

First-in-human evaluation of a novel balloon-expandable transcatheter heart valve in patients with severe symptomatic native aortic stenosis: the MyVal-1 study



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KEYWORDS

- aortic regurgitation
- aortic stenosis
- femoral
- paravalvular leak
- TAVI

Abstract

Aims: The aim of this study was to demonstrate the safety and efficacy of the next-generation balloon-expandable Myval transcatheter heart valve (THV) in an intermediate- or high-risk patient population with severe symptomatic native aortic stenosis.

Methods and results: MyVal-1 was a first-in-human, prospective, multicentre, single-arm, open-label study. Between June 2017 and February 2018, a total of 30 patients were enrolled at 14 sites across India. Mean age was 75.5±6.7 years; 43.3% had coronary artery disease. The mean Society of Thoracic Surgeons score was 6.4±1.8% and 100% of the patients were in New York Heart Association (NYHA) functional Class II/III/IV pre-procedure. The six-minute walk test and Kansas City Cardiomyopathy Questionnaire (KCCQ) scores were recorded. After successful implantation of the Myval THV, 96.6% and 100% were in NYHA functional Class I/II at 30-day and 12-month follow-up, respectively. Outcomes of the six-minute walk test (148.0±87.4 vs 336.0±202.9 m) and KCCQ score (36.6±11.0 vs 65.9±11.4) improved from baseline to 12-month follow-up. The effective orifice area (0.6±0.2 vs 1.8±0.3 cm², p<0.0001), mean aortic valve gradient (47.4±8.8 vs 12.0±3.3 mmHg, p<0.0001), peak aortic valve gradient (71.7±13.0 vs 20.3±5.9 mmHg, p<0.0001) and transaortic velocity (4.5±0.4 vs 2.2±0.4 m/s, p<0.0001) improved substantially from baseline to 12 months post procedure. Four all-cause mortality cases were reported up to 12 months. Moreover, there was no other moderate/severe paravalvular leak, aortic regurgitation or need for new permanent pacemaker (PPM) up to 12-month follow-up.

Conclusions: The MyVal-1 study demonstrated the primary safety and efficacy of the Myval THV with no new PPM requirement up to 12-month follow-up. However, future trials with a larger number of patients and long-term follow-up are warranted to establish the safety and efficacy of the device.

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Abbreviations

AS	aortic stenosis
EOA	effective orifice area
KCCQ	Kansas City Cardiomyopathy Questionnaire
MACCRE	major adverse cardiac cerebrovascular and renal events
NYHA	New York Heart Association
PPM	permanent pacemaker
PVL	paravalvular leak
QoL	quality of life
SAVR	surgical aortic valve replacement
STS	Society of Thoracic Surgeons
TAVR	transcatheter aortic valve replacement
THV	transcatheter heart valve

Introduction

Aortic stenosis (AS) is a common type of valve disorder in the elderly population, and its prevalence is increasing in ageing societies¹. Two decades ago, surgical aortic valve replacement (SAVR) was the only available treatment for AS². In 2002, a “proof-of-concept” case of transcatheter aortic valve replacement (TAVR) was performed by Cribier and his colleagues³. TAVR was introduced as an alternative treatment for selected patients with severe AS who were not eligible for surgery⁴. Moreover, TAVR was found to be non-inferior to SAVR with a lower rate of mortality and reduced cardiac arrest in intermediate- and high-risk patient populations^{5,6}. TAVR has been successfully carried out in more than 200,000 patients across 65 countries, and is currently considered to be the best strategy for treatment of calcific, severe AS in patients with intermediate- to high-risk surgical scores⁷.

Some of the approved TAVR systems (SAPIEN 3, SAPIEN XT [Edwards Lifesciences, Irvine, CA, USA], LotusTM [Boston Scientific, Marlborough, MA, USA], and CoreValve[®],

EvolutTM PRO [Medtronic, Minneapolis, MN, USA]) are well established. However, some reports demonstrated certain challenges during implantation or post procedure in low as well as intermediate and high operative risk patients, which included a requirement for new permanent pacemaker (PPM), paravalvular leak (PVL), increased risk for valve dislocation, annular rupture, aortic regurgitation (AR) and need for a second TAVR implantation⁸⁻¹².

The Conformité Européenne (CE) approved MyvalTM transcatheter heart valve (THV) (Meril Life Sciences Pvt. Ltd., Vapi, India) is a next-generation balloon-expandable TAVR system with features that facilitate accurate positioning and favourable clinical outcomes compared to current-generation TAVR systems. The present study aimed to demonstrate its safety and efficacy in an intermediate- or high-risk patient population with severe symptomatic native AS.

Methods

STUDY DESIGN

MyVal-1 was a first-in-human, prospective, multicentre, single-arm, open-label study (Clinical Trials Registry-India: CTRI/2016/11/007512) performed at 14 sites across India to evaluate the safety and efficacy of the next-generation balloon-expandable Myval THV in symptomatic patients with severe AS. The study protocol was approved by the institutional ethics committees at the participating sites. All patients received and signed informed consent. There was an independent data safety monitoring board that adjudicated all the adverse events.

PATIENT POPULATION

A total of 36 patients were screened for the study. Out of these, six patients were excluded due to reasons shown in **Figure 1**. All the inclusion and exclusion criteria for the implantation of the study device are shown in **Supplementary Appendix 1**.

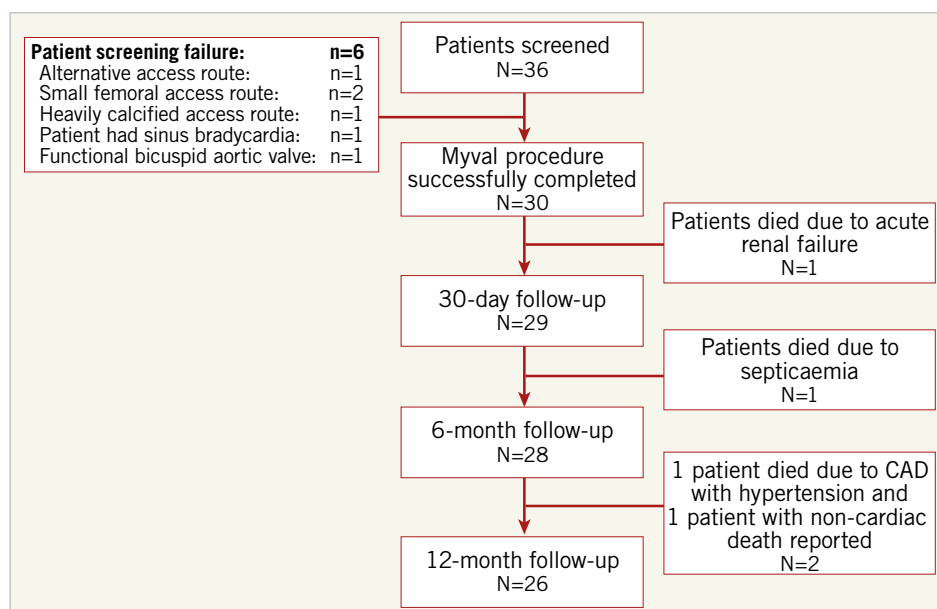


Figure 1. Patient enrolment and disposition.

DEVICE DESCRIPTION AND PROCEDURE

The Myval THV is a balloon-expandable TAVR system (**Figure 2**). The device is characterised by a nickel-cobalt alloy frame which is composed of a single design element – hexagons. These are arranged in a hybrid honeycomb fashion which allows 53% of the frame to have large open cells towards the aortic end and 47% to have closed cells with higher annular radial force towards the ventricular end. This novel design geometry on crimping gives rise to a unique alternative dark-light band-like pattern which allows precise positioning, placement, and deployment of the THV across the native annulus (**Figure 3**). The valve construction material is decellularised bovine pericardium tissue, which receives an anti-calcification treatment and is crafted into a trileaflet valve, fixed at three equipoise vertical commissural posts (separated by 120°) on the metal frame. The lower closed cell part of the valve frame is covered externally with a protective sealing cuff of polyethylene

terephthalate (PET) to form an external buffering. This feature has a significant benefit in terms of minimising or eliminating PVL. The Myval THV is manufactured in diameters of 20 mm, 21.5 mm, 23 mm, 24.5 mm, 26 mm, 27.5 mm, 29 mm, and 32 mm.

The Myval THV is recommended to be crimped on its novel specially designed hi-flex, over-the-wire Navigator™ balloon catheter system (Meril Life Sciences Pvt. Ltd.) prior to insertion within the vessel (**Figure 4**). The Navigator has a unique construction characterised by a proximal deep flexion handle and a distal balloon with two counter-opposing soft stoppers within that create a shallow, low-profile crimping zone and thus a snug fit that prevents any inadvertent dislocation of the Myval THV during negotiation through the sheath or thereafter. Additionally, the delivery system allows flexion of the distal catheter system which ensures trauma-free negotiation across the aortic arch and minimises or eliminates any threat of a periprocedural stroke during

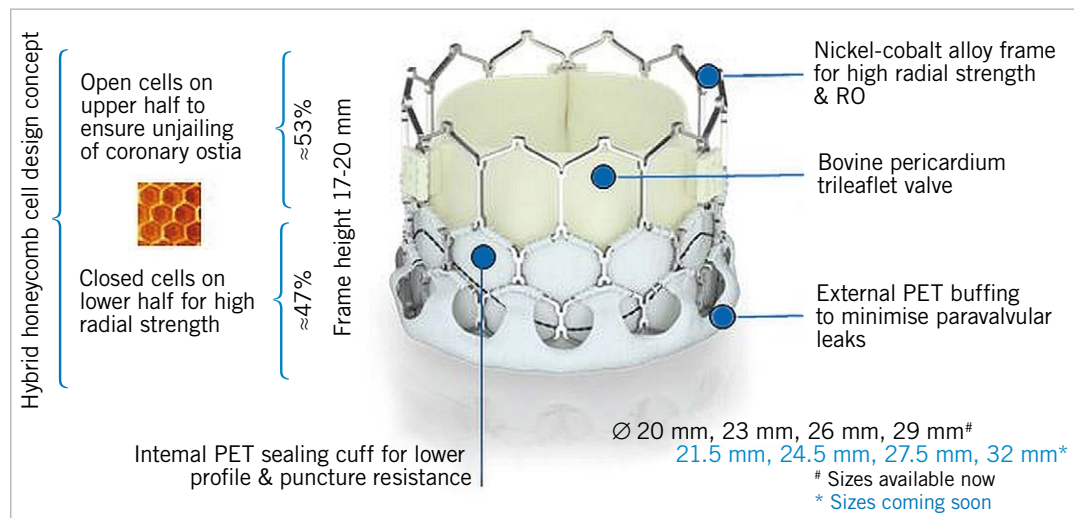


Figure 2. Design of the Myval THV.

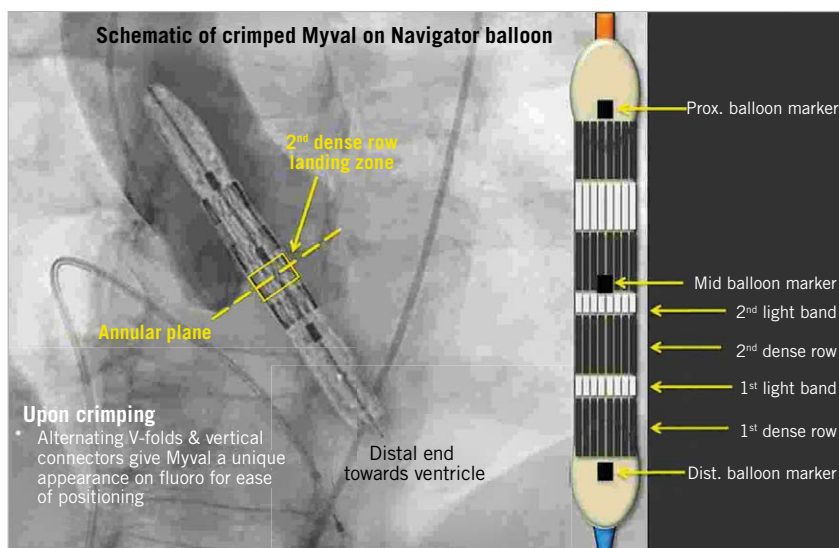


Figure 3. Positioning of the Myval THV.

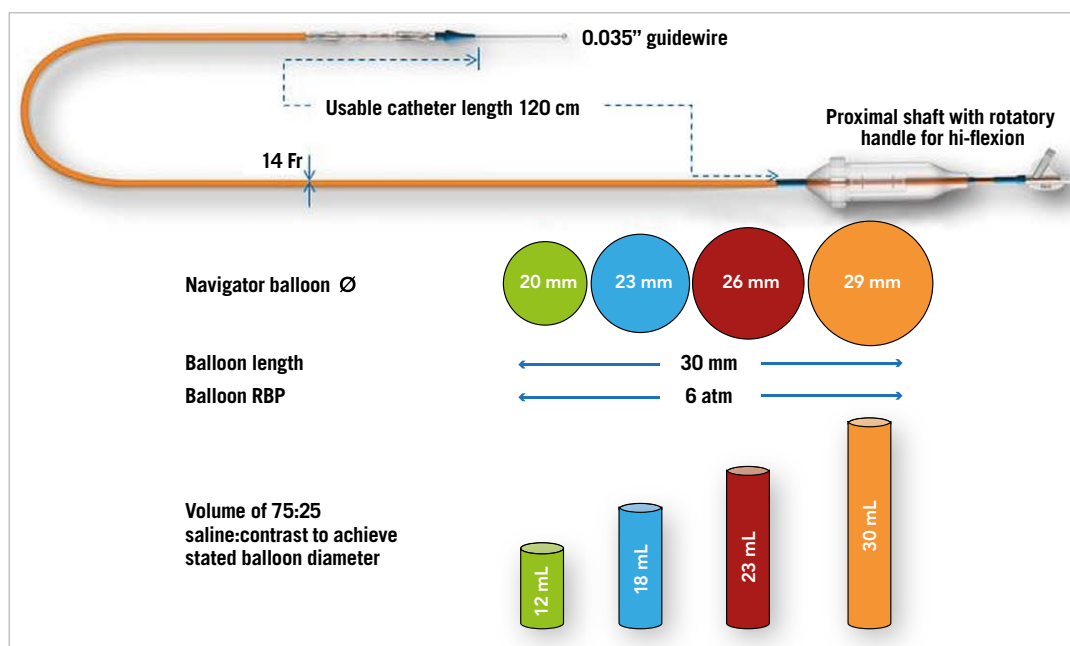


Figure 4. Navigator delivery system for the Myval THV.

arch navigation. Furthermore, the balloon has two internal expansion ports, which facilitate simultaneous expansion distally and proximally (similar to a dog bone), stabilising the valve during deployment and ensuring precision placement. The crimped THV is inserted via a specially designed 22 Fr (THV sizes: 20, 23 and 26 mm) or 24 Fr (THV size: 29 mm) expandable sheath. In situations where the operator is not able to deploy the valve in the desired orthotopic position, the unique sheath design allows valve retraction within the sheath.

All the patients received a loading dose of aspirin (325 mg/day) and clopidogrel (300 mg/day) before the procedure. In most of the cases, using standard percutaneous techniques, a predilatation was performed using an over-the-wire balloon (Mammoth™; Meril Life Sciences Pvt. Ltd.) compatible with a 0.035" guidewire. Once the THV was positioned accurately across the annulus, a dry pacing run at 180-200 bpm was conducted to ensure the valve positioning. The Myval THV was deployed under fluoroscopic guidance by connecting an inflation device pre-filled with a mixture of saline and contrast (75:25) using controlled emptying of the syringe under rapid pacing. Once the THV was fully deployed, the Navigator THV delivery system balloon was fully deflated, and the temporary pacing was stopped. The delivery system was withdrawn from the implantation site, and the post-procedural echo was recorded to check the accuracy of valve deployment, to confirm the absence of any trauma to adjoining zones, to measure the gradients and to check for the presence of AR or PVL. **Figure 5** depicts positioning of the Myval THV in a case example from the MyVal-1 study.

After the procedure, anaesthesia/sedation was reversed, and patients were transferred to the intensive care unit. All the patients were prescribed 75 mg/day aspirin and clopidogrel for at least six to 12 months post procedure.

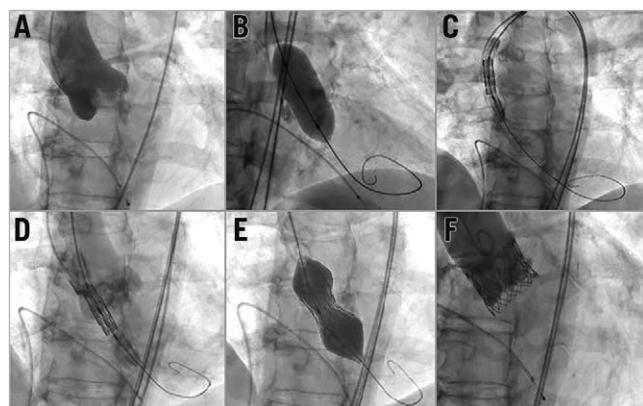


Figure 5. Case example. A) Baseline aortogram. B) Predilatation. C) Navigator flexion avoids scraping against the contralateral arch wall. D) Valve positioning. E) Precise placement and deployment. F) Final orthotopic deployment.

ENDPOINTS AND FOLLOW-UP

Clinical follow-up and echocardiography were performed post procedure and up to 12 months. Thereafter, clinical and echocardiographic follow-up will be performed annually up to five years post procedure. The safety endpoint was Kaplan-Meier survival up to 12-month follow-up. Additional safety endpoints were all-cause death and stroke up to 12-month follow-up. The efficacy endpoints were improvement in NYHA functional classification, effective orifice area (EOA), and six-minute walk test from baseline up to 12-month follow-up. Additionally, quality of life (QoL) as measured by the Kansas City Cardiomyopathy Questionnaire (KCCQ), and freedom from major adverse cardiac cerebrovascular and renal events (MACCRE) were assessed at

follow-up. MACCRE was defined as the composite of cardiovascular death, evidence of prosthetic valve dysfunction (haemolysis, infection, thrombosis, or valve migration), stroke, procedure-associated and/or device-associated adverse cardiac events, or kidney dysfunction. Device success, early safety at 30 days, clinical efficacy after 30 days, myocardial infarction, all-cause death and stroke were defined in accordance with the Valve Academic Research Consortium-2 (VARC-2) definitions¹³. All VARC-2 and the MACCRE definitions are shown in **Supplementary Appendix 2** and **Supplementary Appendix 3**.

STATISTICAL ANALYSIS

Patient demographics, device performance, risk factors, and clinical outcomes were summarised using descriptive statistics for continuous variables and frequency tables for categorical variables. Continuous variables were reported as mean±standard deviation. Categorical variables were expressed as numbers and percentages. All calculations were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC, USA). Change from baseline for NYHA functional class was assessed using the paired Wilcoxon signed-rank test; the six-minute walk test was assessed using a paired t-test. Time-to-event analysis for survival was evaluated by Kaplan-Meier curve.

Results

BASELINE CHARACTERISTICS OF THE STUDY POPULATION

Between June 2017 and February 2018, a total of 30 symptomatic patients (73.3% male) with a mean age of 75.5±6.7 years were enrolled in the study. The number of patients enrolled at each participating site is shown in **Supplementary Table 1**. Baseline and demographic characteristics are listed in **Table 1**.

PROCEDURAL OUTCOMES

The Myval THV was implanted in all 30 patients enrolled in the MyVal-1 study. Procedural details are shown in **Table 2**. There were no cases of coronary obstruction, valve dislocation, annular rupture, or structural damage to the aortic valve apparatus. The placement of a second valve was not required in any of the cases.

ECHOCARDIOGRAPHIC FINDINGS

As shown in **Figure 6**, EOA (1.7±0.3 vs 0.6±0.2 cm², p<0.0001) and mean aortic valve gradient (8.0±2.7 vs 47.4±8.8 mmHg, p<0.0001) improved significantly post procedure as compared to baseline. These results were sustained at 12 months with an EOA of 1.8±0.3 cm² (p<0.0001) and a mean aortic valve gradient of 12.0±3.3 mmHg (p<0.0001), showing significant improvement from baseline to 12-month follow-up. Moreover, peak aortic valve gradient (20.3±5.9 vs 71.7±13.0 mmHg, p<0.0001) and transaortic velocity (2.2±0.4 vs 4.5±0.4 m/s, p<0.0001) remained significantly improved haemodynamically at 12-month follow-up as compared to baseline. Two patients had a mild PVL after Myval THV implantation which was treated by post-dilatation during the procedure itself. This did not result in any patient complication or change in haemodynamic performance.

Table 1. Characteristics of the patients at baseline.

Characteristics		Myval THV (N=30)
Age, years		75.5±6.7
Male		22 (73.3)
Society of Thoracic Surgeons score, %		6.4±1.8
New York Heart Association functional class	I	0 (0.0)
	II	9 (30.0)
	III	16 (53.3)
	IV	5 (16.7)
Previous intervention and history	Coronary artery bypass grafting	5 (16.7)
	Percutaneous coronary intervention	4 (13.3)
	Cerebral vascular disease	1 (3.3)
	Coronary artery disease	13 (43.3)
	Previous myocardial infarction	4 (13.3)
	Peripheral vascular disease	3 (10.0)
	Chronic obstructive pulmonary disease	14 (46.7)
	Extensively calcified aorta	2 (6.7)
	Pulmonary hypertension	5 (16.7)
Computed tomography data		
Aortic root analysis, mm	Left ventricular outflow tract	21.8±2.0
	Perimeter derived	24.0±1.9
Annulus diameter, mm	Area derived	23.6±1.9
Sinus of Valsalva, mm	Left	28.8±1.8
	Right	28.7±1.5
	Non	31.1±2.4
Height of coronary ostia, mm	Left	13.6±1.4
	Right	12.9±1.6
Sinotubular junction, mm		29.3±2.4
Ascending aorta, mm		34.9±3.5
Horizontal annulus		2 (6.9)
Echocardiographic data		
Valve pathophysiology	Effective orifice area, cm ²	0.6±0.2
	Mean aortic valve gradient, mmHg	47.4±8.8
	Peak aortic valve gradient, mmHg	71.7±13.0
	Left ventricular ejection fraction, %	45.5±11.5
	Aortic regurgitation (moderate/severe)	0 (0.0)
	Mitral regurgitation (moderate/severe)	2 (6.7)
Values are n (%) or mean±SD.		

NYHA FUNCTIONAL CLASS AND QoL STATUS

NYHA functional class improved significantly (p<0.0001) from baseline to 12-month follow-up (**Figure 7**). The QoL improved from baseline to 12-month follow-up, according to the KCCQ score (36.6±11.0 vs 65.9±11.4). Outcomes of the six-minute walk test (148.0±87.4 vs 336.0±202.9 m) improved from baseline to 12-month follow-up.

CLINICAL FOLLOW-UP

Clinical outcomes along with MACCRE at different follow-up periods are shown in **Table 3**. Cumulative all-cause mortality

Table 2. Procedural characteristics.

Parameters		Myval (N=30)
Implanted Myval size	20 mm	2 (6.7)
	23 mm	13 (43.3)
	26 mm	11 (36.7)
	29 mm	4 (13.3)
Predilatation with Mammoth balloon	16 mm	7 (23.3)
	20 mm	15 (50.0)
	23 mm	3 (10.0)
	25 mm	1 (3.3)
Post-dilatation		6 (20.0)
Access site	Right common femoral artery	22 (73.3)
	Left common femoral artery	8 (26.7)
Procedural anaesthesia	General anaesthesia	18 (60.0)
	Conscious deep sedation	12 (40.0)
Average hospital stay, days		4.4±1.4
Device success		30 (100.0)
Procedure success		29 (96.7)
Values are n (%) or mean±SD.		

Table 3. Cumulative clinical outcomes up to 12-month follow-up.

Events	Post-procedure (N=30)	30-day follow-up (N=30)	6-month follow-up (N=30)	12-month follow-up (N=30)
All-cause mortality	1 (3.3) [#]	1 (3.3)	2 (6.7)	4 (13.3)
Stroke	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Kidney dysfunction	1 (3.3)	1 (3.3)	1 (3.3)	1 (3.3)
Device-associated and/or procedure-associated adverse cardiac events	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Myocardial infarction	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Major vascular complications	2 (6.7)	2 (6.7)	2 (6.7)	2 (6.7)
Repeat hospitalisation	0 (0.0)	3 (10.0) [*]	3 (10.0)	3 (10.0)
New permanent pacemaker	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Early safety (at 30 days)	–	3 (10.0)	–	–
Clinical efficacy (after 30 days)	–	–	2 (6.7)	4 (13.3)
Values are n (%). [#] patient died due to kidney dysfunction. [*] one patient reported gastroenteritis, one patient had access-site complications and one patient reported fracture in left femur.				

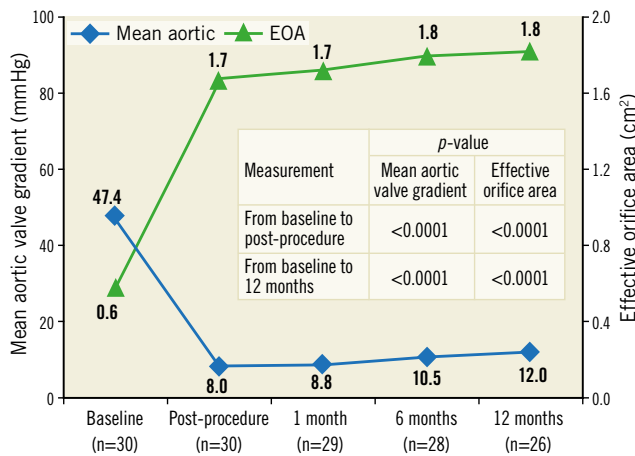


Figure 6. Mean aortic valve gradient and effective orifice area by echocardiography.

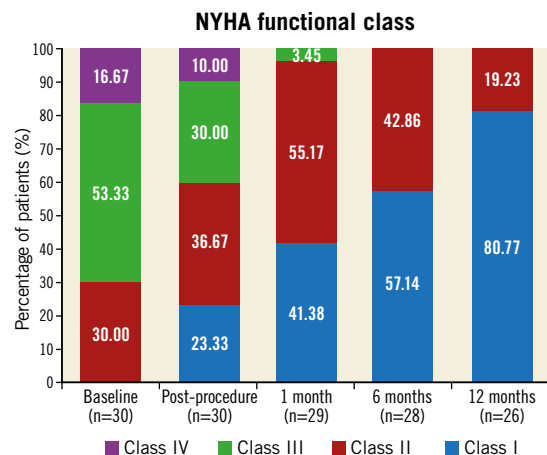


Figure 7. Improvement in NYHA functional class.

at 1-month, 6-month, and 12-month follow-up was 1 (3.3%), 2 (6.7%), and 4 (13.3%), respectively. The Kaplan-Meier survival curve is shown in **Figure 8**. Of the four all-cause mortality cases, one patient died due to acute renal failure post procedure, one patient had died due to septicaemia at six-month follow-up, one patient died due to coronary artery disease with hypertension, and death related to a non-cardiac event was reported in another patient at 12-month follow-up. Major vascular complications were observed in two patients post procedure; no stroke, life-threatening bleeding or myocardial infarction, haemolysis, thrombosis, or valve migration was reported in any of the patients. Three patients were re-hospitalised at 30-day follow-up. All the re-hospitalised patients were successfully treated and discharged. None of the patients required a new PPM up to 12-month follow-up.

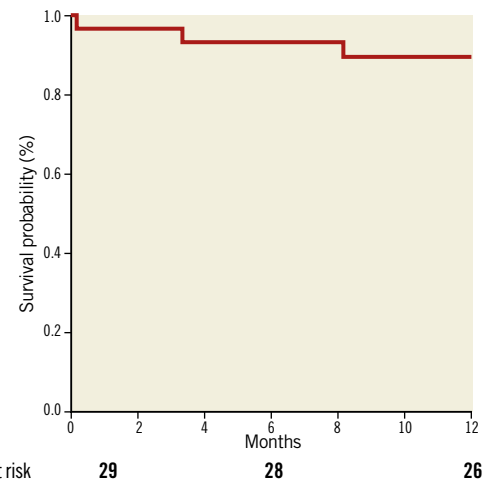


Figure 8. Kaplan-Meier survival curve.

Discussion

The first-in-human MyVal-1 study demonstrated the safety and efficacy of the next-generation balloon-expandable Myval THV implanted using a percutaneous transfemoral approach. The Myval THV was successfully implanted in all 30 patients with a low incidence of 30-day as well as 12-month all-cause mortality (4 out of 30 patients). The results of this study support the use of the Myval THV in intermediate- and high-risk patients with severe symptomatic native AS. No new PPM was required during or after the implantation of the Myval THV. Also, no moderate/severe PVL, haemolysis, thrombosis or valve migration was reported at 12-month follow-up.

Several randomised studies have demonstrated the effectiveness of TAVR over SAVR for symptomatic patients with AS (at low as well as intermediate to high operative risk) with a lower 30-day postoperative mortality rate^{4,5,12,14,15}. The TAVR procedure is generally associated with a risk of acute kidney injury due to a variety of factors such as diabetes mellitus, chronic kidney disease, low glomerular filtration rate, peripheral vascular disease, haemodynamic instability during rapid pacing, previous stroke, and contrast agent volume¹⁶. In our study, one death due to acute renal failure was reported in a patient who was diabetic, hypertensive and had renal insufficiency. The analysis of the SWISS-TAVI registry, which comprised 3,491 consecutive patients, demonstrated a lower rate of in-hospital (2.9%) and 30-day mortality (3.8%) after a TAVR procedure¹⁷. The present study reported similar findings at 30 days with a mortality rate of 3.3%.

TAVR is frequently associated with moderate/severe paravalvular regurgitation (10-12%), which may require repeat intervention^{15,18,19}. In the MyVal-1 study, prosthetic aortic regurgitation was not seen in any patient up to 12-month follow-up. Mild PVL was seen in 7.1% of the patients without any haemodynamic effects. Our data are in accordance with the recently published low-risk PARTNER 3 trial using the SAPIEN 3 valve where mild PVL was seen at a higher rate with TAVR than with surgery (29.4% vs 2.1%)²⁰. Moreover, there was a substantial improvement in aortic valve haemodynamics from baseline in terms of EOA, mean aortic valve gradient, peak aortic valve gradient, and transaortic velocity up to 12-month follow-up.

Other major concerns after TAVR are neurological complications including stroke. Earlier studies have shown a greater risk of stroke within 30 days in TAVR than in SAVR^{18,21}. In the PARTNER-I trial, the 30-day stroke rate was 3.6%²¹. Studies have suggested that in-hospital stroke events, both major and minor, were commonly seen in nonagenarian patients following TAVR¹⁹. In this study, no stroke during the 12-month follow-up was reported in any of the patients. Moreover, a recent study has favoured TAVR over SAVR with shorter hospital stay (3 days vs 7 days)²⁰. Our procedural data are in accordance with that study concerning a shorter hospital stay.

The overall objective of TAVR in AS is to improve QoL, prolong life expectancy and improve NYHA functional class and

six-minute walk test^{18,22}. The QoL outcomes from recent studies have shown significant improvements after TAVR up to 1 month, 6 months, and 1 year²³⁻²⁵. Our results are in line with these observations, with significant improvements in QoL as well as NYHA functional class and six-minute walk test from baseline to 12-month follow-up.

New pacemaker implantation is a predictor of increased 30-day mortality following TAVR in low-flow AS and occurs due to atrioventricular block associated with deeper implantation of the valve^{26,27}. The rates were shown to decrease with newer THV designs and advanced knowledge of predictors of pacemaker implantation²⁸. The lowest pacemaker rate among the currently available valves is reported with the SAPIEN 3 (7.3%) in the PARTNER 3 trial²⁰. Moreover, in the SURTAVI and Evolut Low Risk trials, PPM implantation was required in 25.9% and 17.4% of TAVR patients at 30-day follow-up, respectively^{12,15}. Out of 30 patients evaluated in the MyVal-1 study, there was no new PPM implantation up to 12-month follow-up. This may be attributed to the fact that the design of the Myval THV allows positioning across the landing zone such that 70% of the THV lies in the aorta and 30% in the left ventricle, leading to marginal foreshortening of the frame from the ventricular end and thus resulting in a reduced depth of valve implantation within the left ventricular outflow tract.

Limitations

A limitation of this study is that it is a first-in-human experience, with a small sample size. The present study warrants future trials with larger populations and adequate power to validate the outcomes. Another limitation of the study is the assessment of safety and efficacy at short-term follow-up. Although pre-specified in the study protocol, our study was not statistically powered for clinical endpoints at 12 months, so the results should be considered hypothesis-generating only.

Conclusions

The results of this first-in-human study demonstrate the primary safety and efficacy of the Myval THV in patients with severe AS at intermediate or high risk for surgery. A high rate of device success was achieved without the need for a new PPM implant. The preliminary observations of the MyVal-1 study will serve as a basis for future trials with a larger number of patients and long-term follow-up to establish the safety and efficacy of the Myval THV further.

Impact on daily practice

The MyVal-1 study showed acceptable safety and efficacy of the Myval THV with no need for a new PPM implant up to 12-month follow-up. Besides this, no stroke event was observed during the 12-month follow-up. The results are encouraging, with no device-related adverse events. The MyVal-1 study thus demonstrates that implantation of the Myval THV is safe in severe AS patients at intermediate or high risk for surgery.

Appendix

STUDY COLLABORATOR

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Conflict of interest statement

S.K. Sharma and A. Seth are external scientific advisors to Meril Life Sciences Pvt. Ltd. R.S. Rao, P. Chandra and A. Sonawane are proctors for Myval THV technology and have received honoraria from Meril Life Sciences Pvt. Ltd. The other authors have no conflicts of interest to declare.

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Supplementary data (Original) – 24 April 2019

Supplementary Appendix 1. Inclusion and exclusion criteria of the MyVal-1 study.

Supplementary Appendix 2. Valve Academic Research Consortium-2 (VARC-2) definitions.

Supplementary Appendix 3. Definitions of MACCRE.

Supplementary Table 1. Number of procedures at each participating site.

The supplementary data are published online at:
<https://eurointervention.pconline.com/doi/10.4244/EIJ-D-19-00413>



Corrigendum

DOI: 10.4244/EIJ-D-19-00413C

Corrigendum to: First-in-Human Evaluation of Balloon Expandable Transcatheter Heart Valve in the Treatment of Severe Symptomatic Native Aortic Stenosis: The MyVal-1 Study

EuroIntervention. 2019 Oct 1. [Epub ahead of print]. JAA-658 2019, doi: 10.4244/EIJ-D-19-00413

The authors wish to apologise for the following error:

Supplementary data (Updated) – 17 April 2020

Information on the following has now been corrected and is available online.

- | | |
|--|--|
| 1. Patient screening and informed consent flow chart | 3. Extension of the study |
| 2. Screen failed patients | 4. Corrigendum to the clinical outcomes up to 1-year follow-up |

This has now been corrected online.

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Supplementary data

Supplementary Appendix 1. Inclusion and exclusion criteria of the MyVal-1 study

Inclusion criteria

All patients of this study must meet all of the following inclusion criteria:

1. Patient above 18 years of age who or whose legal representative is willing to sign informed consent form to participate in the study.
2. Patient must have comorbidities such that the Heart Team concur that the predicted risk of operative mortality is $\geq 15\%$ and/or an STS score of ≥ 4 .
3. Patient must have senile degenerative aortic valve stenosis with echocardiographically derived criteria: mean gradient >40 mmHg or jet velocity greater than 4.0 m/s or an initial aortic valve area (AVA) of <0.8 cm².
4. Patient should be symptomatic from his/her aortic valve stenosis, as demonstrated by the New York Heart Association (NYHA) Functional Class \geq II.
5. The patient or the patient's legal representative has been informed of the nature of the study, agrees to its provisions and has provided written informed consent as approved by the Institutional Review Board (IRB) of the respective clinical site.
6. The patient agreed to all required post-procedure follow-up visits.

Exclusion criteria

Patients are excluded from the study if any of the following conditions are present:

1. Patients who are not willing to provide an informed consent form, or whose legal heirs object to their participating in the study.
2. Pregnant and lactating female patients.
3. Evidence of an acute myocardial infarction ≤ 1 month before the intended treatment.
4. Aortic valve is a congenital unicuspid or congenital bicuspid valve or is non-calcified.
5. Mixed aortic valve disease (aortic stenosis and aortic regurgitation with predominant aortic regurgitation $>3+$).
6. Any therapeutic invasive cardiac procedure performed within 30 days of the index procedure (or six months if the procedure was a drug-eluting coronary stent/scaffold implantation).
7. Pre-existing prosthetic heart valve in any position, prosthetic ring, severe mitral annular calcification (MAC), severe (greater than 3+) mitral insufficiency, or Gorlin syndrome.
8. Blood dyscrasias defined as: leukopaenia (WBC $<3,000$ mm³), acute anaemia (Hb <9 mg/dl), thrombocytopenia (platelet count $<50,000$ cells/mm³), history of bleeding diathesis or coagulopathy.
9. Untreated clinically significant coronary artery disease requiring revascularisation.
10. Haemodynamic instability requiring inotropic support or mechanical heart assistance.
11. Need for emergency surgery other than aortic valve replacement with the study device.
12. Hypertrophic cardiomyopathy with or without obstruction (HOCM).
13. Severe ventricular dysfunction with left ventricular ejection fraction (LVEF) <20 .
14. Echocardiographic evidence of intracardiac mass, thrombus or vegetation.

15. Active peptic ulcer or upper GI bleeding within the prior three months.
16. A known hypersensitivity or contraindication to aspirin, heparin, ticlopidine, or clopidogrel, or sensitivity to contrast media, which cannot be adequately premedicated.
17. Native aortic annulus size <18 mm or >28 mm as measured by echocardiogram.
18. Recent (within six months) cerebrovascular accident (CVA) or a transient ischaemic attack.
19. Renal insufficiency and/or end-stage renal disease requiring chronic dialysis.
20. Life expectancy <12 months due to non-cardiac comorbid conditions.
21. Significant aortic disease, including abdominal aortic or thoracic aneurysm defined as maximal luminal diameter 5 cm or greater, marked tortuosity (hyperacute bend), aortic arch atheroma or narrowing (especially with calcification and surface irregularities) of the abdominal or thoracic aorta, severe "unfolding" and tortuosity of the thoracic aorta (applicable for transfemoral patients only).
22. Iliofemoral vessel characteristics that would preclude safe placement of 22 Fr or 24 Fr introducer sheath such as severe obstructive calcification, severe tortuosity or vessel size less than 7 mm in diameter (applicable for transfemoral patients only).
23. Currently participating in an investigational drug or another device study.
24. Active bacterial endocarditis or other active infections.
25. Bulky calcified aortic valve leaflets in close proximity to coronary ostia.

Supplementary Appendix 2. Valve Academic Research Consortium-2 (VARC-2) definitions

Device success

- Absence of procedural mortality.
- Correct positioning of a single prosthetic heart valve into the proper anatomical location.
- Intended performance of the prosthetic heart valve (no prosthesis–patient mismatch and mean aortic valve gradient <20 mmHg or peak velocity <3 m/s, AND no moderate or severe prosthetic valve regurgitation).

Myocardial infarction

- Periprocedural MI (≤ 72 hrs after the index procedure).
- New ischaemic symptoms (e.g., chest pain or shortness of breath), or new ischaemic signs (e.g., ventricular arrhythmias, new or worsening heart failure, new ST-segment changes, haemodynamic instability, new pathological Q-waves in at least two contiguous leads, imaging evidence of new loss of viable myocardium or new wall motion abnormality) AND
- Elevated cardiac biomarkers (preferably CK-MB) within 72 hours after the index procedure, consisting of at least one sample post procedure with a peak value exceeding $15\times$ the upper reference limit for troponin or $5\times$ for CK-MB. If cardiac biomarkers are increased at baseline (99th percentile), a further increase of at least 50% post procedure is required AND the peak value must exceed the previously stated limit.

Stroke

- Disabling stroke: a modified Rankin Scale score of 2 or more at 90 days and an increase in at least one modified Rankin Scale category from an individual's pre-stroke baseline.
- Non-disabling stroke: a modified Rankin Scale score of 2 at 90 days or one that does not result in an increase in at least one mRS category from an individual's pre-stroke baseline.

Early safety (at 30 days)

- All-cause mortality
- All stroke (disabling and non-disabling)
- Life-threatening bleeding
- Acute kidney injury - stage 2 or 3 (including renal replacement therapy)
- Coronary artery obstruction requiring intervention
- Major vascular complication
- Valve-related dysfunction requiring repeat procedure (BAV, TAVI, or SAVR)

Clinical efficacy (after 30 days)

- All-cause mortality
- All stroke (disabling and non-disabling)
- Requiring hospitalisations for valve-related symptoms or worsening congestive heart failure
- NYHA Class III or IV
- Valve-related dysfunction (mean aortic valve gradient ≥ 20 mmHg, EOA ≤ 0.9 – 1.1 cm² and/or DVI < 0.35 m/s, AND/OR moderate or severe prosthetic valve regurgitation)

Supplementary Appendix 3. MACCRE definitions

Cardiovascular death

Any of the following criteria:-

- Death due to proximate cardiac cause (e.g., myocardial infarction, cardiac tamponade, worsening heart failure).
- Death caused by non-coronary vascular conditions such as neurological events, pulmonary embolism, ruptured aortic aneurysm, dissecting aneurysm, or other vascular disease.
- Sudden or unwitnessed death.
- Death of unknown cause.

Procedure-associated and/or device-associated adverse cardiac events

- All procedure-related deaths, including those related to a complication of the procedure or treatment for a complication of the procedure.

- All valve-related deaths including structural or non-structural valve dysfunction or other valve-related adverse events.

Kidney dysfunction (AKIN classification)

Stage 1

Increase in serum creatinine to 150-199% (1.5-1.99 × increase compared with baseline) OR increase of ≥ 0.3 mg/dL (≥ 26.4 mmol/L) OR

Urine output < 0.5 mL/kg/hour for > 6 but < 12 hours

Stage 2

Increase in serum creatinine to 200-299% (2.0-2.99 × increase compared with baseline) OR

Urine output < 0.5 mL/kg/hour for > 12 but < 24 hours

Stage 3

Increase in serum creatinine to $\geq 300\%$ (> 3 × increase compared with baseline) OR serum creatinine of ≥ 4.0 mg/dL (≥ 354 mmol/L) with an acute increase of at least 0.5 mg/dL (44 mmol/L) OR

Urine output < 0.3 mL/kg/hour for ≥ 24 hours OR anuria for ≥ 12 hours

Supplementary Table 1. Number of procedures at each participating site.

Site code	Number of procedures
001	3
002	7
003	1
004	1
005	4
006	2
007	1
008	1
009	1
010	1
011	1
012	1
013	2
014	4
Total	30