

Clinical evaluation of the Hydra self-expanding THV: 30-day results from the GENESIS-II study



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ABSTRACT

BACKGROUND: The Hydra transcatheter heart valve (THV) utilised in the GENESIS-II study is equipped with an active release mechanism for tentacle deployment, distinguishing it from the Hydra THV used in earlier studies.

AIMS: The primary objective of the GENESIS-II study is to assess the ongoing safety and performance of the Hydra THV in treating severe aortic stenosis in patients deemed at high surgical risk.

METHODS: This is a prospective, multicentre, non-randomised, investigational study conducted between November 2021 and November 2023. The study enrolled a total of 40 patients exhibiting high surgical risk and symptomatic severe aortic stenosis from 19 sites across India. The primary safety endpoint of the study was cardiovascular mortality at 30 days, while the primary performance endpoint was device success as defined by Valve Academic Research Consortium-2. The 6-month follow-up of the GENESIS-II study is ongoing.

RESULTS: Among the 40 patients, the average age was 74.4 ± 6.7 years, and 65% were male. The rate of device success was 95%. At 30 days, 2.5% of patients experienced cardiovascular mortality, and the incidence of new permanent pacemaker implantation was 7.9%. There was a progressive enhancement in the effective orifice area, transitioning from 0.6 ± 0.2 cm² at baseline to 1.9 ± 0.6 cm² at 30 days ($p < 0.001$). Similarly, the mean aortic valve gradient demonstrated significant improvement from 53.1 ± 12.5 mmHg at baseline to 8.4 ± 4.0 mmHg at 30 days ($p < 0.001$) post-intervention.

CONCLUSIONS: The Hydra THV is the first device with an active release mechanism for deploying the supra-annular valve. The observed high rates of device success and procedural safety in the GENESIS-II study may support the continued safety and performance of the device.

KEYWORDS: aortic valve stenosis; safety outcomes; transcatheter aortic valve implantation

Over the years, transcatheter aortic valve implantation (TAVI) has paved its way as a less invasive option to surgical aortic valve replacement (SAVR) for treating patients with symptomatic severe aortic stenosis (AS). Initially, TAVI was utilised for patients at high and extreme surgical risk, but it is now also used in patients at intermediate and low surgical risk¹⁻³. Multiple clinical trials, offering the strongest level of scientific support, have demonstrated that TAVI is either superior or non-inferior to SAVR. This has led to an expansion of practice guideline recommendations for TAVI^{4,5}. However, due to their highly selected patient cohorts, the results may not be directly applicable to everyday clinical practice. Real-world scenarios are primarily reflected through registries and studies on various iterations of these devices focusing on valve design, device-related complications, and valve durability⁶.

The incremental improvements in device technology, combined with refined procedural techniques and growing operator experience, have reduced mortality rates and reduced device-related complications following TAVI procedures⁷. With escalating global experience and the accumulation of data, it is becoming increasingly evident that ameliorations in valve designs have a significant impact on clinical outcomes⁸. One such modification has been implemented in the self-expanding, supra-annular Hydra transcatheter heart valve (THV; Vascular Innovations, a subsidiary of Sahajanand Medical Technologies). The Hydra THV utilised in the GENESIS-II study is equipped with an active release mechanism for tentacle deployment, distinguishing it from the Hydra THV used in earlier studies⁹⁻¹¹. In this regard, the primary objective of the GENESIS-II study is to assess the ongoing safety and performance of the Hydra THV in treating severe aortic stenosis in patients at high surgical risk.

Editorial, see page 151

Methods

STUDY DESIGN AND PATIENTS

GENESIS-II was a prospective, multicentre, non-randomised, investigational study. A total of 40 patients with severe aortic stenosis at high surgical risk were enrolled between November 2021 and November 2023 from 19 sites across India. Patients were eligible for enrolment in the study if they were ≥65 years of age and had a Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) score ≥3% or STS-PROM score <3% with the presence of frailty indices and/or existing comorbidities. Their aortic annulus diameter had to meet the following ranges: 17.0-20.0 mm for Hydra 22, 20.0-23.5 mm for Hydra 26, and 23.5-27.0 mm for Hydra 30. All eligible patients had degenerative aortic stenosis (associated with or without more than mild aortic regurgitation) with an echocardiography-derived aortic valve

Impact on daily practice

The introduction of the Hydra transcatheter heart valve with its active release mechanism enhances precision in valve deployment, offering a notable advancement for clinicians treating high-risk patients with severe aortic stenosis. The high rates of device success and procedural safety observed in the GENESIS-II study reinforce its reliability in real-world settings.

area of <1.0 cm² and mean gradient ≥40 mmHg or peak velocity >4.0 m/s or Doppler velocity index (DVI) ≤0.25. Furthermore, patients were required to have a left ventricular ejection fraction >20% and symptomatic aortic stenosis as demonstrated by New York Heart Association (NYHA) Functional Class II or greater. Patients with a congenital bicuspid aortic valve, severe mitral or tricuspid valvular regurgitation or moderate to severe mitral stenosis, an aortic root diameter of <26 mm or >36 mm, a resting LVEF <20%, or a life expectancy less than 24 months were excluded from the study.

STUDY DEVICE

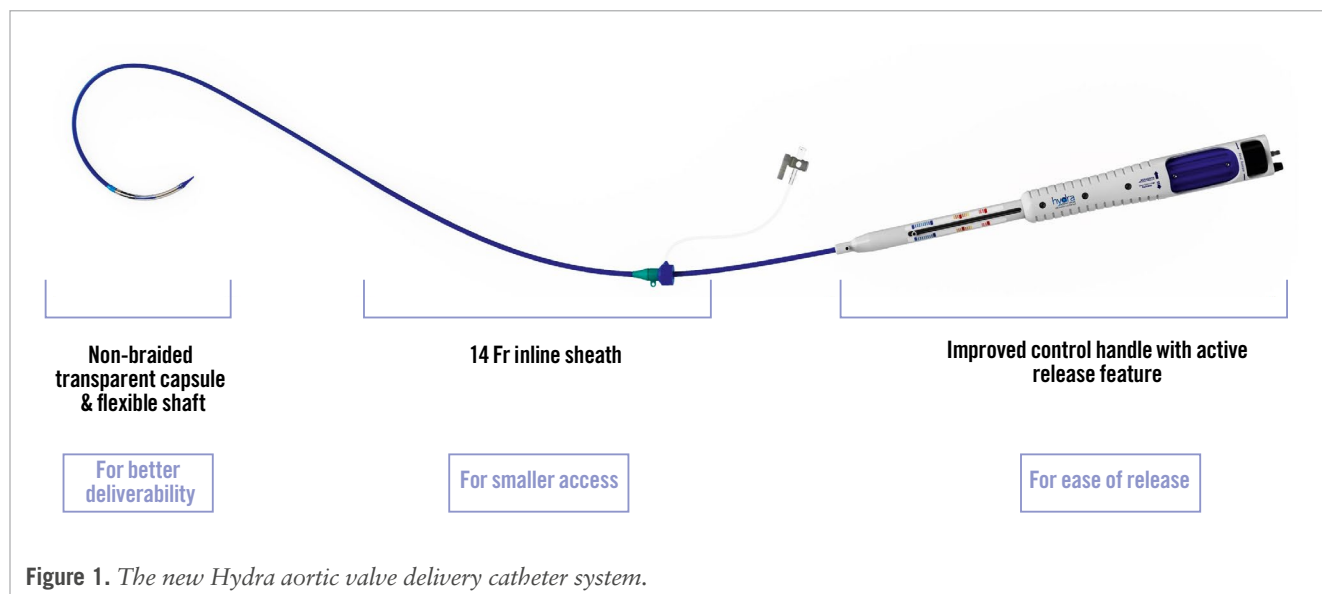
The Hydra THV is a bioprosthetic aortic valve made of a self-expanding nitinol stent frame and three bovine pericardium leaflets in a supra-annular position, designed to provide a large effective orifice area (EOA) and a low transvalvular pressure gradient. A high sealing skirt has been added to the inflow part of the stent frame to mitigate paravalvular leak (PVL). The non-flared inflow part of the stent frame aims to reduce interference with the conduction system and subsequent new conduction abnormalities. The outflow part of the stent frame has three tentacles used for anchoring to the delivery catheter, as well as for alignment with and conformability to the shape of the aorta. Large open cells (≥15 Fr) in the midframe facilitate easy access to the coronary arteries and high flexibility of the Hydra delivery catheter. Further, the two sets of markers on the Hydra THV stent frame help in guiding accurate implantation of the valve at the targeted landing zone. The Hydra THV is available in three sizes of 22, 26, and 30 mm, which cover native aortic annuli with diameters ranging from 17 to 27 mm. The complete details of the Hydra THV, implantation procedure, and concomitant medications have been described elsewhere¹⁰. The Hydra THV used in the GENESIS-II study is equipped with an active release mechanism for tentacle deployment, distinguishing it from the Hydra THV used in earlier studies (Figure 1).

FOLLOW-UP

All patients underwent a clinical follow-up at 30 days, and a 6-month post-implant follow-up is scheduled for all patients.

Abbreviations

AS	aortic stenosis	PVL	paravalvular leak	TAVI	transcatheter aortic valve implantation
EOA	effective orifice area	SAVR	surgical aortic valve replacement	THV	transcatheter heart valve
NYHA	New York Heart Association	STS-PROM	Society of Thoracic Surgeons Predicted Risk of Mortality	VARC	Valve Academic Research Consortium
PPI	permanent pacemaker implantation				



At the 30-day follow-up visit, adverse events, medications, echocardiographic parameters, 6-minute walk tests, NYHA Functional Class status, and need for permanent pacemaker were documented.

ENDPOINTS

The primary safety endpoint of the study was cardiovascular mortality at 30 days, while the primary performance endpoint was device success as defined by Valve Academic Research Consortium (VARC)-2. The secondary endpoints were all-cause death (cardiovascular and non-cardiovascular), acute kidney injury, bleeding, myocardial infarction, vascular access site and access-related complications, periprocedural encephalopathy, all stroke (including disabling and non-disabling stroke), transient ischaemic attack, and need for permanent pacemaker implantation (PPI) at discharge and 30 days. Functional improvement from baseline to 30 days was defined by improvements in 6-minute walk test results and NYHA Class. Haemodynamic improvement was defined in terms of increased EOA and reduced mean aortic gradient at 30 days.

STATISTICAL ANALYSIS

Continuous variables are presented as mean±standard deviation, while categorical variables are expressed as frequency and percentage. Changes from baseline for continuous variables (e.g., EOA, mean aortic gradient) were assessed using paired Student's t-tests. Changes from baseline for categorical variables (e.g., NYHA Functional Class, degree of PVL) were assessed using the Wilcoxon signed-rank test. A p-value<0.05 was considered statistically significant for all tests. All data were analysed using R software, version 4.3.3 (The R Foundation for Statistical Computing).

Results

BASELINE DEMOGRAPHICS

A total of 40 patients were included in the study. The mean age of the patients was 74.4±6.7 years, with a predominance of male patients (65.0%). The mean STS-PROM score

was 3.5±1.6%. Twenty-two (55.0%) patients exhibited NYHA Functional Class II, 14 (35.0%) and 4 (10.0%) patients exhibited Class III and IV, respectively. The baseline characteristics of the patients are outlined in **Table 1**.

ECHOCARDIOGRAPHIC DETAILS AT BASELINE AND PROCEDURAL DETAILS

The mean aortic valve area was 0.6±0.2 cm², and the mean aortic gradient was 53.1±12.5 mmHg. The transfemoral route was used in all patients. The Hydra 26 mm valve was implanted in more than half of the patients (55.0%). A total of 82.5% of patients underwent predilatation, while 47.5% underwent post-dilatation. Overall, 38 patients (95.0%) attained device success; however, one underwent surgical reintervention due to device embolisation, and another patient died during the procedure. The patient who experienced intraprocedural mortality developed hypotension and ventricular fibrillation during the valve predilatation step of the procedure. These complications arose before the valve was implanted, suggesting that they were related to the procedural process rather than the device itself. The echocardiographic and procedural details are described in **Table 2**.

CLINICAL OUTCOMES

At 30-day follow-up, all-cause mortality occurred in one patient. The rate of new permanent pacemaker implantation was 7.5% at 30 days. There was no incidence of stroke at 30-day follow-up. The clinical outcomes at 30-day follow-up are summarised in **Table 3**.

ECHOCARDIOGRAPHIC FINDINGS AND NYHA FUNCTIONAL CLASS

There was a progressive enhancement in EOA, specifically from 0.6±0.2 cm² at baseline to 1.9±0.6 cm² at 30 days (p<0.001), as well as a significant improvement in the mean aortic valve gradient, decreasing from 53.1±12.5 mmHg at baseline to 8.4±4.0 mmHg at 30 days (p<0.001) (**Figure 2**). No moderate or severe PVL was observed at 30-day follow-up (**Figure 3**).

Table 1. Baseline patient characteristics.

Variables	Patients n=40
Age, years	74.4±6.7
Male	26 (65.0)
Body mass index, kg/m ²	25.7±5.0
Body surface area, m ²	1.7±0.2
Diabetes mellitus	17 (42.5)
Hypertension	24 (60.0)
Coronary artery disease	10 (25.0)
Previous CABG	5 (12.5)
Previous PCI	4 (10.0)
History of myocardial infarction ≥6 months	2 (5.0)
History of atrial fibrillation	0 (0)
Left bundle branch block	3 (7.5)
Right bundle branch block	2 (5.0)
Permanent pacemaker	2 (5.0)
Heart failure	1 (2.5)
NYHA Functional Class	
II	22 (55.0)
III	14 (35.0)
IV	4 (10.0)
Prior stroke	1 (2.5)
Prior TIA	2 (5.0)
Peripheral artery disease	2 (5.0)
Chronic kidney disease	2 (5.0)
COPD	4 (10.0)
Asthma	4 (10.0)
Pulmonary hypertension	1 (2.5)
STS-PROM score, %	3.5±1.6
Haemoglobin, g/dl	11.6±1.5
Serum creatinine, µmol/L	1.1±0.3

Values represented as mean±standard deviation or frequency (percentage). CABG: coronary artery bypass grafting; COPD: chronic obstructive pulmonary disease; NYHA: New York Heart Association; PCI: percutaneous coronary intervention; STS-PROM: Society of Thoracic Surgeons Predicted Risk of Mortality; TIA: transient ischaemic attack

At 30 days, the NYHA Functional Class improved from baseline, as shown in **Figure 4**. Improvement in NYHA Functional Class by at least one and at least two functional classes from baseline to 30 days occurred in 73.7% and 34.2% of patients, respectively. The 6-minute walk test distance increased from 217.0±50.9 m at baseline to 275.9±66.4 m at 30 days ($p<0.001$).

Discussion

The main findings from the 30-day follow-up of the GENESIS-II study are as follows: (1) the Hydra THV demonstrated favourable procedural and in-hospital outcomes; (2) there was no increase in mortality rate or PPI rate from in-hospital to 30-day follow-up; (3) there were no incidences of more-than-mild PVL at 30-day follow-up; (4) there was a progressive enhancement in EOA, and the mean

Table 2. Echocardiographic and computed tomography details at baseline and procedural characteristics.

Echocardiographic details at baseline	N=40 patients
Mean aortic gradient, mmHg	53.1±12.5
Aortic valve area, cm ²	0.6±0.2
Moderate or severe aortic regurgitation	8 (20.0)
Moderate mitral regurgitation	4 (10.0)
Moderate tricuspid regurgitation	1 (2.5)
eGFR, mL/min/1.73 m ²	89.5±17.9
LVEF, %	57.7±8.1
Computed tomography details at baseline	
Annulus perimeter, mm	71.5±6.3
Annulus diameter, mm (perimeter-derived)	22.9±2.1
Sinus of Valsalva, mm	
Left	30.6±3.5
Right	29.3±3.1
Non-coronary	31.3±2.7
Height of coronary ostia, mm	
Left	14.4±2.5
Right	16.5±3.2
Sinotubular junction diameter, mm	27.0±3.0
Procedural characteristics	
Transfemoral access	40 (100)
Local anaesthesia and conscious sedation	40 (100)
Implanted size of Hydra valve	
22 mm	2 (5.0)
26 mm	22 (55.0)
30 mm	16 (40.0)
Predilatation	33 (82.5)
Post-dilatation	19 (47.5)
Procedure time, min	116.8±51.3
Fluoroscopy time, min	39.9±9.5
Contrast volume, mL	104.9±11.9
Device success	38 (95.0)*
Duration of hospital stay, days	4.0±2.4

Values represented as mean±standard deviation or frequency (percentage). *Device success defined as per Valve Academic Research Consortium-2 criteria. eGFR: estimated glomerular filtration rate; LVEF: left ventricular ejection fraction

aortic gradient significantly improved up to 30-day follow-up; (5) no major vascular complications were associated with the use of the Hydra THV.

The broad use of the TAVI procedure has been supported by continuous technical advancements in available THVs, aiming to improve procedural safety and efficacy¹²⁻¹⁵. Self-expanding THVs, deployed in a supra-annular position, offer several benefits, including flexibility in valve positioning, improved haemodynamics⁸, and lower permanent pacemaker rates, even in specific patient subgroups like those with a small aortic annulus¹⁶. Moreover, the new iterations of self-expanding THVs have alleviated the issue of higher rates of significant PVL

Table 3. Clinical outcomes up to 30-day follow-up (N=40 patients).

Clinical outcomes	In-hospital	30 days
All-cause mortality	1 (2.5)	1 (2.5)
Cardiovascular mortality	1 (2.5)	1 (2.5)
All stroke	0 (0)	0 (0)
Disabling stroke	0 (0)	0 (0)
Non-disabling/transient ischaemic attack	0 (0)	0 (0)
Life-threatening bleeding	0 (0)	0 (0)
Major bleeding	0 (0)	0 (0)
Major vascular complication	0 (0)	0 (0)
Acute kidney injury	0 (0)	0 (0)
Myocardial infarction	0 (0)	0 (0)
New permanent pacemaker implantation	2 (5.0)	3 (7.5)
In pacemaker-naïve patients	2 (5.3)	3 (7.9)

Values represented as frequency (percentage).

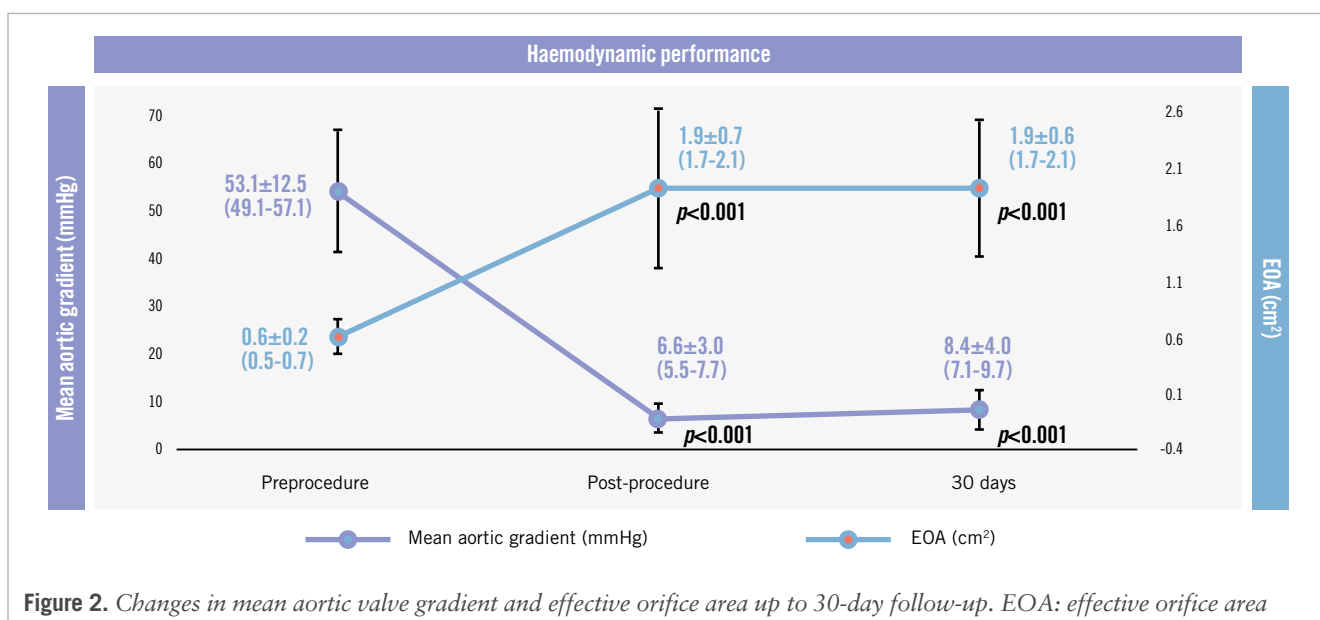


Figure 2. Changes in mean aortic valve gradient and effective orifice area up to 30-day follow-up. EOA: effective orifice area

associated with earlier generations of self-expanding THVs compared to balloon-expandable THVs^{17,18}. The Hydra THV is one such bioprosthetic aortic valve composed of a self-expanding nitinol stent frame and three bovine pericardium leaflets in a supra-annular position. The Hydra aortic valve delivery catheter used in the GENESIS-II study incorporates an active release mechanism for tentacle deployment. This advancement in the device has led to high device success (95.0%) and low all-cause mortality (2.5%) rates at 30 days. There were no incidences of stroke, major bleeding, major vascular complications, acute kidney injury, or myocardial infarction. The rate of new PPI was 7.5% at discharge, with no additional implantations observed up to 30 days of follow-up. This is particularly relevant given that the majority of patients were septuagenarians and had various additional risk factors, including coronary artery disease (25%), diabetes mellitus (42.5%), and hypertension (60%). The low 30-day mortality rate compares positively with other registries

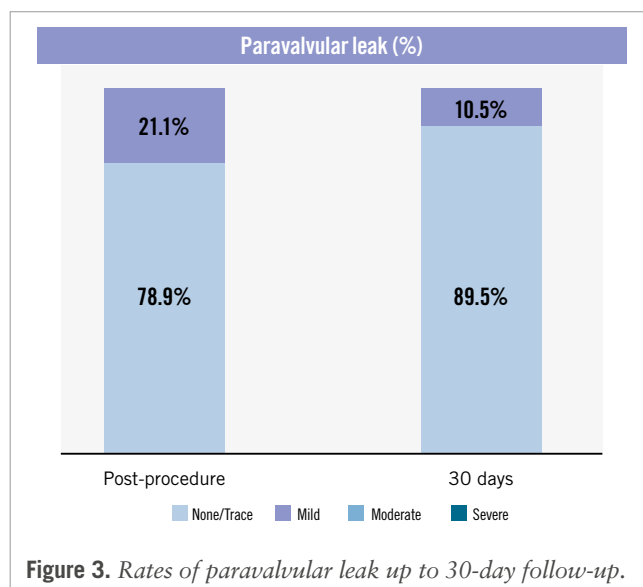
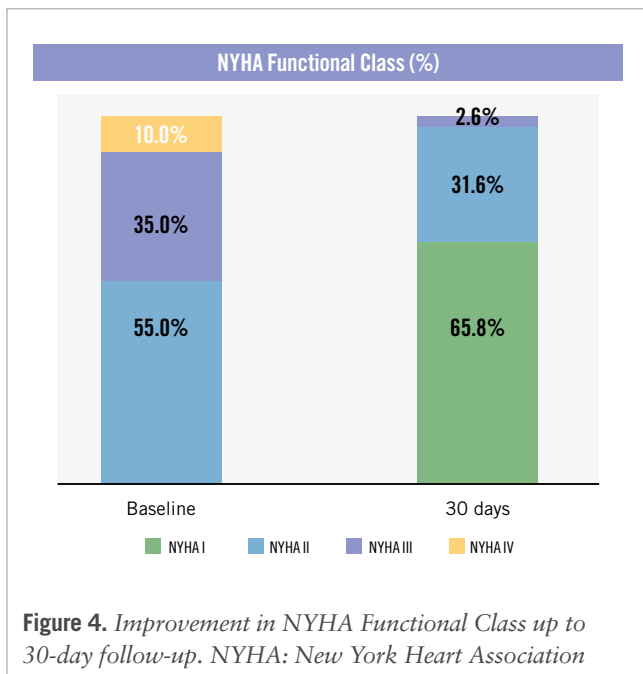


Figure 3. Rates of paravalvular leak up to 30-day follow-up.



involving patients who received either self-expanding or balloon-expandable THVs¹⁹⁻²⁴. A comparative description of patient demographics and 30-day clinical outcomes of various THVs in recent studies^{8,25-27} and the Hydra THV in GENESIS-II have been detailed in **Table 4**.

The 7.5% rate of new PPI observed in the GENESIS-II study is notably lower than the rates reported at 30 days in several other registries: 18.7% in the PORTICO-1 registry (Portico [Abbott])¹⁹, 19.3% in the FORWARD registry (Evolut R [Medtronic])²¹, 20.7% in the FORWARD PRO registry (CoreValve Evolut PRO [Medtronic])²⁴, and 8.3% in the SAVI TF Registry (ACURATE *neo* [Boston Scientific])²³. This is potentially due to the non-flared inflow portion of the Hydra platforms. There has been a reduction in PPI rates observed with the evolution from first-generation THVs to the latest-generation THVs²⁸. Technical modifications, along with improvements in implantation techniques such as the cusp overlap technique, which minimises conduction disturbances, have led to a decrease in PPI rates²⁹.

The moderate or severe PVL observed with previous-generation THVs has clearly been shown to worsen prognosis due to its association with increased rates of heart

Table 4. Comparison of 30-day follow-up studies on TAVI devices.

Device	Hydra	Portico ⁸	Navitor ⁸	Portico ²⁵	Myval ²⁶	SAPIEN THV or Evolut THV ²⁶	Portico DS ²⁷	FlexNav DS ²⁷
Manufacturer name	Vascular Innovations	Abbott	Abbott	Abbott	Meril Life Sciences	Edwards Lifesciences/ Medtronic	Abbott	Abbott
Study name	GENESIS-II Study	-	-	Portico NG Study	Landmark Trial	Landmark Trial	Confidence Registry	Confidence Registry
Patient demographics								
No. of patients	40	139	137	120	384	384	501	500
Age, years	74.4±6.7	82.7 [80.0; 86.0]	83.0 [80.0; 86.0]	83.5±5.4	80.0±5.7	80.4±5.4	81.7±5.4	82.3±5.3
STS score, %	3.5±1.6	-	-	4.0±2.0	2.6 [1.7; 4.0]	2.6 [1.7; 4.0]	4.2±2.9	4.2±2.7
EOA, cm ²	0.6±0.2	0.7 [0.6; 0.9]	0.8 [0.6; 0.9]	0.7±0.2	0.74±0.2	0.72±0.2	0.71±0.2	0.72±0.2
Mean aortic gradient, mmHg	53.1±12.5	41.0 [29.5; 49.5]	41.0 [32.0; 49.0]	46.7±13.4	39.9±14.0	38.7±13.6	43.4±14.5	42.2±15.0
30-day clinical outcomes								
Device success/ technical success, %	95.0	89.2	94.9	-	96.0	97.0	97.4	97.6
All-cause mortality, %	2.5	4.3	5.2	0	2.0	2.0	3.2	2.0
Cardiovascular mortality, %	2.5	-	-	0	2.0	2.0	3.0	1.2
Stroke, %	0	3.6	2.2	3.2	3.0	3.0	2.6	3.2
Disabling stroke, %	0	-	-	0.8	1.0	1.0	1.6	2.0
Major vascular complications, %	0	-	-	0.8	2.0	2.0	6.4	8.2
Need for new PPM, %	7.5	15.3	20.9	15.0	15.0	17.0	19.2	18.9
Moderate or severe PVL, %	0	-	-	1.0	3.0	5.0	2.1	-
EOA, cm ²	1.9±0.6	1.9 [1.7; 2.1]	2.0 [1.7; 2.2]	2.0±0.5	2.02 [1.96; 2.07]	2.05 [1.99; 2.12]	1.82±0.49	-
Mean aortic gradient, mmHg	8.4±4.0	7.0 [6.0; 9.0]	8.0 [6.0; 10.5]	7.4±3.5	8.20 [7.83; 8.56]	7.90 [7.42; 8.37]	7.1±3.7	-

Values represented as mean±standard deviation or median [interquartile range], unless indicated otherwise. EOA: effective orifice area; PPM: permanent pacemaker; PVL: paravalvular leak; STS: Society of Thoracic Surgeons; TAVI: transcatheter aortic valve implantation

failure-related rehospitalisations, valve reinterventions, and mortality at follow-ups after TAVI³⁰⁻³². Nevertheless, the clinical significance of technical improvements enhancing valve performance is evident, resulting in reduced rates of more-than-mild PVL in the latest iterations of THVs. In addition to the low PVL rate observed with the Hydra THV in the GENESIS-II study, an important factor contributing to the excellent performance of the Hydra THV is its outstanding haemodynamic performance across all valve sizes. At the 30-day follow-up, the gradients remained in the single-digit range, even among patients with very small annuli who received the 22 mm Hydra THV. The mean aortic gradient was 8.4 mmHg, and the EOA was measured at 1.9 cm², both of which were comparable to other supra-annular self-expanding THVs like the ACURATE neo2 (Boston Scientific; 7.9 mmHg; 1.7 cm²) and the CoreValve Evolut PRO (6.4 mmHg; 2.0 cm²)³³⁻³⁵.

In the present study, the Hydra THV resulted in significant functional improvement at 30 days. The proportion of patients in NYHA Class III and IV decreased from 35.0% and 10.0% at baseline to 2.6% and 0%, respectively, at 30 days. In the CONFIDENCE registry, the percentage of patients in NYHA Class III/IV decreased from 63.5% at baseline to 11.9% at 30 days after implantation of the Portico THV²⁷. These outcomes demonstrate greater clinical improvement at 30 days compared with those reported for other self-expanding THVs^{21,23,24} and balloon-expandable THVs^{22,36}.

The GENESIS-II study additionally focused on the utilisation of the Hydra THV equipped with an active release mechanism for tentacle deployment, distinguishing it from the Hydra THV used in earlier studies. The device success rate was higher (95.0% vs 92.5%), cardiovascular mortality was lower (2.5% vs 7.5%), and there was an absence of major vascular complications (0% vs 2.5%) in the GENESIS-II study compared with the GENESIS study⁹, though the differences were not statistically significant. The GENESIS-II study population demonstrated comparable haemodynamic outcomes and a substantial reduction in the duration of hospital stay (4 days vs 7 days), with a significantly increased 6-minute walk test distance (275.9±66.4 m vs 229±24 m) in comparison with the GENESIS arm at 30 days. The comparative results of the GENESIS-II and GENESIS studies⁹ demonstrate a clear trend towards improved outcomes due to the more precise and reliable placement of the latest Hydra THV, which incorporates an active release mechanism.

Limitations

This study is limited by its non-randomised design. Furthermore, the relatively long study period and small sample size may introduce potential biases. These biases arise from learning curves and variations in procedural approaches that may have evolved over time.

Conclusions

The Hydra THV is the first device with an active release mechanism for deploying the supra-annular valve. The observed high rates of device success and procedural safety in the GENESIS-II study may support the safety and performance

of the device in treating severe aortic stenosis in patients at high surgical risk.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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