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First-in-man study of transcatheter aortic valve implantations in aortic stenosis using the Hydra self-expanding bioprosthesis

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KEYWORDS

- aortic regurgitation
- femoral
- transcatheter aortic valve implantation (TAVI)

Abstract

Aims: The aim of this study was to document the initial experience with transcatheter aortic valve implantations with the Hydra self-expanding aortic bioprosthetic valve.

Methods and results: Implantation of the Hydra aortic valve was performed in patients with symptomatic, severe aortic stenosis at the King Chulalongkorn Memorial Hospital, Thailand. Surgical treatment was deferred based on Heart Team assessment of an estimated high surgical risk. The Hydra valve was implanted in 15 patients with mean STS score 6.2%, mean age 82 years, mean aortic valve area 0.68 cm^2, mean aortic pressure gradient 49 mmHg. All procedures were performed under general anaesthesia. Percutaneous transfemoral access was used in 13 patients, whereas the remainder had a transaxillary approach. There was one procedural death due to a major vascular complication. At 30-day follow-up, the median aortic valve area and pressure gradient were 1.53 cm^2 and 9 mmHg, respectively. The prevalence of more than mild paravalvular leakage and new permanent pacemaker implantation was 7.7% and 14.3%, respectively. No patient suffered from stroke or TIA.

Conclusions: The Hydra aortic bioprosthetic valve is useful for transcatheter treatment of severe aortic stenosis. Initial results indicate a high haemodynamic performance and complication rates similar to those reported for second-generation transcatheter aortic bioprostheses.

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Abbreviations

AR	aortic regurgitation
AVA	aortic valve area
CABG	coronary artery bypass grafting
COPD	chronic obstructive pulmonary disease
GFR	glomerular filtration rate
LVEDD	left ventricular end-diastolic dimension
LVEF	left ventricular ejection fraction
MR	mitral regurgitation
PCI	percutaneous coronary intervention
PVL	paravalvular leakage
SD	standard deviation
TAVI	transcatheter aortic valve implantation
TEE	transoesophageal echocardiography

Introduction

Transcatheter aortic valve implantation (TAVI) has become a part of the standard therapy for severe aortic stenosis in patients considered at high or prohibitive surgical risk[1-5]. A number of different transcatheter aortic valves are commercially available[6]. Recently, the Hydra Aortic bioprosthesis (Vascular Innovations Co., Ltd., Nonthaburi, Thailand) was developed as a self-expanding system with a mechanism for recapturing the prosthesis during deployment.

The preclinical study on the Hydra Aortic bioprosthesis was conducted in Rigshospitalet, Copenhagen, Denmark. The prostheses were implanted in sheep aortic valves and were explanted after three months. The procedure of implanting the valve is similar to that of TAVI in humans – using percutaneous access from the femoral artery, deployment of the valve at the aortic valve level under fluoroscopy guidance, and assessing the valve function using intracardiac echocardiography, angiography and haemodynamic measurements. The deployment of the valve was possible without any difficulties.

The histology of the eight explanted valves was performed at an independent lab - Innoheart Pvt Ltd, Singapore. The prosthesis showed an intact smooth and undulating morphology and good encapsulation after deployment in the sheep aorta. The materials remained closely integrated with the stent wire. There was a large surface area of the cusps with a smooth appearing surface that signifies good endothelialisation and good interaction of the materials with the circulatory elements. Fibrous and elastic filamentous materials were observed on the surfaces of the cusps and on the underlying surface denuded of endothelial layer, though no excessive fibrin network or thrombi were observed. The valve showed an overall good biocompatibility with the circulation system with limited cusps remaining uncovered by the endothelialisation process.

We report here the initial experience with implantations of the Hydra Aortic bioprosthesis in humans.

Methods

PATIENTS

Implantation of the Hydra Aortic valve was performed in 15 patients with symptomatic, severe aortic stenosis in the period from May 2014 to June 2015 at King Chulalongkorn Memorial Hospital, Thailand. In all cases, surgical treatment was deferred based on Heart Team assessment of an estimated high surgical risk. Patients were thoroughly informed and all gave written consent to the treatment. The study was approved by the ethics committee of King Chulalongkorn Memorial Hospital. The primary endpoint of the study was all-cause mortality at 30 days; secondary endpoints were myocardial infarction (MI), all stroke, bleeding, vascular access complications, and all TIA rates at 30 days.

Preprocedural examinations included transthoracic echocardiography, coronary angiography, and multislice ECG-gated computed tomography (CT) to measure the aortic annulus, aorta, and access vessels. For follow-up, patients had transthoracic echocardiography performed before discharge and at one month after the procedure. Any complications were documented at these time points.

HYDRA AORTIC BIOPROSTHETIC VALVE

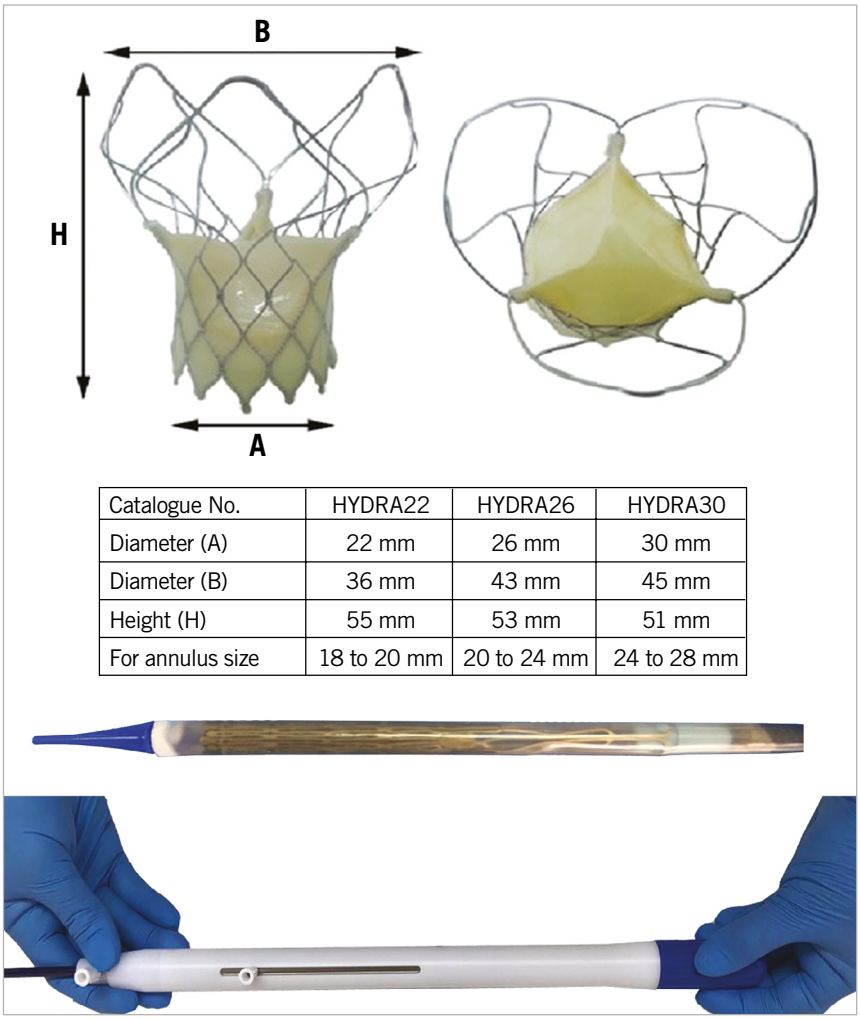
The Hydra Aortic valve consists of a self-expanding stent frame made of nitinol with three leaflets and a sealing cuff made of bovine pericardium **(Figure 1)**. The three tentacles (antennae) on the outflow part of the stent frame are used for fixation to the delivery system and, after deployment, provide flexible anchors at the outflow, which conforms to the shape of the aorta. The inflow section of the frame is non-flared, and exerts a higher radial force than the outflow portion to ensure attachment to the aortic annulus. The valve leaflets are positioned supra-annular of the native aortic valve, and the sealing cuff covers the proximal 12 mm of the inflow portion of the frame. The valve is produced in three sizes, 22, 26, and 30 mm, covering an annulus range of 18 to 28 mm **(Figure 1)**. The bioprosthesis can be fully recaptured, retrieved and repositioned until 80 to 90% of deployment.

DELIVERY SYSTEM

The Hydra valve is implanted using the Hydra Aortic valve delivery system **(Figure 1)**, which has a distal 18 Fr capsule for the Hydra valve and a 12 Fr shaft. The delivery system is introduced into an 18 Fr sheath along a 0.035" stiff wire. The prosthesis is crimped into the distal protective capsule using the single-operator Hydra Aortic valve loading system. The handle at the proximal end of the delivery catheter includes a turning knob for loading/re-sheathing and deploying the valve. Both the delivery system and the loading system are the same for all three valve sizes. The delivery system is suitable only for retrograde implantation.

IMPLANTATION TECHNIQUE

All procedures were performed under general anaesthesia using transoesophageal echocardiography (TEE) and fluoroscopy guidance. The transfemoral route was used in all but two cases, where the transaxillary access was chosen. An 18 Fr sheath was introduced into the access artery, and a pigtail catheter from the contralateral femoral artery was placed in the bottom of the non-coronary cusp for repeated aortic root angiograms during deployment. After



Catalogue No.	HYDRA22	HYDRA26	HYDRA30
Diameter (A)	22 mm	26 mm	30 mm
Diameter (B)	36 mm	43 mm	45 mm
Height (H)	55 mm	53 mm	51 mm
For annulus size	18 to 20 mm	20 to 24 mm	24 to 28 mm

Figure 1. *The Hydra Aortic valve and delivery system. The Hydra Aortic valve consists of a self-expanding stent frame made of nitinol with three leaflets and a sealing cuff made of bovine pericardium. The valve is produced in three sizes, 22, 26, and 30 mm, covering an annulus range of 18 to 28 mm.*

crossing the aortic valve and placement of a 260 cm long Amplatz Super Stiff™ 0.035" wire (Boston Scientific, Marlborough, MA, USA) with a J-tip manually shaped to acquire a pigtail configuration in the left ventricle, predilatation was performed under rapid pacing (160 bpm). The delivery system was then advanced over the stiff wire until the distal part of the valve frame had crossed the aortic valve. Deployment was then begun by rotating the knob clockwise aiming at an implantation depth of ideally 3-5 mm (sealing range 1-10 mm) below the native annulus. In case of a suboptimal position after opening the fully functional inflow portion of the valve, partial or complete re-sheathing and repositioning could be performed. Before final release, tension was released from the delivery system and the guidewire. Valve position, coronary patency, and paravalvular leakage (PVL) were examined with angiography. Deployment was then completed and the detachment of all three tentacles from the delivery system was checked fluoroscopically before withdrawing the delivery system. The function of the implanted valve was assessed with TEE and, in case of more than mild paravalvular leakage, post-dilatation was considered. If suboptimal high or low positioning of the fully deployed valve prosthesis was associated with more than mild paravalvular leakage, a second Hydra valve could be implanted within the first prosthesis. **Figure 2** provides fluoroscopic and angiographic images of the implantation procedure.

STATISTICAL ANALYSIS

Discrete variables are reported as proportions. Continuous variables are reported as mean (standard deviation).

Results

POPULATION

Fifteen patients with severe aortic stenosis were enrolled from May 2014 to June 2015 at King Chulalongkorn Memorial Hospital, Thailand. The clinical characteristics and imaging findings of patients are listed in **Table 1**. All patients were symptomatic; two patients (13.3%) had severe symptoms (NYHA Class III).

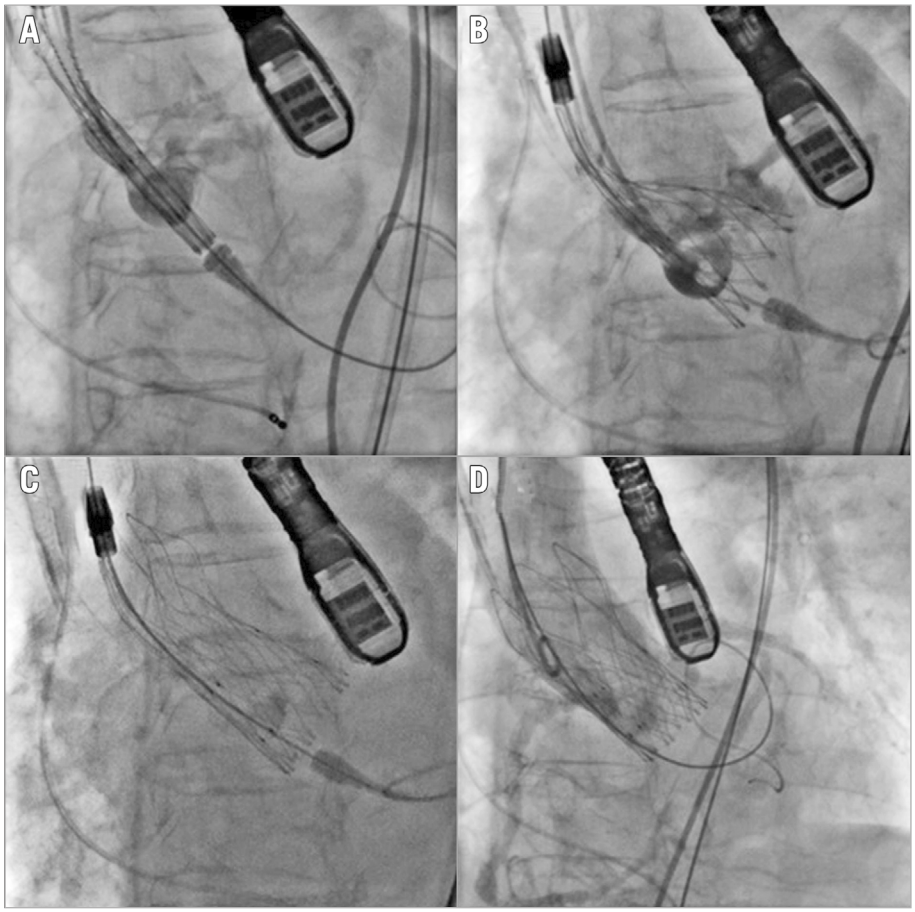


Figure 2. *Implantation of the Hydra Aortic valve. Fluoroscopic and angiographic images of the implantation procedure. A) Angiography in the LAO projection checking depth before deployment of the valve. B) Angiography during deployment. C) Fluoroscopic image at the time of tentacle release. D) Angiography after final release.*

OUTCOMES

Implantation of the Hydra valve was accomplished in all cases (**Table 2** for procedural details). There were no instances of delivery system failure. In five patients valve position was suboptimal after final release and a second Hydra valve was successfully implanted in a correct position. The presence of more than mild paravalvular leakage necessitated post-dilatation in seven cases. Two patients had major vascular complications related to the procedure according to VARC-2 definition. One patient was haemodynamically difficult to control during anaesthesia and systolic blood pressure was temporarily more than 350 mmHg, causing a dissection from the ascending to the descending aorta. This dissection was treated conservatively and the patient had an uneventful recovery. Another patient, treated by the transaxillary approach, required a valve retrieval in the subclavian artery, causing a fatal dissection and rupture of the aortic arch.

Thus, 14 patients survived the post-procedural period. Thirteen patients completed full echocardiographic assessment at 30 days **(Table 3)**. Prosthetic valve haemodynamics are listed in **Table 4**. The mean aortic gradient dropped from 49 mmHg pre-procedure to 9 mmHg. Paravalvular leakage graded more than mild was seen in only one patient and a permanent pacemaker implanted in two patients. Stroke or TIA did not occur in any patient.

Discussion

In this report, we describe the first experiences with the new self-expanding transcatheter Hydra Aortic valve for aortic stenosis in humans deemed ineligible for surgical aortic valve replacement.

SAFETY AND EFFICACY

The one mortality within the first 30 days was not related to the bioprosthetic valve but to the 18 Fr introducer sheath and the post-implantation evaluation of the access function. This complication underlines the need for careful preprocedural evaluation of the access vessels, and for gentle manipulation of sheaths and catheters in elderly and frail patients. Particularly in an Asian population, the vessel size is often smaller than in most reported TAVI studies. Other access-site complications encountered were comparable in frequency to those generally reported[6,7].

Post-procedural valve gradients demonstrated no significant obstruction to flow, and the values are in line with results from

Table 1. Preprocedural clinical characteristics and cardiac imaging findings (n=15).

Characteristic	All patients (n=15)
Sex, male, n (%)	8 (53.3)
Age, years (SD)	82 (4.5)
Body mass index, kg/m^2 (SD)	23.2 (4.4)
Hypertension, n (%)	10 (66.7)
Diabetes, n (%)	2 (13.3)
Previous myocardial infarction, n (%)	1 (6.7)
Previous PCI, n (%)	6 (40.0)
Previous CABG, n (%)	2 (13.3)
Peripheral vascular disease, n (%)	2 (13.3)
Atrial fibrillation, n (%)	2 (13.3)
Previous permanent pacemaker, n (%)	0 (0)
Stroke, n (%)	3 (20.0)
Chronic kidney disease, n (%)	6 (40.0)
e-GFR, mL/min (SD)	51.8 (20.8)
COPD, n (%)	1 (6.7)
STS score (SD)	6.2 (1.4)
EuroSCORE II (SD)	4.3 (1.9)
Echocardiography	
LVEF, % (SD)	60.0 (18.3)
LVEDD, mm (SD)	43.9 (9.2)
Peak aortic gradient, mmHg (SD)	71.8 (21.6)
Mean aortic gradient, mmHg (SD)	49.0 (16.3)
AVA, cm^2 (SD)	0.68 (0.19)
AR grade ≥moderate, n (%)	5 (33.3)
MR grade ≥moderate, n (%)	2 (13.3)
Multislice computed tomography	
Annulus mean diameter, mm (SD)	23.5 (3.4)

AR: aortic regurgitation; AVA; aortic valve area; CABG: coronary artery bypass grafting; COPD: chronic obstructive pulmonary disease; e-GFR: estimated glomerular filtration rate; LVEDD: left ventricular end-diastolic dimension; LVEF: left ventricular ejection fraction; MR: mitral regurgitation; PCI; percutaneous coronary intervention; SD: standard deviation

Table 2. Implantation characteristics.

Implantation characteristic	
Transfemoral access, n (%)	13 (86.7)
Subclavian access, n (%)	2 (13.3)
Mean annulus diameter, mm (SD)	23.1 (3.3)
Mean annulus area, cm^2 (SD)	3.7 (0.9)
Mean annulus planimetry, mm (SD)	69.1 (8.1)
Coronary height – LCA, mm (SD)	11.9 (2.0)
Coronary height – RCA, mm (SD)	12.0 (1.6)
Hydra 26, n (%)	9 (60.0)
Hydra 30, n (%)	6 (40.0)
Predilatation, n (%)	15 (100)
Post-dilatation, n (%)	7 (46.7)
Need for 2nd valve, n (%)	5 (33.3)

Table 3. Clinical outcomes at 30 days post procedure (n=15).

Outcomes at 30 days		
Myocardial infarction, n (%)		0 (0)
Stroke, n (%)		0 (0)
Death, n (%)		1 (6.7)
Bleeding complication, n (%)	Minor	3 (20.0)
	Major or life-threatening	1 (6.7)
Vascular complication, n (%)	Minor	4 (26.7)
	Major	2 (13.3)
New permanent pacemaker, n (%)		2 (14.3)

other transcatheter aortic bioprosthetic valves[6]. In the present study, only one patient (7.7%) had more than mild paravalvular leak at 30-day follow-up. A second valve was needed in five cases; however, this may be due to our learning experience for this new valve technology.

The deployment technique for the Hydra valve is different from the CoreValve® (Medtronic, Dublin, Ireland). The CoreValve has a tendency to move downwards at the time of final release but the Hydra valve seems to be stable at the deployed position. The initial position of the Hydra valve may be a bit lower than that of the CoreValve, which helps to avoid valve pop-up into the aorta. The expanding force of the Hydra is slightly lower compared to the CoreValve. This may be a benefit in terms of less injury to the conduction system; however, in some cases this may require post-deployment balloon inflation to expand the valve, especially if the annulus is calcific.

Atrioventricular block requiring new pacemaker implantation was seen in two patients out of 14 (14.3%), which is in the same range as that reported for second-generation transcatheter aortic bioprosthetic valves. This is a reassuring result as a relatively high rate of pacemaker implantation has been a persistent feature of the most commonly used self-expanding aortic valves[8]. If confirmed in larger populations, this feature could potentially be attributed to the lack of flaring of the inflow end of the prosthesis.

Table 4. Valve performance at 30 days post procedure (n=13, one patient lost to echocardiography follow-up).

Follow-up echocardiography at 30 days		
LVEF, (SD)		69.3 (12.8)
Peak aortic gradient, mmHg (SD)		18.9 (8.7)
Mean aortic gradient, mmHg (SD)		9.4 (4.8)
AVA, cm^2 (SD)		1.53 (0.45)
AR grade, n (%)	None or trace	4 (30.7)
	Mild	8 (61.5)
	Moderate	1 (7.7)
	Severe	0

AR: aortic regurgitation; AVA: aortic valve area; LVEF: left ventricular ejection fraction; SD: standard deviation

Limitations

This is the first implantation of Hydra Aortic bioprosthetic valves in humans. The delivery system cannot retrieve the valve once it is completely deployed, which is not much different from the first generation of the CoreValve delivery system. The delivery system is under development to enable a perfect deployment.

Conclusions

The Hydra Aortic bioprosthetic valve is useful for transcatheter treatment of severe aortic stenosis. Initial results indicate that the haemodynamic performance of the implanted bioprosthesis is satisfactory, and complication rates are similar to those seen with other techniques. Further evaluation in a larger population is needed in order to assess the safety and efficacy of the Hydra Aortic valve more completely and to compare its performance to other treatment options.

Impact on daily practice

TAVI is now an acceptable treatment for symptomatic aortic stenosis patients who have an intermediate to high surgical risk. The Hydra self-expanding bioprosthetic valve may be an alternative device for this procedure.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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