

A new self-expanding aortic stent valve with annular fixation: in vitro haemodynamic assessment[☆]

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Abstract

Objective: Balloon-expandable stent valves require flow reduction during implantation (rapid pacing). The present study was designed to compare a self-expanding stent valve with annular fixation versus a balloon-expandable stent valve. **Methods:** Implantation of a new self-expanding stent valve with annular fixation (Symetis[®], Lausanne, Switzerland) was assessed versus balloon-expandable stent valve, in a modified Dynatek Dalta[®] pulse duplicator (sealed port access to the ventricle for transapical route simulation), interfaced with a computer for digital readout, carrying a 25 mm porcine aortic valve. The cardiovascular simulator was programmed to mimic an elderly woman with aortic stenosis: 120/85 mmHg aortic pressure, 60 strokes/min (66.5 ml), 35% systole (2.8 l/min). **Results:** A total of 450 cardiac cycles was analysed. Stepwise expansion of the self-expanding stent valve with annular fixation (balloon-expandable stent valve) resulted in systolic ventricular increase from 120 to 121 mmHg (126 to 830 ± 76 mmHg)*, and left ventricular outflow obstruction with mean transvalvular gradient of 11 ± 1.5 mmHg (366 ± 202 mmHg)*, systolic aortic pressure dropped distal to the valve from 121 to 64.5 ± 2 mmHg (123 to 55 ± 30 mmHg) N.S., and output collapsed to 1.9 ± 0.06 l/min (0.71 ± 0.37 l/min* (before complete obstruction)). No valve migration occurred in either group. (* = $p < 0.05$). **Conclusions:** Implantation of this new self-expanding stent valve with annular fixation has little impact on haemodynamics and has the potential for working heart implantation in vivo. Flow reduction (rapid pacing) is not necessary.

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1. Introduction

Transluminal artificial heart valve implantation was first reported, in an in vivo experimental study, by Andersen in 1992 [1]. Cribier et al. described the first human clinical implantation in 2002 [2].

Since 2006, literature on percutaneous heart valve therapies burst out, with more than 300 patients cohort published at that date (Pubmed). In 2008, according to European societies' position statement on transcatheter aortic procedure [3], 1200 high-risk patients with severe symptomatic aortic stenosis have been treated using transcatheter aortic valve implantation.

After first feasibility studies (I-REVIVE, US-REVIVAL and RECAST), several clinical trials are on the way (REVIVE, REVIVAL II), and even now, prospective randomised trials are

on the way (PARTNER). Moreover, numerous transcatheter heart valve devices are in development.

However, percutaneous aortic valve replacement has been noteworthy rapidly brought to clinics and lack of experimental studies is significant, for this potentially life threatening procedure. At the time of writing, a Pubmed search with the terms 'percutaneous heart valve' and 'in vitro restriction', brings up only two studies [4,5]. Considering animal studies, the same investigation results in 9 studies for aortic valve before 2002 (date of Cribier first in man publication), 14 studies for aortic valve before 2006 (beginning of large cohort studies).

Haemodynamics during percutaneous aortic valve replacement is a major concern, especially regarding left ventricular overpressure, as procedures are performed on low ejection fraction hearts (part of the high-risk patients). Rapid pacing for these devices (balloon-expandable stent valve) is necessary. While this topic has been briefly studied for percutaneous aortic valvuloplasty [6–10], only one study get onto haemodynamics during percutaneous heart valve therapies [11].

The purpose of this study was to observe in vitro the impact that the new percutaneous heart valve replacement may have

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on haemodynamics. To generate standardised haemodynamic conditions, an in vitro model using an electrohydraulic pulse duplicator was used. Two main type of stent were used: balloon-expandable stent valve (Balloon SV) and self-expanding stent valve (self SV). The new Symetis[®] self-expanding stent valve with annular fixation was assessed.

2. Materials and methods

The design of the in vitro circulatory system (Fig. 1) was based on Dynatek Delta MP3[®] (Dynatek Delta[®], Galena, MO, USA) hydrodynamic pulse duplicator.

This cardiovascular simulator consists of a double-valved left ventricle chamber connected to a compliant vascular loop. Left ventricle is connected with a piston, computer controlled, volumetric pump, with adjustable stroke volume and duration. Pulsatile flow is generated (maximum 10 l/min). Each stroke ejects 30–100 ml of saline solution into the circuit. The system possesses an open reservoir and compliant tubing to simulate venous and arterial system, respectively. In addition, peripheral vascular resistance/compliance and systolic/diastolic aortic pressure were adjusted by using loop clamps.

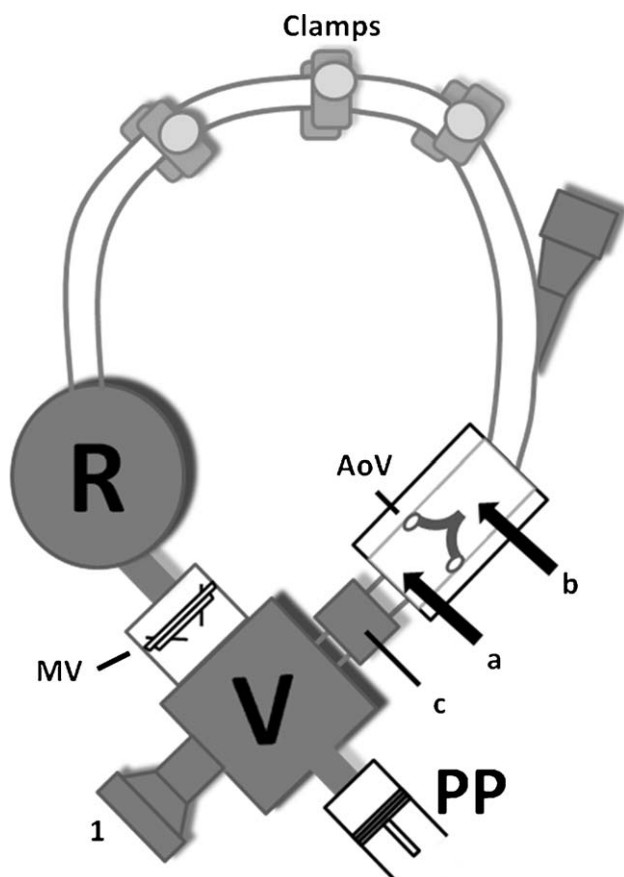


Fig. 1. The cardiovascular simulator. A double-valved (mitral (MV) and aortic valves (AoV)) left ventricle (V) is connected with a piston volumetric pump (PP). A compliant vascular loop and a systemic reservoir (R) simulate arterial and venous systems. Vascular resistance is adjusted by clamps. Piezoelectric (a and b) and ultrasound (c) sensors allow for continuous monitoring and computer control adjustment. Sealed port-access to the circulatory system has been created to simulate transapical (1) and transfemoral (2) routes.

Versatility of the system allows for a large panel of physiological/pathological conditions, with control of dP/dt ratio.

An ultrasonic probe (Transonic[®] Laboratory Tubing Flowmeter T110, Transonic Systems Inc., Ithaca, NY, USA) was placed on the outflow tubing to assess cardiac output. Ventricular and aortic pressure (piezoelectric sensors), flow rates (ultrasound sensor) are monitored continuously (sampling rate: 2000 Hz).

A mechanical valve has been placed in the mitral position. In order to mimic anatomic environment, a stentless bioprosthesis was attached in aortic position. A 25 mm inner diameter stentless porcine aortic bioprosthesis was used. The valve was sutured in a 27 mm inner diameter rigid silicon tube, applying a reimplantation procedure. Soft moss material was fixed under the valve, mimicking annulus, to increase sealing in the non-compliant silicon tube. The tube was then connected to the circulation. Stent valves were implanted in that environment.

Sealed port access to the ventricle has been created for transapical route implantation (33F inside diameter). Another peripheral access has been developed for transfemoral access implantation.

Visualisation of the simulated aortic root was possible through the transparent silicon tube, or by an endoscope inserted through the transarterial access.

Saline (0.9%) was used as fluid.

In this simulated circulation, blood pressure, heart rate and cardiac output can be chosen to mimic physiological/pathological conditions. The testing conditions were set to mimic low cardiac output in an elderly woman at rest (under anaesthesia). The following haemodynamic conditions were produced: pressure, heart and flow rates, stroke volume and systolic duration respectively 120 mmHg systolic, 85 mmHg diastolic, 60 beats/min, 2.8 l/min, 66.5 ml, 35% of cycle.

Stent valves were used: a self-expanding stent valve and a balloon-expandable stent valve.

The new Symetis[®] aortic stent valve (Symetis, Lausanne, Switzerland) was used for self-expanding stent valve implantation. This device consists of an aortic stentless porcine valve that is mounted and sutured in a self-expanding nitinol alloy stent (Fig. 2), with a Dacron interface. The double-crown design of the device is specially adapted to anchor on the aortic annulus and allows self-positioning. Inner diameter of the stent valve used was 25 mm. The device was inserted by means of a self-constructed rigid catheter-based (32F outside diameter) delivery technique through the sealed ventricular port access.

A 23 mm percutaneous valvuloplasty catheter (Cristal Balloon CVB23 × 45/110, Balt, Montmorency, France) was used to simulate balloon-expandable stent valve implantation.

Stepwise of implantation of valved stents was simulated. The positioning of the valved stents into the valve chamber was enabled by means of direct view through the transparent silicone tube. All data (arterial and ventricular pressure, heart rate and cardiac output) were digitised and continuously recorded with the Dynatek Delta software. Seven steps were studied for the balloon-expandable stent valve and eight for the self-expanding stent valve, 30 cycles analysed on each step (16 only for extreme positions with 800 mmHg ventricular pressure). A total of 450 cycles

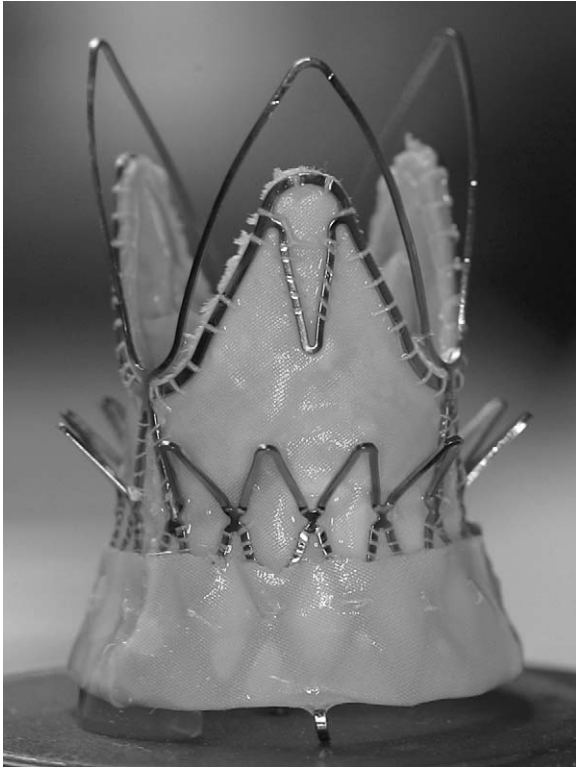


Fig. 2. The new Symetis® aortic stent valve (Symetis, Lausanne, Switzerland).

recorded at 2000 Hz sampling rate for each variable (aortic and ventricular pressure, outflow) resulted in 2,700,000 values to process.

Stepwise implantation of self-expanding stent valve consisted of:

- a. baseline
- b. release-catheter through the valve
- c. superior arch deployed
- d. predelivery position
- e. during delivery
- f. after delivery
- g. self-expanding stent valve without delivery catheter
- h. self-expanding stent valve after balloon dilatation (wall application of the device).

Stepwise implantation of balloon-expandable stent valve consisted of:

- a. baseline
- b. balloon valvuloplasty catheter through the valve
- c. balloon filled with 5 cc saline with 0.5 bar pressure
- d. balloon filled with 10 cc saline with 1 bar pressure
- e. balloon filled with 15 cc saline with 3 bar pressure
- f. balloon filled with 17.5 cc saline with 4 bar pressure
- g. balloon-expandable stent valve.

Delivery is step e on self-expanding stent valve implantation and step f in balloon-expandable stent valve implantation.

Complete obstruction of the simulator was not performed (23 mm balloon in a 25 mm native valve), to prevent explosion of the system at mechanical boundaries.

Data analysed were systolic, diastolic and mean arterial pressure (SAP, DAP, MAP), systolic ventricular pressure (SVP), mean transvalvular gradient, mean outflow and regurgitation fraction (RF). Results were expressed as mean \pm standard deviation.

Mann–Whitney test was used to compare measurements between the two groups, and a *p* value less than 0.05 was considered significant.

3. Results

During self-expanding stent valve implantation, systolic ventricular pressure rose from 120 mmHg to a maximum of 121 ± 0.6 mmHg, as delivery catheter was inserted (step b) (Table 1). Maximum left ventricular outflow obstruction assessed by a mean transvalvular gradient of 11 ± 1.4 mmHg was observed during delivery (step e) (Fig. 3). Systolic arterial pressure decreased to a minimum of 64 ± 2 mmHg during delivery (step e), while cardiac output nadir value was, after delivery catheter pull back, of 1.9 ± 0.07 l/min (Table 2).

For balloon-expandable stent valve implantation, all boundary values were observed during maximum balloon inflation (step f). Differences with SESV were statistically (*p* < 0.05) significant (marked as *), for all boundary values, except for SAP and MAP (Table 3 and Fig. 4).

Stepwise expansion of the balloon-expandable stent valve resulted in a significantly higher systolic ventricular pressure increase from 126 to 830 ± 76 mmHg* (Table 1). Peak left ventricular outflow obstruction with mean transvalvular gradient of 366 ± 202 mmHg* was observed with balloon inflated with 17.5 cc (Fig. 5). Systolic aortic pressure dropped distal to the valve from 123 to 56 ± 31 mmHg (non-significant (N.S.)), and output collapsed to 0.71 ± 0.37 l/min (before complete obstruction)* (Table 2).

Table 1

Systolic ventricular pressure (SVP), mean gradient, systolic arterial pressure (SAP), mean arterial pressure (MAP), diastolic arterial pressure (DAP), during stepwise implantation.

	SVP	Mean gradient	SAP	MAP	DAP
Self SV					
a	119.8 \pm 0.3	0.3 \pm 0.1	121.1 \pm 0.3	108.1 \pm 0.4	93.3 \pm 0.4
b	121.6 \pm 0.6	2.1 \pm 0.1	122.9 \pm 0.6	110.1 \pm 0.7	95.3 \pm 0.7
c	118.6 \pm 0.2	2.3 \pm 0.1	119.7 \pm 0.2	106.6 \pm 0.2	91.1 \pm 0.3
d	79.4 \pm 0.3	5.8 \pm 0.1	79.4 \pm 0.3	60.5 \pm 0.3	38.4 \pm 0.4
e	67.1 \pm 3.6	11 \pm 1.4	64.4 \pm 2.3	43 \pm 2.8	19.1 \pm 3
f	66.7 \pm 0.3	10.1 \pm 0.3	65.7 \pm 0.3	44.4 \pm 0.4	20.4 \pm 0.4
g	83.2 \pm 0.6	7.5 \pm 0.2	82.8 \pm 0.6	63.9 \pm 0.7	41.7 \pm 0.8
h	104 \pm 0.4	3.3 \pm 0.1	104.5 \pm 0.4	88.9 \pm 0.4	70.7 \pm 0.5
Balloon SV					
a	126.2 \pm 0.2	2.9 \pm 0.1	123.3 \pm 0.2	110.2 \pm 0.2	95.8 \pm 0.3
b	120.4 \pm 0.7	3 \pm 0.1	117.4 \pm 0.6	103.4 \pm 0.5	88.1 \pm 0.6
c	122.5 \pm 0.9	7.1 \pm 0.4	117.5 \pm 0.9	103.3 \pm 1	88.1 \pm 1.1
d	136.1 \pm 0.9	15.5 \pm 0.7	120.4 \pm 0.6	107.2 \pm 0.6	92.2 \pm 0.8
e	401.4 \pm 44.2	180 \pm 26.4	106.7 \pm 2.9	94 \pm 3.1	80.6 \pm 3
f	829.7 \pm 76.1	365.9 \pm 202.3	55.8 \pm 30.7	44.1 \pm 24.7	34.3 \pm 21.3
g	121.6 \pm 0.2	1 \pm 0.1	121.3 \pm 0.2	107.8 \pm 0.2	92.5 \pm 0.3

Data are expressed in mmHg. Delivery steps are highlighted.

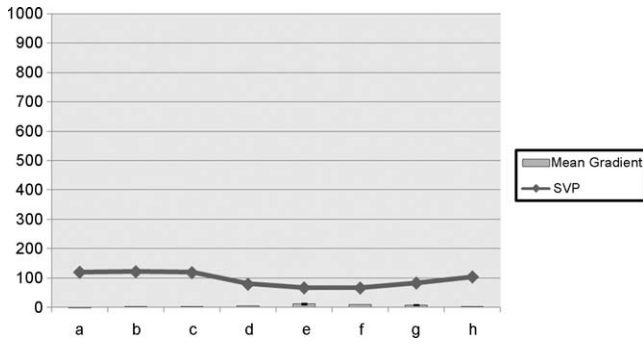


Fig. 3. Systolic ventricular pressure (SVP) (mmHg) and mean aortic gradient (mmHg) during self SV implantation. Delivery is step e.

Table 2
Mean outflow (l/min) and regurgitating fraction (RF) (%) during stepwise implantation. Delivery steps are highlighted.

	Mean output (l/min)	RF%
Self SV		
a	2.70 ± 0.08	11.9 ± 1.5
b	3.57 ± 0.09	12.1 ± 1.4
c	3.53 ± 0.12	13.8 ± 1.1
d	2.66 ± 0.20	37.9 ± 1.4
e	2.32 ± 0.14	46.2 ± 3.0
f	2.39 ± 0.09	45.0 ± 1.0
g	1.88 ± 0.07	39.0 ± 0.9
h	2.24 ± 0.05	25.9 ± 0.8
Balloon SV		
a	2.76 ± 0.05	12.3 ± 1.0
b	2.65 ± 0.11	16.6 ± 1.5
c	2.50 ± 0.08	18.6 ± 1.3
d	2.58 ± 0.05	15.0 ± 1.5
e	2.32 ± 0.08	17.6 ± 1.9
f	0.71 ± 0.37	48.1 ± 25.7
g	2.85 ± 0.12	13.8 ± 1.0

4. Discussion

First in vitro model for aortic stent valve implantation is proposed. Efficient in vitro stent valve implantation assessment, with detailed haemodynamics, can be realised.

Percutaneous stent valve implantation has increasingly become a therapy for aortic stenosis. Haemodynamics during implantation is a critical step, as referred to its consequences (effects on recipient heart and device positioning).

Some in vitro percutaneous valve studies [12–16] have been reported but none of these are relative to haemodynamic conditions during implantation. To our knowledge, this is the first in vitro model of working heart transcatheter aortic valve implantation. The aim of this study was to continuously assess flow and pressure throughout implanta-

Table 3
Systolic ventricular pressure (SVP), mean gradient, systolic arterial pressure (SAP), mean arterial pressure (MAP), at boundaries conditions.

	SVP	Mean gradient	SAP	MAP	Mean output
Self SV	121.6 ± 0.6 (b)	11 ± 1.4 (e)	64.4 ± 2.3 (e)	43 ± 2.8 (e)	1.88 ± 0.07 (g)
Balloon SV	829.7 ± 76.1* (f)	365.9 ± 202.3* (f)	55.8 ± 30.7 (f)	44.1 ± 24.7 (f)	0.71 ± 0.37* (f)

Data are expressed in mmHg and l/min. Letter indicates the step during delivery (self-expanding stent valve: b, release-catheter through the valve; e, during delivery; g, after delivery; balloon-expandable stent valve: f, balloon filled with 17.5 cc saline with 4 bar pressure). *p < 0.05. NS: not significant.

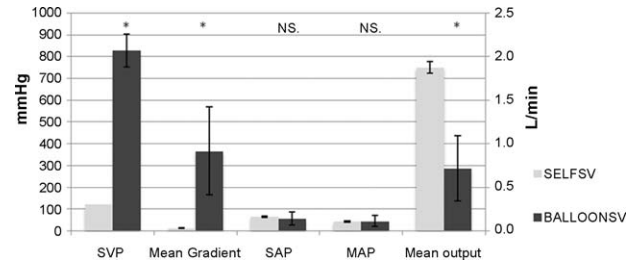


Fig. 4. Systolic ventricular pressure (SVP), mean gradient, systolic arterial pressure (SAP), mean arterial pressure (MAP), at boundaries conditions. Data are expressed in mmHg and l/min. *p < 0.05. NS: not significant.

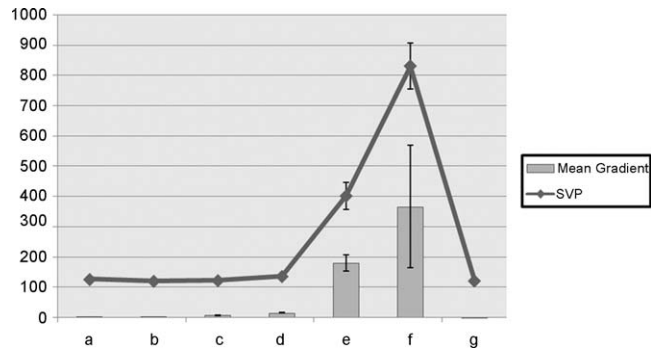


Fig. 5. Systolic ventricular pressure (SVP) (mmHg) and mean aortic gradient (mmHg) during Balloon SV implantation. Delivery is step f.

tion of the two most used kind of stent valves. The new Symetis self-expanding stent valve was assessed.

Some studies about haemodynamics during valvuloplasty have been reported in the late eighties [6–10]. Nevertheless, clinical limited application stopped this research fields early. In vitro evaluation of aortic valvuloplasty [7] revealed that magnitude of transvalvular gradient during obstruction is flow dependant, thus protecting heart failure patients. However, for critical narrowing, minute alterations of orifice size may induce significant changes of this gradient. Suárez De Lezo [8] showed that during occlusion of left ventricle, hypertension is transmitted to all cardiac chambers. Adaption is generated by regurgitation through atrioventricular valves and foramen ovale, acting as escape orifices relieving intracavitary pressures.

Among valved stents, balloon-expandable stent valve devices have been historically developed first and brought to clinic (Cribier–Edwards® aortic prosthesis (Edwards Lifesciences, CA, USA)).

Our results showed clinically significant modifications of haemodynamic status during implantation simulation of balloon-expandable stent valve. As a result of outflow obstruction, systolic pressure rose in the unvented ventricle,

while outflow and arterial pressure dropped distal to the balloon.

Two consequences of this obstruction are concerning. First, acute overpressure occurs on a chronically high pressure exposed ventricle. This issue is real, as percutaneous heart valve procedure has been designed to treat high-risk patients. However, Bittl et al. showed in an in vivo human study, that peak left ventricular systolic pressure during valvuloplasty correlates closely with left ventricular function [6]. Secondly, transvalvular gradient reflects migration forces applied to the delivery system, which may result in device malpositioning.

This study confirms the non-alternative need for flow reduction (rapid pacing) in balloon-expandable stent valve implantation. Nevertheless, evolution of systolic ventricular overpressure (and its ventricular and device positioning consequences) during percutaneous aortic valve implantation under rapid pacing has never been studied.

Various methods have been described to transiently reduce intracardiac flow during interventional procedures. Ventricular fibrillation has been induced to facilitate endovascular stent implantation [18]. Rapid pacing was described by Daehnert et al. [19] in paediatric valvuloplasty and used by Cribier et al. [20,21] during valvuloplasty and valve implantation. A concern with rapid pacing is the potential for provoking ventricular arrhythmias; of particular concern in patients with aortic stenosis hypertrophic hearts. Webb et al. described an occurrence of 3% in 40 consecutive patients, but concealed more frequent arrhythmia in other settings than those used in the study [17]. The author concludes with cautious advice and prudent attitude, by limiting frequency and duration of pacing so far as possible. However, although non-physiological approach, rapid pacing is more and more used in transcatheter valvular procedure field, and is now considered as safe procedure in experienced hands.

Other options could be considered to decrease ventricular outflow (and over-pressure) in percutaneous heart valve procedures. Reducing inflow, by balloon occlusion of proximal vasculature, results in lower output, as described by Marty et al. [22]. Other methods proposed are cardiopulmonary assistance, adenosine-induced ventricular standstill.

Antegrade delivery of the new Symetis self-expanding stent valve showed significantly reduced impact on haemodynamics (as opposed to balloon-expandable stent valves) and thus, potential for working heart implantation in vivo. Throughout delivery, output was maintained, with a nadir SAP value of 64 ± 2.3 mmHg.

The first and only available self-expanding stent valve for clinical use is the Corevalve[®] revalving system [23]. This device, initially implanted under cardio-pulmonary bypass, required, in initial experience, rapid pacing, to improve device positioning. Though not reported in literature, centres using this device now report implantation without rapid pacing.

This study showed the Symetis stent valve can be implanted by antegrade route, on working heart. No flow reduction (rapid pacing) is required (as opposed to balloon-expandable stent valves).

These advantages have two consequences as opposed to balloon-expandable stent valve. No clinically relevant

haemodynamic modifications and output preserve. Left ventricle is not exposed to acute overpressure. This more physiologic approach could be an asset in treating high-risk patients.

Another effect of this is a secure positioning. As gradient is no more than 11 ± 1.4 mmHg, migration forces applied on the delivery catheter are lower than the restraining forces of ventricular introducer valve on the delivery catheter. In predelivery position (step to exactly position the device), only uncovered upper crown is deployed and exposed to the flow. This low profile does not obstruct blood flow. In addition, the design of the stent allows for secured positioning of the device in the aortic annulus. Auto-positioning of the stent after delivery, under diastolic pressure, is a consequence of the double-crown system.

Haemodynamic status during valve implantation is one of the several complex aspects of multifaceted transcatheter aortic valve implantation procedure. It could be, as for access route, one of the factors taken into account for the decision of which delivery system to use for each patient. Numerous other factors will be considered in future assessment of transcatheter valvular device, such as durability of valve and stent of each device.

5. Limitations of the study

The main limitation of the study is the use of a volumetric, non-adaptive pump. A barometric pulse duplicator would have provided less pathologic flow and pressure patterns. However, assessment of self-expanding stent valve implantation procedure was more close to reality than balloon-expandable stent valves, and proved the absence of ventricular over pressure. This study validated the haemodynamic consistency of the new device. This proof of concept is required, but not sufficient, for stepping to in vivo experiment. Moreover, this left ventricle overpressure led us to create a new concept for ventricular venting, before in vivo testing.

Post implantation haemodynamic assessment was not optimal. The rigid silicone tube holding aortic native valve was not molded to receive profiled stent valve. Even with the help of sealing moss, post implant leaks were important, misleading haemodynamic assessment. However, design of the study was not intended to assess haemodynamics after but during implantation.

Saline temperature was ambient. Nitinol requires heating for complete unfolding. This led to non-optimal adaption of the device to the aortic mock-up, increasing parastental leakage.

Another limitation is the use of normal native valve. However, in vitro studies should be undertaken prior to expensive in vivo studies; they should serve as a filter to test and eliminate early designs and techniques. The superior in vivo approach would also be limited by the lack of an experimental animal model with calcified aortic stenosis. Recognition of the multiple limitations of present day models does not invalidate attempts at dissecting the multiple problems of percutaneous aortic valve replacement. Moreover, some authors consider PAVR for wider application than aortic stenosis patients [24].

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Appendix A. Conference discussion

Dr G. Wimmer-Greinecker (Bad Bevensen, Germany): It is absolutely true, that the crucial parts of those procedures are the placement and the positioning of this valve. So let me ask you three questions.

From your manuscript I understand that your setup is a pulsatile one. So what I don't really understand is your comment on the migration forces. Why do you think this is only depending on the transvalvular gradient? I would see this in a nonpulsatile setting, but in a pulsatile setting I think there are more things that contribute to those forces.

The second question is how do those data reflect the two on the market available valves? As we have seen several times during this meeting and also today the CoreValve is still implanted in most cases with rapid pacing. So what is the difference with your valve? Is it the valve itself or is it the delivery system?

And the last question. Have you also tried this experiment under different hemodynamic conditions? I mean, it is not only that we have different individuals but even during a procedure, due to the application of fluids and vasopressors, we do have different hemodynamic conditions. They might vary, and so the situation is not as stable as you have shown in your experiments.

Dr Vergnat: My understanding of the migration forces is that during balloon-expandable stent-valve implantation you have high gradients, with high pressure in the ventricle and low pressure in the aorta. That can move up your delivery balloon catheter towards the aorta. That is why, for me, it is very important. And during self-expanding stent-valve implantation, the flow is going around the delivery device. So the flow is maintained; there is no gradient. Thus you can place your device exactly where you want. The flow is going on, you have the time, and that is it.

Dr Wimmer-Greinecker: But in a pulsatile system, the flow is changing.

Dr Vergnat: In calcified aortic stenosis you mean?

Dr Wimmer-Greinecker: No, I mean the difference between systolic and diastolic pressures.

Dr Vergnat: Yes, but as I showed you on the self-expanding stent-valve assessment, there was no traction on the catheter. I can just leave the catheter inside, and the flow is going on, with the systolic pressure, and diastolic pressure, and it is not moving. If you have a balloon inside, the balloon is going into the aorta. So that is why for me migration forces are very linked during the implantation to the ventriculo-aortic gradients.

About your second question, the difference between this device and the CoreValve device, it is difficult to speak about that, as I never used the CoreValve stent valve, I never had it in the hands and never went into an implantation. But what we have on that device design (Symetis® self expanding StentValve) that you don't have any modification of the gradient. So you can position it very precisely. And then you have this double-crown design that can allow auto-positioning of the device. When you just release it, the device is self-positioning into the aortic annulus with this double-crown design. That could be better. And you can answer me that on calcified leaflets, it would be different. But maybe the future is near [aortic regurgitation indications]

Your last question was, it was not stable during the implantation?

Dr Wimmer-Greinecker: No. You only did this experiment under one kind of hemodynamic condition. So have you tried this at different cardiac outputs?

Dr Vergnat: No, we didn't do that. It could be very interesting. At that outflow you don't have migration forces. I don't think you will find any migration forces in higher output. The second thing is, I don't know if you saw the pressure figures in the ventricle when it was obstructed with the balloon-expandable stent valve. It was 800 mmHg, and I didn't want my system to explode.

Dr P. Kappetein (Rotterdam, The Netherlands): One remark. When you implant the CoreValve device, you don't need rapid pacing. When we started we used extracorporeal circulation, then we found out that rapid pacing was sufficient, and then we discovered that actually you don't need any rapid pacing during the implantation.