Development of an algorithm to plan and simulate a new interventional procedure

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Abstract

OBJECTIVES: The number of implanted biological valves for treatment of valvular heart disease is growing and a percentage of these patients will eventually undergo a transcatheter valve-in-valve (ViV) procedure. Some of these patients will represent challenging cases. The aim of this study was to develop a feasible algorithm to plan and in vitro simulate a new interventional procedure to improve patient outcome.

METHODS: In addition to standard diagnostic routine, our algorithm includes 3D printing of the annulus, hydrodynamic measurements and high-speed analysis of leaflet kinematics after simulation of the procedure in different prosthesis positions as well as X-ray imaging of the most suitable valve position to create a ‘blueprint’ for the patient procedure.

RESULTS: This algorithm was developed for a patient with a degenerated Perceval aortic sutureless prosthesis requiring a ViV procedure. Different ViV procedures were assessed in the algorithm and based on these results the best option for the patient was chosen. The actual procedure went exactly as planned with help of this algorithm.

CONCLUSIONS: Here we have developed a new technically feasible algorithm simulating important aspects of a novel interventional procedure prior to the actual procedure. This algorithm can be applied to virtually all patients requiring a novel interventional procedure to help identify risks and find optimal parameters for prosthesis selection and placement in order to maximize safety for the patient.

Keywords: Transcatheter aortic valve implantation • Valve-in-valve • Simulation • Safety

INTRODUCTION

Transcatheter aortic valve implantation (TAVI) for treatment of severe aortic stenosis (AS) has evolved as an accepted alternative to surgical aortic valve replacement (SAVR) in patients with an elevated risk for surgery [1, 2]. In recent years, TAVI has also been performed for failing bioprosthetic valves in high-risk patients, a so-called valve-in-valve (ViV) procedure [3, 4]. However, compared with standard TAVI, ViV procedures are relatively rare and experience comparatively low, also reflected by the heterogeneous outcomes documented in ViV registries [3]. Major safety issues include device malposition, coronary occlusion and elevated post-procedural gradients as high as 60 mmHg [5]. These data are at least partly due to the fact, that in the past ViV procedures have often been performed on a ‘trial and error’ basis without sufficient evidence resulting in unsatisfactory outcomes [6, 7]. With an ageing population, increasing life expectancy and a significant increase in the use of surgical bioprostheses [8], in particular in younger patients, structural valve deterioration will become more and more prevalent [9, 10]. As a consequence, the number of ViV procedures will rise and the procedure may establish itself as an alternative to redo surgery. In addition, the variety of implanted bioprostheses has increased over time and technical issues will be of growing interest in the near future as new transcatheter heart valves (THVs) as well as sutureless bioprostheses have been released on the market [11, 12].

ViV procedures in new prostheses are particularly challenging as they are comparable with first-in-man trials, which are usually preceded by a significant amount of in vitro and preclinical in vivo experiments [13–15]. However, this is currently not the case for...
these procedures resulting in an accordingly elevated risk for the patient [5]. Numerous problems are conceivable with respect to such first-in-man transcatheter procedures: based on the past experience, the choice of the right THV and the implantation height seem to be of particular importance. Recommendations for the selection of THVs for specific bioprostheses can be found in the ViV App, which was developed to help guide physicians in their planning of such procedures [16]. However, individual patient anatomy is not considered and newly released valves are not yet included.

It was the aim of this study to develop a feasible algorithm utilizing an extended spectrum of imaging, modelling and perfusion modalities on top of standard diagnostic routine to plan and prepare for a new interventional procedure in an in vitro setting. This algorithm was designed to address all potential problems by simulating crucial anatomical, procedural, functional and device-specific aspects in order to detect and solve them in advance—well before the actual patient procedure. This algorithm was initially developed for a patient requiring a ViV procedure into a degenerated sutureless Perceval prosthesis that represented such a challenging case.

**MATERIALS AND METHODS**

**3D printing of aortic annulus, ascending aorta and left ventricular outflow tract**

The implantation site was virtually reconstructed using Mimics™ software by Materialise (Leuven, Belgium) to create a printable 3D model derived from multislice computed tomography (MSCT) data of the respective patient. The anatomy was printed, using a standard MakerBot Replicator 2X with acrylonitrile butadiene styrene filament. It was coated with silicone to improve the surface finish. The model was constructed for better visualization of the implantation site and the understanding of the implantation angles for both transfemoral and transapical approaches. The Perceval prosthesis was integrated into the printed model (Fig. 1A).

**Valve-in-valve procedures**

A 21 mm Perceval prosthesis (kindly provided by Sorin Biomedica, Milan, Italy) was expanded and placed within a custom-made hydrodynamic test compartment, resembling the position of the Perceval within the patient according to data from the virtual reconstruction of the implantation site, and heated to a physiological temperature of 37°C to ensure proper stent expansion. Afterwards, a 23 mm SAPIEN XT (kindly provided by Edwards Lifesciences, Irvine, CA, USA) was implanted into the Perceval using the Ascendra® delivery system as a ViV procedure in two different positions from the ventricular side under direct visual control. X-ray images of both positions were acquired for guidance during the actual procedure. Position 1 was a low implantation with the SAPIEN XT exceeding the bottom end of the Perceval by approximately 2 mm (Fig. 2A straight arrow) and Position 2 was a higher implantation of approximately 2 mm higher than the bottom end of the Perceval stent (Fig. 2B arrow).

**Hydrodynamic measurements**

After ensuring correct positioning of the Perceval and the SAPIEN XT within the aortic root model, hydrodynamic measurements were performed. Measurements were performed with water in a pulse duplicator developed at the Department of Cardiovascular Engineering CVE-AME at the Helmholtz Institute (Fig. 2F) [17]. This system is designed to mimic flow conditions of the left heart and has been employed successfully in comparable studies [18, 19]. It is equipped with a passively filling left atrium, a mitral valve, a silicone ventricle, an interchangeable aortic root and an adjustable peripheral impedance (Fig. 2F) and has been described in detail previously [17]. Briefly, the stroke volume of the ventricle and the beat rate can be adjusted to alter the flow rate of the system (Table 1). Analysed parameters for this study were mean systolic pressure difference, effective orifice area (EOA) and regurgitation volume, derived from flow and pressure data in accordance with similar studies [17].

**High-speed camera recording**

High-speed video recordings (Fastcam 1024 PCI Model 100 K, Photron, San Diego, CA, USA) of valve performance during hydrodynamic testing were analysed in terms of leaflet opening and closing dynamics, leaflet coaptation and possible leaflet-stent-frame interaction.

**X-ray and fluoroscopy**

X-ray pictures (MULTIX Swing, Siemens, Erlangen, Germany) of both ViV positions were taken under direct visual control to have a pattern for the actual procedure (Fig. 2D and E).

**Data acquisition and analyses**

Data acquisition was run across five consecutive cardiac cycles, and transvalvar pressure gradient, regurgitant volume and EOA were determined.

The study was approved by a local institutional review board and the patient gave written informed consent.
RESULTS

Clinical scenario

In 2010, a 77-year old female patient was admitted to our institution due to severe symptomatic AS. The patient underwent an uncomplicated minimally invasive SAVR (MIC-SAVR) with a 21 mm sutureless Sorin Perceval bioprosthesis through a partial upper sternotomy. Intraoperative transoesophageal echocardiography (TOE) showed an excellent result with no signs of paravalvular regurgitation. Unfortunately, 3 years after MIC-SAVR, valve function had gradually declined and the prosthesis showed severe central aortic regurgitation (AR) and AS (mean gradient 49 mmHg, EOA 0.8 cm²) (Fig. 3A). This was clinically paralleled by a decline in exercise capacity to New York Heart Association class III–IV of the now 80-year old patient, making another AVR necessary. Owing to the patients’ risk profile [EuroSCORE I 19%, Society of Thoracic Surgeons Predicted Risk Of Mortality 4.2%, body mass index 32 kg/m²], redo SAVR was associated with an elevated surgical risk. The case was discussed within our heart team and TAVI was decided to be the most feasible option for this high-risk patient. However, a transcatheter procedure into a Perceval prosthesis had not been reported before, therefore multiple challenging safety issues had to be overcome.

Technical considerations and access route

The initial step was to evaluate the specific features of the Perceval. It is a bovine pericardial valve mounted on an elastic nitinol frame, consisting of two rings, one on the annular level

Table 1: Parameters of set measurement points

<table>
<thead>
<tr>
<th>Flow (l/min)</th>
<th>Mean aortic pressure (mmHg)</th>
<th>Heart rate (1/min)</th>
</tr>
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<tbody>
<tr>
<td>Low cardiac output</td>
<td>3</td>
<td>80</td>
</tr>
<tr>
<td>Light exercise</td>
<td>5</td>
<td>100</td>
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Figure 2: ViV with an Edwards SAPIEN XT into a Sorin Perceval prosthesis performed in two positions: In Position 1, the lower border of the SAPIEN valve extended partially beyond the lower margin of the Perceval prosthesis (A, straight arrow) whereas in Position 2, the SAPIEN was positioned in a way that its upper border extended above the opened Perceval leaflets (B, arrow). X-ray pictures of the respective positions (D and E). ViV with CoreValve into Perceval, demonstrating an unfavourable effect of the Perceval stent on deployment of the CoreValve as indicated by the arrows (C). Schematic depiction of the pulse duplicator (F). ViV: valve-in-valve.
inflow) and one at the sinotubular junction (‘outflow’), connected by straight commissural struts and sinusoidal struts, which protrude from the cylindrical geometry to anchor the valve in the sinuses of Valsalva (Fig. 1B). The distal ‘outflow’ ring is a unique feature of the valve, which ensures prosthesis stabilization, but on the other hand represents a potential mechanical obstacle for transfemoral TAVI (Fig. 1B). Second, the majority of ViV procedures have been performed with either the Edwards SAPIEN/SAPIEN XT or the Medtronic CoreValve. The CoreValve did not seem suitable for a ViV procedure into a Perceval as the high Perceval stent design can interfere with the likewise high CoreValve stent and jeopardize proper valve deployment (Fig. 2C arrows). Furthermore, the transapical approach facilitates a more precise control of the prosthesis during deployment of the valve. Therefore, a transapical approach seemed the better option for this patient.

Third, with regard to the unique Perceval stent design, the depth of implantation of the SAPIEN XT seemed a crucial issue. Therefore, two ViV procedures were performed at different implantation heights, a low position (1) and a higher position (2) (Fig. 2A and B).

Hydrodynamic measurements revealed good results for both valve-in-valve positions

Hydrodynamic measurements were performed during a simulated cardiac output of 3 and 5 litres per minute (l/min) with heart rates of 120 and 70/min, respectively, simulating resting conditions and light exercise in a patient. A detailed description of all parameters is given in Table 1. Both ViV positions were stable for the duration of the perfusion test.

Systolic pressure gradient

As expected, we found increased pressure gradients with higher flow rates in both positions. The mean systolic pressure gradient was acceptable during perfusion with 3 l/min (Position 1: 12.80 vs Position 2: 10.85 mmHg) and an increase was observed for both ViV-positions at the higher flow rate of 5 l/min (Position 1: 14.42 vs Position 2: 12.92 mmHg) (Fig. 4A). Compared with Position 1, mean systolic gradients in Position 2 were slightly lower, but with regard to the small anatomy of the annulus and the ‘overstented’ 21 mm Perceval valve both positions showed encouraging and acceptable results.

Effective orifice area

ISO 5840-3 requires an EOA of 1.25 cm² for a 23 mm compartment at a flow rate of 5 l/min [20] and this requirement was met for both implantation positions. EOA was slightly lower for the 3 l/min measurement point (Position 1: 1.05 vs Position 2: 1.08 cm²) and an increase was observed for both ViV positions at a flow rate of 5 l/min (Position 1: 1.61 vs Position 2: 1.65 cm²) (Fig. 4B).

Valvular and paravalvular regurgitation

The amount of regurgitation was analysed in percentage of the stroke volume. The regurgitation volume is calculated from the closure volume and the leakage volume. Evaluation of total regurgitation for both ViV positions showed excellent results for both flow conditions (3 l/min: Position 1: 7.4% vs Position 2: 8.2%/5 l/min: Position 1: 3.3% vs Position 2: 2.8%) (Fig. 4C). According to ISO standards, the overall regurgitation may not exceed 10% of the forward flow for a 23 mm compartment [20]. These requirements were fulfilled by far for all measurements.

High-speed motion analysis of leaflet kinematics

High-speed video recordings of the protheses revealed differences in the opening characteristics in different ViV positions: our analysis showed impaired leaflet motion in Position 1 compared...
with Position 2 (Fig. 5A–D, Video 1). Owing to the higher deployment of the valve in Position 2, the Perceval leaflets were completely pushed aside by the SAPIEN XT stent, resulting in unimpaired valve opening (Figs 2B and 5D, Video 1). In Position 1, however, the leaflets of the Perceval show residual motion and contact with the SAPIEN XT leaflets during systole (Fig. 5C arrows, Video 1). During the closure phase, pinwheeling of the leaflet edges was seen due to underexpansion of the valve. This effect appeared more prominent in Position 1, indicating an unfavourable effect of the Perceval on full deployment of the SAPIEN XT (Fig. 5A and B, Video 1). With regard to the acquired hydrodynamic measurement data and high-speed video analyses, a benefit of Position 2 is evident.

**Patient procedure**

After thorough revision of all results, it was decided to perform the procedure with a 23 mm SAPIEN XT valve in Position 2 via a transapical approach. The procedure was carried out in our hybrid operating room, using a slightly modified version of the previously published technique by Walther et al. [21]. Briefly, the apex was exposed after a left-sided minithoracotomy in a non-rib-spread technique. Two purse string sutures and epicardial pacemaker electrodes were placed on the apex of the left ventricle. The apex was punctured, a guidewire inserted and exchanged to an Amplatz Super Stiff wire. No predilatation was performed to avoid calcium mobilization. The 23 mm SAPIEN XT was inserted through the Ascendra® sheath, advanced and positioned according to the X-ray image of Position 2, which was projected on the monitor as a guide for proper valve position in the predetermined position. The valve was balloon-expanded under rapid pacing in the exact predetermined position and one post-dilatation (+2 ml additional balloon volume) was performed to ensure complete expansion and anchoring of the SAPIEN XT. Intraoperative fluoroscopy and TOE showed an excellent result with no AR, a mean gradient of 8 mmHg and EOA of 1.6 cm² (Fig. 6A–D, Video 2), which was an even better result than expected. The coronaries were unimpaired and there were no signs of myocardial ischaemia on electrocardiography during and after the procedure; no signs of conduction disturbances were observed. The patient was extubated in the operating room and discharged home on Day 7 after an uneventful recovery.

**Valve-in-valve procedure with SAPIEN XT resulted in dilatation of the lower Perceval nitinol stent frame**

As the final result of the patient procedure was better than anticipated, we decided to look for potential explanations. The only procedural difference between our preprocedural simulations and the patient procedure was performance of one post-dilatation.

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**Video 1:** High-speed video recordings of leaflet motion in both ViV positions.

**Figure 4:** Hydrodynamic measurements—hydrodynamic measurements performed in the pulse duplicator revealed good functional results in both positions under both physiological conditions in terms of transvalvular gradients (A), EOA (B) and leakage volumes (C). EOA: effective orifice area.
We speculated that the favourable functional result was a consequence of an increase in diameter of the lower nitinol stent of the Perceval after ‘post-dilatation’ of the SAPIEN XT and decided to simulate this additional step in vitro. The 21 mm Perceval was once again expanded in a size matching silicon annulus, representing a moderately calcified aorta. The 23 mm SAPIEN XT was then implanted at Position 2 within the Perceval, expanded with normal balloon volume (16 ml) and increased balloon volume (18 ml) and the diameter and area under both conditions were quantified. As shown in Fig. 7, this resulted in a 13% increase in orifice area of the overstented Perceval valve. This finding was verified by TTE at 8 weeks follow-up, when a gradient of 14 mmHg and an EOA of 1.6 cm² were measured under resting conditions (Fig. 6E and F, Video 1).

**DISCUSSION**

In an attempt to plan and prepare for a challenging transcatheter ViV procedure, we have developed a new and technically feasible algorithm, simulating important aspects of a novel interventional procedure to optimize procedural success and patient safety.

ViV procedures are increasingly performed for minimally invasive treatment of degenerated bioprostheses in patients deemed inoperable for redo surgery and represent a promising approach in this patient group [5, 22–24]. However, analyses of multinational ViV registries have raised safety concerns as some severe complications are observed more often during ViV procedures, which can have deleterious effects on patient outcome [5]. A very recent innovation in this sector was the development of a ViV App containing recommendations for selection of THV for specific bioprostheses [16]. These recommendations are a unique help in the hands of an experienced physician; however, recently introduced valves, such as the Perceval are not yet included. Furthermore, crucial information regarding the hydrodynamic performance or potential leaflet interactions between the ‘old’ and ‘new’ valve after a ViV procedure is not provided, and in our view is particularly critical for first-time implantations. Finally, according to the manufacturer, the valve design of the Perceval is not suitable for a ViV procedure (Sorin Biomedica personal communication). We therefore felt the necessity to make all efforts to compensate for the lack of experience and evidence regarding this case in order to minimize potential complications.

The 21 mm Perceval prosthesis implanted in this patient has an inner diameter of 19 mm according to the manufacturer’s specifications. These specifications were along our own measurement obtained for hydrodynamic testing (19.2 mm) and MSCT analysis of the patient (18.3 mm), which also revealed a significant degree of eccentricity of the implanted Perceval (Fig. 3B). These dimensions are along the lower margin of the smallest
SAPIEN XT available (23 mm) requiring a minimal inner diameter of 18.0 mm of the degenerated biological valve [16]. Owing to the small dimensions, a satisfactory haemodynamic performance was questionable. Therefore, the depth of implantation of the SAPIEN XT seemed a crucial issue since leaflet motion might be influenced by the Perceval 'outflow' stent. In addition, the Perceval has an inflow section below the leaflets, which must be considered when comparing implantation heights with other surgical prostheses such as an Edwards Perimount or St. Jude Medical Trifecta, which have their leaflets attached at the bottom end of the prosthesis.

Therefore, two ViV procedures were performed at different implantation heights, a low position (1) and a higher position (2). Hydrodynamic measurements were performed with a simulated

Figure 6: Fluoroscopy images of the actual patient procedure—fluoroscopy showed severe AR (A). The Edwards SAPIEN XT valve was implanted according to the X-ray image in the predetermined position (B and C). The final angiogram after one post-dilatation showed an excellent result with no AR and no impairment of the coronaries (D). Eight-week follow-up TTE showed an excellent result with no regurgitation and a low mean gradient (E and F). TTE: transthoracic echocardiography.
cardiac output of 3 and 5 l/min with heart rates of 120 and 70/min, respectively, simulating resting conditions and light exercise in a patient. The 3 l/min measurement point was chosen to reflect the low-flow, high-frequency condition of a patient recovering from cardiac surgery. The 5 l/min condition was chosen to reflect a recovered heart and because it reflects an accepted standard measurement point in comparable studies and international standards [20]. Interestingly, both positions showed good functional results with acceptable transvalvular gradients, EOA and negligibly small leakage volumes. However, high-speed video recordings of the prostheses revealed differences in leaflet kinematics for the two ViV positions. In Position 1, leaflet motion was impaired due to protrusion of the Perceval leaflets over the SAPIEN XT prosthesis (Fig. 2A dashed arrow, Video 1). In contrast, in Position 2 the Perceval leaflets were completely pushed aside by the SAPIEN XT stent, resulting in an unimpaired valve opening. This can result in increased turbulences behind the ViV area and bears the risk to reduce long-term durability. In addition during the closure phase of the SAPIEN XT, pinwheeling of the leaflet edges was seen and this effect appeared more prominent in Position 1 again indicating an unfavourable effect of the Perceval on full deployment of the SAPIEN XT (Video 1).

As the final result of the patient procedure exceeded our expectations, we hypothesized that the favourable functional result was a consequence of an increase in diameter of the lower nitinol stent of the Perceval after post-dilatation of the SAPIEN XT. To avoid additional radiation for the patient and as it is often very difficult to perform exact measurements with MSCT after a ViV procedure due to artefacts [25], we decided to simulate the ‘post-dilatation’ in vitro. Interestingly, this resulted in an increase in EOA of the overstented Perceval and therefore conclusively explained our good functional result. We think that this observation is of utmost importance as our analysis provides interesting insights into the mechanism of a ViV procedure in a sutureless nitinol stent-based valve with important implications for future procedures: on the one hand, the finding that the nitinol stent of a sutureless valve can further dilate after a ViV procedure is beneficial in that aspect as it allows for a better functional result with increased EOA and reduced gradient, even for small valve sizes. On the other hand, excessive oversizing of the implanted nitinol stent may carry a potential risk of annulus perforation or the need for pacemaker implantation due to increased radial forces exerted on aortic annular structures. However, this risk should be fairly low since a procedural step during implantation of the sutureless Perceval valve is resection of the calcified leaflets, leaving an annular wall behind that mostly displays at least some degree of elasticity. This is in contrast to implantation of a self-expandable THV where calcium debris remains around the THV stent, therefore possibly constituting a higher risk regarding this aspect. However, most conventionally implanted biological valves have stent frames made of rigid substances such as cobalt-nickel-alloy, polypropylene or titanium not allowing for a significant dilatation. Therefore, presence or absence of the native valve leaflets, its calcium debris and the stent material of the previously implanted valve should carefully be considered when planning a ViV procedure.

In conclusion, we have developed a new and technically feasible algorithm, using cutting edge technology to simulate important aspects of a novel interventional procedure to optimize procedural success and maximize patient safety. In particular, this algorithm may be helpful for planning of a ViV procedure into a bioprosthesis that has never been performed before or does not seem feasible at
first look. Also, this algorithm can be applied not only for prostheses in aortic position but in all conceivable positions in the heart, even in native valves within a complicated anatomy. This can be particularly important in congenital heart defects in which not only the choice of the THV and its position but also the access route may represent an important aspect. This algorithm allowed us to address potential safety concerns and solve them in advance to ensure a safe and successful ViV procedure. Furthermore, the algorithm revealed unexpected obstacles, which would have influenced patient outcome substantially, if detected during the procedure. Although, initially developed for simulation of a ViV procedure, this algorithm can be applied to virtually all patients requiring a novel interventional procedure to help identify risks and find optimal parameters for prosthestic selection and placement in order to maximize safety for the patient.

**Funding**

ADUMED Foundation.

**Conflict of interest:** Buntaro Fujita: Received travel compensation from Edwards Lifesciences and Symetis.

Smita Scholtz: Proctor for Direct Flow Medical, received speaker honoraria from Medtronic, received travel compensation from Edwards Lifesciences, Medtronic and Direct Flow Medical.

Jochen Börgermann: Proctor and consultant for Medtronic, received speaker honoraria from Symetis, received travel compensation from Medtronic and Symetis.

Stephan Ensminger: Proctor and consultant for Edwards Lifesciences, proctor and member of the SAB of JenaValve, received speaker honoraria from Edwards Lifesciences and Symetis, received travel compensation from Edwards Lifesciences.

The remaining authors do not report a conflict of interest with regard to this manuscript.

**REFERENCES**


[16] Bapat VN. Valve-in-valve app: why and how they were developed and how to use them. EuroIntervention 2014;10:U44–51.


