Postsurgical Complications after Tavi Using First and Second-Generation Transcatheter Heart Valves

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INTRODUCTION

Since the year 2002 a rapid evolution of catheter-based technology to treat severe symptomatic aortic valve stenosis in high risk patients has taken place and these minimally-invasive techniques have become a routine procedure [1]. Transapical as well as transfemoral aortic valve implantation avoiding cardiopulmonary bypass support and midline sternotomy have reduced the threshold to treat formerly inoperable or very high risk patients [2,3].

These encouraging findings have led to a significant increase of TAVI procedures worldwide, and the recently published results gave a further boost for industry and referring physicians to get more involved in this relatively new technology. However, results of TAVI are not yet perfect and several unresolved questions remain to be answered. Beside others, one major challenge is how to reduce present device-related limitations like high-degree atrio-ventricular block in up to 40%, high stroke-rate in up to 14.6% or significant rate of moderate paravalvular leaks in up to 21% of patients [3-6].

Both CE-mark approved 1st generation TAVI systems, the balloon-expandable SAPIEN® valve system as well as the transfemoral Nitinol stent-based Core Valve revalving system® do not provide an anatomical orientation of the prosthesis into the native aortic annulus, bearing a potential risk of coronary blood flow compromise and paravalvular leak. Thus, efforts were made in some of the 2nd generation TAVI devices to overcome these shortcomings and develop TAVI systems allowing for anatomical valve positioning in the aortic root.

In this chapter we aim to summarize the evolution as well as postsurgical complications after TAVI using first and second generation transcatheter heart valves. In conclusion, we would give some perspectives for the future of new devices, which eventually overcome some of the current device limitations.

1ST GENERATION TRANSCATHETER HEART VALVES

Evolution of the Edwards Sapien®

The balloon-expandable Cribier-Edwards valve (Edwards Life sciences, Irvine, CA, USA) was introduced in 2002, which consisted of equine pericardium and a stainless steel frame. Modification of this first prototype resulted in the Edwards SAPIEN® THV, which also consisted of a stainless steel frame, but with bovine pericardial valve tissue and a fabric skirt made of Polyethylene Terephthalate (PET). The RetroFlex™ delivery system accompanying this device was of large diameter (22-24 Fr) and associated with higher rates of vascular complications. In 2010 the Edwards SAPIEN XT™ was launched with a cobalt-chromium stent frame, thinner struts and a low-profile NovaFlex+ delivery system.

The last generation is the SAPIEN 3 valve which consists of a trileaflet pericardial bovine valve mounted in a cobalt-chromium stent with an additional outer cuff to further improve paravalvular sealing. The highly flexible, low-profile TF Commander delivery system is introduced through a nominal 14 (~4,7 mm) or 16 (~5,3 mm) French expandable sheath (eSheath) and consists of a distal short tapered tip and additional features to facilitate valve alignment and positioning.

In a multicentre study of the SAPIEN 3 valve TF implantation was associated with lower mortality and stroke rates as compared to alternative access [7]. In a propensity score-matched, single-centre analysis, SAPIEN 3 was associated with significantly lower rates of ≥ mild paravalvular regurgitation (15.9% versus 46.2%, p=0.003) before hospital discharge compared to SAPIEN XT. No differences in pacemaker rates (9.8% versus 8.8%, p = 0.94) and 30-day mortality (both 5%) were observed [8]. Data comparing the outcome of different SAPIEN generations have been few and several studies are ongoing.

Evolution of the CoreValve®

The self expanding CoreValve® (Medtronic Inc., Minneapolis, MN, USA) was launched in 2007 and consists of bovine (first-generation device, 25 Fr delivery sheath) or porcine (second- and third-generation, 21 Fr and 18 Fr delivery sheaths, respectively) pericardial tissue mounted on a nitinol-frame. The lower profiles of the newer-generation devices were achieved by switching to porcine pericardium and using a more flared outflow design. The stent frame consists of an inflow segment, a supra-annular narrower middle segment containing the leaflets, and a cell designed outflow segment which allows blood flow to the coronary ostia. The low-profile AccuTrak™ delivery system is equipped with features to reduce frictional forces and enhanced control during deployment.

The CoreValve Evolut R™ is the latest generation that has several modifications to make it repositionable, resheathable and recapturable. It is shorter in height and treated with alpha-amino oleic acid, which binds to aldehyde groups within the pericardial tissue to inhibit calcification. The valve comes with the EnVeo™ R delivery system, a very low-profile 14-French sheath.

2ND GENERATION TRANSCATHETER HEART VALVES

Shortcomings had pushed the development of 2nd generation self-expandable Nitinol-based devices which aim to reduce the degree of paravalvular leak and AV-block by anatomical orientated positioning of the valve into the aortic root (Figure 1 & Figure 2). First results using these new TAVI devices are promising.

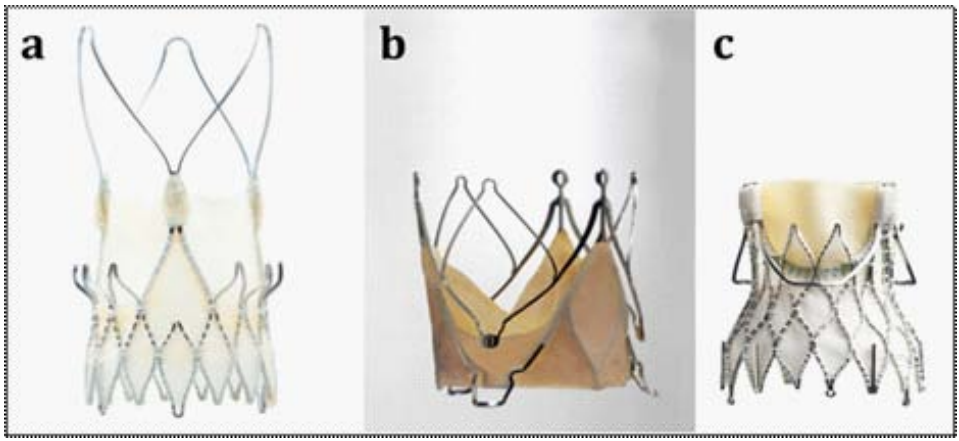

Figure 1: Overview of currently available second-generation transcatheter heart valves. Pictures provided courtesy of (a) Symetis ACURATE neo™ (Symetis SA, Ecublens, Switzerland); (b) JenaValve™ (JenaValve Technology, Munich, Germany); (c) Engager™ (Medtronic, Minneapolis, MN, USA).

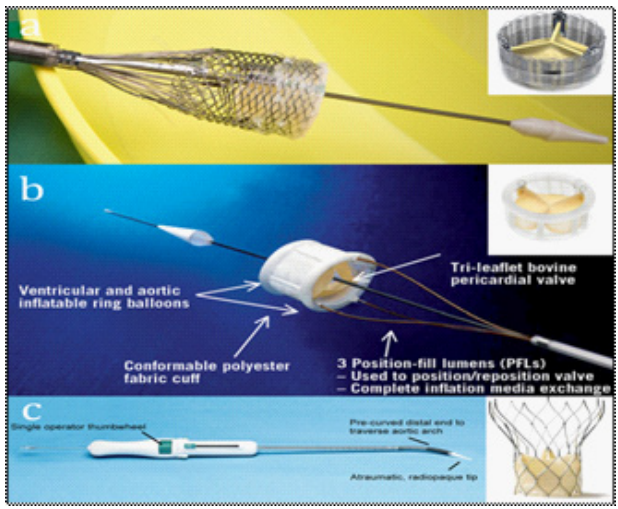

Figure 2: The second-generation transcatheter heart valves (a) Lotus™ Valve System (Boston Scientific, Marlborough, MA, USA); (b) Direct Flow Medical® (Direct Flow Medical Inc., Santa Rosa, CA, USA) and (c) Portico™ Transcatheter Aortic Valve Implantation System (St. Jude Medical, St. Paul, MN, USA).

The Symetis ACURATE neo™ (Symetis SA, Lausanne, Switzerland) consists of an aortic stentless porcine valve that is mounted and sutured on a self-expanding nitinol alloy stent with a Dacron interface. The stent assembly consists of a three stabilization arches ensuring predictable coaxial alignment, commissural totems, inflow-edge hooks, and an upper and lower anchoring crown [9].

The Engager™ Aortic Valve Bioprosthesis (Medtronic Inc., Minneapolis, MN, USA) is a flexible heart valve prosthesis composed of three leaflets, cut from tissue-fixated bovine pericardium, sewn to a polyester sleeve, and mounted on a compressible and self expanding Nitinol frame. The stents consist of a main frame and a support frame. The control arms of the support frame are designed to be placed into the sinus of the aortic root to achieve an anatomically correct position to minimize the risk of coronary obstruction [10].

The JenaValve™ (JenaValve, Munich, Germany) device consists of a self-expandable Nitinol stent designed for subcoronary implantation. Using three Nitinol 'feelers' meant to embrace the native calcified aortic valve leaflets the stent design relies on axial in addition to radial fixation. Inside the Nitinol stent a regular porcine tissue-valve (Elan, Vascutek Inc.) is mounted [11].

The Lotus™ valve (Boston Scientific, Natick, Massachusetts, USA) consists of single braided nitinol wire and 3 bovine pericardial leaflets. During the mechanical deployment the valve is unsheathed and the frame expands to its final diameter and shortens to the final height of 19 mm. The outer surface of the lower half of the frame is covered with an adaptive seal, essentially a polymer membrane that concertinas as the device is expanded. The valve is fully repositionable and resheathable, even in the completely expanded position, allowing for fine control and the potential for removal [12].

The Direct Flow Medical® valve (Direct Flow Medical Inc., Santa Rosa, California, USA) is a novel, polymer-frame percutaneous low-profile aortic valve with an inflatable cuff that can be filled and emptied of contrast, which allows for repositioning if necessary. Once placed in the optimal position, the saline contrast mixture is exchanged for a solidifying polymer that hardens to form the permanent support structure [13].

The Centera™ valve (Edwards Life sciences, Irvine, CA, USA) is a self-expanding valve composed of a nickel-titanium alloy frame and treated trileaflet bovine pericardium. The stent features a unique shape that facilitates self-centering in the annulus, improved fit and therefore reduces PVR. In addition, it minimizes protrusion on either side of the annulus. Although the valve is repositionable and recapturable until final deployment, it is only resheathable if less than 70% deployed [14].

The repositionable Portico™ valve (St. Jude Medical, Minneapolis, Minnesota, USA) consists of a nitinol self-expanding frame, bovine pericardial leaflets, and a porcine pericardial sealing cuff. The outflow portion of the stent frame incorporates 3 retention tabs, which secure the crimped valve to the delivery system. The large cell area design of the frame allow easier engagement of coronary ostia post implantation and a potential to minimise the risk of paravalvular leakage by allowing valve tissue to conform around calcium bricks at the annulus [15].

POSTSURGICAL COMPLICATIONS – WHAT TO LEARN RETROSPECTIVELY?

To propose standardized definitions for important clinical endpoints in transcatheter aortic valve implantation consensus criteria were developed by the 'Valve Academic Research Consortium' (VARC) [16]. Subsequent to the implementation of this first consensus document, recommendations were soon revisited and updated by the VARC-2 position paper [17]. Specific definitions for research of TAVI aimed to provide consistency across studies and included the following clinical endpoints: mortality, myocardial infarction, stroke, bleeding, acute kidney injury, vascular complications, and prosthetic valve performance (Table 1).

1st Generation devices	Study design	n	Results	Reference
Sapien vs. CoreValve	randomized 5 centres	n = 241 Sapien XT (n=121) CoreValve (n=120)	Device success: Sap 95.9%, CV 77.5% ≥ mild pvleak: Sap 4.1%, CV 18.3% ViV: Sap 0.8%, CV 5.8% 30d CV-mortality: Sap 4.1%, CV 4.3% (similar) Bleeding and vascular complications: not different new pacemaker: Sap 17.3%, CV 37.6%	CHOICE trial 2014
	non-randomized 25 centres	n = 870 Sapien (n=410) CoreValve (n=459)	> mild pvleak: Sap 9.6%, CV 17.3% 30d-mortality: Sap 8.5%, CV 5.8% (similar) 1yr mortality: Sap 20.6%, CV 21.7% (similar) myocardial infarction, stroke and vascular complications: not different new pacemaker: Sap 7.4%, CV 24.4%	UK registry (Moat) 2011
	non-randomized 137 centres	n = 4.571 Sapien XT (n=2.604) CoreValve (n=1.943)	in-hospital mortality: Sap 7.9%, CV 6.7% (similar) large mortality differences according approach (TF 5.9%, TA 12.8%, TS and others 9.7%) ViV: Sap 1.4%, CV 3.7% Device embolisation: Sap 0.3%, CV 0.6% Surgical conversion: Sap 3.3%, CV 5.5% > mild pvleak: Sap 6.7%, CV 12.2% myocardial infarction, stroke and vascular complications: not different new pacemaker: Sap 6.0%, CV 23.4%	TAVI Sentinel Pilot registry 2012

	non-randomized 23 centres	n = 861 Sapien (n=460) CoreValve (n=401	Device success: Sap 97.0%, CV 98.0% 30d- and midterm survival (3 yrs): not different ViV: Sap 1.0%, CV 3.0% valve migration: not different myocardial infarction and stroke: not different new pacemaker: Sap 7.0%, CV 29.0%	Belgian registry (Collas) 2015
	non-randomized 33 centres	n = 3980 Sapien (n=2036) CoreValve (n=1897) Portico (n=35) JenaValve (n=3) Direct Flow (n=3)	moderare pvleak: Sap 6.8%, CV 15.6% 1 and 2 yr-mortality: similar ViV: Sap 0.8%, CV 4.0% Surgical conversion: Sap 0.6%, CV 0.4% Emergency PCI: Sap 0.3%, CV 0.3% stroke (Sap 2.7% vs. CV 2.6%) and vascular complications: not different new pacemaker: more frequent after CV, but reduced markedly from ≈29% to ≈15% in more recent years	UK registry (Ludmann) 2015
	Meta-analysis 5 RCTs 28 MCRs	n = 35347 Sapien (n=23745) CoreValve (n=11602)	30d- & 1-yr mortality: similiar ≥ 2+ pvleak, new pacemaker implantation, valve embolization, need for ViV, need for surgical AVR: higher incidence in CoreValve stroke: not different Coronary obstruction: similar	Agarwal et al. 2015

2nd generation devices				
Engager vs. Symetis vs. JenaValve	non-randomized single-center	n = 200 Engager (n=50) JenaValve (n=88) Symetis (n=62)	no more-than-mild pvLeak significant rate of post-dilatation no immediate complications (e.g. annular rupture) Engager: trend towards increased conduction disorders, PM in 30% PM lowest in JV myocardial infarction, AKI, major access site complications not different 1-yr-mortality: 32.1% JV, 29.8% Eng, 12.4% Sym	Seiffert et al. 2015
	non-randomized 2 centres	n = 537 Sapien XT (n=254) CoreValve (n=123) JenaValve (n=62) Engager (n=56) Symetis (n=42)	Sapien XT and 2nd generation valves linked to lower pvLeak	Seiffert et al. 2015 (2)

Lotus	prospensity-score matched single-center	n = 100 Lotus (n=50) CoreValve (n=50)	Device success: Lotus 84.0%, CV 64.0% comparable procedural safety and efficacy CV mortality: Lotus 0.0%, CV 4.0% n.s. ≥ moderate pvleak: Lotus 4.0%, CV 16.7% myocardial infarction, stroke, AKI, major access site complications: not different new pacemaker: Lotus 28.0%, CV 18.0%	Gooley et al. 2015
	non-randomized single-center	n = 78 Lotus (n=26) Sapien 3 (n=52)	Device success: Lotus 96.0%, S3 98.0% comparable procedural safety and efficacy balloon postdilatation: not necessary contrast media: same amount ≥ moderate pvleak: Lotus 0.0%, S3 0.0% myocardial infarction, stroke, AKI, bleeding, vascular complications: not different no mortality, annulus rupture, coronary obstruction, adjunctive PCI new pacemaker: Lotus 27.0%, S3 4.0%	Wöhrle et al. 2015

Direct Flow	prospensity-score matched single-center	n = 120 DFM (n=40) Sapien XT (n=40) CoreValve (n=40)	Device success: similiar balloon postdilatation: not necessary contrast media: less ≥ 2 pvleak: DFM 0%, Sap 7,5%, CV 5.0% 30d-mortality, myocardial infarction, stroke, AKI, blood transfusions, coronary obstruction: not different new pacemaker: DFM 10.0%, Sap 5.0%, CV 37.5%	Zhang et al. 2015
	prospensity-score matched single-center	n = 123 DFM (n=41) Sapien XT (n=41) CoreValve (n=41)	Device success: 97.6% (higher) balloon postdilatation: not necessary contrast media: n.s. less ≥ 2 pvleak: DFM 2.5%, Sap 31.7%, CV 53.6% Device embolisation and ViV: DFM 0%, Sap 0.0%, CV 7.3% 30d-mortality, myocardial infarction, stroke, AKI, major bleeding, coronary obstruction, vascular complications, mean hemodynamic gradient: not different new pacemaker: DFM 17.1%, Sap 7.3%, CV 34.1%	Gustino et al. 2015

5. MORTALITY

To date, the CHOICE trial is the only randomized comparison of the Edwards Sapien XT™ and Medtronic CoreValve®. In this German, investigator-initiated, multicenter, open-label, randomized trial, 241 patients with severe aortic stenosis and at least intermediate surgical risk underwent transcatheter aortic valve replacement [18]. 30-day mortality was comparable between the Edwards Sapien XT™ and Medtronic CoreValve® (4.1% vs. 5.1%, p = 0.77). In the multinational TAVI Sentinel Pilot registry in-hospital mortality was also comparable (Sapien XT™ 7.9% vs.

CoreValve® 6.7%, p = 0.15). Similar results were found for mid-term survival at 1 and 3 years in the recent UK and Belgian TAVI registries [19-22].

Regarding the 2nd generation devices JenaValve™, Medtronic Engager™ and Symetis Acurate™ all-cause mortality at 1 year was 26.1% with better survival in Symetis patients (JenaValve™ 32.1%, Medtronic Engager™ 29.8% and Symetis Acurate™ 12.4%, p = 0.047) [23].

With regard to the Lotus™ Valve System cardiovascular 30-day mortality was not different in a matched comparison with CoreValve® patients (0% vs. 4%, respectively; p = 0.32) [24]. Likewise, no 30-day mortality was found in a non-randomized single-centre study comparing the Lotus™ valve and Sapien 3 [25].

In 2 prospensity-score matched studies 30-day mortality of the Direct Flow Medical® valve was not different compared to the Sapien XT™ and CoreValve® [26,27].

MYOCARDIAL INFARCTION

The CHOICE trial revealed a comparable incidence of periprocedural myocardial infarction between the Edwards Sapien XT™ and Medtronic CoreValve® (0,8% vs. 0.0%, p = 0.99). This is in consistency with an incidence of 0.7% for both valve types in a recent meta-analysis of 35.347 TAVI patients [22].

Comparing the JenaValve™, Medtronic Engager™ and Symetis Acurate™ no cases of intraprocedural coronary obstruction occurred but one myocardial infarction was observed in a patient with diffuse pre-existing coronary artery disease [23].

At present, excellent results with no single case of peri-procedural myocardial infarction can also by stated for recent data of the Lotus™ valve and Direct Flow Medical® valve [24-27]. Further validity of these first results remains to be seen.

STROKE

A serious concern in the beginning was the potentially high stroke rate which was assigned to the balloon valvuloplasty. With regard to CHOICE trial stroke occurred in 5.8% in the balloon-expandable Sapien XT™ group and 2.6% in the self-expandable CoreValve® group (p = 0.33) [18]. Several registries as well as a recently published large meta-analysis demonstrated a similar incidence of stroke at 30-day (2.4% vs. 2.7%) and 1-year (5.2% vs 4.9%) follow-up among the two valve types [19-22,28].

Results of the European Pivotal Trial revealed an incidence of 1.8% of major strokes at 30 days for the Engager™ valve [29]. The observed overall 30-day stroke rate in the multicentre SAVI registry using the Symetis Acurate TA™ device was 2,8% (“early-onset” 0.4% within 48 hours, “late-onset” 2.4% after 48 hours) [30]. In the 30-day results of the JenaValve™ pivotal study 2 of 66 patients (3.0%) developed a stroke [23,31].

There was no significant difference in the incidence of major strokes for the Lotus™ valve compared to CoreValve® and the Sapien 3 (4% vs. 2%, p = 0.56 and 0% vs. 1.9%, p = 0.48, respectively) [24,25]. Comparable results were found for the Direct Flow Medical® valve (5%, p = 0.770 and 0%, p = 0.365) [26,27].

BLEEDING AND VASCULAR COMPLICATIONS

Bleeding complications post-TAVI is frequent and independently associated with impaired clinical outcome at short- and long-term follow-up. TAVI patients with in-hospital bleeding are older and more frequently have previous bleeding events in their past medical history. The majority of bleeding complications are considered access-site related or have been classified as vascular events (66.4%) [32]. Vascular complications are most commonly a consequence of arterial sheath insertion during TF-TAVI. Reported rates of major vascular complications range from 5.5 to 20% [33,34]. The continued efforts towards smaller sheaths should in the future reduce the risk of vascular access problems.

In the Choice trial bleeding as well as vascular complications (major: 9.9% Sapien XT™ and 11.1% CoreValve®, p = 0.76) were not significantly different between the Edwards Sapien XT™ and Medtronic CoreValve® [18]. Regarding the 2nd generation JenaValve™, Medtronic Engager™ and Symetis Acurate™ life-threatening/major bleeding occurred in 13.0% with a higher incidence of bleeding events in JenaValve™ patients (JenaValve™ 17.4%, Medtronic Engager™ 6.0%, Symetis Acurate™ 13.1%, p = 0.179) [23]. Major access site complications, mostly related to bleeding from the apex or thoracic wall occurred in 4.0% of Engager™, 6.5% Symetis Acurate™ and 8.0% JenaValve™ patients, p = 0.663 [23].

With regard to the Lotus™ Valve System life-threatening (3.9% vs. 1.9%), major and minor bleeding was comparable with the Sapien 3 and CoreValve® (p = 0,61 and p = 0,1, respectively) [24,25]. Although sheath sizes for implantation of the Lotus™ valve were clearly higher compared with the Sapien 3, major vascular complications and the need for covered stents at the puncture site were similar (7.7 vs. 5.8%, p = 0.74) [25]. One reason for the observed similar complication rates could be the expansion of the 14 to 16 French sheath up to 24 French during the passage of the Edwards Sapien 3 valve.

Early data of the Direct Flow Medical® valve revealed comparable results for life-threatening (2.4%), major (2.4%) and minor bleeding (4.9%) compared to the CoreValve® and Sapien XT™ [26,27]. A significantly lower rate of major vascular complications was seen in the Direct Flow Medical® subgroup compared with the CoreValve® and Sapien XT™ (0% vs. 15.0% vs. 10.0%, respectively; p = 0.03), associated to differences in vascular closure devices [26]. Comparable results were found by Gustino et al. (2.4% vs. 4.9% CoreValve® vs. 4.9% Sapien XT™, p = 0.812) [27].

ACUTE KIDNEY INJURY

Severe acute kidney injury, defined according to VARC, is a rare event that was found in 4.1% of the Sapien XT™ and 9.4% of CoreValve® patients (p = 0.13) in the randomized CHOICE trial [18].

Second generation transcatheter heart valves showed a comparable incidence of acute kidney injury stage 3, even if their incidence appears to be considerable lower than in the early TAVI era (JenaValve™ 2.3%, Medtronic Engager™ 2.0%, Symetis Acurate™ 3.2%, p = 0.903) [23]. Comparable results of stage 2 or 3 acute kidney injury were found for the Direct Flow Medical® valve possibly related to a numerically lower contrast medium dose used during implantation (2.4% vs. 14.6% CoreValve® vs. 4.9% Sapien XT™; p = 0.081) [27]. The Lotus™ valve, as a differentiated second-generation TAVI valve, showed even no single case of acute kidney injury stage 2 or 3 (0.0% vs. 1.9% Sapien 3, p = 0.48) giving us a preview of the things to come like the worldwide RESPOND and Lotus REPRISE III trial [25].

PROSTHETIC VALVE PERFORMANCE

Residual Paravalvular Leak

As calcified aortic leaflets are not removed during TAVI, incomplete coaptation between the prosthesis and native annulus occurs. Studies have shown that moderate and severe Paravalvular Leaks (PVLs) are associated with a worse outcome and some studies even reveal a higher mortality rate in cases of even mild paravalvular leaks [35]. However, the pivotal CoreValve® trial failed to demonstrate an adverse effect of residual PVL on survival [36]. In cases of more than mild PVLs, post-dilatation or Valve-In-Valve (ViV) implantation should be considered. Another option remains the percutaneous closure with an Amplatzer vascular plug. Due to several factors, the incidence of moderate and severe PVL has been decreasing in recent experience.

The CHOICE study demonstrated a much higher incidence of PVL with the CoreValve® prosthesis despite significant over sizing, the achieved depth of implantation and a liberal use of balloon post-dilatation (≥ mild pvleak: 4.1% Sapien XT™ vs. 18.3% CoreValve®, p ≤ 0.001) [18].

Several characteristics of new transcatheter heart valves address this issue, such as enhanced positioning accuracy, controlled and anatomically correct implantation and improved sealing even in eccentric annular calcifications. With these concepts improved results have been achieved (> mild PVL: 4.0% Engager™, 5.7% JenaValve™ and 0% Symetis Acurate™) [23], however a significant rate of post-dilatation was required, possibly due to lower radial strength of the Nitinol-based stent compared with balloon-expandable transcatheter heart valves. In a second study by Seiffert et al. in 537 patients the Sapien XT™ and the 2nd generation Engager™, JenaValve™ and Symetis Acurate™ were linked to a lower incidence of PVLs [37].

Comparison of the repositionable Lotus™ valve and CoreValve® revealed lower rates of moderate or severe PVLs (4% vs. 16.7%, respectively; p < 0.001) [24]. TAVI with the Lotus™ valve

and balloon-expandable Edwards Sapien 3 resulted in similar acute and 30-day outcomes. In both groups there was no post-procedural moderate or severe PVL [25].

A already low incidence from 0 to 2.5% of moderate or greater PVLs was achieved with the Direct Flow Medical valve [26,27]. The decision whether or not a leak is relevant remains probably one of the most crucial decisions before expanding the indication to younger and intermediate-risk patients.

Conduction Disturbances and Cardiac Arrhythmias

The impact of conduction abnormalities and permanent pacemaker implantation following TAVI is currently not well understood, but available data suggest that there is no significant impact of periprocedural pacemaker implantation upon long-term follow-up [38]. However, this may be an important consideration in the choice of the valve in the future.

Placement of a new permanent pacemaker is more frequent after CoreValve® implantation compared to the Sapien™ prosthesis [18], but reduced markedly from about 29% to almost 15% in more recent years [19-22,28].

A trend towards an increased incidence of conduction disorders was observed possibly due to the stent design of the Medtronic Engager™ valve sealing paravalvular leakage with a skirt covering the lower stent part. Implantation of a permanent pacemaker was performed in 30% when compared with Symetis Acurate™ or JenaValve™ patients [23]. In the study by Seiffert and collegues the incidence of pacemaker implantation was lowest using the JenaValve™ [23].

The need for permanent pacemaker implantation was higher with the repositionable Lotus™ valve compared with the CoreValve® (28.0% vs. 18.0%, $p = 0.23$) and Edwards Sapien 3 (26.9% vs. 3.8%, $p < 0.003$) [24,25]. The results were not powered to identify the cause of increased pacing; however, in the REPRISE II trial, pacemaker insertion was found to correlate with the degree of prosthesis over sizing, which was greater than anticipated because only 2 valve sizes were at that time available. The option to select between 3 different valve sizes may reduce the need for permanent pacing with the Lotus™ Valve System.

The incidence with the Direct Flow Medical® Valve (10.0% to 17.1%) was lower than with the CoreValve® but higher with respect to the Sapien XT™ [26,27]. In order to optimally implant the Direct Flow® and make the inflatable ring conform to the aortic anatomy, pre-dilation of the stenotic aortic valve is mandatory.

Device Success

Device success is a composite endpoint meant to characterize acute device and procedural factors which underlie vascular access, correct positioning and performance of the valve [16]. The Sapien XT™ demonstrated a significantly higher rate of “device success” compared to the CoreValve® (95.9% vs. 77.5%, $p < 0.001$) primarily because of less-frequent moderate or severe aortic regurgitation (4% vs. 18%; $p < 0.001$) and need for a second valve (0.8% vs. 5.8%; $p = 0.03$) [18].

Procedural success rate for the JenaValve™ device was 89.6% and for the Engager™ transapical valve system 94.3% in multicentre CE-mark studies [29,31]. Device success was quite high for the Symetis Accurate™ (98%) [30].

VARC 2–defined device success in Lotus™ compared to CoreValve® patients was 84% and 64%, respectively (p = 0.02) [24]. High, but similiar results were found for the Lotus™ and Sapien 3 (96% vs. 98%, p = 0.61) with comparable procedural safety and efficacy [25]. A quite high procedural success rate was also found for the Direct Flow Medical® valve in a prospensity-matched comparison (Direct Flow Medical® 97.6%, CoreValve® 65.9% and Sapien XT™ 92.7%, p < 0.001) [27].

FUTURE DEVELOPMENTS

Apart from recent advancements, new valve designs and third-generation technology may influence the future of TAVI. Two upcoming devices are shortly described which are fully retrievable and repositionable upon deployment (Figure 3).

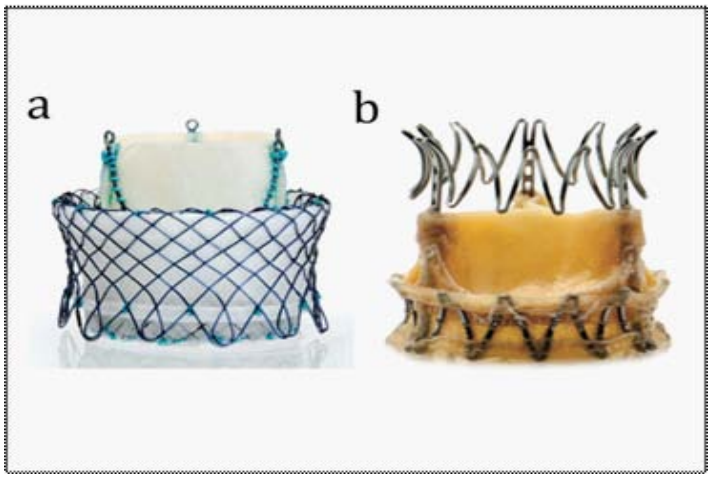

Figure 3: New Nitinol-based self-expandable transcatheter aortic valve systems, which are currently under clinical evaluation. (a) HLT® valve **(**Heart Leaflet Technologies Inc., Maple Grove, MN, USA) and (b) Trinity heart valve (Transcatheter Technologies GmbH, Regensburg, Germany).

One device is the HLT® valve (Heart Leaflet Technologies Inc., Maple Grove, MN, USA) that has porcine leaflets mounted on a self expandable nickel-titanium alloy stent. The valve sits in an intra-annular position and has a flexible tissue frame, isolated from the outer support structure, to reduce commissural stress and preserve flow area even in eccentric, diseased annuli.

The Trinity heart valve (Transcatheter Technologies GmbH, Regensburg, Germany) is a self-expandable valve that consists of three glutaraldehyde-treated bovine pericardial tissue leaflets attached to a nitinol frame. In order to minimize PVL, a pericardial cuff is placed along the lower crown for additional sealing. The supra-annular position of the prosthesis aims at minimizing the risk of atrioventricular block.

Further improvement will allow for controlled deployment without the need for contrast media and rapid ventricular pacing. Low profile TAVI devices might expand transfemoral access and further reduce vascular complications. Future TAVI devices might overcome the reduced durability of established heart valves by even an inner regenerative capacity or superior mechanical and surface properties and higher resistance to calcification.

CONCLUSION

To date, no scientific evidence exists with regard to the optimal choice of a particular prosthesis. New TAVI systems under clinical evaluation demonstrate positive haemodynamic results with low periprocedural complication rates. However, long-term durability of these new valve prostheses remains to be seen. In the near future, growing evidence may enable us to identify particulary suitable devices for a distinct root anatomy and mode of valve failure, allowing us to choose the right valve for the right patient.

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