Doppler haemodynamics and effective orifice areas of Edwards SAPIEN and CoreValve transcatheter aortic valves

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Aims
Transcatheter aortic valve implantation (TAVI) is a new therapy for severe aortic stenosis in high-risk patients. So far, no reference values for the echocardiographic assessment of this new class of heart valves have been established. The aim of our study was to determine Doppler haemodynamics and the effective orifice area (EOA).

Methods and results
We retrospectively analysed the earliest transthoracic echocardiographic examinations of 146 stable patients after successful TAVI (median 8 ± 20 days). Doppler examinations were analysed for peak instantaneous velocity, peak, and the mean systolic gradient. EOA was determined using the continuity equation. Patients with severe paravalvular aortic or mitral valve regurgitation were excluded. The overall peak instantaneous velocity \( n = 146 \) was 2.0 ± 0.4 m/s with a peak systolic gradient of 17.1 ± 7.4 mmHg and a mean gradient of 9.3 ± 4.5 mmHg. The mean EOA was 1.82 ± 0.43 cm\(^2\) with an indexed EOA of 1.0 ± 0.27 cm\(^2\)/m\(^2\). In general, all prostheses showed similar values—with the exception of the Edwards Sapien 23 mm which was associated with higher velocities and peak pressure gradients.

Conclusion
Our study establishes the normal range for Doppler haemodynamics of four transcatheter aortic valve prostheses. Compared with previously published data of surgically implanted bioprostheses percutaneous valves tend to have similar EOA values but lower mean peak velocities and pressure gradients. In comparison with physiological haemodynamics; however, this new class of heart valves is still associated with a mild obstruction.

Keywords
TAVI • Haemodynamics • Aortic stenosis • EOA

Introduction
Age-related calcific aortic stenosis (AS) is the most common cause of AS in adults in developed countries. Its prevalence continues to rise in an ageing society and has been reported to be 4.6% in adults aged 75 years or more.\(^1\) Transcatheter aortic valve implantation (TAVI) represents a new therapeutic option for the substantial number of high-risk patients with severe AS who are not eligible for surgical aortic valve replacement. Since 2002—when the first TAVI in humans was performed by Alain Cribier in France\(^2\)—two distinct devices have been developed and are now routinely implanted in various European centres: First, the third-generation CoreValve® system (Medtronic, Minneapolis, MN, USA) consisting of a trileaflet porcine pericardial tissue valve mounted on a self-expanding multilevel support Nitinol frame which is only licenced for the transfemoral approach. Secondly, the Edwards SAPIEN™ THV system (Edwards Lifesciences, Inc., Irvine, CA, USA) constructed of three bovine-pericardial tissue leaflets mounted onto a balloon-expandable stainless steel frame. The second generation, called Edwards SAPIEN™ XT, uses a cobalt—chromium frame allowing for a lower profile crimping but with the same orifice area. Both Edwards SAPIEN valves are suitable for the transfemoral and transapical approach. All valve types are available in several sizes: the CoreValve® system in 26, 29, and 31 mm; the

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Edwards SAPIEN™ THV in 23 and 26 mm; and the SAPIEN™ XT system additionally in 29 mm. The two largest available types, the SAPIEN™ XT 29 mm and the CoreValve® 31 mm, were not included in our study since only a small number of patients have received these recently introduced prostheses.

Since surgical and transcatheter valve procedures are associated with similar survival rates at 1 year and since survival after TAVI is higher compared with the best medical care, the need for further follow-up evaluation of this new class of biological prosthetic valves is evident. According to the recommendations of the American Society of Echocardiography (ASE) Doppler echocardiography is the method of choice for non-invasive valve evaluation. Therefore, reference values for the Doppler haemodynamics and for the effective orifice area (EOA) have to be defined.

Methods

Study population

A total of 146 consecutive patients that underwent TAVI in our centre between July 2009 and November 2011 (transfemoral approach 124; transapical approach 22) matched our inclusion criteria: (i) stable clinical situation, (ii) sufficient acoustic window with an adequate Doppler examination, (iii) absence of severe paravalvular aortic or mitral valve regurgitation, and (iv) ability to provide informed consent. The earliest complete transthoracic echocardiogram after implantation (median 8.0 ± 19.3 days) was identified for each patient. Patients with severe paravalvular aortic regurgitation or severe mitral valve regurgitation were excluded. The inclusion criteria for TAVI were either the criteria described previously or, in some cases, compassionate use. Written informed consent was obtained from each patient.

Echocardiography and Doppler measurements

Standard transthoracic echocardiography including Doppler analysis was performed according to the guidelines of the ASE on a Vivid 7 Dimension (GE Vingmed, Horten, Norway, M4S 1.5–4.0 MHz transducer). The earliest postoperative two-dimensional and Doppler study for each patient was used for the analysis. Patients were imaged in the left lateral decubitus position. In general, the left ventricular ejection fraction (LVEF) was obtained according to the recommendation of the ASE. The haemodynamic measurements were subsequently performed by a single observer experienced in quantitative echocardiographic analysis. Continuous wave (cw) Doppler examinations were analysed for peak instantaneous velocity. Mean and maximum aortic valve pressure gradients were estimated by the modified Bernoulli equation using the flow velocity time integral over the ejection period in cw-Doppler recordings with a 100 mm/s time scale on the x-axis for all patients. Left ventricular outflow tract (LVOT) velocity was obtained in 120 (82.2%) of the 146 patients. If possible, the Doppler velocity index (DVI) and the aortic EOA were determined by the continuity equation. The EOA index was normalized to the body surface area (BSA) following the recommendations for evaluation of prosthetic valves of the ASE. Stroke volume (SV) and the stroke volume index (SVI) were obtained using the velocity time integral over LVOT, the LVOT diameter, the BSA, and the heart rate. The BSA was calculated by the Mosteller formula. Aortic and mitral regurgitation were assessed according to the recommendations of the ASE.

Patient data

Of the 146 study patients, 65 were male and 81 were female; age range was 47–94 (mean 78.5 ± 8.7 years). CoreValve 26 and 29 mm prostheses were implanted in 40 (27.4%) and 58 patients (39.7%), respectively. In 16 patients, Edwards SAPIEN 23 mm prostheses (6 Edwards SAPIEN THV, 10 Edwards SAPIEN XT; 5 transapical, 11 transfemoral) were implanted; 32 patients received Edwards SAPIEN 26 mm prostheses (15 Edwards SAPIEN THV, 17 Edwards SAPIEN XT; 17 transapical, 15 transfemoral). There were no statistically significant differences between the implanted valve types regarding age, body mass index (BMI), LVEF, SV, and SVI. Baseline data for the different valve types are given in Tables 1 and 2. During Doppler examination, the heart rate ranged from 50 to 116 bpm with a mean of 72.5 ± 11.2 bpm.

Statistics

All results are expressed as mean ± SD with the exception of the examination time after implantation, which is given as median ± SD. Statistics were calculated using SPSS 19.0 (SPSS, Inc., Chicago, IL, USA). The Kruskal–Wallis-H non-parametric test was used to
compare echocardiographic data between the different aortic valve prostheses. *P*-values of <0.05 were considered statistically significant.

**Results**

Doppler data, valve sizes, and the presence of prosthetic regurgitation for the various valve types are given in Table 3 and Figures 1 and 2. The mean peak instantaneous velocity for all prostheses was 2.0 ± 0.4 m/s (range 1.0–3.6 m/s). The mean peak gradient for all prostheses was 17.1 ± 7.4 mmHg (range 4–52 mmHg) with an average mean gradient of 9.3 ± 4.5 mmHg (range 3–36 mmHg). The mean EOA was 1.82 ± 0.43 cm² (range 0.7–3.4 cm²) with an indexed EOA of 1.0 ± 0.27 cm²/m² (range 0.5–2.0 cm²). The mean DVI was 0.54 ± 0.13 (range 0.2–0.8). The mean LVEF and SV were 53.1 ± 11.7% (range 12–70%) and 73.4 ± 21.7 (range 30.0–143.0), respectively. The time from valve replacement to the index Doppler examination ranged from 2 to 118 days. Of the 146 patients, 138 (94.4%) had their index echocardiographic study within 1 month after valve replacement (mean 8.5 ± 4 days). The other eight patients (5.5%) were

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Echocardiographic baseline characteristics</th>
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<tbody>
<tr>
<td>Aortic valve prosthesis</td>
<td>Edwards Sapien 23 mm</td>
</tr>
<tr>
<td>n</td>
<td>16</td>
</tr>
<tr>
<td>Time of examination after implantation, days</td>
<td>7.5 ± 21</td>
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<tr>
<td>LVEF, %</td>
<td>57.5 ± 6.3</td>
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<tr>
<td>HR, bpm</td>
<td>69.4 ± 7.6</td>
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<tr>
<td>SV, mL</td>
<td>73.7 ± 17</td>
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<tr>
<td>SVI, mL/m²</td>
<td>41.3 ± 10.6</td>
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<tr>
<td>AR, n (%)</td>
<td>None</td>
</tr>
<tr>
<td>Mild</td>
<td>9 (56.21/40)</td>
</tr>
<tr>
<td>Moderate</td>
<td>3 (18.8)</td>
</tr>
<tr>
<td>Moderate-to-severe</td>
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</tr>
<tr>
<td>MR, n (%)</td>
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</tr>
<tr>
<td>Mild</td>
<td>9 (56.3)</td>
</tr>
<tr>
<td>Moderate</td>
<td>1 (6.3)</td>
</tr>
<tr>
<td>Moderate-to-severe</td>
<td>1 (6.3)</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD, except time of examination after implantation which is expressed as median ± SD.

LVEF, left ventricular ejection fraction; HR, heart rate; SV, stroke volume; SVI, stroke volume index; AR, aortic regurgitation; MR, mitral regurgitation.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Doppler haemodynamics and EOA for the different transcatheter aortic valve prostheses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic valve prosthesis</td>
<td>Edwards Sapien 23 mm</td>
</tr>
<tr>
<td>n</td>
<td>16</td>
</tr>
<tr>
<td>Peak instantaneous velocity, m/s</td>
<td>2.3 ± 0.4</td>
</tr>
<tr>
<td>Peak systolic gradient, mmHg</td>
<td>21.4 ± 7.1***</td>
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<tr>
<td>Mean systolic gradient, mmHg</td>
<td>11.9 ± 4.2</td>
</tr>
<tr>
<td>EOA, cm²</td>
<td>1.47 ± 0.14***</td>
</tr>
<tr>
<td>Indexed EOA, cm²/m²</td>
<td>0.83 ± 0.15</td>
</tr>
<tr>
<td>DVI</td>
<td>0.49 ± 0.08</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD.

EOA, effective orifice area; DVI, Doppler velocity index.

*P < 0.05 vs. Edwards Sapien 23 mm.

**P < 0.05 vs. Edwards Sapien 26 mm.

***P < 0.05 vs. CoreValve 26 mm.

****P < 0.05 vs. CoreValve 29 mm.
examined, on average, 88.8 ± 18 days after aortic valve implantation.

Using a multiple comparison analysis, only CoreValve 26 mm prostheses compared with Edwards Sapien 23 mm were found to have significantly lower mean peak velocities (1.9 ± 0.4 vs. 2.3 ± 0.4 m/s; P = 0.04) and lower peak gradients (15.5 ± 6.6 vs. 21.4 ± 7.1 mmHg; P = 0.04). In addition, the CoreValve 29 mm valve was identified to have a significantly greater EOA than Edwards Sapien 23 mm prostheses (1.94 ± 0.43 vs. 1.47 ± 0.14 cm²; P = 0.03). In contrast, there were no significant differences regarding the indexed EOA between all analysed valve types (Figure 1 and Table 3).

Thirteen (81.5%) patients with Edwards Sapien 23 mm and thirty (93.8%) patients with Edwards Sapien 26 mm had none or mild prosthetic regurgitation (none, 4; mild, 9, and none, 9; mild, 21, respectively). Of the patients that had received Edwards Sapien 23 and 26 mm valves, 3 (18.8%) and 2 (6.3%) were found to have moderate prosthetic regurgitation. 31 (77.5%) patients with CoreValve 26 mm and 40 (69%) patients with CoreValve 29 mm had none or mild prosthetic regurgitation (none, 8; mild, 23, and none, 19; mild, 21, respectively). Of CoreValve 26 and 29 mm, 8 (20%) and 14 (24.1%) was found to have moderate prosthetic regurgitation. One (2.5%) patient with CoreValve 26 mm and

Figure 1 Peak instantaneous velocity (A), mean gradient (B), effective orifice area (EOA, C), and EOA index (D) of the Edwards Sapien 23 mm (ES 23) and 26 mm (ES 26) prostheses and the CoreValve 26 mm (CV 26) and 29 mm (CV 29) prostheses.

Figure 2 Severity of aortic regurgitation after TAVI of the Edwards Sapien 23 mm (ES 23) and 26 mm (ES 26) prostheses and the CoreValve 26 mm (CV 26) and 29 mm (CV 29) prostheses.
four (6.9%) patients with CoreValve 29 mm had moderate- to-severe prosthetic regurgitation (Figure 2).

Discussion

Percutaneous valve implantation is an evolving new approach for the over 30% of all symptomatic patients with severe AS who cannot undergo surgical treatment due to relevant comorbidities.10 As the non-inferiority of TAVI compared with surgical treatment was recently shown,9 percutaneous treatment of severe AS will likely become a standard method. Therefore and due to increasing experience with this technique the number of implantations will rise and the need for non-invasive evaluation will become even more necessary than it is already today. While assessment of symptomatic patients after valve repair should always start with physical examination, differentiation of symptoms caused by prosthetic valve dysfunction and other conditions needs specific diagnostic tools.5 Echocardiography and Doppler assessment are the method of choice also in patients after TAVI9 and, therefore, normal Doppler values have to be established. The present study determines the normal range for Doppler haemodynamics and EOA of two types of percutaneously implanted bioprosthetic valves (i.e. Edwards SAPIEN and CoreValve) after successful TAVI. As mild paravalvular regurgitation is common,11 especially in patients with CoreValve prostheses, only patients with severe aortic (or mitral) regurgitation were excluded due to alteration of forward-flow haemodynamics. In our experience, the classification of paravalvular regurgitation is even more challenging in percutaneous valves than in conventional, surgically implanted prostheses since the regurgitation jet is often eccentric and crescent-shaped. Moreover, measurement of the vena contracta is frequently not feasible. Vena contracta planimetry by 3D echocardiography might prove to be an accurate methodology for paravalvular AR jet evaluation in the future.11

One limitation of our study is the fact that transoesophageal echocardiography (TEE) was not routinely performed after TAVI. This modality shows higher sensitivity in AR evaluation than trans-thoracic echocardiographic studies in patients with a poor acoustic window and may help to identify posterior paravalvular leaks.5 In patients with treated severe AS, the rate of deceleration of the diastolic regurgitant jet and the derived pressure half-time are not sufficient for paravalvular AR jet evaluation in the future.11 As recommended we used an integrative approach with an emphasis on the flow profile in the thoracic and abdominal aorta since a holodiastolic flow reversal in the descending thoracic aorta indicates an at least moderate AR.5 The strength of the presented data is the additional consideration of haemodynamic parameters such as LVEF and SV since their consideration is required for an adequate interpretation of Doppler data due to the flow dependence.12,13 In most of the published literature about normal values for Doppler gradients this crucial information is missing.14 However, a preserved LVEF does not rule out impaired systolic function and a paradoxical low flow situation resulting in low gradients.15 In consequence, the SV has a greater significance for the flow profile than LVEF alone. Importantly, our study population has normal mean flow haemodynamics with a mean SV of over 70 mL and a SVI of 40 mL/m². In case of treating patients with a low flow haemodynamic situation, our normal values have to be used with caution6,12,14 but the EOA and the DVI should still be valid. In patients with aortic prostheses and narrow LV outflow due to LV hypertrophy, the velocity proximal to the prosthesis may be elevated and should be included in the Bernoulli equation to derive the pressure gradients more accurately. But there is still a good correlation between pressure gradients derived from the simplified Bernoulli equation and haemodynamically measured gradients.16

The present publication was neither designed as a comparison between the different available percutaneous aortic valves nor between other surgically implanted aortic prostheses. Rather, it describes the haemodynamic performances of the Edwards Sapien and the CoreValve transcatheter aortic valves in a large cohort of patients. We performed only a non-invasive evaluation of the different valves and no corresponding invasively measured haemodynamic values were obtained. Yet, a good correlation between cw Doppler data and catheter-based haemodynamics has been shown for prostheses in the aortic position17 and routinely follow-up examinations will be performed non-invasively for the majority of the patients.

Although our four patient groups are not matched, there were no significant differences regarding LVEF, heart rate and SV between the different valves. CoreValve 26 mm prostheses were found to have significantly lower mean peak velocities as well as lower peak and average mean gradients. Furthermore, the CoreValve 29 mm prosthesis had, on average, a significantly greater EOA compared with the Edwards Sapien 23 mm. These findings are consistent with previous studies on aortic prostheses which reported an inverse correlation between valve size and flow velocities.18,19 Although the CoreValve 26 mm had the greatest orifice area indexed to the patient’s BSA no significant difference could be found compared with the other valve types. To describe the function of prosthesis using the indexed EOA is more reasonable since it better reflects the combination of valve function and condition of each patient present. The EOA has to be proportionate to the patient’s body size to keep the haemodynamic parameters low.20–22 Hence, the indexed orifice area was shown to be the only parameter with impact on the clinical outcome.23–26

Taken together, no percutaneous valve can be considered superior regarding the haemodynamic function. Therefore, the decision which valve to implant should be driven by the aortic annulus diameter and the optimal interventional access for each patient.

In comparison with previously published haemodynamic data of mostly stented surgically implanted bioprosthetic aortic valves,5,14,27–40 the percutaneous valves tend to have lower mean peak velocities and pressure gradients. Even the normal values of some stentless valves seem higher than the tested percutaneous valves.51–44 The EOA is similar compared with previously published data of surgically implanted stented bioprosthetic aortic valves. It is not possible to compare the indexed EOA since this parameter is generally not given in the available literature. Our results appear all the more surprising because the diseased and often severely calcific leaflets of the native valve are only crushed against the supporting valvaral sinuses during the valvuloplasty and the following valve implantation and are not surgically
resected. Accordingly, recoil could be expected leading to reduction of the orifice area and an increase in the transvalvular pressure gradients. Nevertheless, our data suggest an improvement of the pressure gradients in this new class of prostheses compared with surgically implanted valves. In comparison with native valves; however, a mild obstruction is still detectable. Thus, a complete normalization of the haemodynamics cannot be expected.

The frequent paravalvular regurgitation could influence the haemodynamic effects additionally. Since the vast majority of index echocardiographic examinations took place in the first month, no information is available about mid-term alterations. In a subgroup analysis; however, no significant differences regarding the EOa and the indexed EOa in patients examined > 1 month after TAVI could be detected.

Importantly, since our study did not include patients after conventional therapy our comparison with surgically implanted valves is only based on previously published data.

In conclusion, Doppler echocardiography is the preferred non-invasive modality for the follow-up evaluation of prosthetic valve function. This study establishes normal Doppler values for Edwards Sapien and CoreValve transcatheter aortic valves but, if available, comparison with the individual baseline values should always be considered.

Acknowledgements

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Conflict of interest: none declared.

References


7. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA et al. Chamber Quantification Writing G, American Society of Echocardiography’s G. Standards C. European Association of E. Recommendations for chamber quantification: a report from the American Society of Echocardiography’s Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005;18:1440–63.


A 70-year-old male diagnosed with idiopathic pulmonary artery dilatation at 23. The patient was asymptomatic until the age of 68, when he started with exertional dyspnoea and was found to have a chronic pulmonary artery dissection with significant pulmonary hypertension. The patient refused surgery. He presents now with symptoms of angina. The chest-X-ray was normal. CT angiography showed the dissection in the axial image and the non-occlusive thrombosis in the right pulmonary artery (asterisk). Panels C and D show the dissection in the axial image and in a three-dimensional reconstruction of the MDCT study (arrows). Panel E corresponds to a multiplanar reconstruction showing a compression of the left main coronary artery by the pulmonary aneurysm (arrow). In addition, an apical myocardial perfusion defect is seen in an MDCT reconstruction on a longitudinal left ventricular plane (Panel F, arrows) probably secondary to the coronary compression.

Surgical replacement of the trunk and the proximal branches of the pulmonary artery and pulmonary thrombo-endarterectomy has been recommended.

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