Flow Characteristics of the Medtronic CoreValve: Difficulties Estimating Aortic Valve Cross-Sectional Area Following Transcatheter Aortic Valve Implantation

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Abstract

**Background:** Echocardiographic evaluation after transcatheter aortic valve implantation (TAVI) includes estimation of effective orifice area (EOA). EOA calculation depends on sub-valvular stroke volume (SV), which depends on sub-valvular diameter and velocity time integral (VTI). The Medtronic CoreValve area changes throughout its length. We aimed to (i) compare SV at two sites of flow acceleration: ‘pre-stent’ and ‘in-stent, pre-valve’, (ii) assess effects of possible differences in sub-valvular SV on EOA, and (iii) assess agreement of measurement of EOA calculation after CoreValve TAVI.

**Methods:** We studied 43 patients after CoreValve implantation. All had transthoracic echocardiography 5-7 days after TAVI. Sub-valvular SV was measured ‘pre-stent’ and ‘in-stent, pre-valve’. Measurement agreement was assessed by root mean square (RMS) differences and Bland-Altman analyses.

**Results:** SV was consistently higher ‘in-stent, pre-valve’ compared with ‘pre-stent’ (62±20ml vs. 53±19ml, p<0.001), so that EOA was correspondingly larger using ‘in-stent, pre-valve’ measurements (1.7±0.5cm² vs. 1.4±0.5cm², p<0.001). Between-observer RMS difference for calculation of EOA was higher ‘in-stent, pre-valve’ compared to ‘pre-stent’ (0.53 cm² vs. 0.23cm², difference from zero 0.17, p=0.002). Though sub-valvular diameter measurements were variable, VTI variability was additionally higher ‘in-stent, pre-valve’ compared to ‘pre-stent’ (0.42cm vs. 0.6cm, difference from zero -1.74, p=0.11).

**Conclusion:** Calculation of EOA after CoreValve TAVI is highly dependent on sub-valvular sample position. EOA may be underestimated using ‘pre-stent’ SV, and overestimated using ‘in-stent, pre-valve’ SV. Limitations in SV reproducibility suggests EOA should be used in conjunction with other indices of valve function in serial assessment of CoreValve function following TAVI.

**Key words:** Transcatheter aortic valve implantation, Effective aortic valve area, Stroke volume, Pre-stent, In-stent pre-valve, Agreement

Introduction

Aortic stenosis is the most frequent type of valvular heart disease in Europe and North America, and Doppler echocardiography is the preferred technique for assessing the severity of native aortic valve stenosis and prosthetic aortic valve function after surgical aortic valve replacement (AVR). Trans-catheter aortic valve implantation (TAVI) is a less-invasive alternative for patients with severe symptomatic aortic stenosis who are at high-risk for surgical AVR. Survival after TAVI is higher compared to medical therapy alone, and is comparable with surgical AVR at 1-year. The need for accurate follow-up assessment of TAVI devices is therefore evident. Echocardiography is the primary imaging modality for the assessment of prosthetic valve function, including after TAVI. The American Society of Echocardiography and The European Association of Echocardiography advocate an integrated approach, using both flow-dependent (mean gradient) and flow-independent (effective orifice area: EOA) assessment. If there is discordance between these measurements, the Doppler velocity index (DVI) is calculated.

Calculation of EOA is performed by echo-Doppler, and is based on the use of the continuity equation. This requires calculation of sub-valvular stroke volume (SV), obtained as the product of velocity time integral (VTI) and cross-sectional area (CSA) measured simultaneously at a pre-defined region below the aortic valve. However, the design of transcatheter devices complicates conventional calculation of EOA due to difficulties pre-specifying the exact sub-valvular region of interest. The two TAVI devices most commonly used in Europe and the USA are the Edwards SAPIEN XT THV device (Edwards Lifesciences, Irvine, California), and the Medtronic CoreValve prosthesis (Medtronic, Minneapolis, Minnesota). There are important shape differences between a fully deployed SAPIEN device and a fully deployed CoreValve. The SAPIEN valve is cylindrical when fully expanded and the neo-aortic leaflets are relatively close to the ventricular end of the device (Figure 1A). In contrast, the CoreValve is hour-glass shaped (minimum dimension at neo-aortic valve leaflet level), and is a longer device, so that the neo-aortic valve leaflets are relatively further away from the ventricular end of the device (Figure 1B). These differences in neo-aortic valve height are confirmed in representational 2-dimensional echo pictures shown in Figures 2A and 2B.

The unique shape of different TAVI devices has specific influence on sub-valvular flow acceleration across the implanted valve. In the SAPIEN device, flow acceleration occurs ‘pre-stent’ and ‘in-stent, pre-valve’. Previous studies thus recommend using sub-valvular SV values ‘pre-stent’ to avoid ‘in-stent’ sub-valvular flow acceleration. However, these studies have assessed only the haemodynamics of the SAPIEN device.
The effect of the site of sub-valvular stroke volume calculation on EOA following CoreValve implantation has received less attention.

The aims of our study were therefore (i) to compare calculated sub-valvular values of SV at two pre-defined sample volume positions; ‘pre-stent’ and ‘in-stent, pre-valve’ in patients undergoing purely CoreValve TAVI, and (ii) to assess the effect of any differences in sub-valvular SV on calculated EOA. We also sought to evaluate the agreement of measurements of sub-valvular SV at both ‘pre-stent’ and ‘in-stent, pre-valve’ levels, and the effect of sub-valvular variability on EOA in a group of patients undergoing CoreValve TAVI.

Methods

Patients

Forty-three consecutive patients with symptomatic severe aortic stenosis who underwent TAVI with a CoreValve at The Royal Brompton Hospital, London, UK were studied. All patients had severe calcific aortic stenosis (aortic valve area ≤1cm² or BSA-indexed AVA <0.6 cm²/m², and mean aortic valve pressure gradient >40mmHg). All underwent CoreValve implantation using transoesophageal and fluoroscopic guidance. The study complied with the Declaration of Helsinki, and was approved by the Royal Brompton Research Committee. All patients provided signed informed consent before the procedure.

Echocardiographic Assessment

All patients had a transthoracic echocardiogram performed by the same echocardiographer between 5 and 7 days after the TAVI procedure. Echocardiograms were obtained using a Philips ie33 echo machine and a SS multifrequency transducer (Andover, Massachusetts, USA). With the subject at rest in the semi-lateral position, standard 2-dimensional parasternal long-axis views were used to determine end-diastolic and end-systolic left ventricular (LV) cavity size (LVedd and LVesd respectively). The same views were also used to obtain a zoomed full screen of the LV outflow tract, native aortic valve (before TAVI), transcatheter device, neo-aortic valve (after TAVI) and aortic root. Apical 5- and 3-chamber views were used to obtain a zoomed full screen of the transcatheter device. The presence of aortic regurgitation (AR) was assessed by colour and continuous wave Doppler in zoomed parasternal long, and short axis windows, 5- and 3-chamber views, and from supra-ternal imaging of proximal descending aorta. Severity was graded semi-quantitatively as none, trivial, mild, moderate or severe according to ASE guidelines7. Mitral regurgitation was also assessed according to ASE guidelines7.

Pulsed wave Doppler was used to obtain sub-valvular VTI at two separate and distinct sites (see below). In general, pulsed-wave spectra were optimised to eliminate spectral broadening and to display modal velocities, and the nominal pulsed-wave sample size was kept constant at 4mm. Pulsed-wave Doppler recordings (both ‘pre-stent’ and ‘in-stent, pre-valve’) were obtained by a single observer in both the 5- and 3-chamber views over 3 consecutive cardiac cycles. Peak velocity and the velocity time integral (VTI) were traced. For all pulsed-wave Doppler recordings, (both ‘pre-stent’ and ‘in-stent, pre-valve’) the average result from the 6 traces obtained from 2 views was reported.

Peak and mean trans-prosthetic pressure gradients were recorded using continuous wave Doppler from the apical 5-chamber, apical 3-chamber, and right parasternal windows, over 3 consecutive cardiac cycles in each window. Highest values were taken. LV end-diastolic (LVEDV) and end-systolic (LVESV) volumes were measured in the apical 4-chamber and 2-chamber windows. Since all patients had either none or trace mitral regurgitation, biplane stroke volume was calculated using volumetric methods by subtracting LVESV from LVEDV. LV ejection fraction was calculated using Simpson’s biplane method. All recordings were made at a sweep speed of 100 mm/s, with a superimposed ECG (lead II).

Figure 1: Comparing distance from base of device to base of aortic valve leaflets in Edwards SAPIEN vs. Medtronic CoreValve in vitro.

A: The distance from the ventricular aspect of the device to the base of the neo-aortic leaflets in the SAPIEN valves is short (7.7mm, 8.7mm, and 11.6mm in 23mm, 26mm, and 29mm SAPIEN devices respectively). Source: Edwards Lifesciences, Irvine, California.

B: In contrast, the distance from the ventricular aspect of the device to the base of the neo-aortic leaflets in the CoreValve (purple semicircle and arrow) is longer, and is always 12mm, irrespective of which CoreValve size is used (Source: Medtronic, Minneapolis, Minnesota).
Site-Specific Measurement of Sub-Valvular SV

Sub-valvular diameter: Using a zoomed 2D parasternal long axis full-screen display, ‘pre-stent’ diameter was measured (in mid-systole, using inner-edge to inner-edge methodology, perpendicular to the TAVI device long axis) just underneath the apical margin of the valve stent. After that, ‘in-stent, pre-valve’ diameter was measured (again using a zoomed parasternal mid-systolic frame, using inner-edge to inner-edge methodology perpendicular to the TAVI device long axis) just below the hinge points of the visible prosthetic leaflets. Cross-sectional area at the ‘pre-stent’ and ‘in-stent, pre-valve’ levels were then calculated as \( \pi (d/2)^2 \), assuming a circular cross-section.

Sub-valvular VTI: Using a zoomed 2D full-screen display of the trans-catheter valve in both an apical 5- and 3-chamber views, ‘pre-stent’ VTI was recorded in mid-systole with the pulsed-wave Doppler sample volume just underneath the apical margin.
There was close agreement between two independent sonographers for calculating effective aortic orifice area (EOA) when sub-valvular measurements were taken ‘pre-stent’ (A) compared to ‘in-stent, pre-valve’ (B). Bland-Altman plots also demonstrated less variability in EOA calculations when sub-valvular measurements were taken ‘pre-stent’ (C) compared to ‘in-stent, pre-valve’ (D).

Doppler velocity index (DVI)
The Doppler velocity index (DVI) was calculated ‘pre-stent’ (using the ratio of the maximum ‘pre-stent’ sub-valvular velocity to the peak trans-prosthetic velocity) and ‘in-stent, pre-valve’ (using the ratio of the maximum ‘in-stent, pre-valve’ sub-valvular velocity to the peak trans-prosthetic velocity). DVI was also obtained for VtI (rather than maximum velocity) using similar methods.

Data analysis
According to previously reported data from the Placement of Aortic Transcatheter Valve (PARTNER) study, the standard deviation for valve area for the SAPIEN valve is approximately 0.5 cm². In a power calculation, a sample size of at least 20 patients was required in order for the present study to have 80% power to detect a mean difference in EOA >60% using 2 different sub-valvular sampling positions in the CoreValve prosthesis at a 5% significance level. Statistical analysis was performed using R Core Team 2013, R Version 3.0.2 (R Foundation for Statistical Computing, Vienna, Austria. URL http://www.R-project.org/) Normally distributed continuous variables were expressed as mean±standard deviation. Continuous variables between groups were compared using paired Student t-tests. A significance level of p<0.05 was employed throughout the study.

Agreement
Fifteen patients were selected randomly to assess agreement of calculated EOA at both ‘pre-valve’ and ‘in-stent, pre-valve’ levels. Between-observer agreement of calculated EOA was determined by having a second and experienced echocardiographer perform a separate echocardiogram on each patient (immediately after the initial full echocardiographic study to minimise patient variability). During the two studies, both sonographers independently performed their own measurements of sub-valvular diameter and VTI, at ‘pre-valve’ and ‘in-stent, pre-valve’ levels. Peak aortic velocity and VTI was measured by only the first sonographer as part of a complete echo examination. Reproducibility was expressed as the root
mean square (RMs) difference (± standard deviation of the difference of the means) between duplicate values. Bland-Altman plots were created to assess variability and bias, determined for both diameter and VtI measurements, at 'pre-valve' and 'in-stent, pre-valve' levels. Finally, the overall effect of agreement of these two measurements, at both sub-valvular sites, on calculated eoA was determined.

Results

Baseline Characteristics

The 43 consecutive patients studied had a mean age of 79±8 years, 21 of whom were male. Before TAVI, all patients had severe symptomatic aortic stenosis (peak and mean trans-aortic pressure gradient were 80±17mmHg and 47±12mmHg respectively, dVI was 0.22±0.06, and calculated aortic valve area was 0.5±0.2cm², Table 1). Sixteen patients received a 26mm CoreValve, 22 patients a 29mm CoreValve, and 5 patients a 31mm CoreValve. A transfemoral route was used in 35 patients, a subclavian route in 3 patients, and a direct aortic approach in 5 patients. Seven patients underwent post-implantation balloon dilatation. Full final valve deployment was achieved in all patients as determined by both fluoroscopic and trans-oesophageal echocardiographic imaging. In no patient was the CoreValve deemed to be low in the LVOT (measured on fluoroscopy as depth of the ventricular end of the TAVI device relative native non-coronary cusp of the aortic valve <10mm). Transthoracic echocardiography was repeated 5-7 days after TAVI. There were significant reductions in peak trans-aortic gradient (to 16±3mmHg), mean trans-aortic gradient (to 5±2mmHg, both p<0.001), SV measured by Simpson’s biplane (from 62±24ml to 54±23ml, p=0.04), but there were no significant change in LV chamber size, chamber volumes, or LVEF (Table 1).

Doppler velocity index (DVI)

Values for both sub-valvular velocity and VTI were significantly higher 'in-stent, pre-valve' compared with 'pre-stent' (Table 2, Figure 3a and 3b). Consequently, DVI was significantly higher...
Table 1: Baseline Echocardiographic Characteristics of the Study Population

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before TAVI</th>
<th>After TAVI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDV (ml)</td>
<td>125±56</td>
<td>121±45</td>
<td>0.23</td>
</tr>
<tr>
<td>LVESV (ml)</td>
<td>63±42</td>
<td>66±43</td>
<td>0.06</td>
</tr>
<tr>
<td>Biplane SV (ml)</td>
<td>62±24</td>
<td>54±23</td>
<td>0.04</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>52±16</td>
<td>46±16</td>
<td>0.06</td>
</tr>
<tr>
<td>LVEDD (mm)</td>
<td>51±10</td>
<td>50±8</td>
<td>0.08</td>
</tr>
<tr>
<td>LVESD (mm)</td>
<td>36±10</td>
<td>36±8</td>
<td>0.81</td>
</tr>
<tr>
<td>Peak trans-aortic gradient (mmHg)</td>
<td>80±17</td>
<td>16±3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean trans-aortic gradient (mmHg)</td>
<td>47±12</td>
<td>5±2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak trans-aortic VTI (cm)</td>
<td>121±23</td>
<td>39±11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Doppler velocity index (V1/V2)</td>
<td>0.22±0.06</td>
<td>See table 2</td>
<td>NA</td>
</tr>
</tbody>
</table>

Data are expressed as mean±SD
LVEDV: left ventricular end-diastolic volume, LVESV: left ventricular end-systolic volume; LVEF: left ventricular ejection fraction, LVEDD: left ventricular end-diastolic diameter; LVESD: left ventricular end-systolic diameter; ; V1: maximum velocity at sub-valvular level; V2 max: maximum trans-prosthetic velocity

when ‘in-stent, pre-valve’ values were used compared to ‘pre-stent’ values (using peak velocity: 0.7±0.2 vs. 0.5±0.1; using peak VTI: 0.7±0.2 vs. 0.5±0.2 respectively, both p<0.001, Table 2).

Sub-Valvular Stroke Volume

‘Pre-stent’: mean diameter was 2.0±0.1cm (Table 2), which corresponded to a cross-sectional area (3.1±0.4cm2); VTI was 16.9±5.2cm, so that calculated SV was 53±20ml. This was not different from SV calculated using Simpson’s biplane method, (53±20ml vs. 55±23ml, p=0.81).

‘In-stent, pre-valve’: mean diameter was smaller (1.7±0.1cm) compared to ‘pre-stent’ (Figure 3) so that cross-sectional area was correspondingly lower (2.3±0.3cm2). However, VTI was significantly higher compared to values ‘pre-stent’ (26.5±7.4cm, Figure 3), so that SV was correspondingly greater (62±20ml, all p<0.001). Calculated SV ‘in-stent, pre-valve’ using Doppler methods was also significantly greater than SV calculated using Simpson’s biplane method (62±20ml vs. 55±23ml, p=0.30).

Calculated Aortic Effective Orifice Area

Consistently higher values of SV at ‘in-stent, pre-valve’ level resulted in larger calculated aortic EOA when ‘in-stent, pre-valve’ values were used compared to ‘pre-stent’ values (1.7±0.5cm² vs. 1.4±0.5cm², p<0.001, Table 2).

Agreement

Discussion

The rapid expansion in the number of patients with severe aortic stenosis receiving a transcatheter aortic implantation has brought a need for precise echo-Doppler evaluation of transcatheter valve function. Previous studies in the relatively short Edwards-SAPIEN valve recommend using the LVOT diameter and velocity “obtained immediately proximal to the stent” (i.e. ‘pre-stent’) to calculate sub-valvular SV. However, site-specific calculation of sub-valvular SV has received little attention in the other widely commercially available device in Europe and the US – the Medtronic CoreValve. We report our experience in patients after receiving the CoreValve prosthesis, and highlight the influence of the precise site of measurement of sub-valvular SV in calculating EOA.

Table 2: Flow Characteristics of the transcatheter CoreValve depending on sub-valvular sample volume positioning

<table>
<thead>
<tr>
<th>Variable</th>
<th>‘Pre-stent’</th>
<th>‘In-stent, pre-valve’</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak sub-valvular velocity (m/s)</td>
<td>0.9±0.2</td>
<td>1.3±0.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak sub-valvular VTI (cm)</td>
<td>16.9±5.2</td>
<td>26.5±7.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak trans-aortic velocity (m/s)</td>
<td>2.0±0.5</td>
<td>2.0±0.5</td>
<td>NA</td>
</tr>
<tr>
<td>Peak trans-aortic VTI (cm)</td>
<td>39±11</td>
<td>39±11</td>
<td>NA</td>
</tr>
<tr>
<td>DVI (V1/V2)</td>
<td>0.5±0.1</td>
<td>0.7±0.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DVI (V1/TI1/TI2)</td>
<td>0.5±0.2</td>
<td>0.7±0.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diameter (cm)</td>
<td>2.0±0.1</td>
<td>1.7±0.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CSA (cm2)</td>
<td>3.1±0.4</td>
<td>2.3±0.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>53±19</td>
<td>62±20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>EOA (cm2)</td>
<td>1.4±0.5</td>
<td>1.7±0.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are expressed as mean±SD
CSA: cross-sectional area; Doppler velocity index (DVI); EOA: effective valve area; SV: stroke volume; VT1: velocity time integral; V1: maximum velocity at sub-valvular level; V2 max: maximum trans-prosthetic velocity; VT1: maximum VT1 at sub-valvular level; VT2 max: maximum trans-prosthetic VTI

Findings

Our study demonstrates significant reductions in both peak and mean trans-aortic gradients, and substantial increases in EOA, one week after CoreValve implantation in consecutive patients undergoing TAVI for severe aortic stenosis. Our study confirmed that there are two regions of flow acceleration in the LV outflow tract after CoreValve: the first at the ventricular aspect of the device (‘pre-stent’), and the second within the valve (‘in-stent, pre-valve’). We found significantly higher values for sub-valvular SV at ‘in-stent, pre-valve’ level, which obviously led to a higher DVI and a larger EOA at ‘in-stent, pre-valve’ level. Our EOA estimations therefore are similar with those of by Jilaihawi et al (15) when * values are used for EOA calculation, while our ‘pre-
EOA: effective orifice area; RMs: root mean square; VtI: velocity time integral

pre-valve’ measurements were used, since EOA is operator-dependent, absolute cut-off values should not be relied upon for clinical decision-making and should be considered in combination with documentation of other measures of valve function. Our results support recently published VARC-2 recommendations, which suggest that the patient’s own initial post-implant study should be used as a reference for long-term follow-up, and that EOA should not be used in isolation in serial follow-up assessment of valve function14.

**Limitations**

Our study lacks a ‘gold-standard’ comparison group for assessment of SV and EOA and thus it is difficult to confirm which site of SV measurement (‘pre-valve’ or ‘in-stent, pre-valve’) is actually correct. We could have compared our EOA calculations with direct measurement of the internal geometric orifice area of a similar group of fully-expanded in-vitro valves, but this would have ignored effect of valve leaflets, and would not have taken into account leaflet distortion at implantation. Three-dimensional imaging may have been helpful in measuring the cross-sectional area of the LVOT17-19. If CoreValve implantation site were low, ‘pre-stent’ diameter and LVOT may have been taken in the LV, but this was not the case in any patient. Finally, we did not take into account pressure recovery phenomenon that may occur downstream of the valve in patients with small aortic diameters; however, the smallest CoreValve used was the 26mm valve, so that this was unlikely to be a major source of error.

**Conclusions**

Our study emphasises the importance of sample volume positioning in calculating sub-oval valve stroke volume, and thus effective aortic valve area, in the functional assessment of a Medtronic CoreValve transcatheter device. Since aortic valve area measurements are operator-dependent, and variable, we suggest that measures of EOA should not be used alone in the assessment of CoreValve function following TAVI. Rather, calculation of effective aortic valve area should be used in conjunction with a description of valve morphology, flow rate, pressure gradients, Doppler velocity index, ventricular function, ventricular size and wall thickness, degree of valve calcification, blood pressure, and functional status. If calculation of EOA is required, this should be performed using ‘pre-stent’ measures, noting in particular the variability associated with ‘in-stent, pre-valve’ VTI measurement. However, since well-established normal transcatheter valve gradients and EOAs based on pre-implant aortic annular dimensions do not exist, the patient’s own initial post-implant study is best placed as a reference for serial comparisons.

**Table 3: Between-observer agreement**

<table>
<thead>
<tr>
<th>‘Pre-stent’</th>
<th>1st Observer</th>
<th>2nd Observer</th>
<th>RMS</th>
<th>Difference from zero (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>EOA (cm²)</td>
<td>1.4±0.5</td>
<td>1.2±0.4</td>
<td>0.30</td>
<td>0.17 (-0.17 → 0.52)</td>
<td>=0.002</td>
</tr>
<tr>
<td>Diameter (cm)</td>
<td>2.1±0.2</td>
<td>2.0±0.5</td>
<td>0.19</td>
<td>0.12 (-0.19 → 0.42)</td>
<td>=0.01</td>
</tr>
<tr>
<td>VTI (cm)</td>
<td>15.1±5.5</td>
<td>14.6±5.3</td>
<td>0.56</td>
<td>0.43 (-0.31 → 1.17)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>‘In-stent, pre-valve’</td>
<td>1st Observer</td>
<td>2nd Observer</td>
<td>RMS</td>
<td>Difference from zero (95% CI)</td>
<td>p</td>
</tr>
<tr>
<td>EOA (cm²)</td>
<td>2.3±0.4</td>
<td>1.9±0.5</td>
<td>0.53</td>
<td>0.34 (-0.52 → 1.21)</td>
<td>= 0.01</td>
</tr>
<tr>
<td>Diameter (cm)</td>
<td>2.08±0.06</td>
<td>1.82±0.11</td>
<td>0.27</td>
<td>0.25 (0.02 → 0.49)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VTI (cm)</td>
<td>25.1±6.4</td>
<td>26.8±6.1</td>
<td>0.42</td>
<td>-1.74 (-9.50 → 6.02)</td>
<td>=0.11</td>
</tr>
</tbody>
</table>

EOA: effective orifice area; RMs: root mean square; VTI: velocity time integral

stent’ values for EOA are consistently lower. Inconsistencies between ‘pre-stent’ and ‘in-stent, pre-valve’ SV measurements could not be attributed to the presence of paravalvular AR, as this was mild in every case and post-TAVI AR severity was not a patient selection criterion. Values of SV calculated using LV volumes were similar to those obtained from ‘pre-stent’ sub-valvular calculation, and significantly lower compared to those obtained from ‘in-stent, pre-valve’ sub-valvular calculation, suggesting ‘pre-stent’ values more likely reflect true sub-valvular SV. Thus ‘pre-stent’ measures should be used when estimating EOA after CoreValve TAVI.

**Error in Calculating Sub-Valvular Volume**

Our study highlights difficulties in EOA calculation after TAVI depending on measurement site of sub-valvular SV. For example, ‘pre-stent’ SV (53±19ml) was significantly lower than ‘in-stent, pre-valve’ SV (62±20ml, p<0.001), despite no loss of mass between the two sites. A possible explanation may be the assumption that the LVOT annulus is circular. At the level of the neo-aortic valve, the device is circular, but within the LVOT, the device takes on the LVOT shape and is likely to be elliptical. Using a circular formula for LVOT would underestimate EOA ‘pre-stent’ and be more accurate ‘in-valve, pre-stent’. Flow acceleration ‘in-stent, pre-valve’ could also account for higher VTI and thus higher SV.

To investigate potential source(s) of error in obtaining in sub-valvular SV calculation, we assessed between-observer agreement for SV and EOA at both ‘pre-stent’ and ‘in-stent, pre-valve’ levels. 95% limits of agreement for EOA were wider ‘in-stent, pre-valve’ compared with ‘pre-stent’, and the largest error was VTI measurement ‘in-stent, pre-valve’. This is unsurprising, since placing the sample volume “approximately 1cm below the neo-aortic valve” to obtain VTI is clearly less exact than placing it “just underneath the apical margin of the valve stalk”. Moreover, flow is not laminar ‘in-stent, pre-valve’, and optimal velocity signals may originate much closer to the valve leaflets. Our results suggest that variability in VTI may be the primary reason for poor agreement between the ‘in-stent, pre-valve’ while diameter measurements accounts for bias measurement between the two observers.

**Clinical Significance**

Our study underlines the difficulties of accurate calculation of valve area, in particular influence of the site of measurement of sub-valvular SV in estimating EOA following CoreValve TAVI, and suggests that SV and EOA are larger when ‘in-stent, pre-valve’ measurements were used. Since EOA is operator-
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