Access Path Angle in Transapical Aortic Valve Replacement: Risk Factor for Paravalvular Leakage

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Background. The aim of this study was to analyze the angle between the left ventricular (LV) long axis and the LV outflow tract (zLV-LVOT) on cardiac computed tomography and to describe its effect on the occurrence of paravalvular leakage (PL), fluoroscopy time, and postoperative creatine kinase-MB levels in transapical transcatheter aortic valve replacement (TA-TAVR).

Methods. High-risk patients with severe aortic stenosis scheduled for TA-TAVR using an Edwards SAPIEN (Edwards Lifesciences, Irvine, CA) prosthesis were retrospectively included. The zLV-LVOT was measured during systole and diastole as far as retrospectively gated data sets were available. The zLV-LVOT was correlated with the occurrence of PL, total fluoroscopy time, and postoperative creatine kinase-MB levels. Interobserver variability was assessed in all cases.

Results. The study included 81 patients (57 women [70.4%], 24 men [29.6%]) with an average age of 81.9 ± 5.8 years. The mean zLV-LVOTs were 61.8 ± 9.9 degrees during systole and 61.1 ± 10.0 degrees during diastole.

There was a minimal, nonsignificant change in the zLV-LVOT between systole and diastole of 0.2 ± 4.1 degrees (p = 0.7). PL was found in 39 patients: grade 0 in 42 (51.9%), grade I in 30 (37.0%), and grade II in 9 (11.1%). Patients with a clinically significant PL (grade ≥ II) showed a significantly greater mean zLV-LVOT than patients with grade I or without PL (mean difference, 13.8 ± 3.2 degrees; p < 0.001). No significant correlation was found between the zLV-LVOT and total fluoroscopy time (r = -0.17, p = 0.16) and postoperative creatine kinase-MB levels (r = -0.1, p = 0.44).

Conclusions. During TA-TAVR, greater zLV-LVOTs were associated with significantly higher grades of PL. Thus, the zLV-LVOT might influence the selection of the transapical implantation path and could have a significant effect on designs for future stents or novel delivery devices.


Transapical (TA) transcatheter aortic valve replacement (TA-TAVR) has proven to be a viable treatment option for elderly, high-risk patients with severe aortic stenosis. Recent studies have shown that TA-TAVR has a comparable 1-year outcome to surgical aortic valve replacement [1, 2]. TA-TAVR leads to a significantly lower all-cause mortality during 1-year follow-up compared with standard medical therapy [3].

Although TA-TAVR has become a routine procedure in numerous medical centers around the globe, paravalvular leakage (PL) remains one of the most common post-interventional complications next to vascular complications, conduction defects, acute kidney injury, and stroke [4, 5]. In particular, intermediate and severe aortic regurgitation appears to have a significant effect on short-term and long-term patient outcomes after surgical aortic valve replacement [6] and in patients treated by TA-TAVR [5, 7]. The presence of mild aortic regurgitation after TA-TAVR is associated with increased late mortality [5]. Abdel-Wahab and colleagues (2012) [7] and Grube and colleagues (2007) [8] found that intermediate and severe PL occurs in up to 17% of patients treated by TA-TAVR, and both studies showed a significant association between clinically significant aortic regurgitation and increased in-hospital mortality. Aortic regurgitation has been used in recent studies as a collective term to describe both paravalvular and transvalvular leakage.

Currently, the Edwards SAPIEN valve (Edwards Lifesciences, Irvine, CA) is the most commonly used prosthesis for the TA approach in Europe and is usually implanted using the fixed, straight, inflexible Ascendra introducer sheath set (Edwards Lifesciences).

Known risk factors for the occurrence of postoperative PL include valvular calcification, which can potentially lead to suboptimal valve deployment [9], and an inappropriately small prosthesis, which results in suboptimal adhesion of the prosthesis to the aortic annulus [10, 11]. Another potential risk factor could be the angle between the left ventricle (LV) long axis and the longitudinal axis of the LV outflow tract (zLV-LVOT) because a greater...
operative creatine kinase (CK)-MB levels. Time, and myocardial damage resulting in elevated post-procedural CK-MB levels would lead to a higher rate of PL, prolonged hospital stay, and increased complications. Our hypothesis was that a greater angle between the LV and LVOT could restrict the positioning of the prosthesis. The LV-LVOT could also have a comparable effect on the occurrence of PL similar to the effect the angle between the LVOT and the ascending aorta has in patients undergoing retrograde transcatheter implantation of the CoreValve prosthesis (Medtronic, Minneapolis, MN), as described by Sherif and colleagues [12].

Computed tomography (CT) has become a standard preoperative imaging modality for three-dimensional assessment of the aortic root and the access path [4]. CT imaging provides accurate dimensions of the aortic root, including the aortic annulus and the ascending aorta, which are important for prosthesis sizing. It also provides information on the suitability of the peripheral access vessels and on extracardiac comorbidities. Initial data indicate that CT-based sizing of the prosthesis, compared with echocardiographic sizing, may lead to better results with reduced rate of PL [13, 14].

This study used CT to examine the LV-LVOT as a possible risk factor for the occurrence of postprocedural complications. Our hypothesis was that a greater angle would lead to a higher rate of PL, prolonged fluoroscopy time, and myocardial damage resulting in elevated postoperative creatine kinase (CK)-MB levels.

Material and Methods

Study Design

This retrospective study included 81 consecutive high-risk patients who had been scheduled for TA-TAVR between February 2007 and May 2010 due to severe symptomatic aortic stenosis. The inclusion criteria were a successful implantation using the Edwards SAPIEN prosthesis, a preoperative electrocardiogram (ECG)-triggered cardiac CT as part of the preoperative planning, and a complete postprocedural hemodynamic assessment using direct aortography and transesophageal echocardiography. Further inclusion criteria were assessment of the postoperative CK-MB levels and available documentation of the total fluoroscopy time. The exclusion criteria were incomplete or unavailable imaging data, the use of an implantation path other than TA, or an implanted prosthesis other than an Edwards SAPIEN.

Image Data Acquisition

CT scans were performed on a 64-row CT (Philips Medical Systems, Cleveland, OH) using a retrospectively ECG-gated technique or on a 128-row dual-source CT (Siemens Healthcare, Erlangen, Germany) using a prospectively ECG-gated technique according to the standard protocol in our facility. The retrospective ECG-gated scan mode provided images during all cardiac phases, and prospective triggering was set to capture the aortic root during late diastole according to the ECG. In total, 100 mL (iodine: 370 mg/mL) or 70 mL (iodine: 400 mg/mL) nonionic iodinated contrast medium were applied before scanning with the 64-row or 128-row CT scanner, respectively.

Image Data Analysis

The CT image analysis, including the LV-LVOT measurement, was completed on SyngoVia V.11 (Siemens Healthcare), a commercially available medical three-dimensional workstation. All measurements were performed by 2 blinded, experienced radiologists (B.F. and C.L.).

Assessment of the zLV-LVOT

The zLV-LVOT describes the deviation from an ideal 180-degree access path and was defined as a direct spatial angle between the LV long axis and the longitudinal axis of the LVOT (Fig 1). The LV long axis was defined as connecting the LV apex and the midpoint of the mitral valve. The LVOT longitudinal axis was defined as the axis orthogonal to the plane of the aortic annulus.

The spatial position of each axis was expressed using left anterior oblique/right anterior oblique and cranial/caudal values of the planes orthogonal to their respective axes. Vector analysis was used to calculate the LV-LVOT as the smallest cutting angle between the 2 planes.

In all of the retrospectively ECG-gated data sets, the LV-LVOT measurements were performed separately during systole and diastole to capture possible dynamic changes during the cardiac cycle. Systole and diastole were determined visually using the functional analysis tool of the workstation. The cardiac phase with an open aortic valve, a closed mitral valve, and minimal filling of the LV was defined as systole, and the cardiac phase with a closed aortic valve, an open mitral valve, and maximal filling of the LV was defined as diastole.

An area-derived effective diameter of the aortic annulus was also measured in all patients in the diastolic phase.
Postoperative CK-MB levels were assessed approximately 8 to 24 hours after the implantation. CK-MB elevation was defined as CK-MB exceeding 24 U/L.

Statistical Analysis
Quantitative variables are expressed as the mean ± standard deviation. The level of significance was defined as p < 0.05 and tested using the Student paired t test. The zLV-LVOT was correlated with the occurrence of PL, the total fluoroscopy time, and postoperative CK-MB levels, and a linear regression analysis was performed using the Pearson correlation coefficient. The null hypothesis was tested using a t distribution. To determine a preliminary prognostic score for the PL, the receiver-operating characteristic curve for the zLV-LVOT (ie, a plot of sensitivity vs 1-specificity for each cutoff value) was plotted, the area under the curve was calculated, and the 95% confidence interval (CI) for the area under the curve was determined using the bootstrap method. Interobserver variability was calculated using the Cronbach α and interclass correlation coefficient. All statistical analyses were performed using SPSS 17 software (IBM Corp, Armonk, NY).

Results
Patient Characteristics
Baseline clinical, procedural, and echocardiographic characteristics are reported in Table 1. Eighty-one patients fulfilled the inclusion criteria. The study population consisted of 57 women (70.4%) and 24 men (29.6%) with an average age of 81.9 ± 5.8 years. All patients had a tricuspid native aortic valve. Retrospective ECG-gated data were available for 66 patients (81.5%), and prospective ECG-triggered data were available for 15 (18.5%). The mean heart rate during image acquisition was 79.7 ± 11.9 beats/min (range, 48 to 108 beats/min). No β-blockers were administered before the examination due to clinical contraindications. The mean area derived effective diameter was 23.0 ± 2.6 mm.

Assessment of the αLV-LVOT
The zLV-LVOT was assessed in all patients. The mean zLV-LVOTs during the systolic and diastolic phases were 61.8 ± 9.9 degrees and 61.1 ± 10.0 degrees, respectively (range, 42.0 to 85.7 degrees). There was only a minimal, nonsignificant dynamic change in the zLV-LVOT between systole and diastole of 0.2 ± 0.1 degrees (95% CI, −1.3 to 0.9 degrees; p = 0.7; Figs 2 and 3). For further analysis, only the late-diastolic zLV-LVOT was assessed.

The interobserver variability analysis of the diastolic zLV-LVOT measurements revealed an optimal intraclass correlation coefficient of 0.85 (95% CI, 0.75 to 0.90; p < 0.001) for average measures and a Cronbach α of 0.85.

PL and αLV-LVOT
Postimplantation hemodynamic assessments were available for all patients. Transesophageal echocardiography and angiography revealed grade I PL in 30 patients

Implantation Procedure
In all patients, the Edwards SAPIEN valves were implanted using the fixed, straight, inflexible Ascendra introducer sheath set. The implantation procedure was performed through a mini left parasternal thoracotomy at the level of fifth intercostal space by placing the introducer sheath set through the apex of the LV straight toward the aortic annulus.

Detection and Grading of PL After TA-TAVR
To detect and quantify PL, an intraprocedural hemodynamic assessment was performed immediately after deployment of the valve using qualitative direct aortography and transesophageal echocardiography. The qualitative aortography was performed in 30-degree right anterior oblique/50-degree left anterior oblique projections, with visual estimation of the amount of contrast medium in the LV during several cardiac cycles [15].

Simultaneously, transesophageal echocardiography was performed using color-flow techniques to quantify the PL using measurements of the width and area of the PL jet at the border between the LVOT and the aortic annulus using the parasternal long-axis view. The results were viewed in relation to the maximum width and area of the LVOT according to Perry and colleagues [16] and divided into the following three groups: grade I = mild, grade II = moderate, and grade III to IV = severe [17].

Fluoroscopy Time and CK-MB levels
Fluoroscopy time was defined as the total time of radiation exposure during the entire implantation procedure expressed in seconds.

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The results of this study indicate that the zLV-LVOT represents an important risk factor for PL in the TA implantation of an Edwards SAPIEN prosthesis. We have demonstrated that the occurrence of significant PL is strongly correlated with a greater zLV-LVOT.

PL is a common complication after TA-TAVR independent of the implanted prosthesis type [11, 12, 18, 19]. PL represents up to 70% of the early postinterventional consequences in elderly patients. However, the occurrence of moderate-grade and high-grade regurgitation or higher was found in 11.1%. Our data corresponded to currently published studies, such as the Placement of Aortic Transcatheter Valve (PARTNER) Cohort A trial, with an incidence of grade II PL or greater in 12.2% of patients [3], and the PARTNER Cohort B trial, with an occurrence of grade II PL or higher in 11.8% of patients [1].

Known risk factors for the occurrence of PL are anatomical or procedural in origin. Anatomical risk factors for PL include an ovoid aortic annulus, valvular calcification, and a bicuspid aortic valve [9, 11, 22]. In contrast, procedural risk factors include a prosthesis/annulus mismatch due to incorrect preoperative sizing.
device malpositioning (too low vs too high), or inadequate predilatation of the native valve [22].

Sherif and colleagues [12] tried to identify new risk factors for PL after CoreValve implantation through a transfemoral approach. These authors found a significantly higher probability of PL in patients with a greater angle between the ascending aorta and the LVOT, especially in combination with a valve placement that was too low [12].

It was rational to test whether the anatomical angle between the LV long axis and the LVOT could play a similar role in the TA approach as it did for transfemoral implantation. Our results indicate that the αLV-LVOT is significantly associated with the occurrence of PL; therefore, the αLV-LVOT should be considered another potential risk factor when evaluating patients for TA-TAVR.

Patients with an αLV-LVOT greater than 69 degrees had a significantly higher risk for a clinically significant PL, with a sensitivity of 89% and specificity of 83%. Therefore, one possibility to lower the rate of PL in patients with an αLV-LVOT exceeding 69 degrees could be an approach through a lower intercostal space or switching to a transfemoral approach. Another way to lower the rate of PL could be to account for the αLV-LVOT in the design of future stents and novel insertion systems.

In most centers, the αLV-LVOT can be measured using CT data, which are routinely acquired before TA-TAVR to...
evaluate the aortic annulus [4]; therefore, no additional imaging is required. Because there is no significant difference in the LV-LVOT during the cardiac cycle, prospectively ECG-triggered CT protocols with low radiation exposure can be used without restriction to assess the LV-LVOT.

Some limitations of this study should be addressed. First, this retrospective study included only a small number of patients with hemodynamically significant PL, and our univariate analysis focused only on the LV-LVOT. Prospective multivariate studies with larger study populations are necessary to validate the influence of the LV-LVOT on the occurrence of significant PL. Second, we only used the Edwards SAPIEN prosthesis; therefore, comparing our results with results for other devices may be inappropriate. Studies with other or advanced prosthesis types should follow.

In conclusion, a greater zLV-LVOT angle during TA-TAVR was associated with a significantly higher rate of PL. Thus, the LV-LVOT might influence the selection of the TA implantation path and have a significant effect on the design of future stents and novel delivery devices.

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Table 2. The Mean Differences in the Angle Between the Left Ventricular Long Axis and the Axis of the Left Ventricular Outflow Tract Depending on the Degree of Paravalvular Leakage

<table>
<thead>
<tr>
<th>Paravalvular Leakage</th>
<th>Difference in Degrees (Mean ± SD)</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 0 vs I</td>
<td>1.1 ± 2.3</td>
<td>−3.4 to 5.7</td>
<td>0.64</td>
</tr>
<tr>
<td>Grade I vs II</td>
<td>12.7 ± 2.9</td>
<td>6.9–18.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Grade 0 + I vs II</td>
<td>13.3 ± 3.2</td>
<td>6.8–19.8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Grade I = mild paravalvular leakage; grade II = moderate paravalvular leakage.

zLV-LVOT = angle between the left ventricular long axis and the axis of the left ventricular outflow tract; CI = confidence interval; SD = standard deviation.

References