



Impact of device-host interaction on paravalvular aortic regurgitation with different transcatheter heart valves[☆]

Ramón Rodríguez-Olivares^{a,b,c}, Nahid El Faquir^a, Zouhair Rahhab^a, Lennart van Gils^a, Ben Ren^a, Rafi Sakhi^a, Marcel L. Geleijnse^a, Ron van Domburg^a, Peter P.T. de Jaegere^a, Jose L. Zamorano Gómez^{b,c}, Nicolas M. Van Mieghem^{a,*}

^a Department of Cardiology, Thoraxcenter, Erasmus MC, Rotterdam, The Netherlands

^b Department of Cardiology, Ramón y Cajal University Hospital, Madrid, Spain

^c Centro de Investigación Biomédica en Red Cardiovascular (CIBERCV), Spain

ARTICLE INFO

Article history:

Received 28 January 2018

Received in revised form 18 April 2018

Accepted 1 May 2018

ABSTRACT

Aims: We sought to evaluate the interaction of different aortic root phenotypes with self-expanding (SEV), balloon-expandable (BEV) and mechanically expanded (MEV) and the impact on significant aortic regurgitation. **Methods and results:** We included 392 patients with a SEV ($N = 205$), BEV ($N = 107$) or MEV ($N = 80$). Aortic annulus eccentricity index and calcification were measured by multi-slice CT scan. Paravalvular aortic regurgitation was assessed by contrast aortography (primary analysis) and transthoracic echocardiography (secondary analysis).

In mildly calcified roots paravalvular regurgitation incidence was similar for all transcatheter heart valves (SEV 8.4%; BEV 9.1%; MEV 2.0% $p = 0.27$). Conversely, in heavily calcified roots paravalvular regurgitation incidence was significantly higher with SEV (SEV 45.9%; BEV 0.0%; MEV 0.0% $p < 0.001$). When paravalvular regurgitation was assessed by TTE, the overall findings were similar although elliptic aortic roots were associated with more paravalvular regurgitation with SEV (20.5% vs. BEV 4.5% vs. MEV 3.2%; $p = 0.009$).

Conclusions: In heavily calcified aortic roots, significant paravalvular aortic regurgitation is more frequent with SEV than with BEV or MEV, but similar in mildly calcified ones. These findings may support patient-tailored transcatheter heart valve selection.

Classifications: Aortic stenosis; multislice computed tomography; transcatheter aortic valve replacement; paravalvular aortic regurgitation.

Condensed abstract: We sought to evaluate the interaction of different aortic root phenotypes with self-expanding (SEV), balloon-expandable (BEV) and mechanically expanded (MEV) and the impact on significant aortic regurgitation. We included 392 patients with a SEV ($N = 205$), BEV ($N = 107$) or MEV ($N = 80$). Aortic annulus eccentricity index and calcification were measured by multi-slice CT scan. Paravalvular aortic regurgitation was assessed by contrast aortography and transthoracic echocardiography. We found that in heavily calcified aortic roots, significant paravalvular aortic regurgitation is more frequent with SEV than with BEV or MEV, but similar in mildly calcified ones.

© 2018 Elsevier Inc. All rights reserved.

1. Introduction

Transcatheter aortic valve implantation (TAVI) is increasingly adopted for treatment of symptomatic severe aortic stenosis [1–5].

Abbreviations: TAVI, transcatheter aortic valve implantation; SEV, self-expanding valve; BEV, balloon-expandable valve; MEV, mechanically-expanded valve; AG, Agatston score; EI, Eccentricity index.

[☆] This work was supported by a grant from the European Association of Percutaneous Interventions (EAPCI).

* Corresponding author at: Department of Interventional Cardiology, Thoraxcenter, Erasmus MC, Room Bd 171, 's Gravendijkwal, 230 3015 CE Rotterdam, The Netherlands.

E-mail address: n.vanmieghem@erasmusmc.nl (N.M. Van Mieghem).

Compared to surgical aortic valve replacement, TAVI is associated with a higher rate of residual paravalvular aortic regurgitation and its occurrence is associated with poor outcome [6,7]. Patient-specific anatomical factors such as aortic root calcification [8], eccentricity [9] and procedure-specific factors such as transcatheter valve type, sizing and depth of implantation [10–12] predict paravalvular regurgitation. The implementation of three-dimensional multi-slice computed tomography as the planning tool of first choice has improved transcatheter heart valve size selection [13], yet the incidence of significant paravalvular regurgitation is still not negligible.

Second-generation heart valves implement sealing fabric to mitigate paravalvular leak albeit sometimes at the expense of more conduction

disorders [14,15]. With the commercial availability of multiple different transcatheter valves designs, device selection may become relevant and a more patient tailored approach may need to consider particular device-host interactions. The aim of this study was thus to evaluate the interaction of different aortic root phenotypes (calcium load and eccentricity index of the aortic annulus) with self-expanding (SEV), balloon-expandable (BEV) and mechanically expanded (MEV) transcatheter heart valves in terms of significant paravalvular regurgitation after implantation.

2. Material and methods

2.1. Patients

This study included all patients who underwent TAVI in our center from November 2005 to December 2015 and had multimodality imaging planning with transthoracic echocardiography, computed-tomography assessment of the aortic valve and peripheral arterial tree [16] and quantification of aortic regurgitation by aortography 5 min after implantation and by transthoracic echocardiography before discharge. A multi-disciplinary heart team consisting of at least 1 cardio-thoracic surgeon and 1 interventional cardiologist deemed all patients at high risk for mortality with surgical aortic valve replacement. TAVI procedure was executed under general or local anesthesia using standard techniques as described [17]. Relevant clinical and procedural data were prospectively collected and entered in a dedicated database. All patients provided written informed consent for the procedure and data analysis for research purposes per Institutional Review Board approval.

The initial TAVI experience was built with Medtronic CoreValve (Medtronic, Minneapolis, MN, USA). In 2012 the Edwards Sapien XT (Edwards Lifesciences, Irvine, CA, USA) was added to our practice. In September 2013 the Lotus valve (Boston Scientific, Natick, Massachusetts) was introduced followed by the Edwards Sapien S3 (Edwards Lifesciences, Irvine, CA, USA) in January 2014. Corevalve Evolut R (Medtronic, Minneapolis, MN, USA) replaced the first generation Corevalve in 2014.

2.2. Multi-slice computed tomography imaging

A second generation dual source (Somatom Definition FLASH, Siemens Healthcare, Forchheim, Germany) computed-tomography, was used for the selection of access site, optimal valve plane and valve size. For the assessment of aortic root calcification, a non-contrast scan was performed in an electrocardiogram-gated, prospective, sequential (step and shoot) mode with a reference tube current of 80 mAs/rotation, a tube voltage of 120 kV and slice thickness of 3 mm at 1.5 mm interval with B35f filtered back projection kernel in the early systolic heart phase depending on the heart rate. The threshold for the detection of calcium was set at 130HU using the SYNGO VIA Calcium score software (Siemens, Forchheim, Germany). The aortic root was defined on axial images as the stretching from the caudal aspect of the aortic annulus to the origin of the left main stem. Agatston score (AG), calcium volume and mass were measured. In cases where aortic root calcification was confluent with adjacent structures (mitral annulus, ascending aorta, coronary arteries) only the stack of images that contained the aortic root were selected.

Eccentricity index of the aortic annulus (EI) was calculated as follows:

$$1 - (\text{Diameter minimum} / \text{Diameter maximum}) \times 100$$

2.3. Assessment of aortic regurgitation

The primary analysis for AR was performed by contrast aortography and a secondary analysis by transthoracic echocardiogram. Contrast

aortography was performed 5 min after device deployment and release. Severity was defined using the Sellers classification (0 = none, 1 = mild, 2 = moderate, 3 = moderate to severe and 4 = severe [18]). A predefined angiography protocol comprised the injection of 15 to 20 ml non-diluted Iodixanol [Visipaque™] at a flow rate of 15 to 20 ml/s via a 6 Fr pigtail that was positioned just above the bioprosthetic leaflets. Cine runs were recorded at a speed of 30 frames/s. Two observers independently scored the angiograms. In case of discrepancy, consensus was reached by including a third observer. The intra- and interobserver variability for the assessment of aortic regurgitation post TAVI according to the Sellers classification were κ 0.70 and 0.78 respectively. Transthoracic echocardiography was acquired and analyzed according to the most recent Valve Academic Research Consortium criteria [19].

For the purpose of this study, aortic regurgitation with a Sellers ≥ 2 by aortography or \geq moderate by transthoracic echocardiogram was considered clinically significant.

2.4. Measurement of depth of implantation

The depth of device implantation was measured by quantitative angiographic analysis with CAAS 5.9 (Pie Medical, Maastricht, The Netherlands). Depth of implantation was defined as the distance from the inflow of the prosthesis to the nadir of the non-coronary and left coronary cusp measured in an optimal projection where the three cusps were aligned.

2.5. Aortic root characteristics

Based on the median values of the AG (2863 [1812 – 4110]) and EI of the aortic annulus (20 [14 – 23] %), four aortic root phenotypes were identified (Fig. 1):

- Phenotype 1: mildly calcified aortic root (AG < 3000) + circular aortic annulus (EI < 20%)
- Phenotype 2: mildly calcified aortic root (AG < 3000) + elliptical aortic annulus (EI \geq 20%).
- Phenotype 3: highly calcified aortic root (AG \geq 3000) + circular annulus (EI < 20%)
- Phenotype 4: highly calcified aortic root (AG \geq 3000) + elliptical aortic annulus (EI \geq 20%).

2.6. Statistical analysis

Normality of the distributions was assessed using Shapiro-Wilk test. Continuous variables with normal distribution are presented as mean \pm standard deviation and differences compared by using the ANOVA test. Median and interquartile range was used for non-normally distributed continuous variables and differences were compared by using the Kruskal-Wallis test. Categorical variables are presented as frequencies and differences were compared using the Pearson chi-square test or Fisher's exact test when applicable.

All statistical tests were two-sided, and a p -value < 0.05 was considered statistically significant. The statistical analyses were performed using SPSS software version 21.0 (SPSS INC., Chicago, IL).

3. Results

3.1. Patient population and baseline characteristics

A total of 392 patients were included in the study. Baseline characteristics are summarized in Tables 1 and 2. Mean \pm SD age was 80 \pm 8 years, 51.8% were male. Mean \pm SD Euroscore was 16 \pm 11. There were no differences across different THV cohorts in terms of calcification (AG SEV 2955 [1909–4276] vs. BEV 2920 [2031–3910] vs. MEV 2528 [1584–3749]; $p = 0.073$) or eccentricity index (SEV 18 [14–23] vs. BEV 20 [13–24] vs. MEV 20 [13–24]; $p = 0.40$).

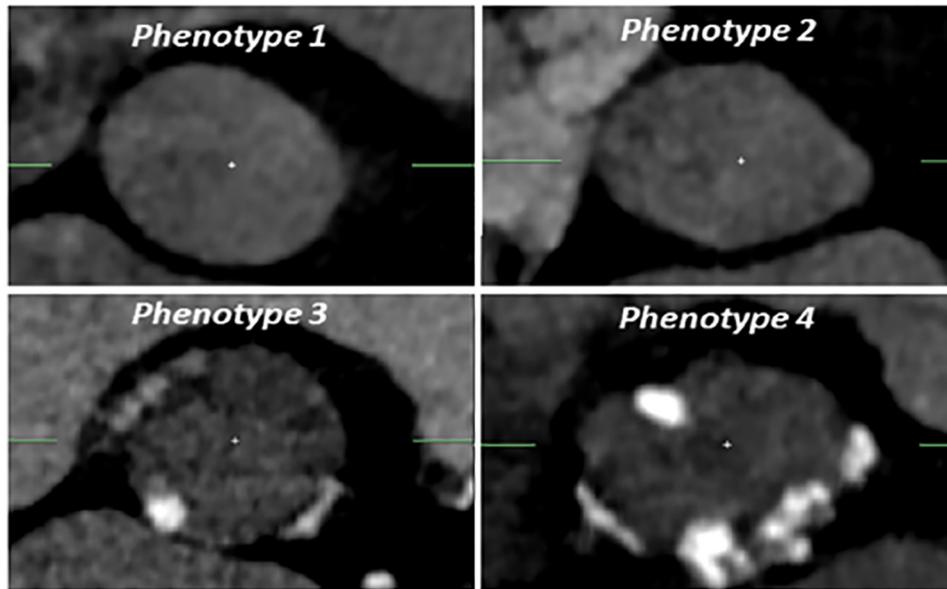


Fig. 1. Example of phenotypes of aortic root created for this study.

3.2. Procedural characteristics and outcomes

Procedural characteristics are summarized in Table 3. Two hundred and five (52.3%) patients received a self-expanding device (197 Corevalve and 8 Corevalve Evolut R), 107 (27.3%) a balloon-expandable valve (33 Edward-SAPIEN XT and 74 Edwards-SAPIEN 3) and 80 (20.4%) a mechanically-expanded valve (Boston Lotus Valve). The rate of balloon pre-dilation was higher in SEV in comparison with MEV and BEV (93.6 vs. 46.7 vs. 17.5% respectively; $p < 0.001$). We did not find differences in depth of implantation at the non-coronary sinus (SEV 6 [4–10] mm; BEV 7 [5–8] mm; MEV 7 [6–8] mm; $p = 0.40$), but a significant difference was found at the left-coronary sinus (SEV 8 [5–10] mm; BEV 6 [5–8] mm; MEV 7 [5–9] mm; $p = 0.015$). The need for balloon post-dilation was similar for SEV (18.0%) and BEV (19.6%) devices and was absent for MEV.

3.3. Aortic regurgitation by aortography and relation with aortic root characteristics

The incidence of significant aortic regurgitation by aortography was 15.3% overall (60 patients), 26.3% in SEV (54 patients), 4.7% in BEV (5 patients) and 1.3% in MEV (1 patients) ($p < 0.001$).

3.4. Comparison among devices

In terms of aortic root calcification, no difference in aortic regurgitation was seen across different devices in mildly calcified aortic roots (AG < 3000) (SEV 8.4%; BEV 9.1%; MEV 2.0% $p = 0.27$). Conversely, in heavily calcified roots (AG > 3000) the rate of significant regurgitation was significantly higher with SEV (SEV 45.9%; BEV 0.0%; MEV 0.0% $p < 0.001$) (Fig. 2A). Aortic regurgitation was more frequent with SEV regardless of EI: aortic regurgitation with EI < 20% for SEV 23.0%; for BEV 5.4%; for MEV 2.3% ($p < 0.001$) and aortic regurgitation with EI > 20% for SEV 31.6%, BEV 3.9%; MEV 0.0% $p < 0.001$ (Fig. 3A). The analysis per phenotype can be found in Fig. 4A.

3.5. Aortic regurgitation by echocardiography and relation with aortic root characteristics

Three-hundred and fifty-two patients out of the 392 initially included in our study, had a good quality transthoracic echocardiogram before discharge. A total of 39 patients had moderate or severe paravalvular regurgitation (11.1%). The frequency of significant paravalvular regurgitation was 16.4% ($n = 31/189$) for the SEV, 6.5% ($n = 6/93$) with BEV and 2.9% ($n = 2/70$) with MEV ($p = 0.002$).

Table 1
Baseline characteristics.

	Total population (n = 392)	SEV (n = 205)	BEV (n = 107)	MEV (n = 80)	p-Value
Age (years)	80 ± 8	80 ± 8	79 ± 8	80 ± 6	0.80
Gender, male N (%)	203 (51.8)	110 (53.7)	59 (55.1)	34 (42.5)	0.17
Body mass index	27 ± 5	27 ± 4	28 ± 6	27 ± 5	0.38
Diabetes mellitus N (%)	113 (28.8)	55 (26.8)	29 (27.1)	29 (36.3)	0.26
Hypertension N (%)	294 (75.0)	135 (65.9)	86 (80.4)	73 (91.3)	<0.001
Atrial fibrillation N (%)	108 (27.8)	49 (24.0)	3 (29.9)	27 (34.6)	0.17
Prior stroke N (%)	87 (22.2)	47 (22.9)	22 (20.6)	18 (22.5)	0.89
Prior myocardial infarction N (%)	79 (20.2)	47 (22.9)	17 (15.9)	15 (18.8)	0.32
Prior coronary artery bypass grafting N (%)	78 (19.9)	46 (22.4)	19 (17.8)	13 (16.3)	0.41
Peripheral vascular disease N (%)	94 (24.0)	43 (21.0)	34 (31.8)	17 (21.3)	0.086
New-York heart association class ≥ III N (%)	278 (74.3)	149 (75.3)	73 (70.9)	56 (76.7)	0.62
Euroscore	16 ± 11	17 ± 11	16 ± 11	14 ± 9	0.055

Table 2
Echocardiographic and computed-tomography data.

	Total Population (n = 392)	SEV (n = 205)	BEV (n = 107)	MEV (n = 80)	p-Value
Echocardiographic data					
Left ventricular ejection fraction (%)	55 [45–64]	52 [42–62]	55 [45–65]	60 [50–65]	0.01
Peak aortic gradient pre (mm Hg)	67 [52–85]	67 [52–85]	73 [52–85]	67 [55–87]	0.94
Mean aortic gradient pre (mm Hg)	41 [31–52]	40 [31–51]	45 [33–56]	41 [30–52]	0.34
Aortic valve area pre-implantation (cm ²)	0.7 [0.6–0.8]	0.7 [0.5–0.8]	0.7 [0.6–0.9]	0.7 [0.6–0.9]	0.016
Aortic regurgitation ≥ grade II (%)	233 (62.0)	202 (62.9)	99 (66.7)	75 (53.3)	0.19
Mitral regurgitation ≥ grade II (%)	286 (75.3)	145 (71.1)	81 (81.8)	60 (77.9)	0.11
MSCT data					
Annulus diameter minimum (mm)	22 [21–24]	22 [21–24]	22 [20–24]	22 [20–23]	0.24
Annulus diameter maximum (mm)	27 [26–29]	27 [26–29]	27 [26–29]	27 [26–29]	0.53
Annulus area (mm ²)	466 [423–529]	470 [422–535]	466 [423–527]	449 [423–517]	0.62
Annulus perimeter (mm)	78 [74–82]	78 [74–83]	79 [73–82]	77 [74–82]	0.67
Annulus eccentricity index	20 [14–23]	18 [14–23]	20 [13–24]	20 [13–24]	0.42
Elliptical annulus (EI > 20%)	166 (42.3)	79 (38.5)	51 (47.7)	36 (45.0)	0.26
Aortic Root Agatston score	2863 [1812–4110]	2955 [1909–4276]	2920 [2031–3910]	2528 [1584–3749]	0.073
Highly calcified aortic root (Agatston score > 3000)	180 (45.9)	98 (47.8)	52 (48.6)	30 (37.5)	0.24

3.6. Comparison among devices

In highly calcified aortic roots, the rate of significant paravalvular regurgitation was higher in SEV vs. BEV and MEV (24.4% vs. 8.9% vs. 3.8%; $p = 0.012$). No differences were found among devices in mildly calcified aortic roots (9.7% vs. 4.2% vs. 2.3%; $p = 0.19$) (Fig. 2B).

Paravalvular regurgitation was more frequent with SEV in EI > 20% (SEV 20.5% vs. BEV 4.5% vs. MEV 3.2%; $p = 0.009$), but not in EI < 20% (13.8% vs. BEV 8.2% vs. MEV 2.6%; $p = 0.12$) (Fig. 3B). The analysis per phenotype can be found in Fig. 4B.

4. Discussion

The key findings of this retrospective observational study can be summarized as follows: 1) Paravalvular regurgitation is more frequent with SEV than with BEV or MEV. 2) Aortic root calcification is associated with more paravalvular regurgitation with SEV but not with BEV or MEV. 3) Aortic annulus circularity does not seem to affect paravalvular regurgitation frequency.

Paravalvular regurgitation impacts long-term outcomes after TAVI. Randomized trials evaluating BEV and SEV unequivocally identified moderate paravalvular regurgitation as an independent predictor of mortality after TAVI [5–7]. In our study moderate paravalvular regurgitation by aortography appeared in 15.6% but more with SEV (26.3%) than with BEV (4.7%) or MEV (1.3%). Moderate paravalvular regurgitation by transthoracic echocardiogram was somewhat lower (11.0%) but consistently higher with SEV (16.0%) than with BEV (6.5%) or MEV (2.9%). The higher moderate aortic regurgitation frequency with SEV by aortography may reflect the inherent capacity of the nitinol Corevalve frame to further expand after deployment. Indeed, aortography was performed approximately 5 min after TAVI as compared to transthoracic regurgitation evaluation several days later. A substudy of the Corevalve US Pivotal Trial demonstrated that at 1 year follow up the degree of aortic regurgitation had improved in the majority of

patients underpinning the hypothesis of continued remodeling and outward expansion of the Corevalve nitinol frame [20].

The optimal imaging technique to assess TAVI related paravalvular regurgitation is controversial and also dependent on the timing and setting. Cardiac magnetic resonance imaging may be considered the standard for aortic regurgitation assessment yet is hampered by logistic and patient related challenges (claustrophobia, permanent pacemaker). Compared to cardiac magnetic resonance, both aortography and transthoracic echocardiography have only modest correlation [21–24]. Because of current trends for a “minimalist TAVI approach” implying local anesthesia with or without sedation, aortography has become the dominant imaging tool to address paravalvular regurgitation in the catheterization laboratory and to guide corrective maneuvers where needed.

Our study is the first to address the interaction of anatomical characteristics with different THV designs in terms of incidence of paravalvular regurgitation after TAVI. Indeed, device composition and mode of implantation may respond differently to a particular anatomical phenotype independent of an operator's experience. Our findings demonstrate SEV was more susceptible for paravalvular regurgitation than BEV or MEV when the aortic annulus is more calcified or ellipsoid. This is consistent with the superior procedural success rates with BEV over SEV in the CHOICE trial driven by a higher frequency of more-than-mild aortic regurgitation with SEV vs. BEV (18.3% vs. 4.1% RR, 0.23; 95% CI, 0.09–0.58; $P < 0.001$) [12].

Aortic root calcification is associated with paravalvular regurgitation [8,25,26] with both SEV and BEV. In our study more than mild aortic regurgitation (assessed by aortography or transthoracic echocardiogram) was more frequent with SEV than with BEV or MEV. Interestingly, this higher frequency of aortic regurgitation was driven by degree of aortic annulus calcification. In heavily calcified annuli there was significantly more paravalvular regurgitation with SEV vs. BEV or MEV (SEV 45.9%; BEV 0.0%; MEV 0.0% $p < 0.001$). In mildly calcified annuli there was no difference in paravalvular regurgitation among the different devices (SEV 8.4%; BEV 9.1%; MEV 2.0% $p = 0.27$). Several reports previously

Table 3
Procedural characteristics.

	Total population (n = 392)	SEV (n = 205)	BEV (n = 107)	MEV (n = 80)	p-Value
Depth of implantation (mm)					
- Non-coronary sinus	7 [5–9]	6 [4–10]	7 [5–8]	7 [6–8]	0.42
- Left coronary sinus	7 [5–9]	8 [5–10]	6 [5–8]	7 [5–9]	0.015
Sizing annulus based on perimeter (%)					
Balloon pre-dilation N (%)	255 (65.2)	191 (93.6)	50 (46.7)	14 (17.5)	<0.001
Balloon post-dilation N (%)	58 (14.8)	37 (18.0)	21 (19.6)	0 (0.0)	<0.001
Residual aortic regurgitation ≥ grade 2 (Aortography)	61 (15.6)	54 (26.3)	5 (4.7)	1 (1.3)	<0.001
Residual paravalvular regurgitation ≥ moderate (transthoracic echocardiography)	39 (11.1)	31 (16.4)	6 (6.5)	2 (2.9)	0.02

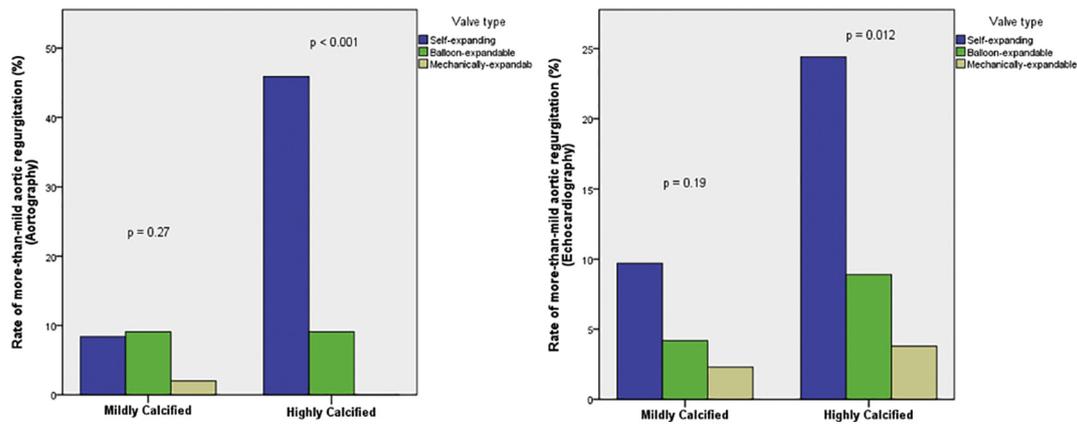


Fig. 2. Rate of more-than-mild aortic regurgitation among devices per calcium burden, A by aortography (Sellers method) and B by transthoracic echocardiography (Valve Academic Research Consortium criteria).

identified an Agatston calcium score > 3000 to predict significant aortic regurgitation or the need of balloon postdilatation [26–28]. In our study, aortic annulus calcification seemed to only affect paravalvular regurgitation frequency with SEV but not with BEV or MEV. In contrast, one report found a relation between Agatston Score > 3000 with significant paravalvular regurgitation [27] and BEV. This study contained a mixed cohort of SEV and BEV and contrary to our study device sizing was not solely based on computed-tomography. Ellipsoid aortic annuli are associated with paravalvular regurgitation after SEV, but not after BEV or MEV [9]. A potential explanation could be that BEV dominates the annular anatomy and remains circular after implantation [29–32], whereas the opposite holds for SEV that appears ellipsoid after implantation [33]. We previously demonstrated more circularity with BEV than with SEV by rotational angiograph [29]. Furthermore, SEV seems associated with more paravalvular regurgitation in aortic annuli with more calcium, smaller areas and more aortic regurgitation at baseline [8]. These differences may be the result of stronger hoop forces with BEV over SEV [32]. Our findings suggest that MEV share similar properties with BEV and seem thus less affected by calcium or annulus eccentricity with lower paravalvular regurgitation rates. However, the flipside of higher hoop strengths and device over host dominance may be a higher risk for aortic rupture with BEV [34] and pacemaker with MEV [14,35].

This study demonstrates specific device-host interactions with a recipient's anatomy. Computer simulation models that integrate transcatheter heart valve biomechanical properties and aortic root characterization by computed-tomography may predict this interaction and resultant aortic regurgitation. A recent series of 60 patients already found good aortic regurgitation prediction with SEV [35,36]. Further

refinement and validation of this concept involving other heart valve designs may eventually catalyze patient tailored transcatheter heart valve design selection.

5. Limitations

Our study has the limitations inherent to its single-center and retrospective nature. We acknowledge possible selection bias because we used 3 different transcatheter heart valve designs with unequal patient distribution and only patients with computer tomography-guided sizing were included. Aortic regurgitation was primarily assessed by contrast angiography. The optimal tool to address aortic regurgitation is controversial. However, the overall results were confirmed when using echocardiography to determine aortic regurgitation.

6. Conclusions

In heavily calcified aortic roots, significant paravalvular aortic regurgitation is more frequent with self-expanding devices than with balloon expandable or mechanically expanded models, but similar in mildly calcified ones. These findings may support patient-tailored transcatheter heart valve selection.

Impact on daily practice

The key finding of our research is that there seem to be a device-host interaction that can explain the incidence of paravalvular leak after TAVI. We saw that paravalvular regurgitation is more frequent with

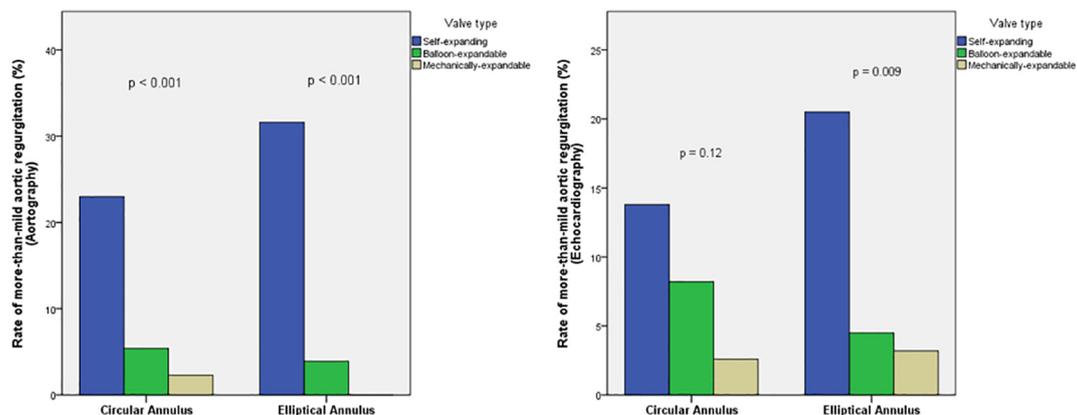


Fig. 3. Rate of more-than-mild aortic regurgitation among devices per eccentricity of the aortic annulus, A by aortography (Sellers method) and B by transthoracic echocardiography (Valve Academic Research Consortium criteria).

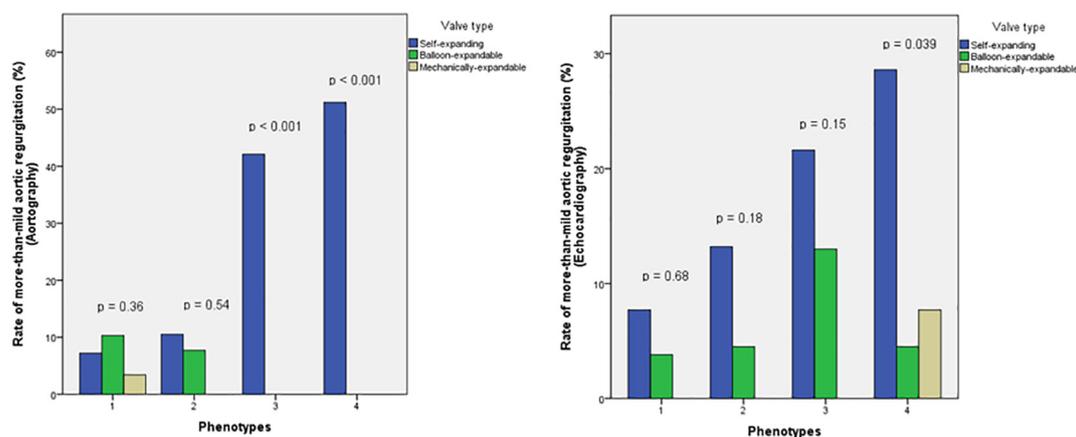


Fig. 4. Rate of more-than-mild aortic regurgitation among devices per phenotype, A by aortography (Sellers method) and B by transthoracic echocardiography (Valve Academic Research Consortium criteria).

self-expanding devices than with balloon-expanding or mechanically-expanded transcatheter heart valves in highly calcified aortic roots, but these differences do not hold for mildly calcified aortic roots. These findings may support patient-tailored transcatheter heart valve selection.

Conflict of interest

Dr. Ramón Rodríguez-Olivares has received a grant from the “European Association of Percutaneous Interventions (EAPCI)” and “Sociedad Española de Cardiología”. Dr. Van Mieghem has received research grants from Claret Medical, Boston Scientific, Medtronic and Edwards Lifesciences. Prof. Dr. de Jaegere is proctor for Boston Scientific. The other authors have no conflict of interest.

References

- Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, et al. PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med* 2010;363:1597–607.
- Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, et al. PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med* 2011;364:2187–98.
- Popma JJ, Adams DH, Reardon MJ, Yakubov SJ, Kleiman NS, Heimansohn D, et al. CoreValve United States Clinical Investigators. Transcatheter aortic valve replacement using a self-expanding bioprosthesis in patients with severe aortic stenosis at extreme risk for surgery. *J Am Coll Cardiol* 2014;63:1972–81.
- Adams DH, Popma JJ, Reardon MJ, Yakubov SJ, Coselli JS, Deeb GM, et al. U.S. CoreValve Clinical Investigators. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med* 2014;370:1790–8.
- Leon MB, Smith CR, Mack MJ, Makkar RR, Svensson LG, Kodali SK, et al. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2016;374:1609–20.
- Kodali SK, Williams MR, Smith CR, Svensson LG, Webb JG, Makkar RR, et al. PARTNER Trial Investigators. Two-year outcomes after transcatheter or surgical aortic-valve replacement. *N Engl J Med* 2012;366:1686–95.
- Kodali S, Pibarot P, Douglas PS, Williams M, Xu K, Thourani V, et al. Paravalvular regurgitation after transcatheter aortic valve replacement with the Edwards sapien valve in the PARTNER trial: characterizing patients and impact on outcomes. *Eur Heart J* 2015;36:449–56.
- Rodríguez-Olivares R, El Faquir N, Rahhab Z, Geeve P, Maugeness AM, van Weenen S, et al. Does frame geometry play a role in aortic regurgitation after Medtronic CoreValve implantation? *EuroIntervention* 2016;12:519–25.
- Wong DT, Bertaso AG, Liew GY, Thomson VS, Cunningham MS, Richardson JD, et al. Relationship of aortic annular eccentricity and paravalvular regurgitation post transcatheter aortic valve implantation with CoreValve. *J Invasive Cardiol* 2013;25:190–5.
- Ali OF, Schultz C, Jabbour A, Rubens M, Mittal T, Mohiaddin R, et al. Predictors of paravalvular aortic regurgitation following self-expanding Medtronic CoreValve implantation: the role of annulus size, degree of calcification, and balloon size during pre-implantation valvuloplasty and implant depth. *Int J Cardiol* 2015;179:539–45.
- Hansson NC, Thuesen L, Hjørtdal VE, Leipsic J, Andersen HR, Poulsen SH, et al. Three-dimensional multidetector computed tomography versus conventional 2-dimensional transesophageal echocardiography for annular sizing in transcatheter aortic valve replacement: influence on postprocedural paravalvular aortic regurgitation. *Catheter Cardiovasc Interv* 2013;82:977–86.
- Abdel-Wahab M, Mehili J, Frerker C, Neumann FJ, Kurz T, Tölg R, et al. CHOICE investigators. Comparison of balloon-expandable vs self-expandable valves in patients undergoing transcatheter aortic valve replacement: the CHOICE randomized clinical trial. *JAMA* 2014;311:1503–14.
- Jilalawi H, Kashif M, Fontana G, Furugen A, Shiota T, Friede G, et al. Cross-sectional computed tomographic assessment improves accuracy of aortic annular sizing for transcatheter aortic valve replacement and reduces the incidence of paravalvular aortic regurgitation. *J Am Coll Cardiol* 2012 Apr 3;59(14):1275–86.
- Meredith IT, Walters DL, Dumontel N, Worthley SG, Tchétché D, Manoharan G, et al. 1-year outcomes with the fully repositionable and retrievable Lotus Transcatheter aortic replacement valve in 120 high-risk surgical patients with severe aortic stenosis: Results of the REPRISE II Study. *JACC Cardiovasc Interv* 2016;9:376–84.
- Tarantini G, Mojoli M, Purita P, Napodano M, D’Onofrio A, Frigo A, et al. Unravelling the (arte)fact of increased pacemaker rate with the Edwards SAPIEN 3 valve. *EuroIntervention* 2015;11:343–50.
- Schultz C, Moelker A, Tzikas A, Piazza N, de Feyter P, van Geuns RJ, et al. The use of MSCT for the evaluation of the aortic root before transcatheter aortic valve implantation: the Rotterdam approach. *EuroIntervention* 2010;6:505–11.
- de Jaegere P, van Dijk LC, Laborde JC, Sianos G, Orellana Ramos FJ, Lighart J, et al. True percutaneous implantation of the CoreValve aortic valve prosthesis by the combined use of ultrasound guided vascular access, Prostar(R) XL and the TandemHeart(R). *EuroIntervention* 2007;2:500–5.
- Sellers RD, Levy MJ, Amplatz K, Lillehei CW. Left retrograde cardioangiography in acquired cardiac disease: technic, indications and interpretations in 700 cases. *Am J Cardiol* 1964;14:437–47.
- Kappetein AP, Head SJ, Généreux P, Piazza N, van Mieghem NM, Blackstone EH, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium–2 consensus document. *J Am Coll Cardiol* 2012;60:1438–54.
- Oh JK, Little SH, Abdelmoneim SS, Reardon MJ, Kleiman NS, Lin G, et al. CoreValve U.S. Pivotal Trial Clinical Investigators. Regression of paravalvular aortic regurgitation and remodeling of self-expanding transcatheter aortic valve: an observation from the CoreValve U.S. pivotal trial. *JACC Cardiovasc Imaging* 2015;8:1364–75.
- Frick M, Meyer CG, Kirschfink A, Altiok E, Lehrke M, Brehmer K, et al. Evaluation of aortic regurgitation after transcatheter aortic valve implantation: aortic root angiography in comparison to cardiac magnetic resonance. *EuroIntervention* 2016;11:1419–27.
- Hartlage GR, Babaliaros VC, Thourani VH, Hayek S, Chrysohoou C, Ghasemzadeh N, et al. The role of cardiovascular magnetic resonance in stratifying paravalvular leak severity after transcatheter aortic valve replacement: an observational outcome study. *J Cardiovasc Magn Reson* 2014;16:93.
- Ribeiro HB, Le Ven F, Larose E, Dahou A, Nombela-Franco L, Urena M, et al. Cardiac magnetic resonance versus transthoracic echocardiography for the assessment and quantification of aortic regurgitation in patients undergoing transcatheter aortic valve implantation. *Heart* 2014;100:1924–32.
- Orwat S, Diller GP, Kaleschke G, Kerckhoff G, Kempny A, Radke RM, et al. Aortic regurgitation severity after transcatheter aortic valve implantation is underestimated by echocardiography compared with MRI. *Heart* 2014;100:1933–8.
- Généreux P, Head SJ, Hahn R, Daneault B, Kodali S, Williams MR, et al. Paravalvular leak after transcatheter aortic valve replacement: the new Achilles’ heel? A comprehensive review of the literature. *J Am Coll Cardiol* 2013;61:1125–36.
- John D, Buellesfeld L, Yuecel S, Mueller R, Latsios G, Beucher H, et al. Correlation of device landing zone calcification and acute procedural success in patients undergoing transcatheter aortic valve implantations with the self-expanding CoreValve prosthesis. *JACC Cardiovasc Interv* 2010;3:233–43.
- Koos R, Mahnken AH, Dohmen G, Brehmer K, Günther RW, Autschbach R, et al. Association of aortic valve calcification severity with the degree of aortic regurgitation after transcatheter aortic valve implantation. *Int J Cardiol* 2011;150:142–5.
- Schultz C, Rossi A, van Mieghem N, van der Boon R, Papadopoulou SL, van Domburg R, et al. Aortic annulus dimensions and leaflet calcification from contrast MSCT predict the need for balloon post-dilatation after TAVI with the Medtronic CoreValve prosthesis. *EuroIntervention* 2011;7:564–72.

- [29] Rodríguez-Olivares R, Rahhab Z, Faquir NE, Ren B, Geleijnse M, Bruining N, et al. Differences in frame geometry between balloon-expandable and self-expanding transcatheter heart valves and association with aortic regurgitation. *Rev Esp Cardiol* 2016;69:392–400.
- [30] Willson AB, Webb JG, Gurvitch R, Wood DA, Toggweiler S, Binder R, et al. Structural integrity of balloon-expandable stents after transcatheter aortic valve replacement: assessment by multidetector computed tomography. *JACC Cardiovasc Interv* 2012;5:525–32.
- [31] Binder RK, Webb JG, Toggweiler S, Freeman M, Barbanti M, Willson AB, et al. Impact of post-implant SAPIEN XT geometry and position on conduction disturbances, hemodynamic performance, and paravalvular regurgitation. *JACC Cardiovasc Interv* 2013;6:462–8.
- [32] Tzamtzis S, Viquerat J, Yap J, Mullen MJ, Burriesci G. Numerical analysis of the radial force produced by the Medtronic-CoreValve and Edwards-SAPIEN after transcatheter aortic valve implantation (TAVI). *Med Eng Phys* 2013;35:125–30.
- [33] Schultz CJ, Weustink A, Piazza N, Otten A, Mollet N, Krestin G, et al. Geometry and degree of apposition of the CoreValve ReValving system with multislice computed tomography after implantation in patients with aortic stenosis. *J Am Coll Cardiol* 2009;54:911–8.
- [34] Barbanti M, Yang TH, Rodès Cabau J, Tamburino C, Wood DA, Jilaihawi H, et al. Anatomical and procedural features associated with aortic root rupture during balloon-expandable transcatheter aortic valve replacement. *Circulation* 2013;128:244–53.
- [35] Schultz C, Rodríguez-Olivares R, Bosmans J, Lefèvre T, De Santis G, Bruining N, et al. Patient-specific image-based computer simulation for the prediction of valve morphology and calcium displacement after TAVI with the Medtronic CoreValve and the Edwards SAPIEN valve. *EuroIntervention* 2016;11:1044–52.
- [36] de Jaegere P, De Santis G, Rodríguez-Olivares R, Bosmans J, Bruining N, Dezutter T, et al. Patient-specific computer modeling to predict aortic regurgitation after transcatheter aortic valve replacement. *JACC Cardiovasc Interv* 2016;9:508–12.