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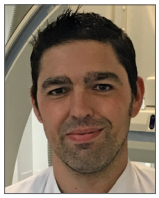
Does frame geometry play a role in aortic regurgitation after Medtronic CoreValve implantation?



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KEYWORDS

- catheter-based coronary valvular interventions
- rotational angiography
- valvular heart disease

Abstract

Aims: Aortic regurgitation (AR) after Medtronic CoreValve System (MCS) implantation may be explained by patient-, operator- and procedure-related factors. We sought to explore if frame geometry, as a result of a specific device-host interaction, contributes to AR.

Methods and results: Using rotational angiography with dedicated motion compensation, we assessed valve frame geometry in 84 patients who underwent TAVI with the MCS. Aortic regurgitation was assessed by angiography (n=84, Sellers) and echocardiography at discharge (n=72, VARC-2). Twenty-two patients (26%) had AR grade ≥2 using contrast angiography, and 17 (24%) by echocardiography. Balloon predilatation and sizing and depth of implantation did not differ between the two groups. Despite more frequent balloon post-dilatation in patients with AR (40.9 vs. 9.7%, p=0.001), the frame was more elliptical at its nadir relative to the patient's annulus (6±13 vs. –1±11%, p=0.046) and occurred in a larger proportion of patients (61.9 vs. 26.8%, p=0.004). Although the Agatston score and the eccentricity of the MCS frame relative to the annulus were independent determinants of AR (odds ratio: 1.635 [1.151-2.324], p=0.006, and 4.204 [1.237-14.290], p=0.021), there was a weak association between the Agatston score and the adjusted eccentricity (Spearman's rank correlation coefficient ρ=–0.24, p=0.046).

Conclusions: These findings indicate that AR can be explained by a specific device-host interaction which can only partially be explained by the calcium load of the aortic root.

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Abbreviations

AR	aortic regurgitation
ESV	Edwards SAPIEN valve
MSCT	multislice computed tomography
MCS	Medtronic CoreValve System
R-angio	rotational angiography
TAVI	transcatheter aortic valve implantation

Introduction

Transcatheter aortic valve implantation (TAVI) is increasingly being used to treat patients with aortic stenosis who are considered too high a risk for surgical valve replacement[1-5]. A vexing clinical problem is the occurrence of paravalvular aortic regurgitation (AR) which is reported to occur more frequently after implantation of the self-expanding Medtronic CoreValve® (MCS) (Medtronic, Minneapolis, MN, USA) than after the balloon-expandable Edwards SAPIEN valve (ESV) (Edwards Lifesciences, Irvine, CA, USA)[6-8].

Patient and procedure-related variables such as aortic root calcification, annular dimensions, depth of implantation and sizing, have been identified as determinants of AR post TAVI[9,10]. However, specific valve-related issues such as the type (i.e., circular vs. non-circular expansion) and degree of valve expansion may play a role as well. There is evidence from multislice computed tomography (MSCT) analysis in selected patients that non-circular expansion and malapposition is more frequent after MCS than ESV valve implantation[11-14]. The question is to what extent this plays a role in the development of AR on top of patient-related and procedural variables. For that purpose, we have adopted a strategy of performing routine rotational angiography (R-angio) using dedicated motion compensation to study frame geometry immediately after valve implantation[15]. The purpose of this study was to assess the correlation between MCS geometric findings by rotational angiography and AR after TAVI.

Methods

PATIENTS

The study population consisted of 98 consecutive patients who underwent TAVI with the MCS valve in whom R-angio with motion compensation was performed[15]. Only patients with sufficient image quality for frame assessment (grade 1,2,3) were included using the following scores:

Grade 1: excellent image quality (struts visible without artefacts).

Grade 2: struts clearly visible, distinction between struts and artefacts possible.

Grade 3: struts visible but in some regions distinction between struts and artefacts cannot be made.

Grade 4: degraded (struts are blurred and distorted).

Grade 5: strongly degraded (struts and artefacts cannot be distinguished) **(Figure 1)**.

A total of 14 patients were excluded from the analysis because of image quality grade 4 (six patients) and grade 5 (eight patients). Therefore, the final study population was 84.

Patients were seen at the outpatient clinic and gave written informed consent for anonymised prospective data collection for clinical research purposes (TAVI Care & Cure project, MEC-2014-277). All patients underwent TAVI under general anaesthesia via the transfemoral approach, except two in whom the subclavian approach was used following Heart Team discussion. MSCT was used for sizing in all except nine patients[16].

ROTATIONAL ANGIOGRAPHY, 3D RECONSTRUCTION AND FRAME ANALYSIS

R-angio was performed immediately after TAVI using the Artis zee biplane angiographic C-arm system (Siemens AG Healthcare, Forchheim, Germany). The technical details have been described before[15]. Cross-sectional short-axis images were used for frame analysis **(Figure 2)**.

Frame analysis: MCS frame analysis was performed at three predefined levels **(Figure 3)**, inflow, nadir and central coaptation of the leaflets[13]. At each of these levels, the minimum diameter (Dmin), maximum diameter (Dmax), area and perimeter were manually measured using the centre point of the strut(s).

Expansion of the frame was calculated by measured perimeter/nominal perimeter. The eccentricity of the frame was calculated by Dmin/Dmax×100. The eccentricity of the frame at the level of the nadir was adjusted to the eccentricity of the native annulus using the following equation: (Eccentricity nadir – Eccentricity native annulus/Eccentricity native annulus)×100, since this part of the frame, that contains the nadir of the bioprosthetic leaflets, is in closest contact with the base of the aortic root and is the part most subjected to the constraining forces of the aortic root.

ASSESSMENT OF AORTIC REGURGITATION

Contrast angiography and Doppler echocardiography were used to assess AR immediately after TAVI and at discharge[17,18]. With respect to contrast angiography, AR severity was defined using the Sellers classification (0=none, 1=mild, 2=moderate, 3=moderate to severe,

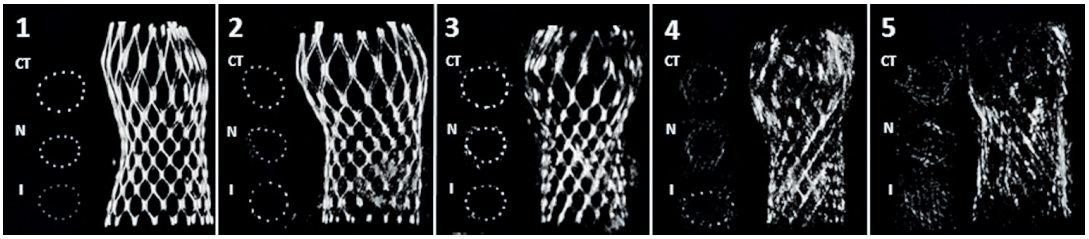

Figure 1. *Image quality of R-angio: grade 1 (best quality) to grade 5 (worst quality). CT: central coaptation of the leaflets; I: inflow; N: nadir*

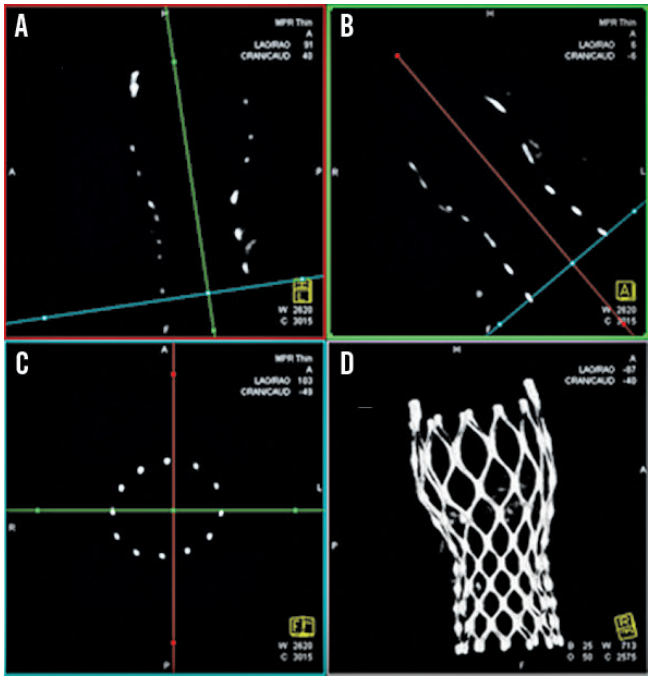

Figure 2. *Acquisition of the multiplanar reformatted short-axis view (C) at the different levels of interest adjusting two longitudinal multiplaner reformatted orthogonal views (A & B) similar to MSCT[16] and the resulting volume-rendered tridimensional reconstruction (D).*

and 4=severe)[17]. For that purpose, an angiography protocol was used consisting of the injection of 20 ml of non-diluted Iodixanol (Visipaque™; General Electric Company, Fairfield, CT, USA) at a flow rate of 20 ml/sec via a 6 Fr pigtail catheter which was positioned above the bioprosthetic leaflets. Cine runs were recorded at a speed of 30 frames/sec. Two observers (independently from one another) scored the angiograms. In case of discrepancy, consensus was reached by including a third observer. The intra- and inter-observer variability for the assessment of AR post TAVR according to the Sellers classification was κ 0.70, 0.60 and 0.78, respectively. A distinction was made between patients with Sellers grade 0-1 and those with Sellers grade 2-4.

Doppler echocardiography was performed before discharge. AR severity was defined by the circumferential extent of the Doppler signal at the inflow of the MCS frame in the parasternal short-axis view (SAX) using the VARC-2 criteria[18]. Echocardiography was available in 72 out of the 84 patients. A distinction was made between none-mild (<10%) and moderate-severe (10-29% and ≥30%) AR.

STATISTICS AND ANALYSIS

Categorical variables are presented as frequencies and percentages and compared using Pearson's chi-square test. Continuous variables are presented as means (±SD) and compared with the Student's t-test. The association between two continuous variables was carried out by using Pearson's or Spearman's rank correlation coefficient test when adequate. To study the independent predictors of AR post TAVI, logistic regression was performed. All characteristics judged to be clinically relevant or to have a pathophysiologic role in AR post TAVI were included in the multivariable logistic regression model. A two-sided alpha level of 0.05 was used to indicate significance. Statistical analyses were performed using SPSS software, Version 21.0 (IBM Corp. Armonk, NY, USA).

The main analysis consisted of the detection of the determinants of AR based on comparing patients with Sellers grade 0-1 and 2-4 on angiography after implantation. The secondary analysis consisted of the assessment of the determinants of AR by comparing patients with no or mild (<10%) and those with moderate or severe AR (10-29% and ≥30%) on the SAX view of the echo-Doppler examination before discharge[18-20].

Results

The baseline clinical and procedural data of all patients and of those with AR grade 0-1 versus those with AR grade ≥2 post TAVI are summarised in **Online Table 1** and **Online Table 2**.

AR grade ≥2 was seen in 22 patients (26%). By univariable analysis, these patients had a lower body weight (68±15 vs. 76±14 kg, p=0.037) and body mass index (23±3 vs. 27±5 kg/m^2, p=0.003), and a lower prevalence of antecedent coronary artery bypass surgery (9.1% vs. 30.6%, p=0.045). They also had more severe aortic stenosis (aortic valve area of 0.61±0.2 cm^2 vs. 0.72±0.2 cm^2 [p=0.034]) with a higher prevalence of AR at baseline by aortography (AR ≥2 81.8% vs. 51.6% [p=0.013]) and a higher Agatston score (4.545±2.005 vs. 2.895±1.698, p=0.001).

From a procedural perspective, there was no difference in predilation strategy, sizing and depth of implantation between the two

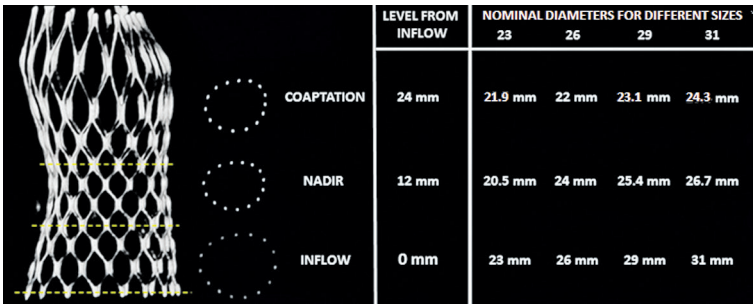

Figure 3. *Cross-sectional view at the three levels of interest of the MCS frame. Nominal perimeters at the various levels of the MCS frame were kindly provided by Medtronic Inc., Minneapolis, MN, USA.*

groups. The only difference was a higher frequency of balloon post-dilatation in patients with AR grade ≥2 (40.9% vs. 9.7%, p=0.001).

With respect to frame geometry **(Table 1)**, there was no difference in the degree of frame expansion or eccentricity at any level between patients with AR grade 0-1 and ≥2. Yet, when relating the degree of frame eccentricity at the level of the nadir with the degree of eccentricity of the native annulus, the frame was more elliptical at its nadir relative to the patient's annulus in patients with AR ≥2 compared to those with AR grade 0-1 (6±13 vs. –1±11%, p=0.046).

Table 1. Rotational angiography analysis.

	Entire cohort (84 patients)	AR 0 or 1 (62 patients)	AR 2, 3 or 4 (22 patients)	*p*-value
Degree of valve expansion at the inflow (%)	83±7	84±7	82±9	0.398
Degree of valve expansion at the nadir (%)	90±3	90±4	91±3	0.502
Degree of valve expansion at the coaptation (%)	97±5	97±5	97±4	0.499
Degree of eccentricity at the inflow (%)	82±8	81±7	82±8	0.617
Degree of eccentricity at the nadir (%)	83±8	84±8	81±7	0.121
Degree of eccentricity at the coaptation (%)	90±6	91±6	88±6	0.150
Degree of eccentricity at the nadir adjusted to the eccentricity of the native annulus (%)*	4±13	6±13	–1±11	0.046
Nadir more elliptical than the native annulus, n (%)	28 (36.4)	15 (26.8)	13 (61.9)	0.004

* negative value denotes that the MCS frame is more elliptical than the native annulus. Degree of valve expansion: measured frame perimeter/nominal frame perimeter ×100

The eccentricity of the frame relative to the patient's annulus was also seen in a larger proportion of patients with AR ≥2 (61.9 vs. 26.8%, p=0.004). In other words, when the valve was more elliptical than the recipient's anatomy (adjusted ellipticity <0) there was significantly more AR than when the valve was less elliptical than the annulus (adjusted ellipticity ≥0).

Spearman's rank correlation coefficient revealed a weak association between Agatston score and the adjusted eccentricity (=-0.24, p=0.046). There was no correlation between prosthesis sizing and adjusted eccentricity (R=0.03, p=0.81).

Multivariate analysis revealed the Agatston score and eccentricity of MCS frame relative to the native annulus to be independent determinants for AR post TAVI (odds ratio: 1.635 [1.151-2.324], p=0.006, and 4.204 [1.237-14.290], p=0.021, respectively) **(Table 2)**.

Repeat analysis based on the circumferential extent of AR on echocardiography before discharge indicated similar findings but lacked statistical power to confirm (**Online Table 3**-**Online Table 5**).

Discussion

The main finding of this study is that, in patients with severe aortic stenosis who received the self-expanding MCS valve, the frame

Table 2. Predictors of AR post TAVI.

	Univariate model OR (CI 95%)	*p*-value	Multivariate model OR (CI 95%)	*p*-value
Weight (kg)	0.961 (0.925-0.998)	0.041		
Body mass index (kg/m^2)	0.805 (0.691-0.938)	0.005		
Aortic valve area (cm^2)	0.074 (0.006-0.869)	0.038		
AR pre-TAVI by aortography grade ≥II	4.219 (1.280-13.901)	0.018		
Agatston score	1.599 (1.156-2.213)	0.005	1.635 (1.151-2.324)	0.006
Post-implantation balloon dilation	6.462 (1.953-21.374)	0.002		
Nadir more elliptical than native annulus	4.442 (1.537-12.832)	0.006	4.204 (1.237-14.290)	0.021

was more elliptical at its nadir relative to the patient's annulus in patients with >mild AR (6±13%) compared to those with no or mild AR (-1±11%). The eccentricity of the frame relative to the patient's annulus was also seen in a significantly larger proportion of patients (61.9 vs. 26.8%, p=0.004) despite a more frequent use of balloon dilatation after valve implantation (40.9 vs. 9.7%, p=0.001). Although the Agatston score and degree of adjusted ellipticity were independent determinants of AR, the Spearman rank correlation analysis indicates that the calcium load of the aortic root only partially explains the degree of adjusted ellipticity.

These data indicate the presence of a specific device-host interaction that, in turn, may suggest the presence of incomplete apposition. Unfortunately, apposition, or the lack thereof, cannot be assessed *in vivo*. This is supported by experimental findings analysing the numerical radial force of the MCS valve that was used in the current population[21]. Tzamtzis et al found that the radial force of the MCS frame rapidly drops with the increasing diameter of the recipient's anatomy and, depending on this diameter, may reach zero[21]. The model did not include elastic coupling between valve and host tissue and may therefore underestimate the radial force exerted by the frame *in vivo* but supports the findings in this clinical study and, therefore, the aetiology of AR. Furthermore, the experimental model of Tzamtzis used a cylindrical surrogate for the annulus while in patients it is often asymmetric[11-14]. Therefore, non-uniform distribution of force along the perimeter of the MCS valve most likely occurs, which, in combination with opposing forces due to calcium, may affect apposition *in vivo*.

Lack of apposition as a cause of AR after MCS, on top of other factors such as sizing and depth of implantation, is supported by the findings in 56 patients treated with the MCS valve in whom geometric analysis of the MCS frame (cardiac CT post TAVI) was correlated with AR on the short-axis view of transthoracic echo-Doppler cardiography (SAX-TTE)[22]. Malposition was reported in 35 patients (63%) and was correlated with the calcium load of the aortic root and the site of AR on SAX-TTE[22]. The role of apposition as a cause of AR and the effects of calcium on apposition are highlighted by the findings in another 110 patients treated with the

MCS valve in whom it was found that aortic root calcification had a higher discriminatory power for the prediction of balloon dilatation after MCS valve implantation to treat AR than sizing (prosthesis to annulus ratio)[23].

Tzamtzis et al also demonstrated a similar biomechanical behaviour in the Edwards SAPIEN valve (stainless steel frame - decreasing radial force with increasing diameter of the recipient anatomy) but found that it was independent of tissue stiffness[21]. This may explain why (at variance with the MCS valve) circularity after ESV implantation is the rule: circularity of the ESV valve was reported in all but two out of 89 patients (98%) and was independent of the native annular anatomy while symmetrical expansion of the MCS frame was seen in only five out of 30 patients (17%)[13,14]. The aggregate of these data indicates that the MCS conforms to the geometry of the patient's annulus while the ESV dictates the geometry of the annulus. Interestingly, in this study patients with AR had a more severe aortic stenosis (AVA) and a higher Agatston score, reflecting more advanced atherosclerotic disease and therefore higher opposing forces to frame expansion. The combination of the experimental findings of Tzamtzis et al and the current clinical findings indicate that some extra degree of oversizing may be needed when using the MCS valve, in particular in such patients, to overcome the calcium load (in addition to correct positioning) or to change the biomechanical properties of the MCS frame at the inflow level. Unfortunately, this study lacks the power to prove this point. Another solution is the use of a repositionable valve which allows the operator to change the depth of implantation so as to avoid or minimise AR[24,25].

In comparison with the CHOICE study which compared valve function between the MCS and ESV, contrast angiography was the principal method used to address the current study objective[8]. AR is most often caused by inappropriate sealing or apposition of the valve, though sometimes it is due to a central leak. This distinction cannot be made by angiography and clarification is needed for proper definition of the eventual additional treatment, such as balloon dilatation in case of malapposition. With respect to quantitative assessment of AR, the limitations of echocardiography are well known[19,20]. MRI has been shown to be the best method but is less available in clinical practice[26,27].

In this study, R-angio was used for the assessment of frame geometry using dedicated prototype software for motion compensation which was validated with MSCT[15]. The advantage of R-angio over MSCT is that it is available on-line in the catheterisation or hybrid operating room. The morphologic information of the valve in combination with haemodynamic (e.g., residual gradient) and/or echocardiographic findings during TAVI may help to tailor or define additional therapeutic measures to improve outcome and valve function[28].

Limitations

The main limitations of the present study are sample size and the absence of independent (core lab) analysis of the parameter of interest. Also, not all patients underwent echocardiography before discharge and we did not perform rotational angiography before and after additional balloon dilatation. A larger sample would have allowed a more comprehensive and robust multivariable analysis. In addition, a larger or multicentric sample with a more heterogeneous distribution of the independent variables – sizing and depth of implantation in particular – would have allowed the assessment of the strength of the reported specific device-host interaction relative to operator- and procedure-related variables such as sizing and depth of implantation. The present analysis also pertains to a selected group of patients (i.e., patients with rotational angiography with sufficient image quality). The absence of independent analysis may affect the validity of the reported point estimate of the target parameter and may explain the difference in AR between this and other studies using contrast angiography. However, we believe that the proposed aetiology of AR in the present population is plausible, in particular considering the experimental analysis of the biomechanical properties of the frame and previous clinical observations.

Conclusions

When the valve is properly implanted, AR post MCS valve implantation is the result of a specific device-host interaction (inadequate frame apposition due to calcium). It is currently unknown how to incorporate the calcium load of the aortic root into the sizing matrix.

Impact on daily practice

When the valve is properly implanted, AR post MCS valve implantation is the result of a specific device-host interaction (inadequate frame apposition due to calcium). The impact of these findings are: 1) clinically, the importance of oversizing when using the MCS valve and the development of an algorithm including calcium of the aortic root in the sizing matrix, and 2) from an R&D perspective, the development of a frame with enhanced hoop force at inflow.

Guest Editor

This paper was guest edited by Alec Vahanian, MD, PhD; Département de Cardiologie, Hôpital Xavier Bichat, Faculté Paris Diderot, DHU FIRE, Paris, France.

Conflict of interest statement

Guenter Lauritsch is an employee of Siemens AG. The other authors have no conflicts of interest to declare. The Guest Editor has carried out low-level consultancy work for Medtronic.

Disclaimer

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References

1. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Brown DL, Block PC, Guyton RA, Pichard AD, Bavaria JE, Herrmann HC, Douglas PS, Petersen JL, Akin JJ, Anderson WN, Wang D, Pocock S; PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med.* 2010;363:1597-607.

2. Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Williams M, Dewey T, Kapadia S, Babaliaros V, Thourani VH, Corso P, Pichard AD, Bavaria JE, Herrmann HC, Akin JJ, Anderson WN, Wang D, Pocock SJ; PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med.* 2011;364: 2187-98.

3. Popma JJ, Adams DH, Reardon MJ, Yakubov SJ, Kleiman NS, Heimansohn D, Hermiller J Jr, Hughes GC, Harrison JK, Coselli J, Diez J, Kafi A, Schreiber T, Gleason TG, Conte J, Buchbinder M, Deeb GM, Carabello B, Serruys PW, Chenoweth S, Oh JK; 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.

4. Adams DH, Popma JJ, Reardon MJ, Yakubov SJ, Coselli JS, Deeb GM, Gleason TG, Buchbinder M, Hermiller J Jr, Kleiman NS, Chetcuti S, Heiser J, Merhi W, Zorn G, Tadros P, Robinson N, Petrossian G, Hughes GC, Harrison JK, Conte J, Maini B, Mumtaz M, Chenoweth S, Oh JK; U.S. CoreValve Clinical Investigators. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med.* 2014;370:1790-8.

5. Mylotte D, Osnabrugge RL, Windecker S, Lefèvre T, de Jaegere P, Jeger R, Wenaweser P, Maisano F, Moat N, Søndergaard L, Bosmans J, Teles RC, Martucci G, Manoharan G, Garcia E, Van Mieghem NM, Kappetein AP, Serruys PW, Lange R, Piazza N. Transcatheter aortic valve replacement in Europe: adoption trends and factors influencing device utilization. *J Am Coll Cardiol.* 2013;62:210-9.

6. O'Sullivan KE, Gough A, Segurado R, Barry M, Sugrue D, Hurley J. Is valve choice a significant determinant of paravalvular leak post-transcatheter aortic valve implantation? A systematic review and meta-analysis. *Eur J Cardiothorac Surg.* 2014;45:826-33.

7. Van Belle E, Juthier F, Susen S, Vincentelli A, Iung B, Dallongeville J, Eltchaninoff H, Laskar M, Leprince P, Lievre M, Banfi C, Auffray JL, Delhaye C, Donzeau-Gouge P, Chevreul K, Fajadet J, Leguerrier A, Prat A, Gilard M, Teiger E; FRANCE 2 Investigators. Postprocedural aortic regurgitation in balloon-expandable and self-expandable transcatheter aortic valve procedures: analysis of predictors and impact on long-term mortality: insights from the FRANCE2 Registry. *Circulation.* 2014;129:1415-27.

8. Abdel-Wahab M, Mehilli J, Frerker C, Neumann FJ, Kurz T, Tölg R, Zachow D, Guerra E, Massberg S, Schäfer U, El-Mawardy M, Richardt G; 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.

9. Généreux P, Head SJ, Hahn R, Daneault B, Kodali S, Williams MR, van Mieghem NM, Alu MC, Serruys PW, Kappetein AP, Leon MB. 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.

10. Athappan G, Patvardhan E, Tuzcu EM, Svensson LG, Lemos PA, Fraccaro C, Tarantini G, Sinning JM, Nickenig G, Capodanno D, Tamburino C, Latib A, Colombo A, Kapadia SR. Incidence, predictors, and outcomes of aortic regurgitation after transcatheter aortic valve replacement: meta-analysis and systematic review of literature. *J Am Coll Cardiol.* 2013;61:1585-95.

11. Ng AC, Delgado V, van der Kley F, Shanks M, van de Veire NR, Bertini M, Nucifora G, van Bommel RJ, Tops LF, de Weger A, Tavilla G, de Roos A, Kroft LJ, Leung DY, Schuijf J, Schalij MJ, Bax JJ. Comparison of aortic root dimensions and geometries before and after transcatheter aortic valve implantation by 2- and 3-dimensional transesophageal echocardiography and multislice computed tomography. *Circ Cardiovasc Imaging.* 2010;3:94-102.

12. Blanke P, Siepe M, Reinöhl J, Zehender M, Beyersdorf F, Schlensak C, Langer M, Pache G. Assessment of aortic annulus dimensions for Edwards SAPIEN Transapical Heart Valve implantation by computed tomography: calculating average diameter using a virtual ring method. *Eur J Cardiothorac Surg.* 2010;38:750-8.

13. Schultz CJ, Weustink A, Piazza N, Otten A, Mollet N, Krestin G, van Geuns RJ, de Feyter P, Serruys PW, de Jaegere P. 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.

14. Binder RK, Webb JG, Toggweiler S, Freeman M, Barbanti M, Willson AB, Alhassan D, Hague CJ, Wood DA, Leipsic J. Impact of post-implant SAPIEN XT geometry and position on conduction disturbances, hemodynamic performance, and paravalvular regurgitation. *JACC Cardiovasc Interv.* 2013;6:462-8.

15. Schultz CJ, Lauritsch G, Van Mieghem N, Rohkohl C, Serruys PW, van Geuns RJ, de Jaegere PP. Rotational angiography with motion compensation: first-in-man use for the 3D evaluation of transcatheter valve prosthesis. *EuroIntervention.* 2015;11:442-9.

16. Schultz CJ, Moelker AD, Tzikas A, Rossi A, van Geuns RJ, de Feyter PJ, Serruys PW. Cardiac CT: necessary for precise sizing for transcatheter aortic implantation. *EuroIntervention.* 2010;6 Suppl G:G6-G13.

17. Sellers RD, Levy MJ, Amplatz K, Lillehey CW. Left Retrograde Cardioangiography in Acquired Cardiac Disease: Technic, Indications and Interpretations in 700 Cases. *Am J Cardiol.* 1964;14:437-47.

18. Kappetein AP, Head SJ, Généreux P, Piazza N, van Mieghem NM, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, van Es GA, Hahn RT, Kirtane AJ, Krucoff MW, Kodali S,

Mack MJ, Mehran R, Rodés-Cabau J, Vranckx P, Webb JG, Windecker S, Serruys PW, Leon MB. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *Eur Heart J.* 2012;33:2403-18.

19. Zoghbi WA, Chambers JB, Dumesnil JG, Foster E, Gottdiener JS, Grayburn PA, Khandheria BK, Levine RA, Marx GR, Miller FA Jr, Nakatani S, Quiñones MA, Rakowski H, Rodriguez LL, Swaminathan M, Waggoner AD, Weissman NJ, Zabalgoitia M; American Society of Echocardiography's Guidelines and Standards Committee; Task Force on Prosthetic Valves; American College of Cardiology Cardiovascular Imaging Committee; Cardiac Imaging Committee of the American Heart Association; European Association of Echocardiography; European Society of Cardiology; Japanese Society of Echocardiography; Canadian Society of Echocardiography; American College of Cardiology Foundation; American Heart Association; European Association of Echocardiography; European Society of Cardiology; Japanese Society of Echocardiography; Canadian Society of Echocardiography. Recommendations for evaluation of prosthetic valves with echocardiography and doppler ultrasound: a report From the American Society of Echocardiography's Guidelines and Standards Committee and the Task Force on Prosthetic Valves, developed in conjunction with the American College of Cardiology Cardiovascular Imaging Committee, Cardiac Imaging Committee of the American Heart Association, the European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography and the Canadian Society of Echocardiography, endorsed by the American College of Cardiology Foundation, American Heart Association, European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography, and Canadian Society of Echocardiography. *J Am Soc Echocardiogr.* 2009;22:975-1014.

20. Zamorano JL, Badano LP, Bruce C, Chan KL, Gonçalves A, Hahn RT, Keane MG, La Canna G, Monaghan MJ, Nihoyannopoulos P, Silvestry FE, Vanoverschelde JL, Gillam LD. EAE/ASE recommendations for the use of echocardiography in new transcatheter interventions for valvular heart disease. *Eur Heart J.* 2011;32:2189-214.

21. 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.

22. Schultz CJ, Tzikas A, Moelker A, Rossi A, Nuis RJ, Geleijnse MM, van Mieghem N, Krestin GP, de Feyter P, Serruys PW, de Jaegere PP. Correlates on MSCT of paravalvular aortic regurgitation after transcatheter aortic valve implantation using the Medtronic CoreValve prosthesis. *Catheter Cardiovasc Interv.* 2011;78:446-55.

23. Schultz C, Rossi A, van Mieghem N, van der Boon R, Papadopoulou SL, van Domburg R, Moelker A, Mollet N, Krestin G, van Geuns RJ, Nieman K, de Feyter P, Serruys PW, de Jaegere P. 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.

24. Piazza N, Martucci G, Lachapelle K, de Varennes B, Bilodeau L, Buithieu J, Mylotte D. First-in-human experience with the Medtronic CoreValve Evolut R. *EuroIntervention.* 2014;9:1260-3.

25. Meredith Am IT, Walters DL, Dumonteil N, Worthley SG, Tchétché D, Manoharan G, Blackman DJ, Rioufol G, Hildick-Smith D, Whitbourn RJ, Lefèvre T, Lange R, Müller R, Redwood S, Allocco DJ, Dawkins KD. Transcatheter aortic valve replacement for severe symptomatic aortic stenosis using a repositionable valve system: 30-day primary endpoint results from the REPRISE II study. *J Am Coll Cardiol.* 2014;64:1339-48.

26. Orwat S, Diller GP, Kaleschke G, Kerckhoff G, Kempny A, Radke RM, Buerke B, Burg M, Schülke C, Baumgartner H. Aortic regurgitation severity after transcatheter aortic valve implantation is underestimated by echocardiography compared with MRI. *Heart.* 2014;100:1933-8.

27. Ribeiro HB, Le Ven F, Larose E, Dahou A, Nombela-Franco L, Urena M, Allende R, Amat-Santos I, Ricapito Mde L, Thébault C, Clavel MA, Delarochelliére R, Doyle D, Dumont E, Dumesnil JG, Pibarot P, Rodés-Cabau J. Cardiac magnetic resonance versus transthoracic echocardiography for the assessment of aortic regurgitation in patients undergoing transcatheter aortic valve implantation. *Heart.* 2014;100:1924-32.

28. Rodríguez-Olivares R, Van Mieghem NM, De Jaegere PP. The role of frame geometry assessment during transcatheter aortic valve replacement by rotational angiography. *JACC Cardiovasc Interv.* 2014;7:e191-2.

Supplementary data

Online Table 1. Baseline characteristics (analysis based on aortic regurgitation by aortography).

Online Table 2. Procedural details (analysis based on aortic regurgitation by aortography).

Online Table 3. Baseline characteristics (analysis based on aortic regurgitation by echocardiography).

Online Table 4. Procedural details (analysis based on aortic regurgitation by echocardiography).

Online Table 5. Rotational angiography analysis (analysis based on aortic regurgitation by echocardiography).

The supplementary data are published online at: http://www.pcronline.com/eurointervention/101st_issue/87

Supplementary data

Online Table 1. Baseline characteristics (analysis based on aortic regurgitation by aortography).

	Entire cohort (84 patients)	AR by aortography grade 0 or 1 (62 patients)	AR by aortography grade 2, 3 or 4 (22 patients)	*p*-value
Age (years)	80±9	79±9	83±7	0.158
Male, n (%)	47 (56.0)	36 (58.1)	11 (50.0)	0.513
Height (cm)	168±10	168±9	169±11	0.595
Weight (kg)	74±14	76±14	68±15	0.037
Body mass index (kg/m^2)	26±5	27±5	23±3	0.003
Body surface area (m^2)	1.8±0.2	1.9±0.2	1.8±0.2	0.090
New York Heart Association Class ≥III, n (%)	59 (72.9)	43 (70.5)	16 (80.0)	0.407
Previous cerebrovascular event, n (%)	22 (26.2)	14 (22.6)	8 (36.4)	0.207
Previous myocardial infarction, n (%)	20 (23.8)	16 (25.8)	4 (18.2)	0.471
Previous coronary artery bypass graft surgery, n (%)	21 (25.0)	19 (30.6)	2 (9.1)	0.045
Previous percutaneous coronary intervention, n (%)	23 (27.4)	15 (24.2)	8 (36.4)	0.271
Diabetes mellitus, n (%)	17 (20.2)	15 (24.2)	2 (9.1)	0.130
Hypertension, n (%)	61 (72.6)	47 (75.8)	14 (63.6)	0.271
Peripheral vascular disease, n (%)	19 (22.6)	14 (22.6)	5 (22.7)	0.989
Pulmonary hypertension, n (%)	5 (6.0)	5 (8.1)	0 (0.0)	0.170
Severe pulmonary hypertension, n (%)	1 (1.2)	1 (1.6)	0 (0.0)	0.549
Chronic obstructive pulmonary disease, n (%)	26 (31.0)	20 (32.3)	6 (27.3)	0.664
Atrial fibrillation, n (%)	21 (25.0)	16 (25.8)	5 (22.7)	0.774
Permanent pacemaker, n (%)	4 (4.8)	4 (6.5)	0 (0.0)	0.222
Logistic EuroSCORE (%)	17±11	17±10	18±13	0.570
Echocardiography & invasive measurements				
Left ventricular ejection fraction (%)	51±14	51±14	52±13	0.794
Aortic valve area (cm^2)	0.69±0.2	0.72±0.2	0.61±0.2	0.034
Peak gradient (mmHg)	72±27	69±28	79±22	0.174
Mitral regurgitation grade ≥II by echocardiography, n (%)	35 (41.7)	23 (37.1)	12 (54.5)	0.154
Aortic regurgitation ≥II by echocardiography, n (%)	35 (41.7)	24 (38.7)	11 (50.0)	0.356
Aortic regurgitation ≥II by aortography, n (%)	50 (59.5)	32 (51.6)	18 (81.8)	0.013
Pre-implantation AR index	26±12	26±12	23±11	0.313
Multislice computed tomography				
Minimal annulus diameter (mm)	22±2	22±3	22±2	0.882
Maximal annulus diameter (mm)	27±3	27±3	27±2	0.650
Mean annulus diameter (mm)	25±2	25±2	24±2	0.856
Perimeter annulus (mm)	78±7	78±7	78±7	0.759
Area annulus (mm^2)	472±85	474±90	466±73	0.740
Eccentricity of the native annulus (%)	81±6	80±6	82±6	0.420
Agatston score	3.349±1.922	2.895±1.698	4.545±2.005	0.001

Online Table 2. Procedural details (analysis based on aortic regurgitation by aortography).

		Entire cohort (84 patients)	AR by aortography grade 0 or 1 (62 patients)	AR by aortography grade 2, 3 or 4 (22 patients)	*p*-value
Access strategy, n (%)					0.394
Transfemoral		82 (97.6)	60 (96.8)	22 (100)	
Trans-subclavian		2 (2.4)	2 (3.2)	0 (0.0)	
Prosthesis size, n (%)					0.310
23 mm		1 (1.2)	1 (1.6)	0 (0.0)	
26 mm		20 (23.8)	14 (22.6)	6 (27.3)	
29 mm		55 (65.5)	39 (62.9)	16 (72.7)	
31 mm		8 (9.5)	8 (12.9)	0 (0.0)	
Balloon predilatation					
Pre-implantation balloon dilation, n (%)		80 (95.2)	58 (93.5)	22 (100.0)	0.222
Balloon nominal/mean annulus diameter ×100 (%)		91±7	91±8	91±5	0.824
Sizing MCS					
Valve size/minimal annulus diameter ×100 (%)		130±10	131±11	129±9	0.357
Valve size/maximal annulus diameter ×100 (%)		105±8	105±8	105±6	0.913
Valve size/mean annulus diameter ×100 (%)		116±7	116±8	115±6	0.575
Valve perimeter/perimeter of the annulus ×100 (%)		114±7	115±7	113±7	0.352
Depth of implantation (mm)					
Left coronary sinus		8±4	8±4	8±4	0.734
Non-coronary sinus		7±4	7±4	7±4	0.807
Balloon post-dilation					
Post-implantation balloon dilation, n (%)		15 (17.9)	6 (9.7)	9 (40.9)	0.001
Balloon nominal diameter/mean annulus diameter ×100 (%)		99±8	101±10	98±6	0.540
Balloon nominal diameter/MCS size ×100 (%)		88±5	88±5	87±5	0.912
AR post TAVI					
Post-implantation AR index (%)		22±10	23±10	20±8	0.267
AR post-implantation by aortography, n (%)	Grade 0	4 (4.8)	4 (6.5)	0 (0.0)	
	Grade I	58 (69.0)	58 (93.5)	0 (0.0)	
	Grade II	20 (23.8)	0 (0.0)	20 (90.9)	
	Grade III	2 (2.4)	0 (0.0)	2 (9.1)	
	Grade IV	0 (0.0)	0 (0.0)	0 (0.0)	
AR post-implantation by echocardiography, n (%)	Mild (<10% circumferential extent of the leakage)	55 (76.4)	48 (88.9)	7 (38.9)	
	Moderate (10-29% circumferential extent of the leakage)	15 (20.8)	5 (9.3)	10 (55.6)	
	Severe (>30% circumferential extent of the leakage)	2 (2.8)	1 (1.9)	1 (5.6)	

Online Table 3. Baseline characteristics (analysis based on aortic regurgitation by echocardiography).

	Entire cohort (72 patients)	AR <10% of circumference by echocardiography (55 patients)	AR ≥10% of circumference by echocardiography (17 patients)	*p*-value
Age (years)	81±8	82±7	76±11	0.012
Male, n (%)	42 (58.3)	32 (58.2)	10 (58.8)	0.963
Height (cm)	169±8	167±9	172±11	0.076
Weight (kg)	74±14	74±14	73±16	0.742
Body mass index (kg/m^2)	26±4	26±4	24±5	0.081
Body surface area (m^2)	1.8±0.2	1.8±0.2	1.8±0.2	0.935
New York Heart Association Class ≥III, n (%)	48 (69.6)	36 (69.2)	12 (70.6)	0.916
Previous cerebrovascular event, n (%)	19 (26.4)	10 (18.2)	9 (52.9)	0.004
Previous myocardial infarction, n (%)	18 (25.0)	14 (25.5)	4 (23.5)	0.873
Previous coronary artery bypass graft surgery, n (%)	18 (25.0)	16 (29.1)	2 (11.8)	0.149
Previous percutaneous coronary intervention, n (%)	15 (20.8)	10 (18.2)	5 (29.4)	0.319
Diabetes mellitus, n (%)	11 (15.3)	9 (16.4)	2 (11.8)	0.645
Hypertension, n (%)	52 (72.2)	44 (80.0)	8 (47.1)	0.008
Peripheral vascular disease, n (%)	16 (22.2)	13 (23.6)	3 (17.6)	0.604
Pulmonary hypertension, n (%)	5 (6.9)	5 (9.1)	0 (0.0)	0.197
Severe pulmonary hypertension, n (%)	1 (1.4)	1 (1.8)	0 (0.0)	0.576
Chronic obstructive pulmonary disease, n (%)	24 (33.3)	18 (32.7)	6 (35.3)	0.844
Atrial fibrillation, n (%)	20 (27.8)	16 (29.1)	4 (23.5)	0.655
Permanent pacemaker, n (%)	3 (4.2)	3 (5.5)	0 (0.0)	0.325
Logistic EuroSCORE (%)	18±11	19±11	14±12	0.154
Echocardiography and invasive measurements				
Left ventricular ejection fraction (%)	51±14	50±14	51±14	0.971
Aortic valve area (cm^2)	0.70±0.2	0.72±0.2	0.66±0.2	0.272
Peak gradient (mmHg)	70±26	68±25	77±26	0.237
Mitral regurgitation grade ≥II by echocardiography, n (%)	30 (41.7)	25 (45.5)	5 (29.4)	0.241
Aortic regurgitation ≥II by echocardiography, n (%)	29 (40.3)	24 (43.6)	5 (29.4)	0.296
Aortic regurgitation ≥II by aortography, n (%)	44 (61.1)	30 (54.5)	14 (82.4)	0.040
Pre-implantation AR index	26±12	25±12	28±12	0.531
Multislice computed tomography				
Minimal annulus diameter (mm)	22±2	22±2	23±2	0.299
Maximal annulus diameter (mm)	27±3	27±3	28±2	0.621
Mean annulus diameter (mm)	25±2	25±2	25±2	0.414
Annulus perimeter (mm)	78±8	78±9	80±7	0.310
Annulus area (mm^2)	480±87	474±87	496±86	0.400
Annulus eccentricity (%)	81±6	80±7	82±6	0.464
Aortic valve Agatston score	3.437±2.014	3.117±1.812	4.317±2.327	0.040

Online Table 4. Procedural details (analysis based on aortic regurgitation by echocardiography).

		Entire cohort (72 patients)	AR <10% of circumference by echocardiography (55 patients)	AR ≥10% of circumference by echocardiography (17 patients)	*p*-value
Access strategy, n (%)					
Transfemoral		70 (97.2)	53 (96.4)	17 (100.0)	
Trans-subclavian		2 (2.8)	2 (3.6)	0 (0.0)	
Prosthesis size, n (%)					
23 mm		1 (1.4)	0 (0.0)	1 (5.9)	
26 mm		17 (23.6)	15 (27.3)	2 (11.8)	
29 mm		47 (65.3)	33 (60.0)	14 (82.4)	
31 mm		7 (9.7)	7 (12.7)	0 (0.0)	
Predilatation					
Pre-implantation balloon dilation, n (%)		68 (94.4)	51 (92.7)	17 (100.0)	0.253
Balloon nominal/mean annulus diameter ×100 (%)		90±7	90±7	90±7	0.911
Sizing MCS					
Valve size/minimal annulus diameter ×100 (%)		129±10	131±9	126±10	0.081
Valve size/maximal annulus diameter ×100 (%)		104±7	104±7	102±6	0.274
Valve size/mean annulus diameter ×100 (%)		115±7	116±7	113±6	0.091
Valve perimeter/perimeter of the annulus ×100 (%)		113±6	114±6	111±7	0.068
Depth of Implantation (mm)					
Left coronary sinus		8±4	7±4	8±4	0.546
Non-coronary sinus		7±4	7±4	7±4	0.937
Balloon post-dilation					
Post-implantation balloon dilation, n (%)		12 (16.7)	5 (9.3)	7 (38.9)	0.003
Balloon nominal diameter/mean annulus diameter ×100 (%)		98±8	96±7	99±9	0.572
Balloon nominal diameter/MCS size ×100 (%)		87±5	85±5	89±5	0.149
Result AR					
Post-implantation AR index		22±9	21±9	24±7	0.217
AR post-implantation by aortography, n (%)	Grade 0	4 (5.6)	4 (7.3)	0 (0.0)	
	Grade I	50 (69.4)	44 (80.0)	6 (35.3)	
	Grade II	16 (22.2)	7 (12.7)	9 (52.9)	
	Grade III	2 (2.8)	0 (0.0)	2 (11.8)	
	Grade IV	0 (0.0)	0 (0.0)	0 (0.0)	

Online Table 5. Rotational angiography analysis (analysis based on aortic regurgitation by echocardiography).

	Entire cohort (72 patients)	AR <10% of circumference by echocardiography (55 patients)	AR ≥10% of circumference by echocardiography (17 patients)	*p*-value
Degree of valve expansion at the inflow (%)	83±7	84±7	81±8	0.260
Degree of valve expansion at the nadir (%)	90±4	90 ± 4	90 ± 4	0.897
Degree of valve expansion at the coaptation (%)	97±5	97±4	97±6	0.482
Degree of eccentricity at the inflow (%)	81±8	81±8	81±7	0.734
Degree of eccentricity valve at the nadir (%)	83±8	84±8	81±9	0.220
Degree of eccentricity valve at the coaptation (%)	90±7	91±6	88±7	0.206
Degree of eccentricity at the nadir adjusted to the eccentricity of the native annulus (%)*	3±11	4±12	–1±9	0.101
Nadir more elliptical than the native annulus, n (%)	24 (36.9)	15 (30.6)	9 (56.2)	0.065

* negative value denotes that the MCS frame is more elliptical than native annulus