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Predictors of Paravalvular Aortic Regurgitation Following Transcatheter Aortic Valve Replacement Using the New Evolut™ PRO System

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Abstract

Background and Objective: The Evolut Pro (EVP) is a novel self-expandable aortic valve. This prosthesis consists of an external porcine pericardial wrap designed to reduce paravalvular leak (PVL), maintaining the benefits of its predecessor. The objective was to assess predictors of PVL using this novel device (d minuscule).

Methods: Twenty-seven consecutive patients with severe symptomatic aortic stenosis undergoing transcatheter aortic valve replacement using the CoreValve EVP bioprosthesis between October 2017 and July 2018, were prospectively recruited.

Patients were divided into two groups according to the presence of PVL: no or trace PVL versus mild or grade II PVL. The groups were compared to identify the demographic, echocardiographic and CT parameters predictive of PVL

Results: Pre-discharge transthoracic echocardiography revealed mild or grade II PVL in 19 cases (70%) (16 patients mild PVL; 3 grade II PVL). There were no patients with grade III or severe (grade IV) PVL. In all patients, the regurgitation was paravalvular. The prosthesis/annulus discongruence (prosthesis diameter – CT mean annular diameter) was significantly related to the occurrence of mild/grade II PVL (4.4±0.9 mm in the mild/moderate PVL group, versus 5±0.5 mm in the group without or trace PVL; p=0.04).

Conclusions: EVP system remains associated with mild or grade II PVL in a significant number of patients. However, hemodynamically significant PVL was not detected in any patient. The prosthesis/annulus discongruence plays a major role in the occurrence of residual PVL.

Key Words

Aortic stenosis • Transcatheter aortic valve replacement • Paravalvular leak • Computed tomography • Echocardiography

Introduction

Transcatheter aortic valve replacement (TAVR) has become standard therapy for patients with severe aortic stenosis who are deemed of at least intermediate risk for surgical valve replacement (SAVR). The current commercially available valves are broadly grouped into balloon-expandable and self-expandable valves [1]. However, there is significant clinical concern regarding the higher incidence of paravalvular leak (PVL) with TAVR as compared to SAVR as this has been associated with poor long-term clinical outcomes [2]. The CoreValve™ system was the first-generation self-expandable valve introduced to the market. The second-generation device was the

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CoreValve™ Evolut™ R System, with a more secure seal protecting against PVL [3, 4]. The latest iteration of this self-expandable valve is named the Evolut Pro system [1]. Based on the prior Evolut™ R platform, this novel valve consists of an external pericardial wrap that ensures a reduction in PVL while retaining other benefits of the previous generation, including a low delivery profile, self-expansion, as well as its ability to recapture and reposition the valve.

The efficacy of the Evolut PRO design has been initially tested by the investigators of the Evolut PRO clinical study [5], conducted as a non-randomized, single-arm prospective registry at eight centers in the USA including a total of sixty well-selected patients. These patients were prospectively followed over 30 days with a primary efficacy endpoint of none or trace aortic regurgitation. The study showed that the Evolut™ PRO system provided excellent hemodynamics and minimal residual aortic regurgitation. There are multiples studies that sought to assess PVL predictors based on anatomical characteristics (defined by computed tomography [CT]) [6-8]. Because Evolut™ PRO is a very new design, apart from the American study [5], there is no additional data available about its safety and efficacy in a "real life" clinical scenario. Moreover, the incidence and determinants of PVL after TAVR with the CoreValve™ Evolut™ PRO remain unknown. We sought to assess predictors of PVL using this novel device.

Methods

Twenty-seven consecutive patients with severe symptomatic aortic stenosis (aortic valve area (AVA) <1 cm^2 or indexed AVA <0.6 cm^2/m^2) undergoing transfemoral TAVI using the Medtronic CoreValve™ Evolut Pro bioprosthesis between October 2017 and July 2018, were prospectively recruited. All patients were previously discussed in a dedicated Heart Team meeting involving cardiac surgeons, interventional cardiologists, experts in cardiac imaging and clinical cardiologists. Our clinical and anatomic selection criteria and device size selection were in accordance with previous recommendations [4]. The prosthesis sizing was based on a combination of echocardiographic and CT measurements but eventually remained at the discretion of the implanting interventional cardiologist. All patients underwent a pre-procedure CT and all images were systematically analyzed using a cardiac application on a dedicated workstation by two independent experienced observers. The best diastolic images at 70 or 80% of the R-R interval were used. The largest (Dmax) and the smallest (Dmin) aortic annulus and left ventricle outflow tract (LVOT) diameters were measured. The mean diameter (Dmean) was derived by averaging the largest and smallest diameter. The circularity of aortic annulus was defined using the eccentricity index using the formula (1 – Dmin/Dmax) [6]. The degree of aortic valve calcification was semi-quantitatively classified as no calcification, mild calcification (small calcium spots), moderate calcification (larger calcium spots), and severe calcification (extensive calcification) as previously described [7]. The "cover index", expressed as a ratio of: ([prosthesis diameter – CT annulus diameter] / prosthesis diameter) x 100, was calculated to assess the congruence between the aortic annulus and the device [8]. Finally, to further explore the value of the difference between prosthesis size and annular size for the prediction of PVL, the difference between the nominal bioprosthesis size and mean CT aortic annulus diameter was assessed [9]. Following a predefined protocol, pre-discharge transthoracic echocardiographic was obtained in all patients. PVL was systematically graded, by an independent experienced operator blinded to angiographic data and procedural results, using multiple parameters including regurgitation color jet density and width, circumferential extent of turbulent regurgitation color jet around the aortic annulus for PVL, descending and abdominal aorta diastolic flow reversal on pulsed wave Doppler, and pressure half- time of aortic regurgitation on continuous wave Doppler signal, as previously defined [10].

For data analysis patients were divided into two groups according to the presence of PVL: no or trace PVL versus mild or grade II PVL. The groups were compared to identify the demographic, echocardiographic and CT parameters predictive of PVL. The data are expressed as the mean ± the standard deviation (SD). The differences between the means were calculated using Student's t-test after assessing normality. The differences in categorical variables were analyzed using Chi-square tests. Univariate analysis was used to identify the most significant predictors of PVL. The

Table 1. Baseline clinical, echocardiographic and CT characteristics.

	All (n=27)	No/trace PVL (n= 8)	Mild/gradeII PVL (n=19)	P value
Patients Characteristics				
Age (years)	85±4.3	83±2.4	86±4.8	0.1
Female	22 (81%)	7 (87%)	15 (79%)	0.6
BSA (mm^2)	1.6±0.1	1.6±0.1	1.6±0.1	0.5
Echo Parameters				
AVA (mm^2)	0.74±0.16	0.72±0.15	0.75±0.17	0.7
Peak gradient (mmHg)	68±21	65±24	69±21	0.6
LVEF (%)	64±13	63±14	64±13	0.9
CT Parameters				
Mean annulus (mm)	23±1.8	22.5±1.7	23.2±1.9	0.4
Annulus área (mm^2)	403±63	387±53	410±67	0.4
Annulus perimeter (mm)	697±114	699±54	697±132	0.9
Mean LVOT (mmHg)	21.9±2.7	20.7±2.5	22.4±2.6	0.1
Eccentricity index	0.22±0.05	0.23±0.06	0.21±0.05	0.5
Cover index	16.6±3.3	18.1±2.1	16±3.6	0.07
Moderate/severe valve calcification	70%	63%	87%	0.4
Prosthesis diameter – CT mean annular diameter (mm)	4.6±0.9	5±0.5	4.4±0.9	0.04

Data are presented as mean ± standard deviation or as number (percentage) of patients. AVA = aortic valve area. BSA = body surface area. LVEF = left ventricle ejection fraction. LVOT = left ventricle outflow tract. NYHA = New York Heart Association; TAVI = Transcatheter aortic valve implantation; PPM = Permanent pacemaker

level of statistical significance was set at $p \leq 0.05$. All statistical analyses were performed using SPSS Statistics version 18.

Results

Baseline clinical, CT and procedural characteristics are shown in Table 1. All 27 patients (mean age, 85±4 years, 81% of females) had severe aortic stenosis (mean AVA, 0.74±0.16 cm^2). An iliofemoral access route was used in all the cases, and 33% of patients required balloon post-dilatation. Left bundle branch block was developed in five cases and a pacemaker was required in 15% of patients due to new conduction system abnormalities. There were no deaths or major adverse cardiac events (MACE) during hospitalization.

Pre-discharge transthoracic echocardiography revealed mild or grade II PVL in 19 cases (70%) (16 patients mild PVL; 3 grade II PVL). There were no patients with grade III or severe (grade IV) PVL. In all patients the regurgitation was paravalvular. Factors associated with the presence of PVL are presented in Table 1. The prosthesis/annulus discongruence (prosthesis diameter – CT mean annular diameter) was significantly related to the occurrence of mild/grade II PVL (4.4±0.9 mm in the mild/moderate PVL group, versus 5±0.5 mm in the group without or trace PVL; p=0.04). However, no significant differences were found using area and perimeter values to calculate prosthesis/annulus discongruence. Moreover, no differences were observed when the body surface area (BSA) was taken into account. Other factors such as eccentricity index, cover index, degree of annular calcification, mean annular

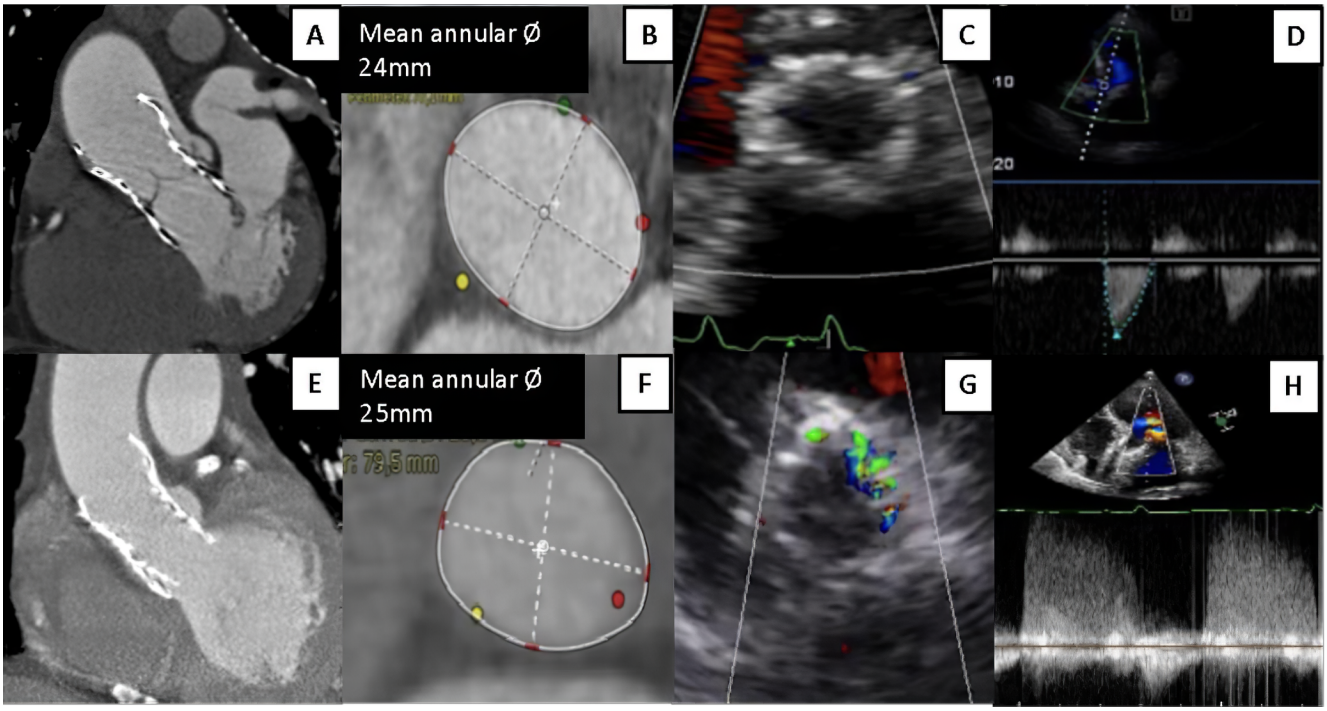

Figure 1. TOP: *Panels A, B, C, D* correspond to a patient without PVL after implantation of an Evolut PRO #29. ***Panel A.*** coronal CT image post TAVR shows mild oversizing with respect to the aortic annulus. ***Panel B.*** oblique transverse CT view showing a mean aortic annular diameter of 24 mm. ***Panel C.*** color Doppler in short axis view at the pre-discharge transthoracic echocardiography with no PVL. ***Panel D.*** Continuous wave Doppler through the aortic valve without any diastolic signal. **BOTTOM:** *Panels E, F, G, H* correspond to a patient with grade II PVL after implantation of a Evolut PRO #29. ***Panel E.*** coronal CT image post TAVR shows that TAVR is not oversized with respect to the aortic annulus. ***Panel F.*** oblique transverse CT view measuring a mean aortic annular diameter of 25 mm. ***Panel G.*** color Doppler in short axis view at the pre-discharge transthoracic echocardiography depicting a color jet around the aortic annulus of grade II PVL. ***Panel H.*** Continuous wave Doppler through the aortic valve with a continuous diastolic signal caused by the PVL.

and LVOT diameter, and baseline aortic regurgitation were not related to the occurrence of significant PVL.

Discussion

This study shows that PVL may still occur after TAVI using the novel CoreValve™ Evolut™ PRO system even when careful sizing, including systematic CT evaluation and technique, is used. In addition, our study demonstrates that the occurrence of mild or grade II PVL is related to a lower degree of oversizing, measured as the disconcordance between prosthesis diameter and mean CT aortic annular diameter (Figure 1). This novel insight may be clinically useful to optimize the implantation of this new device. In the Evolut PRO clinical registry, none to trace PVL was observed in 72.4% of patients while the remaining 27.6% experienced mild PVL at 30 days. There were no patients with moderate or severe PVL [5]. Compared with that study, the only currently available using this valve, our study demonstrated the presence of mild or grade II PVL in 70% of the patients. The different criteria used for PLV assessment (systematic blinded echocardiographic review in our study) and patients characteristics (truly unselected cases in our study) could help to explain this apparently divergent findings.

The presence of significant PVL has been shown to be associated with worse short-term outcomes and increased in-hospital mortality [11]. In fact, the identification of PVL predictors has been widely investigated but with controversial results [12]. Consistent results have been found by other authors with different valve systems. In patients treated with the Edwards

Sapien valve, Detaint et al. reported the occurrence of significant PVL to prosthesis/annulus discongruence [13] and Schultz et al. suggested that improved prosthesis sizing, based on mean annulus diameter on CT, helped to reduce PVL with the Medtronic Corevalve™ [14]. To best of our knowledge, however, this is the first study systematically correlating residual PVL following Evolut™ PRO TAVR with the prosthesis/annulus discongruence. Our findings underscore that appropriate sizing using CT (aiming for mild oversizing) remains critical to avoid residual PVL even with the use of the novel Evolut™ PRO System.

In our experience, the Evolut™ PRO's new design is secure, but it is still associated with a significant incidence of residual mild/grade II PVL, higher than previously reported [4]. Only the prosthesis/annulus discongruence, as measured by CT, was identified as a PVL predictor. Nevertheless, further studies are required to fully define the clinical repercussion of PVL, the clinical utility of assessing prosthesis/annulus discongruence in this setting, and to define other PVL predictors. Because the Evolut™ PRO system is a very new design, only a limited number of patients were included in the present study. Likewise, the potential clinical implications of the degree of PVL detected in our study (mild/grade II) should be established in larger studies.

Conclusion

In conclusion, Evolut™ PRO system remains associated with mild or grade II PVL in a significant number of patients. However, hemodynamically significant PVL was not detected in any patient. The prosthesis/annulus discongruence plays a major role in the occurrence of residual PVL.

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Conflict of Interest

The authors have no conflict of interest relevant to this publication.

Comment on this Article or Ask a Question

References

1. Dhruv M, Islam YE, Anthony AB. From CoreValve to Evolut PRO: Reviewing the Journey of Self-Expanding Transcatheter Aortic Valves. Cardiol Ther. 2017;6:183– 192. DOI: 10.1007/s40119-017-0100-z
2. 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;61:1125–1136. DOI: 10.1016/j.jacc.2012.08.1039
3. Eberhard S, Alexander J, Tommaso G, Stephan VB, Ulrich H, Walter KK, et al. Transcatheter aortic valve implantation with the new-generation Evolut RTM Comparison with CoreValve® in a single-center cohort. IJC Heart & Vasculature. 2016;12:52–56. DOI: 10.1016/j.ijcha.2016.06.002
4. Forrest JK, Mangi AA, Popma JJ, Khabbaz K, Reardon MJ, Kleiman NS, et al. Early Outcomes With the Evolut PRO Repositionable Self-Expanding Transcatheter Aortic Valve With Pericardial Wrap. JACC Cardiovasc Interv. 2018;11:160-168. DOI: 10.1016/j.jcin.2017.10.014
5. Luigi F. M, Wim BV, Ben R, Carl S, Nicolas MV, Osama IS, et al. Prediction of paravalvular leakage after transcatheter aortic valve implantation. Int J Cardiovasc Imaging. 2015;31:1461–1468 DOI: 10.1007/s10554-015-0703-1
6. Leipsic J, Gurvitch R, Labounty TM, Min JK, Wood D, Johnson M, et al. Multidetector computed tomography in transcatheter aortic valve implantation. JACC Cardiovasc Imaging. 2011;4:416-429. DOI: 10.1016/j.jcmg.2011.01.014
7. Delgado V, Ng AC, van de Veire NR, van der Kley F, Schuijf JD, Tops LF, et al. Transcatheter aortic valve implantation: role of multi-detector row computed tomography to evaluate prosthesis positioning and deployment in relation to valve function. Eur Heart J. 2010;31:1114-1123. DOI: 10.1093/eurheartj/ehq018
8. Detaint D, Lepage L, Himbert D, Brochet E, Messika-Zeitoun D, Lung B, et al. Determinants of significant paravalvular regurgitation after transcatheter aortic valve: implantation impact of device and annulus discongruence. JACC Cardiovasc Interv. 2009;2:821-827. DOI: 10.1016/j.jcin.2009.07.003
9. Willson AB, Webb JG, Labounty TM, Achenbach S, Moss R, Wheeler M, et al. 3- dimensional aortic annular assessment by multidetector computed tomography predicts moderate or severe paravalvular regurgitation after transcatheter aortic valve replacement: a multicenter retrospective analysis. J Am Coll Cardiol. 2012;59:1287-1294. DOI: 10.1016/j.jacc.2011.12.015
10. Leon MB, Piazza N, Nikolsky E, Blackstone EH, Cutlip DE, Kappetein AP, et al. Standardized endpoint definitions for transcatheter aortic valve implantation clinical trials: a consensus report from the Valve Academic Research Consortium. Eur Heart J. 2011;32:205-217. DOI: 10.1093/eurheartj/ehq406
11. Abdel-Wahab M, Zahn R, Horack M, Gerckens U, Schuler G, Sievert H, et al. Aortic regurgitation after transcatheter aortic valve implantation: incidence and early outcome. Results from the German transcatheter aortic valve interventions registry. Heart. 2011;97:899-906. DOI: 10.1136/

hrt.2010.217158
12. Schultz CJ, Weustink A, Piazza N, Otten A, Mollet N, Krestin G, et al. Geometry and Degree of Apposition of the CoreValve ReValving System. J Am Coll Cardiol. 2009;54:911-918. DOI: 10.1016/j.jacc.2009.04.075
13. Detaint D, Lepage L, Himbert D, Brochet E, Messika-Zeitoun D, Iung B, et al. Determinants of significant paravalvular regurgitation after transcatheter aortic valve: implantation impact of device and annulus discongruence. JACC Cardiovasc Interv. 2009;2:821-827. DOI: 10.1016/j.jcin.2009.07.003
14. Schultz CJ, Tzikas A, Moelker A, Rossi A, Nuis RJ, Geleijnse MM, et al. Correlates on MSCT of paravalvular aortic regurgitation after transcatheter aortic valve implantation using the Medtronic CoreValve prosthesis. Catheter Cardiovasc Interv. 2011;78:446-455. DOI: 10.1002/ccd.22993

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