International Journal of Cardiology 283 (2019) 73–77

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Intraprocedural valve-in-valve deployment for treatment of aortic regurgitation following transcatheter aortic valve replacement: An individualized approach☆

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ARTICLE INFO

Article history:
Received 2 May 2018
Received in revised form 4 September 2018
Accepted 28 December 2018
Available online 2 January 2019

Keywords:
Transcatheter aortic valve replacement
Valve-in-valve
Paravalvular leak
Aortic regurgitation

ABSTRACT

Background: Aortic regurgitation (AR) following transcatheter aortic valve replacement (TAVR) is usually due to paravalvular leak, is more common with self-expanding valves and is associated with adverse outcomes. Treatment of AR with a second valve (valve-in-valve) has been reported, however the mechanism of benefit is unclear. We hypothesized that location of the initial valve in relation to the aortic annulus should guide positioning of the second valve.

Methods: We assessed the outcomes of valve-in-valve deployment for treatment of AR following implantation of self-expanding valves in a single-center TAVR registry. Location of the initial valves was defined as supra-annular, intra-annular or infra-annular according to the position of the device pericardial skirt relative to the annulus. Positioning of the second valve was selected according to the location of the initial valves.

Results: Among 285 TAVR patients who received Corevalve or Evolut-R valves, 11 (3.8%) underwent valve-in-valve deployment due to AR. Position of initial valves was supra-annular in 6 cases (group-1), intra-annular in 3 cases (group-2) and infra-annular in 2 cases (group-3). In group-1, second valves were implanted 9 ± 4 mm lower than the initial valves. In group-2, second valves were implanted 7 ± 4 mm higher than the initial valves. In group-3, second valves were implanted 9 ± 1 mm higher than the initial valves. Valve-in-valve deployment reduced AR grade in all 3 groups.

Conclusions: Valve-in-valve deployment decreased AR grade during TAVR procedures. We suggest that positioning of the second valve should be guided by the location of the initial valve relative to the aortic annulus.

1. Background

Transcatheter aortic valve replacement (TAVR) is commonly performed in patients with severe symptomatic aortic stenosis. The procedure involves percutaneous implantation of a metallic frame containing the prosthetic valve within the aortic annulus. An impermeable pericardial skirt covers the inflow section of the device in-order to prevent regurgitation of blood from the aortic root to the left ventricle between the frame struts. Aortic regurgitation (AR) following TAVR is demonstrated in up to 70% of cases, is usually due to paravalvular leak (PVL) [1] and is graded as moderate or severe in up to 21% of patients [2]. Paravalvular leak results from incomplete sealing between the skirt segment of the device and the aortic annulus, is more common with self-expanding (SE) valves than with balloon-expandable valves [3] and is associated with adverse patient outcomes and increased mortality [4,5]. Mechanisms of PVL include frame underexpansion due to annular or valvular calcification, device undersizing relative to the annulus and inaccurate placement of the skirt segment of the frame so that it is at a supra-annular (too high) or infra-annular (too low) position, thus precluding apposition between the impermeable skirt and aortic annulus. Various techniques for treatment of AR following TAVR have been reported in non-randomized studies. Treatment options include balloon postdilation to optimize frame expansion, pulling the frame proximally in cases of infra-annular positioning and closure of the orifice between the frame and annulus with a vascular plug. Deployment of a second valve within the initial valve (VIV) has been reported in several case series [6–11] and has been performed in up to 8.5% of the cases [6], however the mechanism of benefit of VIV in this setting has not been described. We hypothesized that positioning of the second valve should be selected according to location of the initial valve in relation to the aortic annulus. The aim of the present study was to describe the procedural and clinical outcomes of such an individualized VIV strategy in a cohort of patients with moderate to severe AR following implantation of SE valves.

☆ The authors have no conflicts of interest to declare. All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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https://doi.org/10.1016/j.ijcard.2018.12.079
0167-5273/

2. Methods

2.1. Study design

All patients with severe symptomatic aortic stenosis who underwent TAVR at the Lady Davis Carmel Medical Center were documented in a prospective institutional registry. Clinical, demographic and procedural variables were recorded. Patients referred for TAVR were assessed by the hospital heart team and underwent cardiac computed tomography angiography (CCTA) to assess the anatomy of the heart, aortic valve, aorta and peripheral vessels. Patients who underwent intraprocedural VIV implantation for treatment of moderate to severe AR following deployment of the initial SE valve were retrospectively identified. Clinical and echocardiographic follow-up was performed at planned visits to the TAVR clinic and via a computerized database (Horizon) which documents all diagnostic and therapeutic procedures that patients undergo. The primary study endpoint was predischarge AR grade assessed by echocardiography. Secondary endpoints were 30-day and 1-year mortality and need for repeat valve interventions. The study was approved by the hospital review board.

2.2. Design of SE valves

The inflow section of Medtronic SE prostheses is cone-shaped and the diameter of the narrow mid-section of the frame is 13–29% smaller than the device inlet, depending on valve type and size. The frames of Corevalve and Evolut-R valves consist of diamond-shaped cells, with an impermeable pericardial skirt attached to the inflow section. The axial length of the lower cell of Corevalve frames is 8 mm and of Evolut-R frames is 10 mm. The height of the pericardial skirt on Corevalve frames is 12 mm, on Evolut-R valves sizes 23 & 26 mm is 13 mm and on Evolut-R valves sizes 29 & 34 mm is 14 mm (Fig. 1A). The recommended implantation depth below the aortic annulus is 4–8 mm for Corevalve and 3–5 mm for Evolut-R.

2.3. Procedural details

TAVR procedures were performed under general anesthesia. The majority of cases (95%) were performed via transfemoral vascular access. Patients received pre- and postprocedural dual antiplatelet therapy with aspirin and clopidogrel. During the TAVR procedure patients received unfractionated heparin (70 U/kg) and the activated clotting time was maintained above 250 s. Selection of valve type and size was based on CCTA measurements of the aortic annulus and root. Sizing of SE valves was based on the measurement of the perimeter of the aortic annulus. Balloon predilation of the aortic valve was performed at the discretion of the operators when the valvular and annular calcification demonstrated on CCTA and fluoroscopy were considered to be severe.

The valves were deployed under fluoroscopic control following delineation of the aortic annular plane by injection of contrast media into the aortic root. The annular plane was defined as the line connecting the nadir of the 3 coronary sinuses. Deployment of SE valves was based on fluoroscopic analysis of the perpendicular distance from the annular plane to the lower edge of the prosthesis frame, using the axial length of the distal cell of the specific valve as a reference. Infra-annular deployment was determined when the distance from the device inlet to the annular plane was longer than the skirt height (≥12 mm for Corevalve, ≥13 mm for Evolut-R sizes 23 and 26 mm and ≥14 mm for Evolut-R sizes 23 and 26 mm). Supra-annular deployment was determined when the device inlet was located above the annular plane. Intraprocedural assessment of AR grade was based on aortography with injection of 20 ml contrast media into the aortic root and assessment of left ventricular filling [12]. Predischarge assessment of AR grade was performed by echocardiography [13,14].

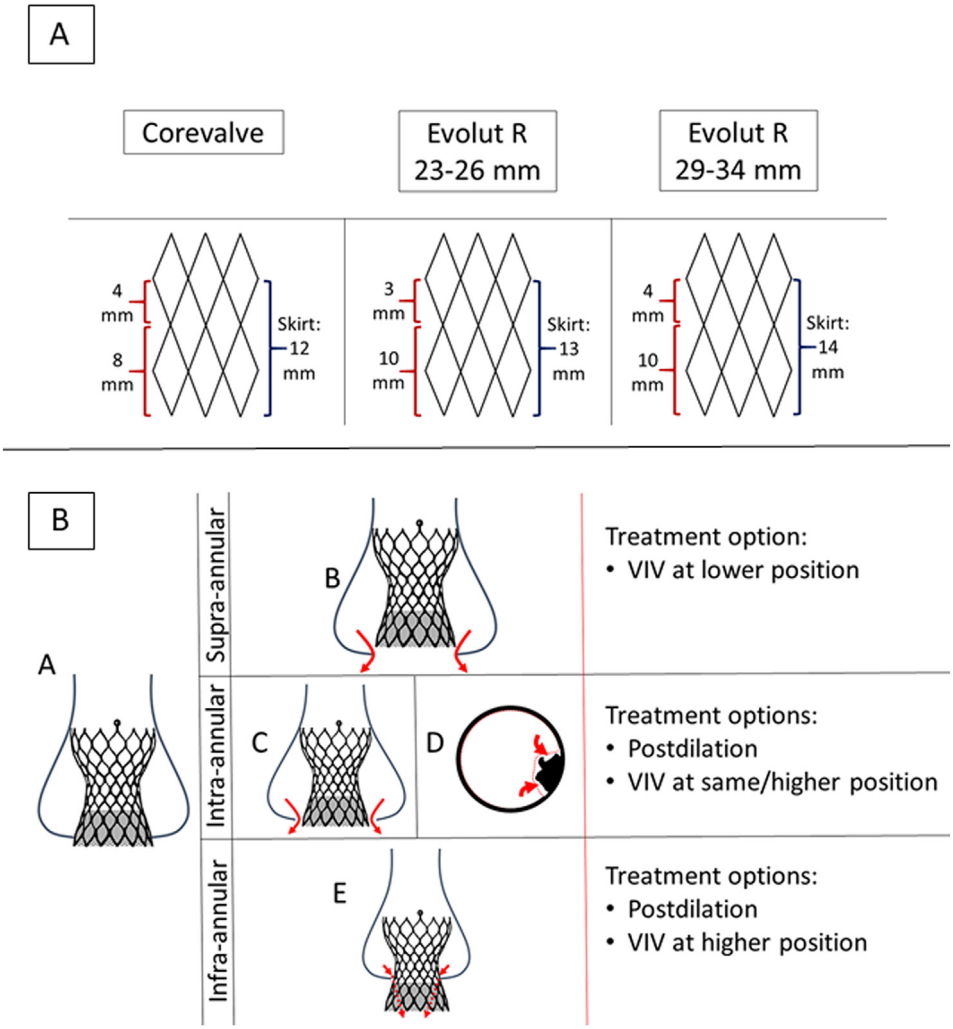

Fig. 1. A) Design of Corevalve and Evolut-R self-expanding valves. The axial length of the lowest cell within the device frame and the height of the impermeable pericardial skirt attached to the inlet of the prosthesis vary between different devices and device sizes. B) Mechanisms of paravalvular leak according to site of valve deployment in relation to the aortic annulus and potential treatment strategies. A: Correct positioning of the prosthesis (4–8 mm below the annulus for Corevalve and 3–5 mm below the annulus for Evolut-R). B: Supra-annular positioning. C: Intra-annular positioning of an undersized prosthesis. D: Incomplete expansion of an intra-annular device due to calcification (cross-sectional view). E: Infra-annular device with location of the whole skirt segment below the annular plane. (VIV = valve-in-valve implantation).

2.4. Intraprocedural treatment of AR

Treatment of moderate to severe AR following valve implantation was selected according to the presumed mechanism. Valve postdilation was the default approach when the initial valve was located at an intra-annular position, in-order to optimize apposition of the skirt segment of the device frame to the annulus. Decision to perform VIV implantation was made when AR grade was not reduced to ≤2 following balloon postdilation of the initial valve, or when postdilation was not considered to be likely to reduce the AR grade. The size of the second valve was the same as that of the initial valve. Position of the second valve was selected according to location of the initial valve. If the initial valve was at a supra-annular location, the second valve was deployed at an intra-annular position. If the initial valve was at an intra-annular location, the second valve was deployed at a slightly higher intra-annular position. If the initial valve was at an infra-annular location, the second valve was deployed at an intra-annular position.

3. Results

Among 388 patients who underwent TAVR at our medical center between March 2010 and October 2017, 285 (73%) received SE valves (Corevalve or Evolut-R, Medtronic, Minneapolis, USA). Eleven patients (3.8%) with moderate to severe AR following deployment of a SE valve underwent VIV implantation. Three additional patients in whom SE valves embolized to the ascending aorta without development of AR, who were treated by implantation of additional distal overlapping valves within the aortic annulus, were not included in the current analysis. Patient demographic and clinical characteristics are detailed in Table 1 and procedural details are detailed in Table 2. All patients had tricuspid native aortic valves and the valve calcium score measured by CT was 4989 ± 2044 HU (Range: 2690–9487). Ten patients (91%) underwent the procedure via transfemoral vascular access and the remaining patient underwent the procedure via subclavian access. The initial valve types implanted were Corevalve in 5 patients (45%) and Evolut-R in the remaining 6 patients (55%).

Within the VIV cohort, balloon predilation prior to implantation of the initial valves was performed in 6 cases, postdilation prior to VIV implantation was performed in 10 cases and postdilation following VIV implantation was performed in 3 patients. All 6 cases of supra-annular position of the initial valve resulted from valve migration following postdilation of a prosthesis which was initially located at an intra-annular position. Postdilation of the initial valve was omitted in a single patient (patient #10) in whom the whole skirt segment of the frame was located at an infra-annular position. Postdilation was performed in the other patient with infra-annular position of the first valve (patient #11) since the correct location of the device was not initially recognized. Mean AR grade prior to VIV was 3.6 ± 0.5. The second valves implanted were of the same size and type as the initial ones except for one case (Case #8), in whom an Evolut-R valve size 29 mm was initially deployed and the second valve was a 31 mm Corevalve due to unavailability of another valve of the same size.

The patients who underwent VIV were categorized into 3 groups according to location of the initial prosthesis in relation to the aortic annulus (Fig. 1B). The initial valves were supra-annular in 6 cases (group-1), intra-annular in 3 cases (group-2) and infra-annular in 2 cases (group-3). Valve-in-valve positioning is detailed in Fig. 2A and illustrative angiographic images are presented in Fig. 1-supplementary data. In Group-1, the initial valves were deployed at an intra-annular location but migrated to a supra-annular location ranging 1–4 mm above the annular plane following balloon postdilation. These cases were treated by implantation of second valves at an intra-annular position in-order to achieve annular sealing, with the inlet of the second valves located 4–13 mm below the annular plane and 9 ± 4 mm lower than the initial valves. In Group-2, the initial valves were deployed 2–9 mm below the annular plane. In these cases, AR was attributed to incomplete device expansion and lack of apposition of the skirt segments of the frames to the annulus or to device undersizing relative to the annulus. In these patients the second valves were deployed 0–2 mm above the annular plane and 7 ± 4 mm higher than the initial valves, in-order to increase the radial force of the prosthesis and to optimize frame expansion. In Group-3, the inlet of the initial valves was located 14–16 mm below the annular plane. In these cases, AR was attributed to location of the upper edge of the impermeable skirt below the annular level thus permitting blood flow from the aortic root to the left ventricle between the uncovered frame struts. In these patients the second valves were deployed 4–8 mm below the annulus and 9 ± 1 mm higher than the initial valves, in-order to create continuous annular sealing and to increase the radial force of the prosthesis.

Valve-in-valve implantation reduced degree of AR in all cases (Fig. 2B). Final aortography at the end of the procedure demonstrated grade 1.5 ± 0.8 AR, and predischarge echocardiography demonstrated grade 0.4 ± 0.7 AR. Preprocedural grade of mitral regurgitation was 0.6 ± 0.8 and decreased to 0.5 ± 0.8 on predischarge echocardiography. During 613 ± 697 (range: 28–2251) days of follow-up no patients died or required repeat valve interventions. Five (45%) patients required implantation of permanent pacemakers and a single patient was readmitted for treatment of heart failure.

4. Discussion

In a cohort of patients who underwent TAVR with deployment of SE valves, VIV implantation was used for treatment of moderate to severe AR in 11 patients and reduced degree of AR in all cases.

Our VIV treatment protocol mandated positioning of the second valves according to location of the initial valves relative to the annular plane and was based on hypothesized mechanisms of benefit of VIV in different settings of PVL. When the position of the initial valves was supra-annular, PVL resulted from the presence of a gap between the device inlet and the aortic annulus. In this setting, implantation of second valves below the annular plane was designed to achieve annular sealing. When the initial valves were implanted at an intra-annular location, PVL may have resulted from either frame underexpansion

Table 1
Demographic and clinical patient characteristics.

Group	Age (yrs)	Height (cm)	Weight (kg)	Gender	STS score	Log euroscore-2 score	Diabetes	HTN	GFR (ml/min)	Mean AV gradient	AVA (Cm^2)	EF (%)	Annulus perimeter (mm)	AV Ca score (HU)
1	95	170	65	Male	12.8	10.9	No	Yes	35	64	0.90	33	81	3326
1	75	167	59	Male	3.0	4.8	No	Yes	43	56	0.30	18	94	7294
1	78	169	76	Male	1.2	2.1	No	Yes	83	59	0.86	60	83	5442
1	78	160	63	Male	4.8	4.1	Yes	Yes	63	80	0.70	45	77	5792
1	89	178	81	Male	9.3	9.3	No	No	46	31	0.97	40	81	3008
1	81	67	159	Female	4.7	12.6	No	No	63	51	0.69	60	76	2690
2	86	168	68	Male	5.1	1.7	No	Yes	57	46	0.88	55	90	5456
2	89	168	63	Male	4.1	4.4	No	Yes	43	73	0.89	65	84	9487
2	89	178	80	Male	4.4	5.4	No	No	65	40	0.99	32	98	4898
3	83	168	74	Male	10.7	14.8	Yes	Yes	35	33	0.84	34	82	3925
3	80	180	80	Male	2.8	4.5	No	Yes	72	41	0.83	60	79	3556

STS = society of thoracic surgeons; HTN = hypertension; GFR = glomerular filtration rate; AV = aortic valve; AVA = aortic valve area; EF = ejection fraction; HU = Hounsfield units.

Table 2
Procedural details.

Group	Vascular access	Valve type	Pre-dilation (mm)	1st valve (mm)	1st valve location[a] (mm)	Post-dilation (mm)	AR after 1st valve	2nd valve (mm)	2nd valve location[a] (mm)	2nd post-dilation (mm)	Final AR (angio)	Final AR (echo)
1	Femoral	Evolut R	–	29	4	24	3	29	4	–	2	0
1	Femoral	Corevalve	22	31	2	29	3	31	4	–	2	2
1	Femoral	Evolut R	22	34	2	28	4	34	4	–	1	0
1	Subclavian	Corevalve	20	29	2	23	4	29	13	–	2	0
1	Femoral	Evolut R	–	34	1	26	4	34	6	28	1	0
1	Femoral	Evolut R	–	29	1	24	3	29	10	26	1	1
2	Femoral	Corevalve	24	31	-2	28	4	31	0	30	3	0
2	Femoral	Evolut R	22	29	−8	26	3	31	−2	–	2	1
2	Femoral	Corevalve	–	31	−9	28	4	31	0	–	2	0
3	Femoral	Corevalve	23	29	−14	–	4	29	4	–	1	0
3	Femoral	Evolut R	–	29	−16	24	4	29	8	–	0	0

AR = aortic regurgitation; angio = angiography; echo = echocardiography.
[a] Location of valve inlet relative to annular plane, negative numbers indicate infra-annular location of device.

due to the presence of annular calcific spicules or from valve undersizing. In this setting, implantation of second valves at the same level of the initial valves or slightly higher was intended to increase the radial force exerted by the frame and achieve annular sealing. When the initial valves were implanted at an infra-annular position, PVL was due to location of the whole skirt segment below the annulus.

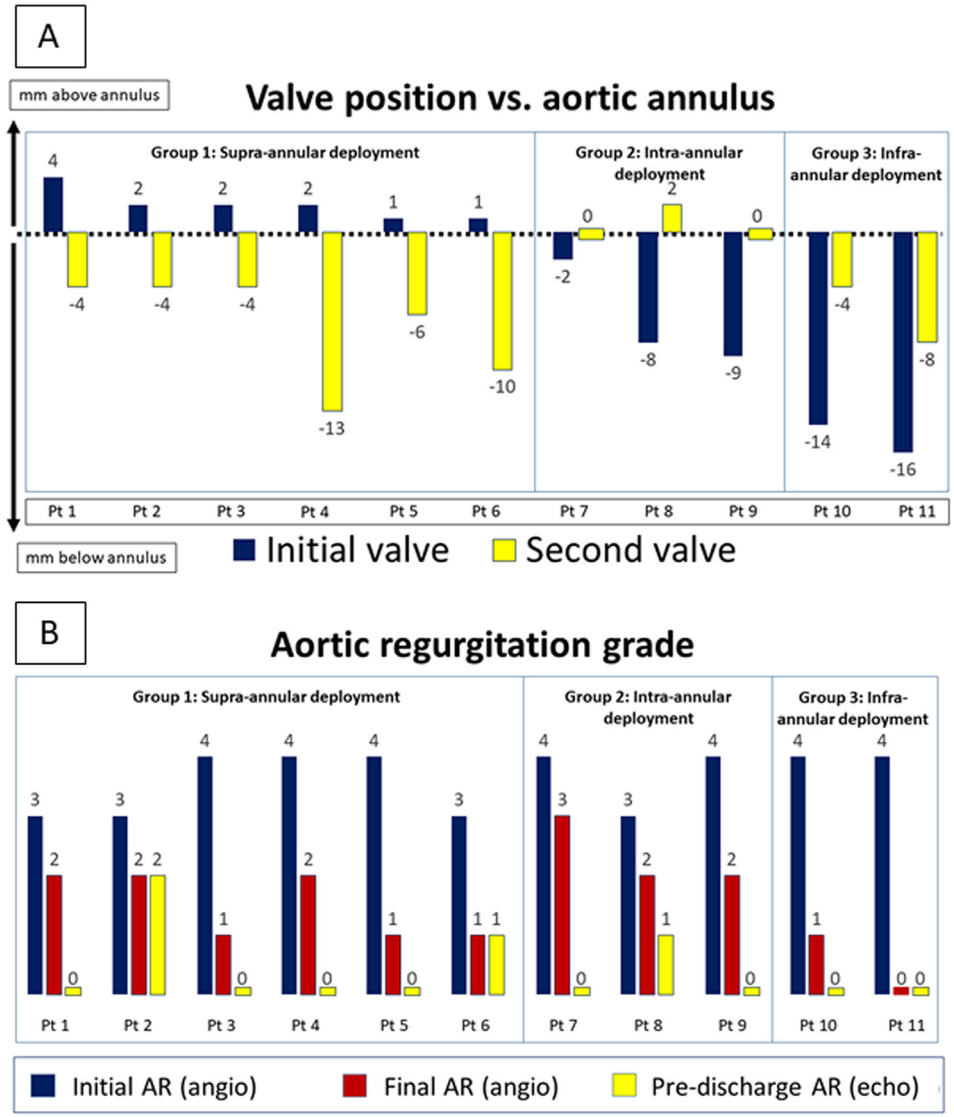

Fig. 2. A) Site of deployment of initial and second valves in relation to the aortic annulus. Supra-annular deployment was defined as location of the device inlet above the aortic annulus. Infra-annular deployment was defined as presence of the whole skirt segment of the device frame below the aortic annulus. B) Degree of aortic regurgitation (AR) following initial valve deployment and following second valve deployment (by aortography) and prior to discharge (by echocardiography).

Higher placement of the second valves was aimed at increasing the expansion of the upper segment of the frame located within the annulus and creating a continuous overlapping impermeable skirt segment extending to the annulus.

The VIV technique for treatment of PVL was described by Piazza et al. in a cohort of 5 patients [6] and was subsequently reported in several cohorts of patients who underwent TAVR with implantation of Corevalve prostheses (Table 1-supplementary data). Different definitions of "high" and "low" deployment have been used. Piazza et al. defined high implantation when the device inlet was placed above the annular plane and low implantation when the whole skirt segment was located within the left ventricle >12 mm below the annular plane [6]. In a more recent study, low implantation was defined as implantation of the device flow >6 mm below the annular plane [11]. Napodano et al. defined high and low implantations when the device inlet was located <4 mm and >12 mm below the annular plane, respectively [10]. Our study is the first to report use of VIV following implantation of Evolut-R devices. For the purpose of the present study, device deployment was categorized according to the relationship between the skirt segment and the annular plane, and low implantation was defined specifically for each device according to the length of the skirt segment. Several angiographic methods for determination of depth of device deployment in relation to the aortic annulus have been reported. Piazza et al. measured implantation depth separately from the right coronary or noncoronary leaflet and from the left coronary leaflet to the ventricular end of the prosthesis [6]. Koifman et al. measured the distance from the noncoronary cusp to the base of the device [11]. Napodano et al. used quantitative angiographic digital techniques to measure the distance between the annulus and device inlet [10]. In the present study we used aortography to align the nadir of the three coronary sinuses along a line representing the annular plane, and then measured the perpendicular distance from this plane to the device inlet using the axial length of the lowest cell of the device frame as a reference.

The study has several important limitations. Like previous studies of this topic, this is a single-center analysis of a small cohort of patients undergoing intraprocedural VIV with SE valves, however VIV implantation for treatment of severe AR following TAVR is rarely used and larger studies are unlikely to be conducted. Since intraprocedural echocardiography was not performed, it was not possible to verify the specific mechanism of regurgitation or to confirm that AR was due to paravalvular and not valvular leak, however occurrence of AR following TAVR is acknowledged to be due to PVL in most cases. These limitations are characteristic of studies of this topic (summarized in Table 1-supplementary data). Due to the small sample size, no attempt was made to identify predictors of AR following SE valve implantation or to compare outcomes of patients undergoing VIV to those of the rest of the TAVR cohort. The VIV technique for treating AR following TAVR entails various potential hazards such as creation of flow disturbance and thrombogenicity which may impact long-term outcomes, however no adverse effects were documented in the present study. As all techniques for treating AR following TAVR have been reported in non-randomized case-series, the aim of the present study was not to compare the utility of VIV to other approaches such as snaring the valve or use of vascular plugs, but to suggest a conceptual framework for use of this strategy.

In conclusion, intraprocedural VIV implantation is an effective strategy for treatment of AR following TAVR with deployment of SE valves. We suggest that positioning of the second valves should be individualized according to the location of the initial valves in relation to the annular plane. The continuing requirement to perform VIV for treatment of AR in the era of repositionable Evolut-R valves suggests an unmet need for more predictable valve deployment.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2018.12.079.

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