Anatomical and Procedural Features Associated With Aortic Root Rupture During Balloon-Expandable Transcatheter Aortic Valve Replacement

Marco Barbanti, MD; Tae-Hyun Yang, MD, Josep Rodès Cabau, MD; Corrado Tamburino, MD; David A. Wood, MD; Hasan Jilaihawi, MD; Phillip Blanke, MD; Raj R. Makkar, MD; Azeem Latib, MD; Antonio Colombo, MD; Giuseppe Tarantini, MD; Rekha Raju, MD; Ronald K. Binder, MD; Giang Nguyen, MD; Melanie Freeman, MD; Henrique B. Ribeiro, MD; Samir Kapadia, MD; James Min, MD; Gudrun Feuchtner, MD; Ronen Gurtvich, MD; Faisal Alqoofi, MD; Marc Pelletier, MD; Gian Paolo Ussia, MD; Massimo Napodano, MD; Fabio Sandoli de Brito, Jr, MD; Susheel Kodali, MD; Bjarne L. Norgaard, MD; Nicolaj C. Hansson, MD; Gregor Pache, MD; Sergio J. Canovas, MD; Hongbin Zhang, PhD; Martin B. Leon, MD; John G. Webb, MD; Jonathon Leipsic, MD

Background**—**Aortic root rupture is a major concern with balloon-expandable transcatheter aortic valve replacement (TAVR). We sought to identify predictors of aortic root rupture during balloon-expandable TAVR by using multidetector computed tomography.

Methods and Results**—**Thirty-one consecutive patients who experienced left ventricular outflow tract (LVOT)/annular/aortic contained/noncontained rupture during TAVR were collected from 16 centers. A caliper-matched sample of 31 consecutive patients without annular rupture, who underwent pre-TAVR multidetector computed tomography served as a control group. Multidetector computed tomography assessment included short- and long-axis diameters and cross-sectional area of the sinotubular junction, annulus, and LVOT, and the presence, location, and extent of calcification of the LVOT, as well. There were no significant differences between the 2 groups in any preoperative clinical and echocardiographic variables. Aortic root rupture was identified in 20 patients and periaortic hematoma in 11. Patients with root rupture had a higher degree of subannular/LVOT calcification quantified by the Agatston score (181.2±211.0 versus 22.5±37.6, *P*<0.001), and a higher frequency of ≥20% annular area oversizing (79.4% versus 29.0%, *P*<0.001) and balloon postdilatation (22.6% versus 0.0%, *P*=0.005). In conditional logistic regression analysis for the matched data, moderate/severe LVOT/subannular calcifications (odds ratio, 10.92; 95% confidence interval, 3.23–36.91; *P*<0.001) and prosthesis oversizing ≥20% (odds ratio, 8.38; 95% confidence interval, 2.67–26.33; *P*<0.001) were associated with aortic root contained/noncontained rupture.

Conclusions**—**This study demonstrates that LVOT calcification and aggressive annular area oversizing are associated with an increased risk of aortic root rupture during TAVR with balloon-expandable prostheses. Larger studies are warranted to confirm these findings. **(*Circulation*. 2013;128:244-253.)**

Key Words: annular calcification ■ annular rupture ■ multidetector computed tomography ■ transcatheter heart valves

Transcatheter aortic valve replacement (TAVR) is now considered an effective treatment for patients with severe aortic stenosis at high risk for conventional surgical aortic valve replacement.[1,2] Although TAVR has been shown to be an effective therapy, limitations do remain. Recently, 3-dimensional multidetector computed tomography (MDCT) measurements have been shown to provide a deeper understanding of aortic annular geometry and allow for prediction

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From St Paul's Hospital, Vancouver, Canada (M.B., T.-H.Y., D.A.W., R.R., R.K.B., G.N.,M.F., H.Z., J.G.W., J.L.); Ferrarotto Hospital, University of Catania, Italy (M.B., C.T.); Busan Paik Hospital, Inje University, South Korea (T.-H.Y.); Quebec Heart & Lung Institute, Laval University, Quebec City, Canada (J.R.C., H.B.R., J.M.); Cedars-Sinai Heart Institute, Los Angeles, CA (H.J., R.R.M.); University Hospital Freiburg, Germany (P.B., G.P.); EMO-GVM Centro Cuore Columbus and San Raffaele Scientific Institute, Milan, Italy (A.L., A.C., M.N.); University of Padua, Padua, Italy (G.T.); Cleveland Clinic, Cleveland, OH (S.K.); Innsbruck Medical University, Innsbruck, Austria (G.F.); The Royal Melbourne Hospital, Melbourne, Australia (R.G.); University of Calgary, Calgary, Canada (FA.); New Brunswick Heart Centre, Saint John, Canada (M.P.); Department of Cardiovascular Disease, Tor Vergata University of Rome, Italy (G.P.U.); Hospital Israelita Albert Einstein Sao Paulo, Brazil (F.S.d.B.); Columbia University Medical Center/New York-Presbyterian Hospital, New York, NY (S.K., M.B.L.); Skejby Hospital, Aarhus University, Aarhus, Denmark (B.L.N., N.C.H.); and University General Hospital of Valencia, Valencia, Spain (S.J.C.).

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Correspondence to Jonathon Leipsic, MD, St. Paul's Hospital, 1081 Burrard St, V6Z 1Y6, Vancouver, BC, Canada. E-mail jleipsic@providencehealth.bc.ca

of paravalvular regurgitation, which is considered a significant complication of TAVR.[3,4] Rupture of the aortic root or annulus remains a major concern, particularly with balloon-expandable prostheses.[5,6] Recently, it has been suggested that contained rupture of the aortic root, as evidenced by echocardiographic findings of periaortic hematoma, is associated with aggressive balloon-expandable transcatheter heart valve (THV) oversizing.[7] Previous reports, however, have been limited in their ability to identify predictors of annular/aortic root rupture owing to their small cohort size and single-center design.[6] The aim of this multicenter international collaboration was to determine whether anatomic features identifiable on MDCT could help determine the predictors of aortic root rupture during balloon-expandable TAVR.

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Methods

Study Population

Thirty-seven consecutive patients with left ventricular outflow tract (LVOT)/annular/aortic root rupture complicating balloon-expandable TAVR were collected from 16 centers across Canada, Italy, Austria, Australia, Brazil, Spain, Germany, Sweden, Denmark and the United States. Edwards SAPIEN and SAPIEN XT THVs (Edwards Lifesciences, Irvine, CA) were implanted by using standard techniques.[8–12] Preliminary analysis was performed on an historical cohort of 150 consecutive TAVR patients without aortic root rupture who underwent preprocedure MDCT at 1 center (St Paul's Hospital, Vancouver, BC, Canada) to identify a comparable group. A caliper-matched sample of 62 patients (31 patients for each group) with similar baseline characteristics was obtained. During the time frame for case gathering, the total number of TAVR procedures performed by using balloon-expandable THV in all centers involved was 3067. The noncontained aortic root rupture rate was 0.9% (n=30). Ten patients with noncontained aortic root rupture were excluded from this study because MDCT was not available (n=7) or because of the matching process (n=3) (Table I in the online-only Data Supplement).

MDCT Protocol and Measurements

MDCT examinations were performed on either a 64-slice Discovery HD 750 high-definition or volume computed tomography scanner (GE Healthcare, Milwaukee, WI), a Siemens first- or second-generation Dual-Source scanner (Siemens Healthcare, Erlangen, Germany), or a Toshiba Aquilion One 320 row scanner (Toshiba Medical Systems, Tokyo, Japan). Multiple CT scan protocols were used as per site specific practice. All scans were performed with ECG gating. Heart rate reduction with β-blockade was not performed because interpretation of the coronary arteries was not required and ß-blockade might be a potential risk in patients with severe aortic stenosis.

MDCT Image Analysis

All MDCT examinations were evaluated by 2 cardiac CT readers (J.L. and T.H.Y.). The data sets were reconstructed to achieve a double-oblique transverse reconstruction at the level of the virtual basal ring (aortic annulus) in a fashion described previously.[13] In addition, multiplanar reconstructions of the LVOT and ascending aorta were reconstructed. The LVOT/subannular and ascending aortic dimensions (short axis, long axis, and area) were also taken by using double-oblique transverse reformats of these structures. The height from the insertion of the aortic valve cusps to the ostia of the coronary arteries and to the sinotubular junction was also measured.[13] Aortic annular eccentricity was calculated as: 1 – short diameter/long diameter.[3] Aortic valve calcification was graded semiquantitatively as follows: grade 1, no calcification; grade 2, mildly calcified (small isolated spots); grade 3, moderately calcified (multiple larger spots); and grade 4, heavily calcified (extensive calcifications of all cusps).[14] The LVOT was separately analyzed for the presence, amount, and location of calcification. If present, the distribution of calcification and extent was also assessed in a semiquantitative fashion as follows: mild, 1 nodule of calcium extending <5 mm in any dimension and covering <10% of the perimeter of the LVOT; moderate, 2 nodules of calcification or 1 extending >5 mm in any direction or covering >10% of the perimeter of the LVOT; severe, multiple nodules of calcification of single focus extending >1 cm in length or covering >20% of the

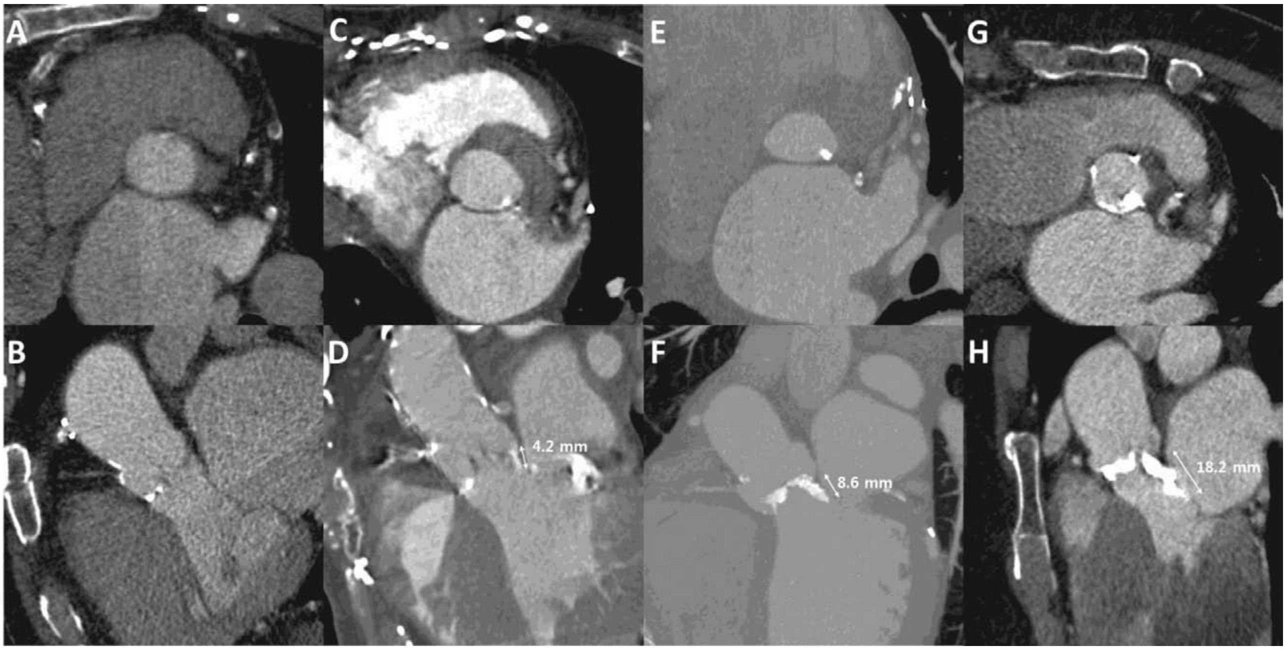

Figure 1. MDCT reconstruction of the LVOTs in 4 different patients undergoing evaluation pre-TAVR in double-oblique transverse (**A**, **C**, **E**, and **G**) and coronal (**B**, **D**, **F**, and **H**) projections displaying varying degrees of LVOT calcification: **A**, **B**, none; **C**, **D**, mild; **E**, **F**, moderate; and **G**, **H**, severe. LVOT indicates left ventricular outflow tract; MDCT, multidetector computed tomography; and TAVR, transcatheter aortic valve replacement.

perimeter of the LVOT (Figure 1). Formal LVOT calcification scoring was also performed by using an Hounsfield units threshold of 800 to allow for determination of an Agatston score for the calcification in the LVOT on a contrast-enhanced computed tomography angiography as described by Ewe et al.[15] Finally, the location of LVOT calcification, when present, in relation to the 3 aortic cusps/sinuses was determined. All image data were analyzed offline on a 3-D workstation (AW 4.4, GE Healthcare, Waukasha, WI).

Difference Between THV Size and Annular Size

The difference between the nominal THV size and MDCT annular dimensions was assessed by multiple means. The THVs used in this cohort had a nominal external diameter of 23, 26, and 29 mm, as reported by the manufacturer. When fully expanded, these prostheses would be expected to have an area of 4.15 cm^2, 5.31 cm^2, and 6.61cm^2; and a circumference of 72.3 mm, 81.7 mm, and 91.1 mm, respectively. These values are derived from the formulae of a circle where area=π×$radius^2$ and circumference=π×diameter.

Comparing the nominal THV area with the preprocedural MDCT-measured annular dimensions allows evaluation of the degree of over- or undersizing. A THV was deemed oversized when the nominal THV area was greater than the MDCT annular area. The percentage of oversizing (positive value) or undersizing (negative value) was calculated by using the formulae (THV area/annular area − 1)×100 and (THV circumference/annular circumference − 1)×100. The eccentricity index of the aortic annulus was calculated as 1 − short diameter/long diameter.

Statistical Analyses

In preliminary analysis, continuous variables with normal and skewed distribution are presented as means±standard deviation. Categorical variables are presented as frequency and group percentage. The Student *t* test and the Fisher exact test were used for comparison of normally distributed continuous and categorical variables, respectively. Median and interquartile range were given for skewed variables, and paired *t* test–based testing was used. For binary variable, conditional logistic regression was used. Caliper-matched analysis was conducted where random 1-to-1 matching data sets were constructed on selected confounders that include sex, baseline aortic valve area, baseline mean transaortic gradient, and annular area on CT. For sex, perfect matching was used; for other variables, close-distance matching was used where 1 U of standard deviation of the matching variable was used. Conditional logistic regression was used on the matched data to assess study variables' association with the root rupture outcome. All tests were 2-tailed and a probability value ≤0.05 was considered statistically significant. All statistical analyses were performed by using SPSS 18.0 (IBM SPSS Statistics, IBM Corp.) software.

Results

Clinical, demographic and echocardiographic characteristics are summarized in Table 1. The median age of the entire cohort was 83.1 (interquartile range, 80–88) years and 74% of patients were women. There were no significant differences between the 2 groups in any preoperative clinical and echocardiographic variables, indicating the effectiveness of the matching. Diagnosis of aortic root rupture/hematoma was most frequently made by angiography and transesophageal echocardiogram (32.3%), transesophageal echocardiogram alone (29.0%), and MDCT (22.6%); less commonly it was made during urgent open-chest surgery (9.7%), with angiography alone (3.2%), or postmortem on autopsy (3.2%).

MDCT Data

MDCT measurements of the aortic root structures are listed in the Table 2. Patients with aortic root rupture had a higher burden of LVOT/ subannular calcification (calcium score, 181.2±211.0 versus 22.5±37.6, P<0.001), whereas no difference in the rate of moderate/severe aortic cusp calcification was noted (83.9% versus 87.1%, P=0.892). When present, localization of LVOT calcification below the left coronary cusp (69.6% versus 66.7%, P=0.563) and the noncoronary cusp (60.9% versus 46.7%, P=0.389) was not significantly different between groups; LVOT calcification localized below the right coronary cusp was present only in patients experiencing annular rupture (30.4% versus 0.0%, P=0.019). The 2 groups had similar annular sizes with measurements of the basal ring area (3.93±0.90 cm^2 versus 4.11±0.80 cm^2, P=0.108), as well as maximum (24.7±2.9 mm versus 25.4±2.6 mm, P=0.075), minimum (19.4±2.2 mm versus 19.6±2.2 mm, P=0.380) and

Table 1. Baseline Characteristics

	Overall (n=62)	Study Group (n=31)	Control Group (n=31)	*P* Value
Clinical variables				
Age, y, median (IQR)	83.1 (80–88)	83 (80.5–87)	83.2 (79.3–89.8)	0.970
Female sex, n (%)	46 (74.2)	23 (74.2)	23 (74.2)	1.000
Previous myocardial infarction, n (%)	8 (12.9)	5 (16.1)	3 (9.7)	0.484
Previous PCI, n (%)	16 (25.8)	9 (29.0)	7 (22.6)	0.594
COPD, n (%)	18 (29.0)	8 (25.8)	10 (32.3)	0.484
Porcelain aorta, n (%)	9 (14.5)	4 (12.9)	5 (16.1)	0.706
STS score, %, median (IQR)	7.5 (4.9–9.1)	7.8 (4.9–8.9)	7.5 (5.5–9.2)	0.433
Echocardiographic variables				
Mean transaortic gradient, mm Hg	49.4±14.6	51.1±13.8	47.7±15.4	0.375
Aortic valve area, cm^2	0.6±0.2	0.6±0.2	0.6±0.2	0.848
Left ventricular ejection fraction, %, median (IQR)	60 (55–65)	58 (52.5–62.5)	65 (60–65)	0.051

Female sex, mean transaortic gradient, and aortic valve area are matching variables. COPD indicates chronic obstructive pulmonary disease; IQR, interquartile range; PCI, percutaneous coronary intervention; and STS, Society of Thoracic Surgery.

mean (22.0±2.4 mm versus 22.5±2.3 mm, P=0.411) diameters. Similarly, the 2 groups had comparable sinus of Valsalva maximum (median 30.5, interquartile range [28.3–32] versus 29.1 [27.2–32.6] mm, P=0.579) and minimum (median 29, interquartile range [24.9–30.9] versus 27.4 [26.4,30.4], P=0.866) diameters, and LVOT area (3.88±0.97 cm^2 versus 4.26±0.88 cm^2, P=0.085). Both groups showed similar annular eccentricity (eccentricity index: 21.3±6.4 versus 22.9±5.4, P=0. 328).

Procedural Data and In-Hospital Outcomes

Patients who experienced aortic root rupture (Figure 2) had a greater degree of area-based prosthesis oversizing (30.5±15.8% versus 11.3±19.7%, P<0.001) and higher frequency of postdilatation (22.6% versus 0.0%, P=0.005). Postdilatation was performed with a balloon identical in diameter to the THV deployment balloon in 5 cases, and balloons 1 mm and 2 mm bigger in the remaining 2 cases (Table 3). Aortic root and sizing characteristics, procedural variables, and outcomes of patients with aortic root rupture and periaortic hematoma are listed in Table 4. Among these patients, the site of rupture was the annulus in 21 (67.7%), sinus of Valsalva in 5 (16.1%), LVOT in 3 (9.7%), and sinotubular junction in 2 (6.4%). Root injury was represented by an uncontained rupture in 20 cases (64.5%) and by a contained periaortic rupture/hematoma in 11 cases (35.5%). Patients with rupture were more likely to undergo conversion to surgery (38.7% versus 0.0%, P<0.001). Aortic root rupture was associated with marked increases in mortality, stroke, and bleeding (Table 5). Table 6 reports in-hospital outcomes in the study group, divided according to the occurrence of uncontained and contained rupture.

Predictors of Aortic Root Rupture

In conditional logistic regression analysis for the matched data, moderate/severe LVOT/subannular calcifications (odds ratio, 10.92; 95% confidence interval, 3.23–36.91; P<0.001) and prosthesis oversizing ≥20% (odds ratio, 8.38; 95% confidence interval, 2.67–26.33; P=<0.001) were associated with aortic root contained/noncontained rupture.

Table 2. MDCT Aortic Root Characteristics

	Overall (n=62)	Study Group (n=31)	Control Group (n=31)	P Value
Aortic annulus				
Max diameter, mm	25.1±2.8	24.7±2.9	25.4±2.6	0.075
Minimum diameter, mm	19.5±2.2	19.4±2.2	19.6±2.2	0.380
Mean diameter, mm	22.3±2.3	22.0±2.4	22.5±2.3	0.411
Area*, cm^2	4.02±0.85	3.93±0.90	4.11±0.80	0.108
Eccentricity index, n	22.1±5.9	21.3±6.4	22.9±5.4	0.328
Left ventricular outflow tract				
Area, cm^2	4.07±0.93	3.88±0.97	4.26±0.88	0.085
Calcification, n (%)	38 (61.3)	23 (74.2)	15 (48.4)	0.046
Degree of calcification, n (%)				
None	25 (40.3)	8 (25.8)	17 (54.8)	<0.001
Mild	11 (17.7)	2 (6.5)	9 (29.0)	
Moderate	18 (29.0)	13 (41.9)	5 (16.1)	
Severe	8 (12.9)	8 (25.8)	0 (0.0)	
Calcium score, n, median (IQR)	20 (0–118)	105.5 (5–243.2)	0 (0–28)	<0.001
Aortic root				
SV max diameter, mm, median (IQR)	29.8 (27.4–32)	30.5 (28.3–32)	29.1 (27.2–32.6)	0.579
SV minimum diameter, mm, median (IQR)	28.6 (26.3–30.8)	29 (24.9–30.9)	27.4 (26.4–30.4)	0.866
STJ max diameter, mm	27.1±3.6	27.4±4.0	26.9±3.2	0.462
STJ minimum diameter, mm	26.4±3.5	26.5±3.8	26.3±3.3	0.724
STJ height, mm	16.7±2.1	17.2±1.9	16.2±2.1	0.098
STJ/aortic annulus max diameter ratio	1.07±0.11	1.09±0.11	1.05±0.12	0.111
STJ/aortic annulus minimum diameter ratio	1.38±0.16	1.40±0.16	1.37±0.15	0.350
Other				
Aortic cusps calcification, n (%)	177 (100)	22 (100)	150 (100)	-
Degree of aortic cusps calcification, n (%)				
Mild	9 (14.5)	5 (16.1)	4 (12.9)	0.205
Moderate	31 (50.0)	18 (58.1)	13 (41.9)	
Severe	22 (35.5)	8 (25.8)	14 (45.2)	

IQR indicates interquartile range; MDCT, multidetector computed tomography; STJ, sinotubular junction, and SV, sinus of Valsalva.
*Matching variable

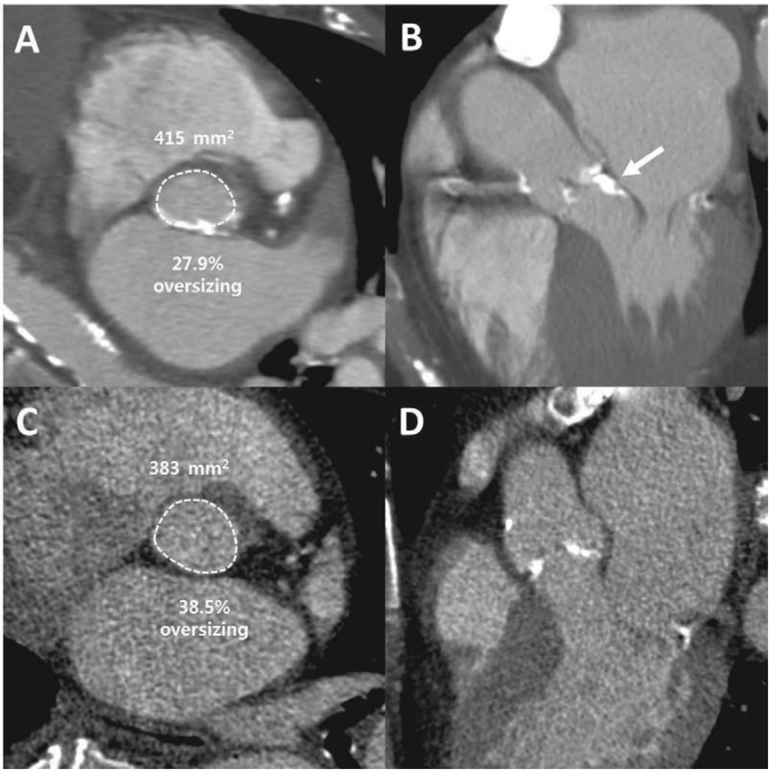

Figure 2. Case examples of 2 patients who underwent TAVR with a 26-mm (**A**, **B**) and a 23-mm (**C**, **D**) SAPIEN XT valve. In these cases, significant annular area oversizing (27.9% and 38.5%, respectively) resulted in different outcomes. The case showed in **A** and **B** (MDCT double-oblique transverse and coronal projections, respectively) with severe LVOT calcification (white arrow) experienced annular rupture during TAVR complicated by procedural death. The second case (**C** and **D**) displays an absence of LVOT calcification and, despite comparable prosthesis oversizing, this patient underwent an uneventful TAVR. LVOT indicates left ventricular outflow tract; MDCT, multidetector computed tomography; and TAVR, transcatheter aortic valve replacement.

Discussion

The data presented represent the largest assessment of patients who have experienced annular contained/noncontained rupture. This complication is a particular concern with balloon-expandable prostheses because of the significant force applied during balloon deployment.[5,6] To date, owing to its relative rarity and cumulative LVOT and annulus rupture rate of 1.1%, according to a recent meta-analysis,[16] we have

Table 3. Procedure Variables

	Overall (n=62)	Study Group (n=31)	Control Group (n=31)	*P* Value
Approach, n (%)				
Femoral	43 (69.4)	23 (74.2)	20 (65.4)	0.403
Apical	16 (25.8)	5 (16.1)	11 (35.5)	
Aortic	2 (3.2)	2 (6.5)	0 (0.0)	
Axillary	1 (1.6)	1 (3.2)	0 (0.0)	
Prostheses type, n (%)				
SAPIEN	55 (88.7)	27 (87.1)	28 (90.3)	0.662
SAPIEN XT	7 (11.3)	4 (12.9)	3 (9.7)	
Prostheses size, n (%)				
23 mm	34 (54.8)	11 (35.5)	23 (74.2)	<0.001
26 mm	25 (40.3)	17 (54.8)	8 (25.8)	
29 mm	3 (4.8)	3 (9.7)	0 (0.0)	
Balloon postdilatation, n (%)	7 (11.3)	7 (22.6)	0 (0.0)	0.005
Valve-in-valve, n (%)	3 (4.8)	2 (6.5)	1 (3.2)	0.571
Prosthesis oversizing, %	20.9±20.2	30.5±15.8	11.3±19.7	<0.001
Prosthesis oversizing ≥20%, n (%)	33 (53.2)	24 (77.4)	9 (29.0)	0.007
Conversion to surgery, n (%)	12 (19.4)	12 (38.7)	0 (0.0)	<0.001
Hemodynamic support, n (%)	10 (16.1)	10 (32.3)	0 (0.0)	0.001
Hemodynamic support type, n (%)				
ECMO	3 (4.8)	3 (9.7)	0 (0.0)	0.001
CPB	6 (9.7)	6 (19.3)	0 (0.0)	0.001

CPB indicates cardiopulmonary bypass; and ECMO, extracorporeal membrane oxygenation.

Table 4. Aortic Root and Sizing Characteristics, Procedural Variables, and Outcomes of Patients With Aortic Root Rupture

Patients	Annulus Measurements Area (Max/Min Diameter)	LVOT Calcification	Approach	Prosthesis	Size, mm	Balloon Post dilatation	Relative Area Oversizing, %	Lesion Site	Lesion Type	Hemodynamic Support	Treatment	Mortality*
Patient 1	334.0 mm² (23.0×19.7 mm)	Moderate	Femoral	Sapien XT	26	No	58.96	Annulus	Rupture	ECMO	Conservative	Yes
Patient 2	480.0 mm² (29.1×21.3 mm)	Moderate	Subclavian	Sapien XT	26	Yes	10.61	LVOT/VSD	Rupture	CPB	ViV†	Yes
Patient 3	361.0 mm² (23.6×17.9 mm)	None	Femoral	Sapien XT	23	No	15.09	SV	Hematoma	CPB	Surgical	No
Patient 4	278.9 mm² (19.4×16.7 mm)	None	Femoral	Sapien XT	23	No	48.97	SV	Rupture	CPB	Surgical	Yes
Patient 5	646.0 mm² (31.0×25.1 mm)	Moderate	Femoral	Sapien XT	29	Yes	2.25	Annulus	Rupture	None	Surgical	Yes
Patient 6	271.4 mm² (20.4×17.1 mm)	Severe	Femoral	ES	23	No	53.09	Annulus	Rupture	CPB	Surgical	Yes
Patient 7	323.8 mm² (22.4×17.2 mm)	None	Femoral	Sapien XT	23	No	28.31	STJ	Hematoma	None	Conservative	No
Patient 8	295.7 mm² (22.1×17.0 mm)	None	Apical	Sapien XT	23	No	40.51	Annulus	Hematoma	CPB	Conservative	No
Patient 9	530.0 mm² (29.9×22.4 mm)	Moderate	Femoral	Sapien XT	29	No	24.63	LVOT/VSD	Rupture	None	Conservative	No
Patient 10	371.9 mm² (23.6×18.6 mm)	Moderate	Aortic	Sapien XT	23	No	11.72	Annulus	Rupture	None	Surgical	Yes
Patient 11	339.0 mm² (24.6×18.6 mm)	Moderate	Femoral	Sapien XT	23	No	22.56	SV	Rupture	None	Conservative	Yes
Patient 12	370.0 mm² (24.4×20.0 mm)	Severe	Femoral	Sapien XT	26	No	43.49	Annulus	Rupture	None	Surgical	Yes
Patient 13	488.6 mm² (27.6×20.1 mm)	Moderate	Apical	ES	29	No	35.19	Annulus	Rupture	CPB	Surgical	Yes
Patient 14	310.0 mm² (23.8×17.6 mm)	None	Femoral	Sapien XT	23	No	34.02	SV	Rupture	None	Conservative	Yes
Patient 15	393.4 mm² (24.1×19.7 mm)	Moderate	Femoral	Sapien XT	26	Yes	34.96	Annulus	Hematoma	None	Conservative	No
Patient 16	280.0 mm² (19.6×18.8 mm)	Severe	Femoral	Sapien XT	23	No	48.38	LVOT/VSD	Rupture	ECMO	Surgical	Yes
Patient 17	415.0 mm² (27.1×17.5 mm)	Severe	Femoral	Sapien XT	26	Yes	27.93	Annulus	Rupture	ECMO	Surgical	Yes
Patient 18	545.0 mm² (29.8×23.2 mm)	Mild	Aortic	Sapien XT	26	Yes	-2.58	STJ	Rupture	None	Surgical	Yes
Patient 19	517.0 mm² (26.4×22.6 mm)	Severe	Femoral	ES	26	No	2.69	Annulus	Hematoma	None	Conservative	No
Patient 20	400.0 mm² (23.5×20.0 mm)	Moderate	Apical	Sapien XT	26	No	32.73	Annulus	Rupture	None	Surgical	No
Patient 21	390.0 mm² (25.2×18.8 mm)	Moderate	Femoral	Sapien XT	26	No	36.14	Annulus	Rupture	None	Surgical	No
Patient 22	291.7 mm² (22.4×15.1 mm)	Moderate	Femoral	Sapien XT	23	Yes	42.43	LVOT/VSD	Rupture	CPB	ViV†	No
Patient 23	397.0 mm² (25.1×21.1 mm)	Mild	Femoral	Sapien XT	26	No	33.74	Annulus	Rupture	None	Conservative	Yes
Patient 24	341.0 mm² (23.2×18.2 mm)	Moderate	Apical	Sapien XT	26	Yes	55.70	SV	Hematoma	None	Conservative	No
Patient 25	402.0 mm² (24.7×25.5 mm)	Mild	Femoral	Sapien XT	26	No	32.07	Annulus	Hematoma	None	Conservative	No
Patient 26	393.0 mm² (26.4×19.9 mm)	Moderate	Femoral	Sapien XT	26	No	35.10	Annulus	Rupture	None	Conservative	Yes

(Continued)

Table 4. Continued

Patients	Annulus Measurements Area (Max/Min Diameter)	LVOT Calcification	Approach	Prosthesis	Size, mm	Balloon Post dilatation	Relative Area Oversizing, %	Lesion Site	Lesion Type	Hemodynamic Support	Treatment	Mortality*
Patient 27	439.0 mm² (27.1×20.8 mm)	Severe	Femoral	ES	26	No	20.94	Annulus	Hematoma	None	Conservative	No
Patient 28	436.5 mm² (24.0×21.6 mm)	Moderate	Femoral	Sapien XT	26	No	21.63	Annulus	Hematoma	None	Conservative	No
Patient 29	448.4 mm² (26.3×18.9 mm)	Severe	Femoral	Sapien XT	26	No	18.41	Annulus	Hematoma	None	Conservative	No
Patient 30	414.0 mm² (24.7×19.3 mm)	Moderate	Femoral	Sapien XT	26	No	28.24	Annulus	Rupture	None	Drainage	Yes
Patient 31	335.0 mm² (22.7×17.1 mm)	Mild	Apical	Sapien XT	26	No	24.02	Annulus	Hematoma	Conservative	CPB	No

CPB indicates cardiopulmonary bypass; ECMO, extracorporeal membrane oxygenation; ES, Edwards-SAPIEN; LVOT, left ventricular outflow tract; STJ, sinotubular junction; SV, sinus of Valsalva; ViV, valve-in-valve; and VSD, ventricular septal defect.

*In-hospital

†Second prosthesis implanted to seal the VSD.

lacked the ability to confidently identify anatomic and procedural features that may increase the risk of this significant complication.

Analysis of MDCT performed before TAVR suggests that there are at least 2 important features associated with annular rupture/periaortic hematoma: (1) moderate or severe LVOT/subannular calcification, and (2) significantly oversized prostheses (≥20% area oversizing). Calcification in the LVOT may be a particular concern, because this is a rigid, thin-walled structure. Recently, Hayashida et al showed that significant calcification located in a vulnerable area as revealed by MDCT might be a possible mechanism for annular rupture in 2 cases of balloon-expandable TAVR.[17] Some have suggested that the location of LVOT calcification might also increase the risk of annular rupture. Theoretically, trigonal calcification may impart greater rigidity to the annulus and make it prone to rupture, whereas more anterior calcification may not impart as great of a risk. Interestingly, our findings actually revealed that in >30% of patients experiencing annular rupture, LVOT calcification was located underneath the right coronary cusp without a single patient in the control group having similar calcification. Although interesting and contradictory to traditional thinking, further study is needed to better understand how the location of calcification may or may not impact the risk of annular injury from TAVR.

Interestingly, the severity of aortic valvular calcification does not appear to play a significant role in root rupture, perhaps because the calcified leaflets are generally accommodated within the capacious sinus of Valsalva. Importantly, however, although our data did not show a significant relationship in univariate analysis, caution should still be exercised when performing TAVR on patients with heavily calcified aortic valve cusps in the setting of shallow sinuses of Valsalva, because this has been shown to result in perforation of a shallow sinus/narrow root on intraprocedural transesophageal echocardiogram and potentially increase the risk of coronary occlusion. (Figure 3)

Walther et al[9] suggested that diameter oversizing by ≈10% (based on transesophageal echocardiographic measurement) is desirable to avoid severe paravalvular regurgitation, but, in the presence of a rigid aortic root, excessive oversizing should be avoided. Similarly, our and other groups have shown that

Table 5. In-Hospital Outcomes

	Overall (n=62)	Study Group (n=31)	Control Group (n=31)	*P* Value
Mortality, n (%)	16 (25.8)	15 (48.4)	1 (3.2)	<0.001
Cardiovascular mortality, n (%)	15 (24.2)	14 (45.2)	1 (3.2)	0.013
Disabling stroke, n (%)	4 (6.4)	4 (12.9)	0 (0.0)	0.056
Nondisabling stroke, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	
Life-threatening bleeding, n (%)	14 (22.6)	14 (45.2)	0 (0.0)	<0.001
Major bleeding, n (%)	1 (1.6)	1 (3.2)	0 (0.0)	
Minor bleeding, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	
RBC transfusions, n (%)	17 (27.4)	13 (41.9)	4 (12.9)	0.032
Periprocedural MI, n (%)	3 (4.8)	3 (9.7)	0 (0.0)	0.119
Spontaneous MI, n (%)	1 (1.6)	1 (3.2)	0 (0.0)	0.001
New PPM, n (%)	5 (8.1)	4 (12.9)	1 (3.2)	0.215

MI indicates myocardial infarction; PPM, permanent pacemaker; and RBC, red blood cell.

Table 6. In-Hospital Outcomes in Patients With Contained and Uncontained Rupture

	Study Group (n=31)	Uncontained Rupture (n=20)	Contained Rupture (n=11)	*P* Value
Mortality, n (%)	15 (48.4)	15 (75.0)	0 (0.0)	<0.001
Cardiovascular mortality, n (%)	14 (45.2)	14 (70.0)	0 (0.0)	<0.001
Disabling stroke, n (%)	4 (12.9)	2 (10.0)	2 (18.2)	0.447
Nondisabling stroke, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	
Life-threatening bleeding, n (%)	14 (45.2)	12 (60.0)	2 (18.2)	0.049
Major bleeding, n (%)	1 (3.2)	0 (0.0)	1 (9.1)	
Minor bleeding, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	
RBC transfusions, n (%)	13 (41.9)	10 (50.0)	3 (27.3)	0.200
Periprocedural MI, n (%)	3 (9.7)	2 (10.0)	1 (9.1)	0.719
Spontaneous MI, n (%)	1 (3.2)	1 (5.0)	0 (0.0)	0.645
New PPM, n (%)	4 (12.9)	2 (10.0)	2 (18.2)	0.447

MI indicates myocardial infarction; PPM, permanent pacemaker; and RBC, red blood cell.

annular area oversizing is essential to mitigate the risk of significant paravalvular regurgitation.[3,4] Although important for THV selection, Blanke et al[7] recently showed that severe prosthesis oversizing of the area-derived annular diameter (>20%) was associated with contained rupture of the aortic root in 3 patients undergoing TAVR with balloon-expandable prostheses. In our study, relative prosthesis area oversizing of ≥20% was found to be a strong predictor of contained/noncontained root rupture, but, importantly, our findings suggest that that this risk may be amplified by other root modifiers such as significant LVOT/ subannular calcification. This might explain why significant annular area oversizing in historical cohorts does not necessarily result in annular rupture.[18] Oversizing a patient with significant LVOT calcification should confer the greatest clinical concern (Figure 4). This awareness may allow more patient-specific THV selection through integration of MDCT data to allow the most appropriate valve choice with more modest oversizing (or even undersizing) of those patients with features that would predispose them to potential annular rupture through the selection of a smaller valve size or balloon underfilling[18] to control the degree of annular/LVOT stretch. It is important to recognize, however, that, although we have identified anatomic and procedural factors that are strongly predictive of annular rupture, this event remains rare, and our model allows simply for the estimation of a probabilistic risk. The majority of patients with these root modifiers still undergo TAVR without annular rupture. For our analysis, we used annular area to assess the degree of oversizing because we have consistently found it to be the most reproducible annular measurement[3,4,14] and also the most predictive

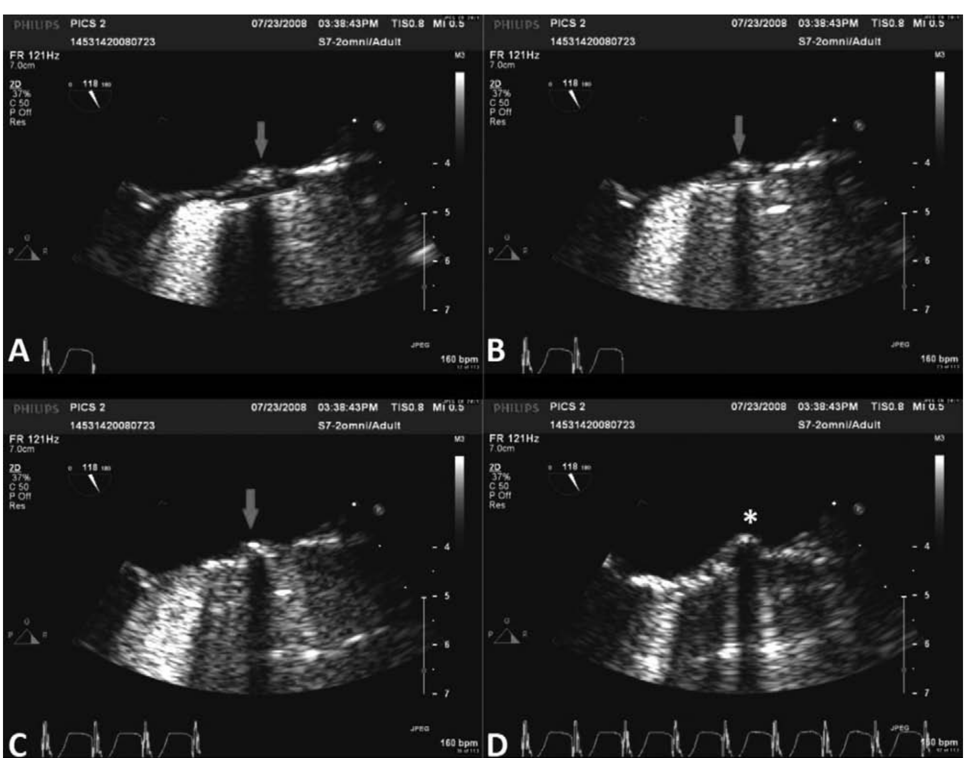

Figure 3. Intraprocedural transesophageal echocardiogram sequences obtained during an Edwards-SAPIEN valve deployment (**A** through **C**). **D**, The deployment resulted in perforation (*) of the sinus of Valsalva by a heavily calcified aortic valve cusp leaflet (red arrow) folded up toward the sinus wall by the stent (red line).

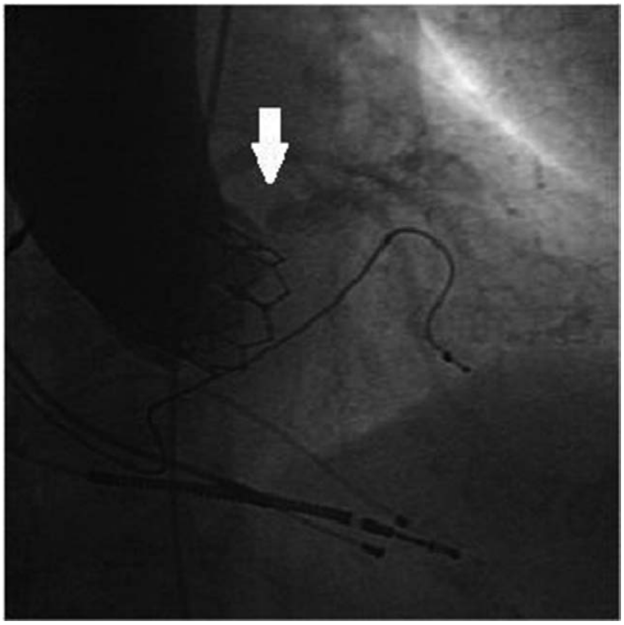

Figure 4. Angiography after SAPIEN XT valve deployment showing a flaw and irregular periaortal extravasation of the contrast (white arrow) in the pericardial space after uncontained annulus rupture.

of greater than mild paravalvular regurgitation.[3,4] Others have suggested that annular sizing should be performed with perimeter or circumference measures of the annulus owing to its lesser variability across the cardiac cycle.[19] Significant limitations in these measurements remain, however, owing to the lack of appropriate tools on all MDCT image review workstations, resulting in, at times, erroneous measurements and a lower degree of reproducibility.[18] It is important, however, to recognize that the implication of oversizing the annular area by 10% is very different from a similar percentage of perimeter/circumference oversizing and certainly from the area-derived diameter as described by Blanke et al.[7] For example, annular area oversizing by 20% is approximately equivalent to 10% perimeter oversizing.

Balloon postdilatation has also been shown to be an effective strategy to reduce significant paravalvular regurgitation.[20] In our analysis, balloon postdilatation confers an odds ratio with a high statistical association with aortic rupture, but, because of the rarity of data for such an estimation, no definitive conclusion can be made on its association with the outcome. However, our data would recommend that greater caution should be taken when oversizing or performing balloon postdilatation in patients with significant LVOT calcification.

Finally, our collaboration has confirmed that aortic root rupture is associated with very high mortality (48%) and morbidity.[5] However, although uncontained aortic root rupture and periaortic hematoma may belong to the spectrum of the same pathology caused by either the forces of the preceding valvuloplasty, valve deployment or balloon postdilatation, a distinction in terms of prognosis between these 2 entities has to be made. In our study, none of the 11 patients who experienced contained rupture/hematoma died during the hospitalization, or required a surgical conversion to open-chest aortic valve replacement. Four patients with uncontained rupture survived. Interestingly, none of them experienced significant hemodynamic compromise. Two patients had annular rupture, and the procedure was successfully converted into conventional aortic valve replacement. The other 2 patients had a ventricular septal defect treated conservatively in 1 case, and with successful implantation of a second prosthesis in a lower position to seal it in the second case.

Study Limitations

Although this is the largest patient series of this rare complication, our study remains limited by the relatively small number of patients who experienced aortic root rupture. Six patients with aortic rupture/hematoma were excluded from the final analysis owing to the lack of matching controls; aortic root and sizing characteristics, procedural variables, and outcomes of such patients are presented in Table I in the online-only Data Supplement). Additionally, we realize that the incidence of periaortic hematoma/contained rupture might be underestimated, but, importantly, the purpose of our study was not to determine the frequency of annular rupture/periaortic hematoma but rather to help identify anatomic predictors of these serious clinical events, and, in this aspect, we designed a case-control study owing to feasibility concerns. We recognize that a case-control study does not provide the same level of evidence as a randomized, control trial, our selection of controls through careful caliper matching can help mitigate the confounding effects, particularly with respect to the interested study variables. As such, we believe that the results of this analysis are of valuable clinical relevance and may serve as an important starting point for larger cohort studies.

Conclusions

Our data demonstrate that LVOT calcification and aggressive annular area oversizing are associated with an increased risk of aortic root contained/noncontained rupture during TAVR with balloon-expandable prostheses. Larger studies are warranted to confirm these findings.

Disclosures

Drs Wood, Jilaihawi, Binder, Kodali, Cabau, Leon, Webb, and Leipsic are consultants to Edwards Lifesciences. Drs Ussia and Latib are consultants to Medtronic Inc. The other authors report no conflicts.

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CLINICAL PERSPECTIVE

Aortic root rupture, albeit infrequently observed, remains a significant concern with balloon-expandable transcatheter valve prostheses, owing to its extremely poor prognosis. To date, owing to its relative rareness (≈1%), we have lacked the ability to confidently identify predictors of these significant complications. Recently, 3-dimensional computed tomography has been shown to provide excellent anatomic detail and accurate assessment of the complex anatomic shape of the aortic root, allowing for the prediction of paravalvular regurgitation and other transcatheter aortic valve replacement—related complications. In this multicenter study, 31 consecutive patients who experienced left ventricular outflow tract/annular/aortic contained/noncontained rupture during balloon-expandable transcatheter aortic valve replacement were compared with a propensity-matched control group of 31 consecutive patients without annular rupture who underwent pre-transcatheter aortic valve replacement computed tomography. In addition to confirming the extremely poor prognosis of annular rupture (48% in-hospital mortality rates), we identified 2 important features associated with this complication: (1) moderate or severe left ventricular outflow tract/ subannular calcification, and (2) significantly oversized prostheses (≥20% area oversizing). Clinical implications of these findings are important, because they support a more patient-specific approach to transcatheter heart valve sizing with the integration of both 3-dimensional annular dimensions and also information regarding potential root modifiers such as left ventricular outflow tract calcification of multidetector computed tomography.

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Anatomical and Procedural Features Associated With Aortic Root Rupture During Balloon-Expandable Transcatheter Aortic Valve Replacement

Marco Barbanti, Tae-Hyun Yang, Josep Rodès Cabau, Corrado Tamburino, David A. Wood, Hasan Jilaihawi, Phillip Blanke, Raj R. Makkar, Azeem Latib, Antonio Colombo, Giuseppe Tarantini, Rekha Raju, Ronald K. Binder, Giang Nguyen, Melanie Freeman, Henrique B. Ribeiro, Samir Kapadia, James Min, Gudrun Feuchtner, Ronen Gurtvich, Faisal Alqoofi, Marc Pelletier, Gian Paolo Ussia, Massimo Napodano, Fabio Sandoli de Brito, Jr, Susheel Kodali, Bjarne L. Norgaard, Nicolaj C. Hansson, Gregor Pache, Sergio J. Canovas, Hongbin Zhang, Martin B. Leon, John G. Webb and Jonathon Leipsic

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SUPPLEMENTAL MATERIAL

Supplemental Table

Supplemental Table 1. Aortic root and sizing characteristics, procedural variables and outcomes of patients with aortic root rupture excluded from the final analysis due to lack of matching controls (from #32 to #37) or due to not available baseline CT (from #38 to #44).

Patient #	Annulus measurements Area (Max/Min diameter)	LVOT Calcification	Approach	prosthesis	Size (mm)	Balloon post-dilation	Relative area oversizing (%)	Lesion site	Lesion type	Hemodynamic support	Treatment	Mortality*
Patient #32	335.0 mm^2 (22.7x17.2 mm)	Severe	Femoral	Sapien XT	23	No	24.02	Unknown	Rupture	None	Surgical	Yes
Patient #33	323.8 mm^2 (22.4x17.2 mm)	None	Femoral	Sapien XT	23	No	28.31	STJ	Hematoma	None	Conservative	No
Patient #34	417.2 mm^2 (23.2x19.5 mm)	None	Femoral	Sapien XT	26	No	27.26	Annulus	Hematoma	CPB	Conservative	No
Patient #35	625.0 mm^2 (30.9x25.0 mm)	Moderate	Apical	Sapien XT	29	No	5.68	SV	Rupture	None	Surgical	Yes
Patient #36	286.3 mm^2 (22.6x14.7 mm)	None	Femoral	ES	23	Yes	45.12	Unknown	Rupture	ECMO	Conservative	Yes
Patient #37	313.8 mm^2 (23.1x16.9 mm)	None	Femoral	Sapien XT	23	No	32.40	LVOT/VSD	Hematoma	None	Conservative	No
Patient #38	N/A	N/A	Femoral	Sapien XT	26	No	N/A	Annulus	Rupture	CPB	ViV†	Yes
Patient #39	N/A	N/A	Apical	Sapien XT	26	No	N/A	LVOT/VSD	Rupture	None	Conservative	Yes
Patient #40	N/A	N/A	Femoral	Sapien XT	26	No	N/A	Annulus	Rupture	CPB	Surgical	Yes
Patient #41	N/A	N/A	Femoral	Sapien XT	26	No	N/A	Annulus	Rupture	None	Conservative	Yes
Patient #42	N/A	N/A	Apical	ES	23	No	N/A	Annulus	Rupture	None	Surgical	Yes
Patient #43	N/A	N/A	Femoral	ES	26	Yes	N/A	Unknown	Rupture	None	Conservative	Yes
Patient #44	N/A	N/A	Femoral	Sapien XT	26	No	N/A	SV	Rupture	CPB	Surgical	No

Abbreviations: LVOT, Left Ventricular Outflow Tract; **VSD,** Ventricular Septal Defect; **SV,** Sinus of Valsalva; **ES,** Edwards-SAPIEN; **STJ,** Sino-Tubular Junction; **CPB,** Cardio-Pulmonary Bypass; **ECMO,** ExtraCorporeal Membrane Oxygenation; **ViV,** Valve-in-Valve.

*In-hospital

†Second prosthesis implanted to seal the leak