



**Universiteit
Leiden**
The Netherlands

Transcatheter Aortic Valve Replacement in Pure Native Aortic Valve Regurgitation

Yoon, S.H.; Schmidt, T.; Bleiziffer, S.; Schofer, N.; Fiorina, C.; Munoz-Garcia, A.J.; ... ; Makkar, R.R.

Citation

Yoon, S. H., Schmidt, T., Bleiziffer, S., Schofer, N., Fiorina, C., Munoz-Garcia, A. J., ... Makkar, R. R. (2017). Transcatheter Aortic Valve Replacement in Pure Native Aortic Valve Regurgitation. *Journal Of The American College Of Cardiology*, 70(22), 2752-2763.
doi:10.1016/j.jacc.2017.10.006

Version: Not Applicable (or Unknown)
License: [Leiden University Non-exclusive license](#)
Downloaded from: <https://hdl.handle.net/1887/95002>

Note: To cite this publication please use the final published version (if applicable).

Transcatheter Aortic Valve Replacement in Pure Native Aortic Valve Regurgitation



Sung-Han Yoon, MD,^a Tobias Schmidt, MD,^b Sabine Bleiziffer, MD,^c Niklas Schofer, MD,^d Claudia Fiorina, MD,^e Antonio J. Munoz-Garcia, MD,^f Ermela Yzeiraj, MD,^g Ignacio J. Amat-Santos, MD,^h Didier Tchetché, MD,ⁱ Christian Jung, MD,^j Buntaro Fujita, MD,^k Antonio Mangieri, MD,^l Marcus-Andre Deutsch, MD,^{c,m} Timm Ubben, MD,^b Florian Deuschl, MD,^d Shingo Kuwata, MD,ⁿ Chiara De Biase, MD,ⁱ Timothy Williams, MD,^o Abhijeet Dhoble, MD,^p Won-Keun Kim, MD,^q Enrico Ferrari, MD,^r Marco Barbanti, MD,^s E. Mara Vollema, MD,^t Antonio Miceli, MD,^u Cristina Giannini, MD,^v Guiherme F. Attizzani, MD,^w William K.F. Kong, MD,^x Enrique Gutierrez-Ibanes, MD,^y Victor Alfonso Jimenez Diaz, MD,^z Harindra C. Wijeyesundera, MD,^{aa} Hidehiro Kaneko, MD,^{bb} Tarun Chakravarty, MD,^a Moody Makar, MD,^a Horst Sievert, MD,^{cc} Christian Hengstenberg, MD,^{md,dd} Bernard D. Prendergast, MD,^{ee} Flavien Vincent, MD,^{ff} Mohamed Abdel-Wahab, MD,^{gg} Luis Nombela-Franco, MD,^{hh} Miriam Silaschi, MD,ⁱⁱ Giuseppe Tarantini, MD,^{jj} Christian Butter, MD,^{bb} Stephan M. Ensminger, MD,^k David Hildick-Smith, MD,^o Anna Sonia Petronio, MD,^v Wei-Hsian Yin, MD,^{kk} Federico De Marco, MD,^{ll} Luca Testa, MD,^{ll} Nicolas M. Van Mieghem, MD,^{mmm} Brian K. Whisenant, MD,ⁿⁿ Karl-Heinz Kuck, MD,^b Antonio Colombo, MD,^l Saibal Kar, MD,^a Cesar Moris, MD,^{oo} Victoria Delgado, MD,^t Francesco Maisano, MD,ⁿ Fabian Nietlispach, MD,ⁿ Michael J. Mack, MD,^{pp} Joachim Schofer, MD,^g Ulrich Schaefer, MD,^d Jeroen J. Bax, MD,^t Christian Frerker, MD,^b Azeem Latib, MD,^l Raj R. Makkar, MD^a

ABSTRACT

BACKGROUND Limited data exist about safety and efficacy of transcatheter aortic valve replacement (TAVR) in patients with pure native aortic regurgitation (AR).

OBJECTIVES This study sought to compare the outcomes of TAVR with early- and new-generation devices in symptomatic patients with pure native AR.

METHODS From the pure native AR TAVR multicenter registry, procedural and clinical outcomes were assessed according to VARC-2 criteria and compared between early- and new-generation devices.

RESULTS A total of 331 patients with a mean STS score of 6.7 ± 6.7 underwent TAVR. The early- and new-generation devices were used in 119 patients (36.0%) and 212 patients (64.0%), respectively. STS score tended to be lower in the new-generation device group (6.2 ± 6.7 vs. 7.6 ± 6.7 ; $p = 0.08$), but transfemoral access was more frequently used in the early-generation device group (87.4% vs. 60.8%; $p < 0.001$). Compared with the early-generation devices, the new-generation devices were associated with a significantly higher device success rate (81.1% vs. 61.3%; $p < 0.001$) due to lower rates of second valve implantation (12.7% vs. 24.4%; $p = 0.007$) and post-procedural AR \geq moderate (4.2% vs. 18.8%; $p < 0.001$). There were no significant differences in major 30-day endpoints between the 2 groups. The cumulative rates of all-cause and cardiovascular death at 1-year follow-up were 24.1% and 15.6%, respectively. The 1-year all-cause mortality rate was significantly higher in the patients with post-procedural AR \geq moderate compared with those with post-procedural AR \leq mild (46.1% vs. 21.8%; log-rank $p = 0.001$). On multivariable analysis, post-procedural AR \geq moderate was independently associated with 1-year all-cause mortality (hazard ratio: 2.85; 95% confidence interval: 1.52 to 5.35; $p = 0.001$).

CONCLUSIONS Compared with the early-generation devices, TAVR using the new-generation devices was associated with improved procedural outcomes in treating patients with pure native AR. In patients with pure native AR, significant post-procedural AR was independently associated with increased mortality. (J Am Coll Cardiol 2017;70:2752–63)

© 2017 by the American College of Cardiology Foundation.



Listen to this manuscript's audio summary by JACC Editor-in-Chief Dr. Valentin Fuster.



From the ^aDepartment of Interventional Cardiology, Cedars-Sinai Heart Institute, Los Angeles, California; ^bDepartment of Cardiology, Asklepios Klinik St. Georg, Hamburg, Germany; ^cClinic for Cardiovascular Surgery, German Heart Center Munich, Germany; ^dDepartment of General and interventional Cardiology, University Heart Center, Hamburg, Germany; ^eCardiothoracic Department, Spedali Civili Brescia, Brescia, Italy; ^fHospital Universitario Virgen de la Victoria, Spain; ^gHamburg University Cardiovascular Center, Hamburg, Germany; ^hInstitute of Heart Sciences, Hospital Clínico Universitario de Valladolid, Valladolid, Spain; ⁱDepartment of Cardiology, Clinique Pasteur, Toulouse, France; ^jDivision of Cardiology, Pulmonology, and Vascular Medicine, University Hospital Dusseldorf, Dusseldorf, Germany; ^kDepartment of Thoracic and Cardiovascular Surgery, Heart and Diabetes Center NRW, Ruhr-University Bochum, Bad Oeynhausen, Germany; ^lInterventional Cardiology Unit, EMO-GVM Centro

The prevalence of aortic regurgitation (AR) increases with age, occurring in up to 2% of individuals over 70 years of age (1). Symptomatic patients with chronic severe AR have a poor prognosis and therefore should undergo surgery. However, in the aging population, an increasing number of patients with symptomatic severe AR have

excessive comorbidities or a clinical condition that contraindicates open heart surgery, and most of them are deemed a high surgical risk and often treated conservatively.

Since the first report of successful transcatheter aortic valve replacement (TAVR), the growing experience, accumulated

ABBREVIATIONS AND ACRONYMS

AR = aortic regurgitation

CI = confidence interval

HR = hazard ratio

TAVR = transcatheter aortic valve replacement

Cuore Columbus & San Raffaele Scientific Institute, Milan, Italy; ^mSan Raffaele Hospital, Milan, Italy; ⁿGerman Center for Cardiovascular Research, Partner Site Munich Heart Alliance, Munich, Germany; ^oUniversity Heart Center, University Hospital Zurich, Zurich, Switzerland; ^pSussex Cardiac Centre, Brighton and Sussex University Hospitals NHS Trust, Brighton, United Kingdom; ^qDepartment of Cardiology, University of Texas Health Science Center, Houston, Texas; ^rKerckhoff Heart and Thorax Center, Department of Cardiology/Cardiac Surgery, Bad Nauheim, Germany; ^sCardiac Surgery Unit, Cardiocentro Ticino Foundation, Lugano, Switzerland; ^tDivision of Cardiology, Ferrarotto Hospital, University of Catania, Catania, Italy; ^uDepartment of Cardiology, Leiden University Medical Center, Leiden 2333 ZA, the Netherlands; ^vIstituto Clinico Sant'Ambrogio, Gruppo Ospedaliero San Donato, Milan, Italy; ^wDepartment Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy; ^xThe Valve and Structural Heart Interventional Center, University Hospitals Case Medical Center, Cleveland, Ohio; ^yDepartment of Cardiology, National University Heart Centre, Singapore; ^zDepartment of Cardiology, Hospital General Universitario Gregorio Marañon, Madrid, Spain; ^{aa}Cardiology Department, University Hospital of Vigo, Vigo, Spain; ^{ab}Division of Cardiology, Sunnybrook Health Science Centre, Toronto, Ontario, Canada; ^{ac}Heart Center Brandenburg in Bernau and Brandenburg Medical School, Bernau, Germany; ^{ad}Department of Cardiology and Vascular Medicine, CardioVascular Center, Frankfurt, Germany; ^{ae}Klinik für Herz- und Kreislauferkrankungen, Deutsches Herzzentrum München, Technische Universität München, Munich, Germany; ^{af}Department of Cardiology, St Thomas' Hospital, London, United Kingdom; ^{ag}Department of Cardiology, CHU Lille, Inserm, U1011, Université Lille, Lille, France; ^{ah}Heart Center, Segeberger Kliniken, Bad Segeberg, Germany; ^{ai}Division of Cardiology, Hospital Clinico San Carlos, Madrid, Spain; ^{aj}Department of Cardiac Surgery, University of Halle, Halle, Germany; ^{ak}Department of Cardiac, Thoracic and Vascular Sciences, University Hospital of Padova, Padova, Italy; ^{al}Division of Cardiology, Heart Center, Cheng Hsin General Hospital, Taipei, Taiwan; ^{am}Department of Cardiology, IRCCS Pol San Donato, San Donato Milanese, Milan, Italy; ^{an}Interventional Cardiology, Thoraxcenter, Erasmus Medical Center, Rotterdam, the Netherlands; ^{ao}Division of Cardiovascular Diseases, Intermountain Heart Institute, Salt Lake City, Utah; ^{ap}Hospital Universitario Central de Asturias, Oviedo, Spain; and the ^{aq}Department of Cardiovascular Disease, Baylor Scott and White Health Care System, Plano, Texas. The Department of Cardiology at the Leiden University Medical Center has received research grants from Edwards Lifesciences, Biotronik, Medtronic, and Boston Scientific. Dr. Bleiziffer has served as a consultant to Medtronic; and as a proctor for Medtronic, JenaValve, and Boston Scientific. Dr. N. Schofer has received travel support from Edwards Lifesciences, St. Jude Medical, and Boston Scientific; and honoraria from Boston Scientific. Dr. Dhoble has served as a proctor for Edwards Lifesciences; and as a consultant for St. Jude Medical. Dr. Kim has served as a proctor for Symmetis and St. Jude Medical. Dr. Ferrari has served as a proctor and consultant for Edwards Lifesciences. Dr. Barbanti has served as a consultant for Edwards Lifesciences. Dr. Miceli has served as a consultant for LivaNova. Dr. Attizzani has served as a proctor for Edwards Lifesciences and Medtronic; on the speakers bureaus for Medtronic and Abbott Vascular; and as a consultant to Abbott Vascular, Medtronic, Edwards Lifesciences, and St. Jude Medical. Dr. Wijesundera has received research grants from Edwards Lifesciences and Medtronic. Prof. Sievert has received study honoraria, travel expenses, and consulting fees from Ablative Solution, Ancona Heart, Bioventrix, Boston Scientific, Carag, Cardiac Dimensions, Celonova, Cibiem, Comed B.V., Contego, Hemoteq, Kona Medical, Lifetech, Maquet Getinge Group, Medtronic, Occlutech, PFM Medical, St. Jude Medical, Terumo, Trivascular, Valtech, and Vascular Dynamics. Dr. Hengstenberg has served as a proctor for Edwards Lifesciences and Symetis; and has received travel compensation from Edwards Lifesciences, Medtronic, and Symetis; and speakers honoraria from Edwards Lifesciences and Symetis. Dr. Prendergast has received research funding from Edwards Lifesciences; and speakers fees from Edwards Lifesciences, Boston Scientific, and Symetis. Dr. Abdel-Wahab has served as a proctor for Boston Scientific; and has received an institutional research grant from St. Jude Medical. Dr. Nombela-Franco has served as a proctor for St. Jude Medical. Dr. Silaschi has served as a consultant from JenaValve Technologies; and has received travel compensation from Edwards Lifesciences. Dr. Ensminger has served as a proctor for JenaValve and Edwards Lifesciences; has received speakers honoraria from Edwards Lifesciences, JenaValve, and Symetis; has served as a consultant for JenaValve and Edwards Lifesciences; and has received travel compensation from Edwards Lifesciences, JenaValve, and Symetis. Dr. Hildick-Smith has served as a proctor for and on the advisory boards of Medtronic, Edwards Lifesciences, and Boston Scientific. Dr. Petronio has served as a consultant for Medtronic, Boston Scientific, and Abbott. Dr. Van Mieghem has received research grants from Claret Medical, Boston Scientific, Medtronic, and Edwards Lifesciences. Dr. Whisenant has served as a consultant for Edwards Lifesciences, Johnson & Johnson, and Boston Scientific. Dr. Kuck has received research grants and contracts from Medtronic, Biotronik, Biosense Webster, and Stereotaxis; and has served as a consultant for Edwards Lifesciences, Boston Scientific, and Abbott Vascular. Dr. Kar has received research grants and consulting fees from Abbott Vascular, Boston Scientific, and St. Jude Medical. Dr. Delgado has received speakers fees from Abbott Vascular. Dr. Maisano has served as a consultant for Edwards Lifesciences, Medtronic, St. Jude Medical, Abbott Vascular, and Valtech; and has received royalties from Edwards Lifesciences. Dr. Nietispach has served as a consultant for Abbott, Edwards Lifesciences, St. Jude Medical, Direct Flow Medical, and Medtronic; and is a shareholder of Edwards Lifesciences. Dr. Frerker has served as a proctor for Medtronic, Boston Scientific, Abbott, and St. Jude Medical; and has received speakers honoraria from Edwards Lifesciences; and travel compensation from Edwards Lifesciences, Medtronic, Boston Scientific, and St. Jude Medical. Dr. Latib has served on the Medtronic advisory board; has received honoraria from Abbott Vascular; and has served as a consultant for Direct Flow Medical. Dr. Chakravarty has received research support from Edwards Lifesciences. Dr. Makkar has received grants from Edwards Lifesciences and Abbott Vascular; and personal fees from Abbott Vascular, Cordis, St. Jude Medical, and Medtronic. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

knowledge, and technological development lead to an expanded use of TAVR in a lower surgical risk population, as well as use in other valvular positions or pathologies such as pure native AR (2-8). However, pure native AR has been considered a contraindication for TAVR due to absent aortic valve calcification and the subsequent difficulty in anchoring the transcatheter valves. The initial report of TAVR using the early-generation self-expanding prostheses for pure native AR showed high rates of procedural complications (9). However, the new-generation devices with retrievability and repositioning capacity, external sealing cuff, or unique anchoring mechanisms could potentially overcome the procedural challenges in treating pure native AR. Therefore, we aimed to create an international multicenter registry of TAVR in pure native AR and evaluate the procedural and clinical outcomes of TAVR in patients with pure native AR, taking into consideration the technological developments of transcatheter valves.

SEE PAGE 2764

METHODS

STUDY DESIGN AND PATIENT POPULATION. The pure native AR TAVR registry is an international, multicenter, observational study that enrolled all consecutive patients with symptomatic severe AR undergoing TAVR. The registry was initiated in August 2016, and a total of 40 centers from Europe, North America, and Asia-Pacific participated in the registry. Patients were considered candidates for the procedure if they had severe AR with comorbid conditions that would preclude surgical valve replacement. Patients with aortic stenosis defined as a peak aortic jet velocity on continuous-wave Doppler of >2.5 m/s were excluded from this study. We collected data retrospectively for cases performed before study initiation and prospectively thereafter. This study was approved by the institutional review board of each institution, and all patients provided written informed consent for TAVR and the use of anonymous clinical, procedural, and follow-up data for research. For retrospective analysis of clinically acquired and anonymized data, the institutional review board of some institutions waived the need for written patient informed consent.

STUDY DEVICES AND TAVR PROCEDURE. Patients were selected for TAVR at the institutional level after discussions by the multidisciplinary heart team. Device size was selected based on 3-dimensional computed tomographic and transesophageal echocardiographic measurements. The access site and type of

device were determined by the multidisciplinary heart team. All TAVR procedures were conducted in accordance with local guidelines using standard techniques via transfemoral or nontransfemoral access, and the self-expanding transcatheter valves (the CoreValve/Evolut R [Medtronic, Minneapolis, Minnesota], Portico [St. Jude Medical, Minneapolis, Minnesota], and Acurate [Symetis SA, Ecublens, Switzerland]), the balloon-expandable transcatheter valves (the Sapien XT/Sapien 3 [Edwards Lifesciences, Irvine, California]), and other transcatheter valves (JenaValve [JenaValve Technology, Munich, Germany], Lotus [Boston Scientific, Natick, Massachusetts], Direct Flow [Direct Flow Medical, Santa Rosa, California], and J-Valve [JieCheng Medical Technology CO., Suzhou, China]) were implanted (10-20).

DATA COLLECTION. Data collection included baseline clinical, laboratory, echocardiographic, and computed tomographic data, as well as procedural data and clinical follow-up data at pre-specified time points (1, 6, and 12 months and yearly thereafter). Follow-up was obtained by clinical visits and/or through telephone contacts, and information about cause of death and rehospitalization was collected. Referring cardiologists, general practitioners, and patients were contacted whenever necessary for further information. All data provided by each institution were anonymized and centrally collected, and all inconsistencies were resolved directly with local investigators and onsite data monitoring.

ENDPOINTS AND DEFINITIONS. The primary endpoints of the present study were all-cause and cardiovascular mortality rates at 1 year. Secondary endpoints were rehospitalization, device success, and other 30-day major clinical endpoints defined according to the VARC (Valve Academic Research Consortium-2) criteria (21). Other endpoints included procedure- and device-related complications, and echocardiographic assessment of the valve and cardiac function at post-procedure. No echocardiographic core laboratory was used, and all echocardiographic data were site reported. The severity of post-procedural AR was qualitatively assessed and graded using transthoracic echocardiography at each institution according to established guidelines and VARC-2 criteria (21). The perimeter and area oversizing indexes were defined as: [(device nominal perimeter or area)/(annulus perimeter or area measured by computed tomography) - 1] \times 100, respectively.

STATISTICAL ANALYSIS. Patients were stratified according to whether they received the early-generation devices (the CoreValve and Sapien XT) or the new-generation devices (the Evolut R, Sapien 3,

JenaValve, Lotus, Direct Flow, Acurate, Portico, and J-Valve). Continuous variables are presented as mean ± SD and compared using the Student's *t*-test or Mann-Whitney *U* test. Categorical variables are presented as counts or percentages, and compared using the chi-square or Fisher exact test. Receiver-operating characteristic curve analysis was performed, and areas under the curve were calculated to assess the discriminative powers of device sizing parameters for post-procedural AR ≥ moderate. Cumulative rates of death or rehospitalization were calculated using the Kaplan-Meier survival analysis, and the log-rank test was used for comparisons across the groups. For rehospitalization, data were censored at the time of death or the end of the observation period. Univariable Cox regression models were used to evaluate potential predictors of all-cause mortality or rehospitalization at 1-year follow-up. Statistically significant variables with a *p* value of <0.10 by univariable analysis were included in the multivariable model. The final model was determined by backward elimination procedures with a threshold of *p* < 0.10. The proportional hazards assumption was confirmed by examination of log (-log [survival]) curves and by testing of partial (Shoenfeld) residuals, and no relevant violations were found. The estimated hazard ratio (HR) with 95% confidence interval (CI) was provided by the Cox model. All statistical analyses were performed using SPSS software version 24.0 (SPSS, Chicago, Illinois) or MedCalc (MedCalc Software, Mariakerke, Belgium). A 2-sided *p* value of <0.05 was considered to be of statistical significance.

RESULTS

BASELINE CHARACTERISTICS. A total of 331 patients with symptomatic, severe pure native AR were treated with TAVR across 40 participating centers between September 2007 and February 2017. The baseline characteristics of the study population are shown in **Table 1**. Of the study population, 119 patients (36.0%) had TAVR with the early-generation devices and 212 patients (64.0%) received the new-generation devices. In the overall cohort, approximately one-half of patients were male with a mean age of 74.4 years, and had increased surgical risk scores with a mean STS (Society of Thoracic Surgeons) score of 6.7 ± 6.7%, and EuroSCORE II (European System for Cardiac Operative Risk Evaluation II) of 9.8 ± 10.7%. All patients were discussed by the multidisciplinary heart team, taking into account increased surgical risk scores (STS score ≥8%: 28.0%), as well as other factors, including frailty (48.9%),

TABLE 1 Baseline Characteristics

	Overall (N = 331)	Early-Generation Devices (n = 119)	New-Generation Devices (n = 212)	<i>p</i> Value
Age, yrs	74.4 ± 12.2	74.2 ± 13.1	74.5 ± 11.6	0.81
Female	159 (48.0)	51 (42.9)	108 (50.9)	0.16
NYHA functional class III or IV	293 (88.5)	107 (89.9)	186 (87.7)	0.55
STS score	6.7 ± 6.7	7.6 ± 6.7	6.2 ± 6.7	0.08
Euro SCORE II	9.8 ± 10.7	11.7 ± 12.9	8.9 ± 9.4	0.03
Creatinine, mg/dl	1.4 ± 1.0	1.5 ± 1.1	1.4 ± 1.0	0.48
Hypertension	255 (77.0)	88 (73.9)	167 (78.8)	0.32
Diabetes mellitus	43 (13.0)	22 (17.6)	22 (10.4)	0.06
Chronic pulmonary disease	98 (29.6)	28 (23.5)	70 (33.0)	0.07
Peripheral vascular disease	65 (19.6)	20 (16.8)	45 (21.2)	0.33
Prior cerebrovascular accident	33 (10.0)	8 (6.7)	25 (11.8)	0.14
Coronary artery disease	156 (47.1)	52 (43.7)	104 (49.1)	0.35
Prior myocardial infarction	72 (21.8)	23 (19.3)	49 (23.1)	0.42
Prior PCI	90 (27.2)	29 (24.4)	61 (28.8)	0.39
Prior CABG	49 (14.8)	20 (16.8)	29 (13.7)	0.44
Prior mitral valve surgery	29 (8.8)	7 (5.9)	22 (10.4)	0.17
Prior permanent pacemaker	51 (15.4)	22 (18.5)	29 (13.7)	0.25
Atrial fibrillation	115 (34.7)	36 (30.3)	79 (37.3)	0.20
Echocardiographic findings				
LVEF, %	45.7 ± 14.6	44.5 ± 14.3	46.3 ± 14.8	0.28
Ascending aorta diameter, mm	36.0 ± 7.6	36.7 ± 8.3	35.5 ± 7.0	0.35
Mitral regurgitation ≥ moderate	113 (35.4)	40 (35.1)	73 (35.6)	0.93
Pulmonary hypertension	88 (26.6)	38 (31.9)	50 (23.6)	0.10

Values are mean ± SD or n (%).
CABG = coronary artery bypass graft surgery; EuroSCORE = European System for Cardiac Operative Risk Evaluation; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; STS = Society of Thoracic Surgeons.

porcelain aorta/previous radiation therapy/hostile chest (8.9%), severe pulmonary disease prohibiting intubation (6.4%), neurological disorders (4.2%), previous cardiac surgery for heart transplantation/congenital heart disease/aortic dissection (3.9%), critical pre-procedural state such as left ventricular assist device (3.5%), cancer (3.5%), end-stage liver failure (1.9%), and/or combination of other comorbidities such as poor left ventricular ejection fraction, severe pulmonary hypertension, or mitral regurgitation (8.1%). Surgical risk scores tended to be lower in the new-generation device group compared with the early-generation device group (STS score 6.2 ± 6.7% vs. 7.6 ± 6.7%; *p* = 0.08; EuroSCORE II 8.9 ± 9.4% vs. 11.7 ± 12.9%; *p* = 0.03). There were no significant differences between the 2 groups in terms of age, baseline New York Heart Association functional class, and other comorbidities except trends of more frequent chronic pulmonary disease (33.0% vs. 23.5%; *p* = 0.07) and less frequent diabetes mellitus (10.4% vs. 17.6%; *p* = 0.06) in the new-generation device group. There were no significant differences in echocardiographic findings between the 2 groups. The data regarding the etiology of AR were available

TABLE 2 Procedural Data

	Overall (N = 331)	Early-Generation Devices (n = 119)	New-Generation Devices (n = 212)	p Value
General anesthesia	192 (58.0)	58 (48.7)	134 (63.2)	0.01
Local anesthesia	139 (42.0)	58 (51.3)	78 (36.8)	0.01
Access site				
Transfemoral access	233 (70.4)	104 (87.4)	129 (60.8)	<0.001
Non-transfemoral access	98 (29.6)	15 (12.6)	83 (39.2)	<0.001
Transapical access	80 (24.2)	4 (3.4)	76 (35.8)	<0.001
Trans-subclavian access	10 (3.0)	4 (3.4)	6 (2.8)	0.79
Transaortic access	6 (1.8)	5 (4.2)	1 (0.5)	0.02
Transcarotid access	2 (0.6)	0 (0.0)	2 (1.7)	0.13
Device type				
Sapien XT	9 (2.7)	9 (7.6)	–	
Sapien 3	41 (12.4)	–	41 (19.3)	
CoreValve	110 (33.2)	110 (92.4)	–	
Evolut R	50 (15.1)	–	50 (23.6)	
JenaValve	64 (19.3)	–	64 (30.2)	
Direct Flow	35 (10.6)	–	35 (16.5)	
J-Valve	1 (0.3)	–	1 (0.5)	
Engager	7 (2.1)	–	7 (3.3)	
Portico	3 (0.9)	–	3 (1.4)	
Acurate	5 (1.5)	–	5 (2.4)	
Lotus	6 (1.8)	–	6 (2.8)	
Procedure time, min	102.1 ± 65.6	89.8 ± 50.2	109.1 ± 72.1	0.047
Fluoroscopy time, min	22.2 ± 17.8	29.1 ± 23.2	18.4 ± 12.5	<0.001
Contrast agent, ml	162.2 ± 88.7	180.1 ± 95.2	150.9 ± 82.7	0.01
Balloon pre-dilation	26 (7.9)	7 (5.9)	19 (9.0)	0.32
Balloon post-dilation	47 (14.2)	23 (19.3)	24 (11.3)	0.045

Values are n (%) or mean ± SD.

in 251 patients (76.8%): the majority of patients exhibited severe AR due to degenerative changes of the aortic cusps (56.6%), annular dilation (23.1%), and other etiologies (Online Figure 1).

PROCEDURAL DATA. Procedural and computed tomography findings are summarized in Table 2 and Online Table 1, respectively. Pre-procedural computed tomography assessment was performed in the majority of patients (84.9%), with a higher rate in the new-generation device group (90.6% vs. 74.8%; $p < 0.001$). The mean aortic annulus diameter, area, and perimeter were 25.2 mm, 488.0 mm², and 79.3 mm, respectively, without significant differences between the 2 groups. Aortic valve calcification was absent or mild in the majority of patients (85.9%), without significant difference between the 2 groups. The ascending aorta was assessed in 252 patients (81.0%), with a mean diameter of 36.5 mm, and 68 patients (27.0%) had a dilated ascending aorta with a diameter of more than 40 mm.

In terms of procedural data, patients in the new-generation device group had more frequent general

anesthesia (63.2% vs. 48.7%; $p = 0.01$) and nontransfemoral approach (39.2% vs. 12.6%; $p < 0.001$) compared with those in the early-generation device group. The most frequently used prosthesis was the CoreValve (33.2%), followed by the JenaValve (19.3%), Evolut R (15.1%), Sapien 3 (12.4%), Direct Flow (10.6%), and other devices. Compared with the patients in the early-generation device group, the patients in the new-generation device group had a longer procedure time (109.1 ± 72.1 min vs. 89.8 ± 50.2 min; $p = 0.047$) but had a shorter fluoroscopy time (18.4 ± 12.5 min vs. 29.1 ± 23.2 min; $p < 0.001$) and a smaller contrast agent volume (150.9 ± 82.7 ml vs. 180.1 ± 95.2 ml; $p = 0.01$). Balloon pre-dilation was performed in 7.9% of patients due to absence of pre-procedural computed tomography (1.5%), any aortic valve calcification (6.6%), and/or initial experience (2.1%). Balloon post-dilation was less frequently performed in the new-generation device group compared with the early-generation device group (11.3% vs. 19.3%; $p = 0.045$).

PROCEDURAL AND CLINICAL OUTCOMES. The procedural and clinical outcomes of the study population are summarized in Table 3. In the overall cohort, procedure-related death, conversion to conventional surgery, coronary obstruction, aortic root injury, and re-intervention were observed in 10 (3.0%), 12 (3.6%), 4 (1.2%), 5 (1.5%), and 14 patients (4.2%), respectively. There was no significant difference in new permanent pacemaker insertion rates between the 2 groups, but the new-generation devices were associated with a lower incidence of second valve implantation (12.7% vs. 24.4%; $p = 0.007$). With respect to echocardiographic findings, post-procedural left ventricular ejection fraction was similar between the 2 groups ($43.5 \pm 14.2\%$ vs. $44.3 \pm 14.5\%$; $p = 0.68$), whereas the new-generation devices were associated with a lower incidence of post-procedural AR \geq moderate (4.2% vs. 18.8%; $p < 0.001$), which resulted in significantly higher device success rate with the new-generation devices (81.1% vs. 61.3%; $p < 0.001$) (Central Illustration).

In terms of 30-day clinical outcomes, all-cause and cardiovascular death were observed in 36 patients (10.9%) and 32 patients (9.7%), respectively. Compared with the early-generation devices, the new-generation devices tended to be associated with a higher rate of stroke (5.7% vs. 1.7%; $p = 0.08$) but a lower rate of stage 2 or 3 acute kidney injury (6.1% vs. 11.8%; $p = 0.07$). There were no significant differences in other major 30-day endpoints between the 2 groups. Given that the median number of TAVR procedures at each institution was 7, patients were

divided into the early experience group (the first 7 cases) and the late experience group (the eighth case and thereafter). There were no significant differences in procedural and clinical outcomes between the 2 groups, except that the late experience was associated with a reduction in major vascular complication (1.8% vs. 6.8%; $p = 0.02$) (Online Figure 2).

OUTCOMES ACCORDING TO DEVICE TYPE. With stratification according to the device type, including the CoreValve, Evolut R, Sapien 3, JenaValve, and Direct Flow devices, procedural outcomes are shown in Figure 1. Compared with the CoreValve, the JenaValve was associated with a significantly lower incidence of second valve implantation (9.4% vs. 26.4%; $p = 0.007$). Similarly, compared with the CoreValve, the new-generation devices (with the exception of the Direct Flow) were associated with a lower incidence of post-procedural AR \geq moderate (Evolut R 4.0% vs. 18.2%; $p = 0.016$; Sapien 3 0.0% vs. 18.2%; $p = 0.003$; JenaValve 1.6% vs. 18.2%; $p = 0.001$). Accordingly, the new-generation devices were associated with higher device success rates compared with the CoreValve. There were no significant differences in new permanent pacemaker insertion rates between the devices. In terms of 30-day clinical outcomes, the JenaValve and Direct Flow were associated with higher rates of stroke (overall $p = 0.001$; JenaValve 7.8%; Direct Flow 17.1%; CoreValve 0.9%; Evolut R 2.0%; Sapien 3 0.0%), whereas there were no significant differences in other major 30-day endpoints between devices (Online Figure 3).

IMPACT OF AORTIC VALVE CALCIFICATION, ANNULUS SIZE, AND DILATED AORTA. The procedural and clinical outcomes were analyzed according to the degree of aortic valve calcification (none or mild vs. moderate) (Online Table 2). None or mild aortic valve calcification was associated with less frequent device success (70.6% vs. 87.2%; $p = 0.03$), which was consistently observed when using the early-generation devices (53.4% vs. 83.3%; $p = 0.02$). However, there were no significant associations between the aortic valve calcification and procedural outcomes when using the new-generation devices (Online Figure 4). Similarly, the procedural outcomes were analyzed according to the mean annulus diameter (mean diameter <25.2 mm vs. ≥ 25.2 mm) and diameter of ascending aorta (<40 mm vs. ≥ 40 mm). In the overall cohort, larger annulus was associated with less frequent device success (70.2% vs. 86.0%; $p = 0.005$), due to higher rates of second valve implantation (21.2 vs. 8.4%; $p = 0.009$) and post-procedural AR \geq moderate (8.7% vs. 2.8%; $p = 0.07$) (Online Figure 5). When using the early-generation

TABLE 3 Procedural and Clinical Outcomes

	Overall (N = 331)	Early-Generation Devices (n = 119)	New-Generation Devices (n = 212)	p Value
Procedural outcomes				
Procedure-related death	10 (3.0)	5 (4.2)	5 (2.4)	0.35
Conversion to conventional surgery	12 (3.6)	4 (3.4)	8 (3.8)	0.85
Coronary obstruction	4 (1.2)	0 (0.0)	4 (1.9)	0.30
Aortic root injury	5 (1.5)	2 (1.7)	3 (1.4)	>0.99
Need for second valve implantation	55 (16.6)	29 (24.4)	27 (12.7)	0.007
New permanent pacemaker*	51 (18.2)	17 (17.5)	34 (18.6)	0.83
Re-intervention	14 (4.2)	6 (5.0)	8 (3.8)	0.58
Echocardiographic findings at discharge				
Mean gradient, mm Hg	9.3 \pm 4.8	7.7 \pm 4.9	10.2 \pm 4.5	<0.001
LVEF, %	44.0 \pm 14.3	43.5 \pm 14.2	44.3 \pm 14.5	0.68
Aortic regurgitation \geq moderate	29 (9.6)	21 (18.8)	8 (4.2)	<0.001
Device success	246 (74.3)	73 (61.3)	172 (81.1)	<0.001
Clinical outcomes at 30 days				
All-cause mortality	36 (10.9)	16 (13.4)	20 (9.4)	0.26
Cardiovascular mortality	32 (9.7)	14 (11.8)	16 (8.5)	0.33
Stroke	14 (4.2)	2 (1.7)	12 (5.7)	0.08
Bleeding	39 (11.8)	18 (15.1)	21 (9.9)	0.16
Major	25 (7.6)	12 (10.1)	13 (6.1)	0.19
Life-threatening	14 (4.2)	6 (5.0)	8 (3.8)	0.58
Major vascular complication	14 (4.2)	7 (5.9)	7 (3.3)	0.26
Acute kidney injury (stage 2 or 3)	27 (8.2)	14 (11.8)	13 (6.1)	0.07

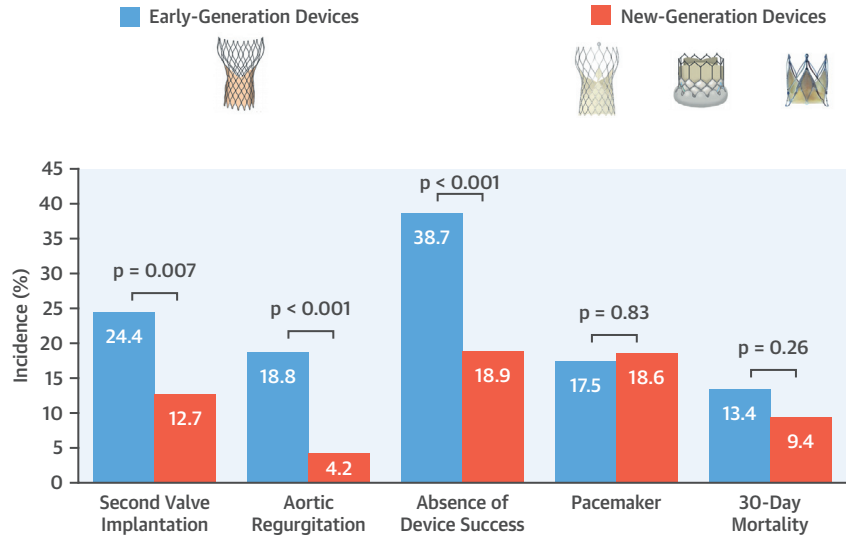
Values are n (%) or mean \pm SD. *280 patients without prior pacemakers were analyzed. LVEF = left ventricular ejection fraction; LVOT = left ventricular outflow tract.

devices, dilated aorta was associated with more frequent post-procedural AR \geq moderate (35.7% vs. 9.2%; $p = 0.002$) and less frequent device success (35.7% vs. 69.2%; $p = 0.003$) (Online Figure 6). However, there were no significant associations between procedural outcomes and dilated aorta when using the new-generation devices.

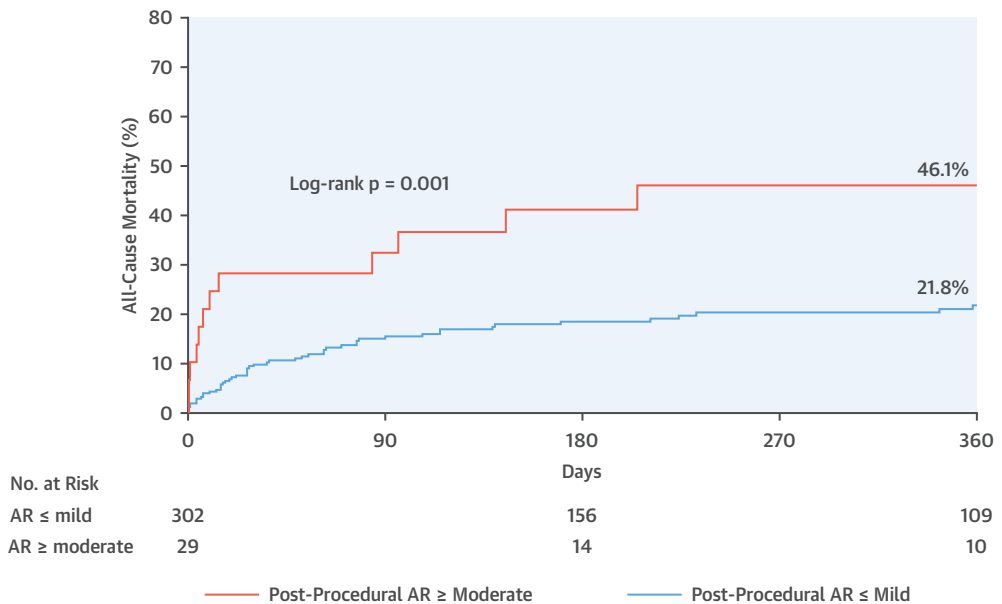
DEVICE SIZING AND POST-PROCEDURAL AORTIC REGURGITATION. The mean perimeter oversizing indexes were $14.8 \pm 9.5\%$ for the CoreValve and $19.9 \pm 11.6\%$ for the Evolut R. The mean area oversizing indexes were $13.6 \pm 13.9\%$ for the Sapien 3, $10.4 \pm 8.7\%$ for the JenaValve, and $24.9 \pm 18.6\%$ for the Direct Flow. Among patients with none or mild aortic valve calcification, 87 patients treated with the self-expanding valves had available computed tomography data. Receiver-operating characteristic curve analysis for predicting post-procedural AR \geq moderate identified cutoff value of perimeter oversizing index as 15% (area under the curve 0.76; $p < 0.001$; sensitivity 81%; specificity 63%). When using the self-expanding valves, a higher degree of perimeter oversizing index ($\geq 15\%$) was associated with less frequent post-procedural AR \geq moderate (4.0% vs. 24.3%; $p = 0.005$).

CENTRAL ILLUSTRATION TAVR for Pure Native Aortic Valve Regurgitation

Outcomes According to Devices



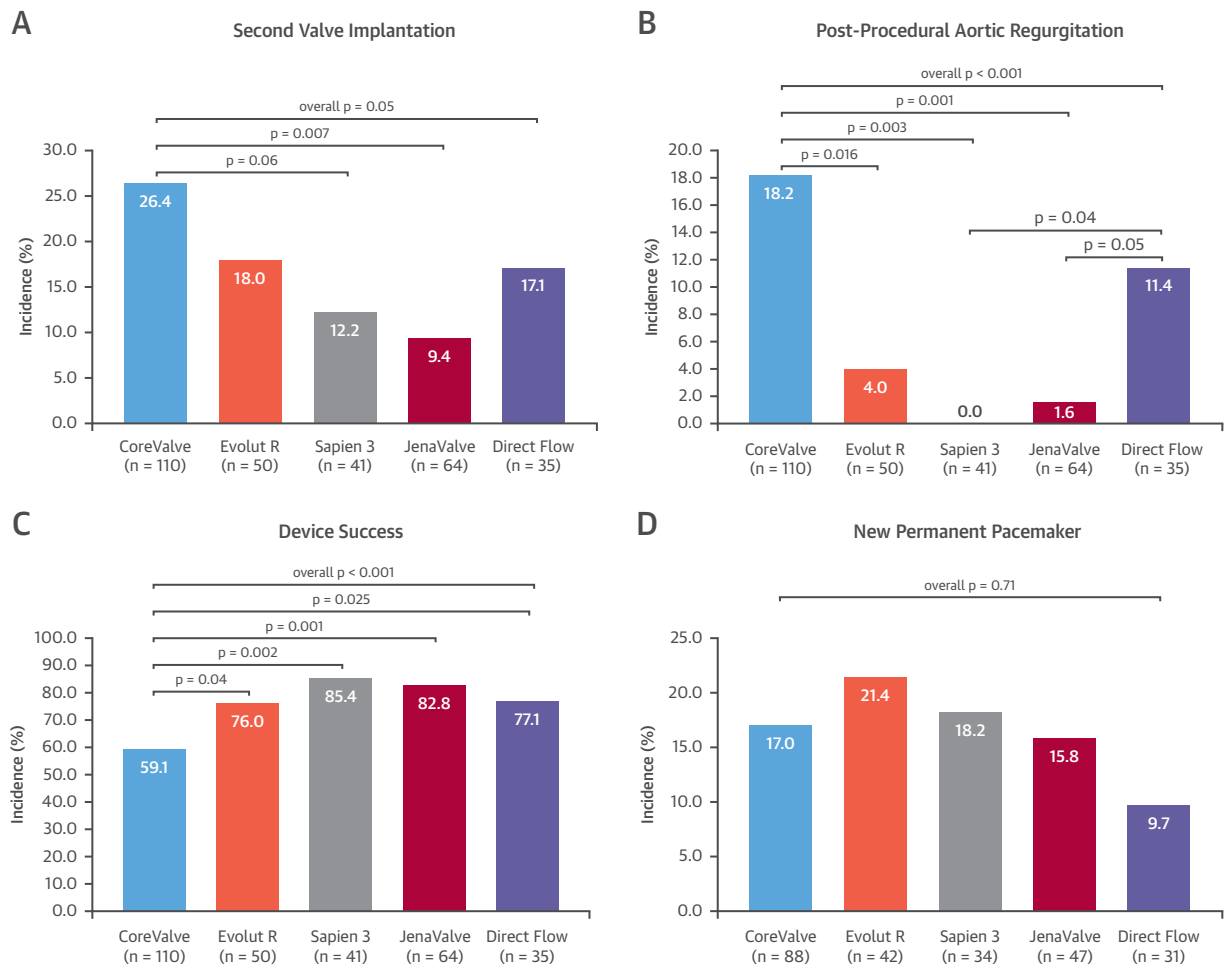
Mortality and Post-Procedural Aortic Regurgitation



Yoon, S.-H. et al. *J Am Coll Cardiol.* 2017;70(22):2752-63.

Incidences of second valve implantation, post-procedural aortic regurgitation (AR) ≥ moderate, device success, new permanent pacemaker insertion, and 30-day mortality following transcatheter aortic valve replacement (TAVR) for patients with pure native AR using the early- and new-generation devices are shown (top). The cumulative 1-year all-cause mortality rates in patients with post-procedural AR ≥ moderate (orange line) and those with post-procedural AR ≤ mild (blue line) after TAVR in pure native AR are shown (bottom).

FIGURE 1 Procedural Outcomes According to Devices

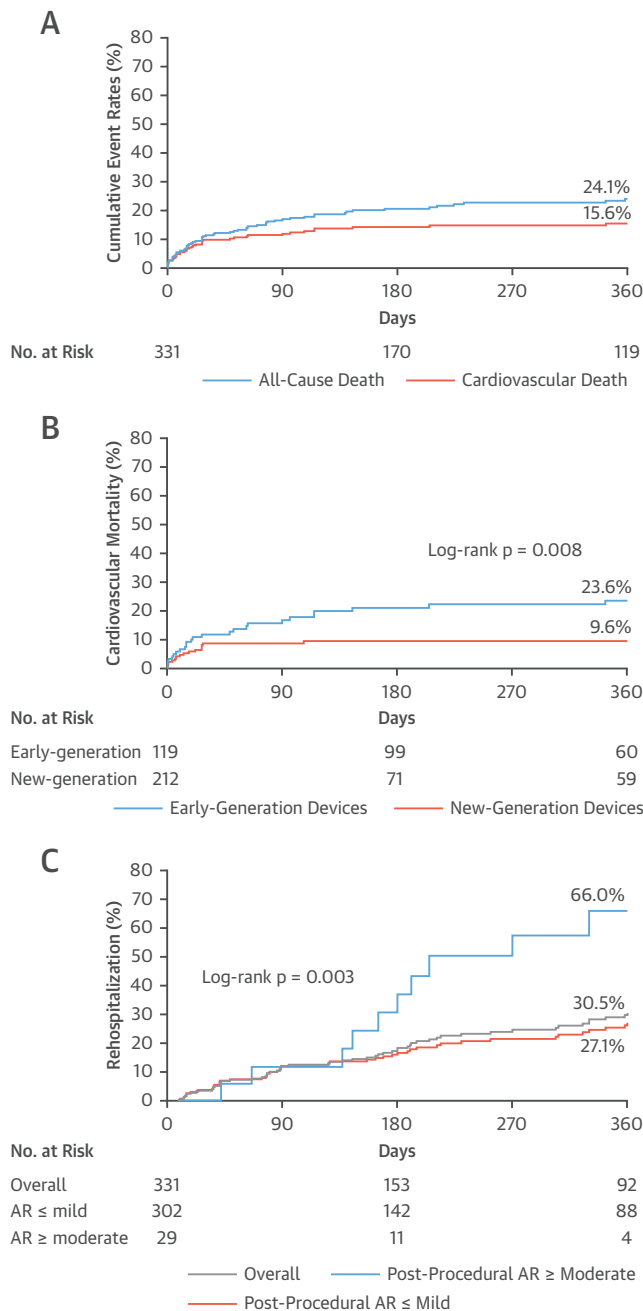


Incidences of (A) second valve implantation, (B) post-procedural aortic regurgitation \geq moderate, (C) device success, and (D) new permanent pacemaker insertion following transcatheter aortic valve replacement for patients with pure native aortic regurgitation using the CoreValve, Evolut R, Sapien 3, JenaValve, and Direct Flow devices are shown.

MID-TERM MORTALITY AND REHOSPITALIZATION. Over a median follow-up period of 200 days (interquartile range: 40 to 500 days), 82 patients died in the overall cohort (42 patients in the early-generation device group and 40 patients in the new-generation device group). The cumulative event rates for all-cause and cardiovascular death at 1-year follow-up were 24.1% and 15.6%, respectively (Figure 2A). The cumulative event rates for all-cause death at 1-year follow-up were significantly higher in patients with post-procedural AR \geq moderate compared with those with post-procedural AR \leq mild (46.1% vs. 21.8%; log-rank $p = 0.001$) (Central Illustration). Although there were no significant differences in 1-year all-cause

mortality between the early- and new-generation device groups (28.8% vs. 20.6%; log-rank $p = 0.13$) (Online Figure 7), the new-generation devices were associated with a lower 1-year cardiovascular mortality (9.6% vs. 23.6%; log-rank $p = 0.008$) (Figure 2B). Over the entire follow-up period, 72 patients experienced rehospitalization (39 patients in the early-generation device group and 33 patients in the new-generation device group). The overall cumulative event rate of rehospitalization at 1-year follow-up was 30.5% with significant higher rate of rehospitalization in the patients with post-procedural AR \geq moderate compared with those with post-procedural AR \leq mild (66.0% vs. 27.1%; log-rank $p = 0.003$) (Figure 2C).

FIGURE 2 Kaplan-Meier Curves



(A) The overall all-cause (blue line) and cardiovascular mortality rates (orange line) at 1-year follow-up in patients undergoing transcatheter aortic valve replacement (TAVR) for pure native aortic regurgitation (AR) are shown. (B) The cumulative 1-year cardiovascular mortality rates in patients with the early-generation devices (blue line) and those with the new-generation devices (orange line) after TAVR in pure native AR are shown. (C) The cumulative 1-year rehospitalization rates of the overall cohort (gray line), patients with post-procedural AR ≥ moderate (blue line), and those with post-procedural AR ≤ mild (orange line) after TAVR in pure native AR are shown. Event rates were compared using the log-rank test.

After adjustment with multivariable analysis, STS score (HR: 1.03; 95% CI: 1.00 to 1.06; $p = 0.037$), left ventricular ejection fraction $\leq 45\%$ (HR: 1.78; 95% CI: 1.07 to 2.94; $p = 0.026$), baseline mitral regurgitation \geq moderate (HR: 2.11; 95% CI: 1.29 to 3.45; $p = 0.003$), and post-procedural AR \geq moderate (HR: 2.85; 95% CI: 1.52 to 5.35; $p = 0.001$) were all independently associated with 1-year all-cause mortality (Table 4). On multivariable analysis, independent predictors for rehospitalization at 1-year follow-up were baseline mitral regurgitation \geq moderate (HR: 1.96; 95% CI: 1.17 to 3.28; $p = 0.011$) and post-procedural AR \geq moderate (HR: 2.85; 95% CI: 1.44 to 5.64; $p = 0.003$) (Online Table 3).

DISCUSSION

The present study is the largest study to our knowledge that evaluated the safety, efficacy, and clinical outcomes of TAVR in patients with pure native AR. The major findings of the present study are as follows: 1) In the overall cohort, TAVR in pure native AR was associated with relatively high rates of procedural complications, particularly when using the early-generation devices; 2) However, the new-generation devices were associated with improved procedural outcomes with lower rates of second valve implantation and post-procedural AR \geq moderate; and 3) Post-procedural AR \geq moderate was associated with increased all-cause mortality and rehospitalization.

The previous major trials established TAVR as a standard treatment for inoperable or increased surgical risk patients with severe aortic stenosis (3-6). The majority of currently available transcatheter devices are designed for treating calcified aortic stenosis, relying on the fixation of the transcatheter valve within an extensively calcified annulus. In case of pure native AR, the large aortic annulus with minimal calcification challenges the anchoring of the prosthesis. Therefore, patients with predominant AR are not indicated for TAVR according to the current guidelines (22). However, accumulated experience and advancement of device technology lead to the increased off-label use of TAVR for untreated patients with significant valvular disease other than severe aortic stenosis (23). Given the increasing number of patients with valvular heart disease in the aging population, these unmet needs will keep increasing, and therefore, understanding the outcomes of TAVR in patients with pure native AR is essential.

With technological development of transcatheter valves designed for treating patients with aortic

“stenosis,” the new-generation devices possess new specific features: namely, retrievability and repositioning capacity, an external sealing cuff, and a unique anchoring mechanism with clipping of the native aortic valve cusps. The initial report by Roy et al. (9) showed high rates of second valve implantation and post-procedural AR \geq moderate after TAVR in pure native AR using the CoreValve system. However, the improved outcomes of TAVR with increased experience of the new-generation devices in “aortic stenosis” lead to applying these new technologies to treatment of pure native AR. Recently, several studies demonstrated the acceptable clinical outcomes of TAVR using the new-generation devices in patients with pure native AR (24-27). However, these studies were limited in sample size, type of device, and follow-up period. Furthermore, limited data exist about the impact of the absence of sufficient aortic valve calcification and dilation of ascending aorta on outcomes of TAVR in pure native AR.

In the present study, the overall cohort exhibited an intermediate to high surgical risk profile with mean STS score and EuroSCORE II of 6.7% and 9.8%, respectively. Although there was a trend of lower surgical risk scores in the new-generation device group compared with the early-generation device group, the indications of TAVR were thoroughly discussed by the multidisciplinary heart team and took into account, not only the STS score, but also other factors such as frailty, neurological disorders, liver failure, and porcelain aorta. The rate of non-transfemoral access was higher in the new-generation device group (39.2% vs. 12.6%; $p < 0.001$) because of the predominant use of transapical access for the JenaValve (98.4%). Relatively high rates of stroke with the JenaValve and Direct Flow were probably due to transapical access, complex procedures, and baseline comorbidities of patients.

In the overall cohort, relatively high rates of procedural complications were observed. Given that the outcomes in patients with moderate aortic valve calcification were comparable to those in the population with severe “aortic stenosis,” procedural challenges of TAVR in pure AR may be attributed to the lack of sufficient calcification and subsequent difficulties in anchoring the devices. Due to poor visibility of the aortic annulus on fluoroscopy and regurgitation of contrast into the ventricle, there is a need for increased contrast volume for opacification, and placing an additional pigtail catheter may help the optimal positioning. In addition to the absence of aortic valve calcification, dilation of the ascending

TABLE 4 Predictors of All-Cause Mortality

	Univariable Model		Multivariable Model	
	HR (95% CI)	p Value	HR (95% CI)	p Value
Age, yrs	1.00 (0.98-1.02)	0.98		
Female	1.05 (0.65-1.72)	0.84		
NYHA functional class IV at baseline	1.33 (0.79-2.26)	0.29		
STS score	1.03 (1.01-1.06)	0.019	1.03 (1.00-1.06)	0.037
Creatinine, mg/dl	1.00 (0.80-1.25)	0.99		
Peripheral vascular disease	1.42 (0.81-2.50)	0.23		
Chronic pulmonary disease	1.34 (0.80-2.25)	0.26		
Prior cerebrovascular accident	0.78 (0.31-1.94)	0.59		
Prior coronary artery bypass graft surgery	1.41 (0.84-2.37)	0.19		
LVEF \leq 45%	1.89 (1.15-3.10)	0.012	1.78 (1.07-2.94)	0.026
Mitral regurgitation \geq moderate at baseline	1.99 (1.22-3.25)	0.006	2.11 (1.29-3.45)	0.003
Pulmonary hypertension	1.41 (0.83-2.40)	0.20		
Transfemoral access	0.81 (0.48-1.34)	0.41		
New-generation devices	0.69 (0.42-1.12)	0.13		
Need for second valve implantation	1.69 (0.93-2.96)	0.087		
Post-procedural aortic regurgitation \geq moderate	2.72 (1.45-5.10)	0.002	2.85 (1.52-5.35)	0.001
Late experience	0.83 (0.50-1.36)	0.46		

CI = confidence interval; HR = hazard ratio; other abbreviations as in Table 1.

aorta may contribute to the increased rate of valve embolization. Therefore, the possibility of valve dislocation and subsequent need for second valve implantation should be considered during the planning process. Given the relatively high rates of complications, general anesthesia and intraprocedural echocardiography assessment of post-procedural AR would help to optimize the procedural results. In terms of device sizing, a relatively higher degree of device oversizing was associated with a reduction in post-procedural AR rates when using the self-expanding valves, which confirms the importance of pre-procedural computed tomography assessment in this population as well. Further studies are required to evaluate the optimal sizing for other valves in treating pure native AR.

The association between new-generation devices and improved procedural outcomes was affected by multiple factors. Even in patients without sufficient aortic valve calcification or those with a dilated aorta, more accurate positioning and lower rates of post-procedural AR and second valve implantation were achieved with the device enhancements: longer stent frame, new delivery system, and sealing skirt in the Sapien 3; recapturability/repositionability, reduced overall height, and redesigned stent frame with

optimized radial force in the Evolut R; and new anchoring mechanism with clipping of the native aortic valve cusps in the JenaValve. In addition, several factors would contribute to the improved outcomes: 1) more frequent use of pre-procedural computed tomography assessment; 2) more frequent general anesthesia with intraprocedural transesophageal guidance; 3) more frequent transapical access; and 4) improved patient selection and accumulated procedure experience. Although the new-generation devices were associated with relatively high rates of second valve implantation in patients with a larger annulus, it should be noted that the second valve implantation was not associated with increased 1-year all-cause mortality. More importantly, the technological advancement of transcatheter valves succeeded in eliminating or reducing post-procedural AR in the pure native AR population. Given the significant impact of post-procedural AR on long-term mortality, this advantage of the new-generation devices should be highlighted.

The mid- and long-term mortality may be affected by procedural complications, as well as baseline comorbidities. The present study showed the higher mid-term mortality in patients with post-procedural AR \geq moderate compared with those with post-procedural AR \leq mild. The impact of post-procedural AR on increased mortality, which is well recognized in the aortic stenosis population (28), was consistently observed in the present pure native AR population. Furthermore, our cohort showed the increased rehospitalization rates in patients with significant post-procedural AR. The advantage of new-generation devices over the early-generation devices was observed in 1-year cardiovascular mortality, which may be due to decreased post-procedural AR as well as fewer baseline comorbidities in the new-generation device group.

The present study showed that the patient characteristics in pure native AR were not identical to those in severe aortic stenosis. The majority of patients had reduced left ventricular ejection fraction, and one-third of patients had significant mitral regurgitation and/or pulmonary hypertension, which may render patients with pure native AR more vulnerable and contribute to the relatively higher short- and mid-term mortality than is observed in aortic stenosis patients. Furthermore, due to lack of randomized studies in pure native AR, the findings in the present study need cautious interpretation. TAVR in pure native AR should be considered for patients deemed high surgical risk after consultation with the multidisciplinary heart team, and the generalization

of this procedure should be recommended only after further investigation. Further device development dedicated for treating pure native AR, establishment of device sizing guideline in this population, and accumulation of procedural experience and scientific knowledge are awaited to provide improved procedural and clinical outcomes in the future.

STUDY LIMITATIONS. First, evaluating the impact of a specific treatment using an observational study could lead to weaker conclusions than using a randomized trial because of confounding factors. Also, this study had the inherent limitations due to lack of center-independent adjunction of adverse events and an independent core laboratory to assess aortic regurgitation severity. The outcomes in this study could differ from those in “real-world” practice due to potential selection biases. Finally, device selection was not randomized, but rather at the operator’s discretion, and patient selection, as well as operator experience, may have affected the observed outcomes.

CONCLUSIONS

Compared with the early-generation devices, TAVR using the new-generation devices was associated with improved procedural outcomes in treating patients with pure native AR. In patients with pure native AR, significant post-procedural AR was independently associated with increased mortality.

ADDRESS FOR CORRESPONDENCE: Dr. Raj R. Makkar, Department of Interventional Cardiology, Cedars-Sinai Heart Institute, 8700 Beverly Boulevard, Los Angeles, California 90048. E-mail: Raj.Makkar@cshs.org.

PERSPECTIVES

COMPETENCY IN PATIENT CARE AND

PROCEDURAL SKILLS: Compared with earlier-generation devices, newer-generation TAVR devices are associated with better procedural outcomes in patients with pure native AR. In these cases, significant post-procedural AR was associated with mortality.

TRANSLATIONAL OUTLOOK: Additional studies are needed to evaluate long-term outcomes and optimal selection of patients and device types for TAVR in pure native AR.

REFERENCES

1. Singh JP, Evans JC, Levy D, et al. Prevalence and clinical determinants of mitral, tricuspid, and aortic regurgitation (the Framingham Heart Study). *Am J Cardiol* 1999;83:897-902.
2. Adams DH, Popma JJ, Reardon MJ, et al. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med* 2014;370:1790-8.
3. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med* 2011;364:2187-98.
4. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med* 2010;363:1597-607.
5. Reardon MJ, Van Mieghem NM, Popma JJ, et al. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2017;376:1321-31.
6. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2016;374:1609-20.
7. Dvir D, Webb JG, Bleiziffer S, et al. Transcatheter aortic valve implantation in failed bioprosthetic surgical valves. *JAMA* 2014;312:162-70.
8. Yoon SH, Bleiziffer S, De Backer O, et al. Outcomes in transcatheter aortic valve replacement for bicuspid versus tricuspid aortic valve stenosis. *J Am Coll Cardiol* 2017;69:2579-89.
9. Roy DA, Schaefer U, Guetta V, et al. Transcatheter aortic valve implantation for pure severe native aortic valve regurgitation. *J Am Coll Cardiol* 2013;61:1577-84.
10. Cribier A, Eltchaninoff H, Tron C, et al. Treatment of calcific aortic stenosis with the percutaneous heart valve: mid-term follow-up from the initial feasibility studies: the French experience. *J Am Coll Cardiol* 2006;47:1214-23.
11. Webb JG, Pasupati S, Humphries K, et al. Percutaneous transarterial aortic valve replacement in selected high-risk patients with aortic stenosis. *Circulation* 2007;116:755-63.
12. Ye J, Cheung A, Lichtenstein SV, et al. Transapical transcatheter aortic valve implantation: 1-year outcome in 26 patients. *J Thorac Cardiovasc Surg* 2009;137:167-73.
13. Meredith Am IT, Walters DL, Dumonteil N, et al. Transcatheter aortic valve replacement for severe symptomatic aortic stenosis using a repositionable valve system: 30-day primary endpoint results from the REPRIS II study. *J Am Coll Cardiol* 2014;64:1339-48.
14. Schofer J, Colombo A, Klugmann S, et al. Prospective multicenter evaluation of the direct flow medical transcatheter aortic valve. *J Am Coll Cardiol* 2014;63:763-8.
15. Grube E, Laborde JC, Gerckens U, et al. Percutaneous implantation of the CoreValve self-expanding valve prosthesis in high-risk patients with aortic valve disease: the Siegburg first-in-man study. *Circulation* 2006;114:1616-24.
16. Binder RK, Rodes-Cabau J, Wood DA, et al. Transcatheter aortic valve replacement with the SAPIEN 3: a new balloon-expandable transcatheter heart valve. *J Am Coll Cardiol Intv* 2013;6:293-300.
17. Seiffert M, Diemert P, Koschyk D, et al. Transapical implantation of a second-generation transcatheter heart valve in patients with noncalcified aortic regurgitation. *J Am Coll Cardiol Intv* 2013;6:590-7.
18. Wei L, Liu H, Zhu L, et al. A new transcatheter aortic valve replacement system for predominant aortic regurgitation implantation of the J-Valve and early outcome. *J Am Coll Cardiol Intv* 2015;8:1831-41.
19. Kempfert J, Holzhey D, Hofmann S, et al. First registry results from the newly approved ACURATE TA TAVI system. *Eur J Cardiothorac Surg* 2015;48:137-41.
20. Willson AB, Rodes-Cabau J, Wood DA, et al. Transcatheter aortic valve replacement with the St. Jude Medical Portico valve: first-in-human experience. *J Am Coll Cardiol* 2012;60:581-6.
21. Kappetein AP, Head SJ, Genereux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *Eur Heart J* 2012;33:2403-18.
22. Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2017;70:252-89.
23. Hira RS, Vemulapalli S, Li Z, et al. Trends and outcomes of off-label use of transcatheter aortic valve replacement: insights from the NCDR STS/ACC TVT registry. *JAMA Cardiol* 2017;2:846-54.
24. Seiffert M, Bader R, Kappert U, et al. Initial German experience with transapical implantation of a second-generation transcatheter heart valve for the treatment of aortic regurgitation. *J Am Coll Cardiol Intv* 2014;7:1168-74.
25. Schofer J, Nietlispach F, Bijklic K, et al. Transfemoral implantation of a fully repositionable and retrievable transcatheter valve for noncalcified pure aortic regurgitation. *J Am Coll Cardiol Intv* 2015;8:1842-9.
26. Urena M, Himbert D, Ohlmann P, et al. Transcatheter aortic valve replacement to treat pure aortic regurgitation on noncalcified native valves. *J Am Coll Cardiol* 2016;68:1705-6.
27. Wendt D, Kahlert P, Pasa S, et al. Transapical transcatheter aortic valve for severe aortic regurgitation: expanding the limits. *J Am Coll Cardiol Intv* 2014;7:1159-67.
28. Athappan G, Patvardhan E, Tuzcu EM, et al. 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.

KEY WORDS aortic regurgitation, transcatheter valve implantation

APPENDIX For supplemental figures and tables, please see the online version of this paper.