ORIGINAL INVESTIGATIONS

Cardiovascular Magnetic Resonance to Evaluate Aortic Regurgitation After Transcatheter Aortic Valve Replacement

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ABSTRACT

BACKGROUND Residual aortic regurgitation (AR) following transcatheter aortic valve replacement (TAVR) is associated with greater mortality; yet, determining AR severity post-TAVR using Doppler echocardiography remains challenging. Cardiovascular magnetic resonance (CMR) is purported as a more accurate means of quantifying AR; however, no data exist regarding the prognostic value of AR as assessed by CMR post-TAVR.

OBJECTIVES This study sought to evaluate the effect of AR assessed with CMR on clinical outcomes post-TAVR.

METHODS We included 135 patients from 3 centers. AR was quantified using regurgitant fraction (RF) measured by phase-contrast velocity mapping CMR at a median of 40 days post-TAVR, and using Doppler echocardiography at a median of 6 days post-TAVR. Median follow-up was 26 months. Clinical outcomes included mortality and rehospitalization for heart failure.

RESULTS Moderate-severe AR occurred in 17.1% and 12.8% of patients as measured by echocardiography and CMR, respectively. Higher RF post-TAVR was associated with increased mortality (hazard ratio: 1.18 for each 5% increase in RF [95% confidence interval: 1.08 to 1.30]; p < 0.001) and the combined endpoint of mortality and rehospitalization for heart failure (hazard ratio: 1.19 for each 5% increase in RF; 95% confidence interval: 1.15 to 1.23; p < 0.001). Prediction models yielded significant incremental predictive value; CMR performed a median of 40 days post-TAVR had a greater association with post-TAVR clinical events compared with early echocardiography (p < 0.01). RF \ge 30% best predicted poorer clinical outcomes (p < 0.001 for either mortality or the combined endpoint of mortality and heart failure rehospitalization).

CONCLUSIONS Worse CMR-quantified AR was associated with increased mortality and poorer clinical outcomes following TAVR. Quantifying AR with CMR may identify patients with AR who could benefit from additional treatment measures. (J Am Coll Cardiol 2016;68:577-85) © 2016 by the American College of Cardiology Foundation.



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ABBREVIATIONS AND ACRONYMS

AR = aortic regurgitation

CMR = cardiovascular magnetic resonance

LVOT = left ventricular outflow tract

PVL = paravalvular leak

TAVR = transcatheter aortic valve replacement

TTE = transthoracic echocardiography

VARC-2 = Valve Academic Research Consortium-2

ranscatheter aortic valve replacement (TAVR) is a rapidly expanding alternative to conventional surgical aortic valve replacement for patients with high operative risk (1). Yet, residual aortic regurgitation (AR) secondary to paravalvular leak (PVL) remains a procedural limitation (2,3). Moderate or severe residual AR post-TAVR is associated with increased shortand long-term mortality, and some studies also suggest that poorer outcomes are associated with mild AR (4,5). Although Doppler echocardiography has been the most common method used for AR assessment following TAVR, its accurate quantification is challenging, as the AR jets are often multiple and eccentric (6-9). Furthermore, acoustic shadowing from the annulus and left ventricular outflow tract (LVOT) calcifications and Doppler attenuation from the prosthetic valve stent may also interfere with the accurate quantification of regurgitant jets.

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Cardiovascular magnetic resonance (CMR) imaging is a noninvasive imaging modality that is considered the "gold-standard" method for assessing left ventricular mass, volume, and function (3,10,11). Likewise, CMR permits direct quantification of AR with high accuracy and reproducibility by using the technique of phase-contrast velocity mapping (12-14). In the context of native aortic valves, CMR-AR quantification has been correlated with clinical outcomes, including the need for surgery at long-term follow-up (12). Recent studies in the TAVR field have shown that echocardiography may underestimate or overestimate the severity of AR as compared with CMR, and a lack of agreement in AR severity between the 2 techniques has been observed in close to one-half of TAVR patients (9,15-17). However, few data exist to date on the clinical value of quantifying AR severity with CMR post-TAVR. The objective of this study was therefore to evaluate the effect of AR as determined by CMR following TAVR on clinical outcomes.

METHODS

STUDY POPULATION. This was a multicenter study including 135 patients who underwent TAVR due to

severe symptomatic aortic stenosis. Patients underwent CMR within a median of 40 days (range 6 to 105 days) following TAVR, and transthoracic echocardiography (TTE) examinations were performed within a median of 6 days (range 6 to 22 days) after the procedure. The CMR and TTE examinations were performed in similar hemodynamic conditions. Patients were eligible for TAVR if they were considered to be at high or prohibitive surgical risk as evaluated by a heart team composed of interventional cardiologists and cardiac surgeons. TAVR procedures were performed with the use of both balloon- and selfexpanding valves, as reported previously (1). All clinical events during the follow-up period were defined according to Valve Academic Research Consortium-2 (VARC-2) criteria, and data were prospectively collected in a dedicated database (18). The clinical endpoints of the study included mortality, rehospitalization for heart failure, and the need for valve reintervention. The study was performed in accordance with the local ethics committee at each center, and all patients signed informed consent forms before the procedures.

The echocardiographic and CMR results for some of the patients included in this study have been reported previously (9,16,17).

DOPPLER ECHOCARDIOGRAPHY MEASUREMENTS.

All TTE examinations were performed and analyzed at each participating center. The following measurements were obtained in all patients: aortic annulus diameter, left ventricular ejection fraction calculated with the biplane Simpson method, mean transvalvular gradient calculated with the Bernoulli formula, and the valve effective orifice area calculated by the continuity equation. AR was graded using an integrative multiparametric approach on the basis of semiguantitative and qualitative parameters, which mainly included visual assessment of the number of jets, jet width (parasternal and apical views), and the circumferential extent of PVL regurgitation, following the American Society of Echocardiography and VARC-2 recommendations (6,7,18). AR was classified as none/trace, mild, and moderate/severe (7,19-21).

CMR MEASUREMENTS. The CMR examinations were performed using a 1.5-T Philips Achieva (Philips

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TABLE 1 Clinical and Procedural Characteristic Population (N = 135)	s of the Study
Clinical variables	
Age, yrs	$\textbf{79.7} \pm \textbf{8.4}$
Male	69 (51.1)
BMI, kg/m ²	$\textbf{26.2} \pm \textbf{4.6}$
NYHA functional class	
1-11	25 (19.5)
III-IV	103 (80.5)
Diabetes	35 (25.9)
Hypertension	101 (74.8)
Coronary artery disease	70 (51.9)
Prior CABG	41 (30.4)
History of atrial fibrillation	52 (38.5)
Peripheral vascular disease	39 (28.9)
COPD	40 (29.6)
eGER. ml/min	64.5 + 22.1
STS-PROM. %	5.2 (3.4-8.9)
LogEuroSCORE %	17 7 (11 1-26 5)
Echocardiography pre-TAVR	
LVEF. %	54 + 13
Mean aortic gradient mm Hg	48 + 19
Aortic valve area cm ²	0.68 ± 0.20
Procedural variables	0.00 ± 0.20
Success*	103 (76 3)
Approach	105 (70.5)
Transfemoral	94 (69 6)
Transanical	37 (27.4)
Transaortic	4 (3 0)
Prosthesis type	1 (3.0)
Edwards-Sanien	37 (27 4)
	89 (66 O)
Sanien 3	3 (2 2)
CoreValve	3 (2.2)
Portico	3 (2.2)
Prosthesis size mm	5 (2.2)
23	56 (41 5)
26	67 (49 6)
29	11 (8 2)
31	1 (0.7)
30-day outcomes	. (617)
Maior vascular complications	4 (3 0)
Major bleeding	3 (2 2)
Conversion to open heart surgery	2 (1 5)
Need for a second valve	2 (15)
Stroke	0
Death	0
Hospitalization length, days	9 (6-13)
	3 (3 13)

Values are mean \pm SD, n (%), or median (interquartile range). *Following VARC-2 criteria (18).

BMI = body mass index; CABG = coronary arterial bypass graft; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; LogEuroSCORE = logistic EuroSCORE predicted risk of mortality; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; STS-PROM = Society of Thoracic Surgeons predicted risk of mortality; TAVR = transcatheter aortic valve replacement.

TABLE 2Post-TAVR Early Transthoracic Echocardiography andCMR Characteristics of the Study Population ($n = 135$)		
Echocardiography Early Post-TAVR (Median of 6 Days Post-TAVR)		
LVEF, %	56 ± 12	
Mean aortic gradient, mm Hg	12 ± 7	
Aortic valve area, cm ²	1.50 ± 0.54	
Multiparametric AR grade		
0/I	56 (41.8)	
II	55 (41.1)	
III	20 (14.9)	
IV	3 (2.2)	
CMR (Median of 40 Days Post-TAVR)		
Heart rhythm during CMR		
Sinus	100 (74.1)	
Atrial fibrillation	31 (22.9)	
Paced	4 (3.0)	
Mean heart rate, beats/min*	71 ± 14	
Left ventricular end diastolic volume, ml	$\textbf{155.2} \pm \textbf{54.3}$	
Left ventricular end systolic volume, ml	$\textbf{68.5} \pm \textbf{46.8}$	
Left ventricular cardiac output, l/s	$\textbf{6.1} \pm \textbf{1.5}$	
LVEF, %	58.2 ± 13.7	
Left ventricular mass, g	$\textbf{124.9} \pm \textbf{37.4}$	
Total forward volume, ml	72 (59 to 88)	
Total backward volume, ml	3 (-6 to 13)	
Regurgitant fraction, %	14 (7 to 23)	
AR grade according to CMR		
0/I: <15%	72 (54.1)	
II: 15-29%	44 (33.1)	
III/IV: ≥30%	17 (12.8)	

Values are mean \pm SD, n (%), or median (interquartile range [IQR]). Echocardiography performed early after TAVR, over a median of 6 days (IQR: 6 to 22 days) as opposed to 40 days (IQR: 6 to 105 days) for CMR. *All patients, including those in sinus rhythm, atrial fibrillation, and paced rhythm.

AR = aortic regurgitation; CMR = cardiac magnetic resonance; other abbreviations as in Table 1.

Healthcare, Best, the Netherlands) or Siemens Avanto 1.5-T scanner (Erlangen, Germany) with dedicated phased-array cardiac coil during successive endexpiratory breath-holds. Potential issues with breath-holds were reported only in a minority of patients (3.7%), and it was adequately resolved in all of them with the reduction in the number of temporal phases to shorten breath-hold duration. Cine imaging of cardiac function was performed by steady-state free precession technique, at 30 phases per cardiac cycle (by vectorcardiographic gating), in 8 to 14 parallel short-axis, 2-chamber, and 4-chamber planes, and in 2 orthogonal LVOT planes. Typical parameters included a repetition time of around 4 ms and an echo time of 2 ms, varying with slice orientation; typically 25 phases per cardiac cycle; and a reconstructed in-plane resolution of 1 mm. The slice thickness usually was in the range of 6 to 8 mm. The typical temporal resolution of the cine balanced steady-state

	Univariate Model		Multivariate Model	
	HR (95% CI)	p Value	HR (95% CI)	p Value
Death (n $=$ 31)				
Coronary artery disease	0.25 (0.05-1.30)	0.098	0.24 (0.04-1.44)	0.118
COPD	2.73 (1.37-5.44)	0.005	2.76 (1.74-4.37)	< 0.001
Regurgitant fraction, %*	1.12 (1.09-1.15)	< 0.001	1.18 (1.08-1.30)	< 0.001
Death and rehospitalization for heart failure ($n = 41$)				
Diabetes	1.46 (1.20-1.79)	< 0.001	1.04 (0.79-1.39)	0.765
COPD	2.15 (1.80-2.56)	< 0.001	2.29 (1.92-2.73)	< 0.001
Regurgitant fraction, %*	1.17 (1.16-1.19)	< 0.001	1.19 (1.15-1.23)	< 0.001

free precession sequences was 30 to 40 ms, depending on the heart rate. The slice for the through-plane phase-contrast flow imaging was placed perpendicular to the direction of flow, approximately 10 mm above the aortic prosthesis. This adequate distance to the prosthesis was kept, as phase-contrast acquisitions may be prone to magnetic field inhomogeneities. Sequences for orthogonal images in at least 2 views were used to ensure that the image plane was truly perpendicular to the flow direction. Velocity encoding maximum value was set at 200 cm/s. Caution was taken to exclude the prosthesis from the acquisition slice to avoid artifacts. However, if significant turbulence, aliasing, or prosthesis stentrelated artifacts were seen in the velocity image, the acquisition was repeated a few millimeters downstream from the valve, and/or with a higher-velocity window (velocity was increased by 50 cm/s). Still, in 2 patients the flow-volume curves were not diagnostic and were finally rejected. Each phase-contrast velocity mapping acquisition produced 2 cine images: 1 magnitude image and 1 phase image.

For assessment of AR, a region of interest identifying the aortic root was defined, and flow was integrated for the whole cardiac cycle to provide forward and regurgitant flow through the aortic valve per cardiac cycle. The regurgitant fraction (RF) was calculated as follows: (regurgitant volume/total forward volume) \times 100. CMR grades of AR were defined according to RF, using similar reference cut-point values as previously described in the VARC-2 criteria: none/trace (RF <15%), mild (16% to 29%), and moderate/severe (≥30%) (18). Left ventricular volumes and ejection fractions were calculated with the use of end-diastolic and -systolic endocardial semiautomated tracings. The intraobserver and interobserver agreement weighted kappas have been published elsewhere (9,16,17).

STATISTICAL ANALYSIS. Continuous variables were tested for distribution normality with the Shapiro-Wilk test and are expressed as mean \pm SD or median (25th to 75th interquartile range [IQR]). Categorical variables are reported as n (%). Univariate and multivariate Cox proportional hazard models were used to determine the predictors of cumulative allcause mortality; the combined endpoint of all-cause mortality and rehospitalization for heart failure; as well as the combined endpoint of cardiac mortality, rehospitalization for heart failure, and valve reintervention. The variables with a probability value <0.10 were included in the multivariate regression model. To check the proportionality assumption, an artificially time-dependent covariate was added to the model. For all variables in the final models, the proportional hazards assumptions were not rejected as local tests linked to the time-dependent covariates were not significant. All analyses were performed using a hierarchical method to account for betweencenter variability. A receiver-operating characteristic curve analysis was used to determine the best RF value cut-off predicting increased all-cause mortality and combined all-cause mortality + rehospitalization for heart failure at 2-year follow-up. To determine whether CMR-quantified AR offered additional value in predicting clinical events beyond that of AR quantified by echocardiography, the incremental value of CMR-determined AR grade was assessed using the net reclassification index (NRI). Logistic regression was used to determine predicted probabilities for the 2-year combined endpoint in each patient, using the background model. The probabilities were then ranked and categorized into tertiles (<13%, 13% to <17%, and \geq 17% for all-cause mortality; and <19%, 19% to <27%, and ≥27% for all-cause mortality and rehospitalization for heart failure). After a CMR grade of AR was added into the model, patients were reclassified according to the predicted probability of the combined endpoint at 2 years. The NRI quantified the net improvement in risk reclassification (higher predicted probability of the combined endpoint in 2-year nonsurvivors; lower predicted probability of death in 2-year survivors). The results were considered significant with p values <0.05. Analyses were conducted using the SAS statistical package, version 9.4 (SAS Institute Inc., Cary, North Carolina) and Statistical Package for Social Sciences, version 20 (SPSS Inc., IBM, Armonk, New York).

RESULTS

Baseline and procedural characteristics of the study population are shown in Table 1.

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ECHOCARDIOGRAPHIC AND CMR DATA AFTER TAVR. Post-TAVR TTE and CMR characteristics are shown in **Table 2**. Regarding the TTE data after TAVR, the mean aortic gradient and aortic valve area were 12 ± 7 mm Hg and 1.50 ± 0.54 cm², respectively. The AR grade according to the multiparametric TTE approach was moderate and severe in 14.9% and 2.2% of the patients, respectively. Therefore, 82.9% of the patients presented mild or less AR by TTE. During CMR, 100 patients (74%) were in sinus rhythm with an average heart rate of 71 ± 14 beats/ min. The median RF as determined by CMR was 14% (range 7% to 23%), and moderate/severe AR by CMR was present in 12.8% of the patients.

CLINICAL EFFECT OF AR MEASURED BY CMR. A total of 31 patients (23.0%) had died at a median follow-up of 26 months (range 13 to 41 months). The causes of death were cardiac (n = 16), sepsis (n = 6), pulmonary (n = 4), cancer (n = 3), and bleeding (n = 2). There were 16 rehospitalizations for heart failure and 8 transcatheter valve reinterventions (second transcatheter valve in 4, vascular plug in 3, and surgical aortic valve replacement in 1 patient). The variables associated with a higher risk of mortality and the combined endpoint of mortality and rehospitalization for heart failure are shown in Table 3. Greater RF as determined by CMR post-TAVR was independently associated with late cumulative all-cause mortality (hazard ratio [HR]: 1.18 for each 5% increase in RF; 95% confidence interval [CI]: 1.08 to 1.30; p < 0.001) and the combined endpoint of late cumulative all-cause mortality and rehospitalization for heart failure (HR: 1.19 for each increase of 5%; 95% CI: 1.15 to 1.23; $p\,<$ 0.001). Greater RF was also independently associated with the combined endpoint of late cardiovascular mortality, rehospitalization for heart failure, or reintervention in the transcatheter valve (HR: 1.25 for each increase of 5%; 95% CI: 1.17 to 1.34; p < 0.001). In all models, CMRquantified AR performed at a median of 40 days provided significant additive model prediction value to that of early (median of 6 days) post-TAVR echocardiographic AR grade and the other clinical variables (p < 0.05 for all models). Also, after adding CMR-quantified AR to the background model, the NRI in predicting the 2-year outcomes of mortality and the combined endpoint of mortality and rehospitalization for heart failure was 15% (p < 0.03 for both).

 $RF \ge 30\%$ best identified patients who were at greater risk of 2-year mortality (area under the curve: 0.678, sensitivity = 39%, specificity = 70%; p = 0.001) and mortality and rehospitalization for



Kaplan-Meier survival curves for cumulative all-cause mortality according to the cardiac magnetic resonance (CMR) aortic regurgitation (AR) grade at a median of 40 days post-TAVR (**A**), and early (median of 6 days post-TAVR) transthoracic echocardiographic (TTE) AR grade (**B**). RF = regurgitant fraction.

heart failure (area under the curve: 0.679, sensitivity = 39%, specificity = 70%; p = 0.001). Kaplan-Meier survival curves according to differing degrees of RF after TAVR and those according to the TTE-AR grades are shown in **Figures 1** and **2**, respectively. RF on CMR \geq 30% was associated with higher all-cause mortality (35.1% vs. 13%; p = 0.032) and mortality and rehospitalization for heart failure



heart failure (HF) according to the CMR AR grade at a median of 40 days post-TAVR (A), and early (median of 6 days post-TAVR) TTE AR grade (B). Abbreviations as in Figure 1.

> (47.3% vs. 15.2%; p = 0.002) at 2-year follow-up (Central Illustration). The mortality at 2 years was numerically higher in patients with moderate-severe AR as evaluated by TTE (compared to those with mild or less AR), but these differences did not reach statistical significance (19.6% vs. 15.2%; p = 0.70). A similar result was observed regarding the combined endpoint of mortality and rehospitalization for heart failure (TTE, moderate-severe AR group: 32% vs. 17.6% in the mild or less AR group; p = 0.175) at 2-year follow-up.

DISCUSSION

The present study demonstrates that a higher RF as determined by CMR was associated with poorer clinical outcomes after a median follow-up of ~2 years post-TAVR, with increased rates of mortality and rehospitalization due to heart failure. CMR-RF ≥30% post-TAVR best predicted poorer clinical outcomes, and CMR-AR grading performed at a median of 40 days post-TAVR was associated with a significant added value for the prediction of clinical events in addition to early (median 6 days post-TAVR) TTE.

TAVR technology has evolved significantly in recent years; however, transcatheter heart valves are still associated with a much higher rate of residual AR, chiefly paravalvular regurgitation, as compared with surgical aortic valve replacement. Although the incidence of residual post-TAVR AR may approach 70%, it is moderate-to-severe in ~12% of the time, also affecting the device success rates. Consistent with our results, device success rates have been lower in the recent studies using the VARC-2 criteria (2,3,8,9). However, the rate of device success was slightly lower in our study, mainly secondary to a >10% incidence of at least moderate AR as evaluated by echocardiography. Importantly, in a recent meta-analysis including 45 studies and 12,926 patients (4), moderateto-severe PVL was associated with an increased rate of short- and mid-term mortality, whereas studies evaluating the effect of mild PVL on outcomes have yielded conflicting results (5,22,23). Although the use of newer transcatheter valve technologies with enhanced antiparavalvular leak properties have been associated with a significant decrease in paravalvular leaks post-TAVR, the rates of mild AR as evaluated by TTE still remain close to 30% (24-26). The precise quantification of AR post-TAVR is therefore of paramount importance, and yet it faces enormous challenges, as the currently available methods for assessing AR are imprecise with limited validation.

Although TTE has been the most commonly used method to quantify AR post-TAVR, this technology still has a number of shortcomings, partially due to the frequent observation of the multiple, irregular, and eccentric paravalvular jets (6-9). Likewise, the quantitative and semiquantitative parameters proposed in the American Society of Echocardiography/ European Association of Echocardiography guidelines (6) may be difficult to measure (e.g., vena contracta width, jet width to LVOT diameter ratio) or less reliable (e.g., pressure half-time of the continuous wave Doppler aortic regurgitant envelope) post-TAVR. This is mainly due to the acute nature of the regurgitation and the reduced compliance of the left ventricle (9).

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Therefore, the precise quantification of paravalvular jets by TTE may be compromised by an ensuing underestimation or overestimation of AR severity.

Misclassification of AR grade by TTE has been shown in previous studies comparing TTE with CMR for AR assessment post-TAVR (9,15,17,27), although different cut-off points for determining AR grade by CMR were used (9,15-17,19). The cut-offs proposed in the VARC-2 for defining moderate and severe AR were used in the present study (18). Of note, this misclassification in AR grade may partially explain the association between mild AR post-TAVR as evaluated by TTE and mortality in some studies (4,5). It is also important to note that recent reports have used color Doppler 3-dimensional (3D) echocardiography to improve the evaluation of both regurgitant jets and the planimetry of the vena contracta area in native AR and AR post-TAVR (28,29). Similarly, a recent study comparing CMR quantification of AR with 2dimensional and 3D echocardiography demonstrated that 3D assessment could significantly improve AR quantification post-TAVR (15). Unfortunately, no 3D echocardiography analysis was included in the present study, so future studies will have to determine if 3D methods are reproducible and may indeed be associated with a more precise quantification of AR.

Prior studies in the TAVR field have consistently shown the negative clinical effect of significant AR after TAVR as evaluated by TTE (2-4). Hartlage et al. (16) reported in a cohort of 21 patients the potential clinical value of CMR for evaluating AR post-TAVR. The present study confirmed that CMR performed

Downloaded for Anonymous User (n/a) at Brazilian Society of Cardiology from ClinicalKey.com by Elsevier on March 26, 2021. For personal use only. No other uses without permission. Copyright ©2021. Elsevier Inc. All rights reserved. at a median of 40 days post-TAVR may improve the prediction of poorer clinical outcomes. There appears to be a stepwise increase in clinical events including mortality and rehospitalization for heart failure according to the differing grades of RF post-TAVR. However, this correlation was more prominent in those patients with an RF \geq 30%, which is consistent with a prior study in the context of native aortic valves (12). Myerson et al. (12) showed that a >33% in RF was associated with an increased incidence of cardiac events, including heart failure symptoms and the need for valve replacement, over a mean follow-up of \sim 3 years. However, unlike the work of Myerson et al. (12), we failed to find an association between the regurgitant volume and clinical outcomes. This may be explained by the fact that AR following TAVR is more an acute form of AR that occurs in patients with pre-existing severe AS and concentric LV hypertrophy, generally with a small LV cavity (30). In this context, a small regurgitant volume may actually correspond to a large RF with a significant effect on clinical outcomes. These findings thus suggest that RF may be superior to regurgitant volume to assess the severity of PVL early after TAVR, and may help in further identifying those patients with truly significant AR. Therefore, such patients might benefit from additional interventions, including paravalvular leak closure, second valve/post-dilation, and possibly surgical aortic valve replacement, to improve late clinical outcomes.

STUDY LIMITATIONS. The patients were not consecutive and a selection bias might have influenced the results. However, the fact that TTE results were similar to those obtained in prior TAVR studies makes this possibility unlikely. TTE and CMR examinations were not performed on the same day for the majority of the patients; this precluded the direct comparison between echocardiography and CMR at the same time-point post-TAVR in assessing the degree of AR and their relative predictive power for clinical outcomes. The results of this study were obtained in patients undergoing TAVR mostly with a balloon-expandable

valve, and may not apply to those patients receiving a self-expanding valve. Although this study represents the largest series of patients evaluated with CMR post-TAVR, the study included a relatively small cohort of patients/events, and the results require confirmation in future larger-scale studies.

CONCLUSIONS

A higher degree of CMR-quantified AR post-TAVR was associated with increased mortality and poorer clinical outcomes. Quantifying AR by CMR may help to identify those patients with significant residual AR and the eventual need for additional intervention following TAVR. Future studies are necessary to determine the effect of implementing CMR post-TAVR in improving the treatment of and outcomes associated with AR post-TAVR.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE: In patients with AR after TAVR, a regurgitant fraction \geq 30% as measured by CMR at a median of 40 days is associated with increased mortality and rehospitalization for heart failure.

TRANSLATIONAL OUTLOOK: Further studies are needed to define the value of CMR in guiding therapeutic interventions to improve outcomes in patients with AR following TAVR.

REFERENCES

1. Rodes-Cabau J. Transcatheter aortic valve implantation: current and future approaches. Nat Rev Cardiol 2011;9:15-29.

2. Genereux P, Head SJ, Hahn R, et al. Paravalvular leak after transcatheter aortic valve replacement: the new Achilles' heel? A comprehensive review of the literature. J Am Coll Cardiol 2013;61:1125-36.

3. Lerakis S, Hayek SS, Douglas PS. Paravalvular aortic leak after transcatheter aortic valve

replacement: current knowledge. Circulation 2013; 127:397-407.

4. 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.

5. Kodali SK, Williams MR, Smith CR, et al. Twoyear outcomes after transcatheter or surgical aortic-valve replacement. N Engl J Med 2012;366: 1686-95.

6. Zoghbi WA, Chambers JB, Dumesnil JG, et al. Recommendations for evaluation of prosthetic valves with echocardiography and Doppler ultrasound: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Task Force on Prosthetic Valves, developed in conjunction with the American College of Cardiology Cardiovascular Imaging Committee, Cardiac Imaging Committee of the American Heart Association, the European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography and the Canadian Society of Echocardiography. J Am Soc Echocardiogr 2009;22:975-1014. guiz 1082-4.

7. Zoghbi WA, Enriquez-Sarano M, Foster E, et al. Recommendations for evaluation of the severity of native valvular regurgitation with twodimensional and Doppler echocardiography. J Am Soc Echocardiogr 2003;16:777-802.

8. Hahn RT, Pibarot P, Stewart WJ, et al. Comparison of transcatheter and surgical aortic valve replacement in severe aortic stenosis: a longitudinal study of echocardiography parameters in cohort A of the PARTNER trial (Placement of Aortic Transcatheter Valves). J Am Coll Cardiol 2013;61:2514-21.

9. Ribeiro HB, Le Ven F, Larose E, et al. Cardiac magnetic resonance versus transthoracic echocardiography for the assessment and quantification of aortic regurgitation in patients undergoing transcatheter aortic valve implantation. Heart 2014;100:1924-32.

10. Hudsmith LE, Petersen SE, Francis JM, Robson MD, Neubauer S. Normal human left and right ventricular and left atrial dimensions using steady state free precession magnetic resonance imaging. J Cardiovasc Magn Reson 2005;7:775-82.

11. Lorenz CH, Walker ES, Morgan VL, Klein SS, Graham TP Jr. Normal human right and left ventricular mass, systolic function, and gender differences by cine magnetic resonance imaging. J Cardiovasc Magn Reson 1999;1:7-21.

12. Myerson SG, d'Arcy J, Mohiaddin R, et al. Aortic regurgitation quantification using cardiovascular magnetic resonance: association with clinical outcome. Circulation 2012;126:1452-60.

13. Sherif MA, Abdel-Wahab M, Beurich HW, et al. Haemodynamic evaluation of aortic regurgitation after transcatheter aortic valve implantation using cardiovascular magnetic resonance. Euro-Intervention 2011;7:57-63. **14.** Sondergaard L, Lindvig K, Hildebrandt P, et al. Quantification of aortic regurgitation by magnetic resonance velocity mapping. Am Heart J 1993;125: 1081-90.

15. Altiok E, Frick M, Meyer CG, et al. Comparison of two- and three-dimensional transthoracic echocardiography to cardiac magnetic resonance imaging for assessment of paravalvular regurgitation after transcatheter aortic valve implantation. Am J Cardiol 2014;113:1859-66.

16. Hartlage GR, Babaliaros VC, Thourani VH, et al. The role of cardiovascular magnetic resonance in stratifying paravalvular leak severity after transcatheter aortic valve replacement: an observational outcome study. J Cardiovasc Magn Reson 2014;16:93.

17. Orwat S, Diller GP, Kaleschke G, et al. Aortic regurgitation severity after transcatheter aortic valve implantation is underestimated by echocar-diography compared with MRI. Heart 2014;100: 1933-8.

18. 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. J Am Coll Cardiol 2012;60:1438-54.

19. Gabriel RS, Renapurkar R, Bolen MA, et al. Comparison of severity of aortic regurgitation by cardiovascular magnetic resonance versus transthoracic echocardiography. Am J Cardiol 2011;108: 1014–20.

20. 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.

21. 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.

22. Gilard M, Eltchaninoff H, lung B, et al. Registry of transcatheter aortic-valve implantation in high-risk patients. N Engl J Med 2012;366:1705-15.

23. Van Belle E, Juthier F, Susen S, et al. Post-procedural aortic regurgitation in balloon-

expandable and self-expandable transcatheter aortic valve replacement procedures: analysis of predictors and impact on long-term mortality: insights from the FRANCE2 Registry. Circulation 2014;129:1415-27.

24. Webb J, Gerosa G, Lefevre T, et al. Multicenter evaluation of a next-generation balloon-expandable transcatheter aortic valve. J Am Coll Cardiol 2014;64:2235-43.

25. 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 REPRISE II study. J Am Coll Cardiol 2014;64:1339-48.

26. 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.

27. Crouch G, Tully PJ, Bennetts J, et al. Quantitative assessment of paravalvular regurgitation following transcatheter aortic valve replacement. J Cardiovasc Magn Reson 2015;17:32.

28. Goncalves A, Almeria C, Marcos-Alberca P, et al. Three-dimensional echocardiography in paravalvular aortic regurgitation assessment after transcatheter aortic valve implantation. J Am Soc Echocardiogr 2012;25:47-55.

29. Perez de Isla L, Zamorano J, Fernandez-Golfin C, et al. 3D color-Doppler echocardiography and chronic aortic regurgitation: a novel approach for severity assessment. Int J Cardiol 2013;166: 640–5.

30. Jerez-Valero M, Urena M, Webb JG, et al. Clinical impact of aortic regurgitation after transcatheter aortic valve replacement: insights into the degree and acuteness of presentation. J Am Coll Cardiol Intv 2014;7:1022-32.

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