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Clinical Impact of Aortic Regurgitation After Transcatheter Aortic Valve Replacement

Insights Into the Degree and Acuteness of Presentation

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ABSTRACT

OBJECTIVES The aim of this study was to determine the impact of the degree of residual aortic regurgitation (AR) and acuteness of presentation of AR after transcatheter aortic valve replacement (TAVR) on outcomes.

BACKGROUND The degree of residual AR after TAVR leading to excess mortality remains controversial, and little evidence exists on the impact of the acuteness of presentation of AR.

METHODS A total of 1,735 patients undergoing TAVR with balloon-expandable or self-expanding valves were included. The presence and degree of AR were evaluated by transthoracic echocardiography; acute AR was defined as an increase in AR severity of ≥1 degree compared with pre-procedural echocardiography.

RESULTS Residual AR was classified as mild in 761 patients (43.9%) and moderate to severe in 247 patients (14.2%). The presence of moderate to severe AR was an independent predictor of mortality at a mean follow-up of 21 ± 17 months compared with none to trace (adjusted hazard ratio [HR]: 1.81, 95% confidence interval [CI]: 1.32 to 2.48; $p < 0.001$) and mild AR (adjusted HR: 1.68, 95% CI: 1.27 to 2.24; $p < 0.001$) groups. There was no increased risk in patients with mild AR compared with those with none to trace AR ($p = 0.393$). In patients with moderate to severe AR, acute AR was observed in 161 patients (65%) and chronic AR in 86 patients (35%). Acute moderate to severe AR was independently associated with increased risk of mortality compared with none/trace/mild AR (adjusted HR: 2.37, 95% CI: 1.53 to 3.66; $p < 0.001$) and chronic moderate to severe AR (adjusted HR: 2.24, 95% CI: 1.17 to 4.30; $p = 0.015$). No differences in survival rate were observed between patients with chronic moderate to severe and none/trace/mild AR ($p > 0.50$).

CONCLUSIONS AR occurred very frequently after TAVR, but an increased risk of mortality at ~2-year follow-up was observed only in patients with acute moderate to severe AR. (J Am Coll Cardiol Intv 2014;7:1022–32)

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Residual aortic regurgitation (AR) is considered to be one of the most important limitations of transcatheter aortic valve replacement (TAVR) with an incidence of mild or more than mild paravalvular leaks of >50% in most series, which markedly exceeds that observed after standard surgical aortic valve replacement (1–3). Several studies have shown that the presence of moderate to severe residual AR after TAVR is one of the strongest predictors of acute mortality and at mid-term follow-up (1–14). However, efforts to determine the clinical impact of mild residual AR have yielded inconsistent results (4,6,11,13–17), and whether mild AR after TAVR is associated with poorer outcomes remains controversial. Further clarification of this issue is of high clinical relevance, especially considering both the high incidence of mild AR after TAVR and the potentially deleterious effects and costs associated with additional measures for the treatment of paravalvular leaks in such cases (e.g., balloon post-dilation, implantation of a second valve, paravalvular leak closure) (18–20).

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The early negative effect of residual AR on TAVR candidates contrasts with the clinical evidence on the impact of moderate or even severe AR in the overall population, which commonly progress slowly, with a long latency period before the appearance of symptoms or complications (21,22). It was recently suggested that the acuteness of residual AR after TAVR might have an impact on late mortality. In particular, the worsening of ≥2 degrees in AR after TAVR was found to be associated with increased mortality (4). However, the degree of AR in this group of patients was not detailed, no adjustment for confounding factors was performed, and whether the impact of the acuteness of presentation of AR was independent of the occurrence of moderate to severe AR was not determined. Moreover, few data exist on the impact of residual AR on cardiovascular outcomes, including cardiac (rather than global) mortality and echocardiographic parameters (6,17,23). The objectives of this study, therefore, were the following: 1) to evaluate the impact of the severity and acuteness of AR after TAVR on clinical outcomes (global and cardiovascular) and 2) to assess the impact of residual AR on left ventricular ejection fraction (LVEF) and mitral regurgitation (MR) changes as evaluated by echocardiography.

METHODS

STUDY POPULATION. A total of 1,783 consecutive patients undergoing TAVR with balloon-expandable valves (982 patients) and self-expanding valves (753 patients) at 8 centers were evaluated. Forty-eight patients were excluded because of the following reasons: unsuccessful procedure without valve implantation in 30 patients, death during the first 24 h after TAVR before an echocardiogram was performed in 17 patients, and concomitant transcatheter mitral valve-in-valve implantation in 1 patient. Therefore, the final study population consisted of 1,735 patients. Details about the number of patients, and type of valves in each center are provided in Online Figure 1. Eligibility for TAVR, valve type, and access

ABBREVIATIONS AND ACRONYMS

AR = aortic regurgitation
CI = confidence interval
HR = hazard ratio
LVEF = left ventricular ejection fraction
MR = mitral regurgitation
TAVR = transcatheter aortic valve replacement
VARC-2 = Valve Academic Research Consortium 2

TABLE 1 Baseline Clinical Characteristics and Echocardiographic and Procedural Findings According to the Severity of AR After TAVR

	All (n = 1,735)	None to Trace AR (n = 727)	Mild AR (n = 761)	Moderate to Severe AR (n = 247)	p Value
Clinical characteristics					
Age, yrs	81 ± 7	80 ± 7	81 ± 7*	80 ± 8	0.002
Male	848 (48.9)	306 (42.1)	402 (52.8)*	140 (56.7)†	<0.001
Body mass index, kg/m^2	27 ± 5	27 ± 5	27 ± 5*	26 ± 5†	<0.001
Hypertension	1,417 (81.7)	634 (87.3)	595 (78.2)*	188 (76.1)†	<0.001
Diabetes	553 (31.9)	252 (34.7)	238 (31.3)	63 (25.6)†	0.024
NYHA functional class ≥3	1,403 (80.9)	585 (80.5)	620 (81.5)	198 (80.2)	0.833
Chronic atrial fibrillation	403 (23.2)	140 (19.3)	208 (27.3)*	55 (22.3)	0.001
CABG	413 (23.8)	181 (24.9)	182 (23.9)	50 (20.2)	0.337
COPD	548 (31.6)	243 (33.4)	220 (29.2)	83 (33.6)	0.165
eGFR <60 ml/min	955 (55.0)	401 (55.2)	410 (53.9)	144 (58.3)	0.561
STS-PROM score, %	7.7 ± 5.2	7.3 ± 5.1	8.1 ± 5.3*	7.6 ± 5.0	0.003
Logistic EuroSCORE, %	20.8 ± 13.9	20.3 ± 13.7	21.5 ± 14.1	20.5 ± 13.9	0.119
Echocardiographic findings					
LVEF <40%	327 (18.8)	119 (16.4)	146 (19.2)	62 (25.1)†	0.011
Aortic mean gradient, mm Hg	46 ± 17	45 ± 16	47 ± 16*	49 ± 18†	<0.001
Aortic valvular area, cm^2	0.65 ± 0.20	0.67 ± 0.21	0.63 ± 0.18*	0.64 ± 0.18	0.018
Systolic pulmonary artery pressure >55 mm Hg	268 (15.4)	98 (13.5)	125 (16.4)	45 (18.1)	0.116
Procedural findings					
Approach					<0.001
Transfemoral/subclavian	1,282 (73.9)	463 (63.7)	607 (79.8)*	212 (85.8)†‡	
Transapical/transaortic	453 (26.1)	264 (36.3)	154 (20.2)	35 (14.2)	
Prosthesis type					<0.001
Self-expanding valve	753 (43.4)	281 (38.7)	325 (42.7)	147 (59.5)†‡	
Balloon-expandable valve	982 (56.6)	446 (61.3)	436 (57.3)	100 (40.5)	
Prosthesis size					<0.001
20–23	452 (26.1)	225 (30.9)	182 (23.9)	45 (18.2)	
26	870 (50.1)	352 (48.4)	402 (52.8)	116 (47.0)†‡	
29–31	413 (23.8)	150 (20.6)	177 (23.3)*	86 (34.8)†‡	

Values are mean ± SD or n (%). *p < 0.05 versus none/trace. †p < 0.05 versus none/trivial. ‡p < 0.05 versus mild.

AR = aortic regurgitation; CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration ratio; 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.