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Transcatheter Aortic Valve Replacement

Outcomes of Patients With Moderate or Severe Mitral Regurgitation

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Objectives The aim of this study was to evaluate the impact of mitral regurgitation (MR) on outcomes after transcatheter aortic valve replacement (TAVR) and the impact of TAVR on MR.

Background Little is known of the influence of MR on outcomes after TAVR.

Methods The outcomes of patients with mild or less (n = 319), moderate (n = 89), and severe (n = 43) MR were evaluated after TAVR at 2 Canadian centers.

Results Patients with moderate or severe MR had a higher mortality rate than those with mild or less MR during the 30 days after TAVR (adjusted hazard ratio: 2.10; 95% confidence interval: 1.12 to 3.94; p = 0.02). However, the mortality rates after 30 days were similar (adjusted hazard ratio: 0.82; 95% confidence interval: 0.50 to 1.34; p = 0.42). One year after TAVR, moderate MR had improved in 58%, remained moderate in 17%, and worsened to severe in 1%, and 24% of patients had died. Severe MR had improved in 49% and remained severe in 16%, and 35% of patients had died. Multivariate predictors of improved MR at 1 year (vs. unchanged MR, worse MR, or death) were a mean transaortic gradient ≥40 mm Hg, functional (as opposed to structural) MR, the absence of pulmonary hypertension, and the absence of atrial fibrillation.

Conclusions Moderate or severe MR in patients undergoing TAVR is associated with a higher early, but not late, mortality rate. At 1-year follow-up, MR was improved in 55% of patients with moderate or severe MR at baseline. Improvement was more likely in patients with high transaortic gradients, with functional MR, without pulmonary hypertension and without atrial fibrillation. (J Am Coll Cardiol 2012;59:2068–74) © 2012 by the American College of Cardiology Foundation

Mitral regurgitation (MR) is present in most patients with severe aortic stenosis. In patients undergoing surgical aortic valve replacement, the reported prevalence of moderate or severe MR ranges from 13% to 74% (1–3). Such patients often undergo concomitant mitral valve repair or replacement.

Similarly, large series have reported moderate or severe MR in 22% to 48% of patients undergoing transcatheter aortic valve replacement (TAVR) (4–10), although in this setting, MR is typically left untreated. In fact, patients with severe MR have generally been excluded from formal evaluation, and outcomes in patients with MR have not been a focus of evaluation (11–13). Consequently, little is known about the impact of MR on clinical outcomes after TAVR and the impact of TAVR on MR (12,14).

Methods

Study population. Between January 2005 and July 2010, a total of 478 patients underwent TAVR for the treatment of severe symptomatic aortic stenosis at 2 Canadian centers, St. Paul's Hospital (Vancouver, British Columbia, Canada), and the Quebec Heart and Lung Institute (Quebec City, Quebec City, Canada), with the balloon expandable Cribier-Edwards, Edwards SAPIEN, or SAPIEN XT valve (Edwards

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Lifesciences, Irvine, California). Patients were excluded from analysis if they had mitral valve prostheses or received a non-balloon-expandable valves, leaving a final study population of 451 patients. All patients provided written informed consent for the procedure.

Data collection and definitions. Clinical and echocardiographic data were prospectively entered into a dedicated database at baseline, hospital discharge, 30 days, and annually. Transthoracic echocardiography was performed before TAVR, at a median of 3 days after TAVR (but before discharge), and after 1 year by senior echocardiographers according to the guidelines of the American Society of Echocardiography (15). MR severity was graded as none or trivial, mild, moderate, or severe according to the American College of Cardiology/American Heart Association/European Society of Cardiology recommendations, integrating structural, Doppler, and quantitative parameters (16). Left ventricular ejection fraction (LVEF) was calculated using the biplane Simpson's method. The severity of mitral annular calcification was graded according to Nair et al. (17). MR was classified on the basis of transthoracic and, in case of ambiguity, transesophageal echocardiography as predominantly functional or ischemic (no or minor associated pathology of the mitral valve leaflets, annulus, and chordate or papillary muscles on echocardiography) or predominantly structural or organic. Pulmonary hypertension was defined as a pulmonary artery systolic pressure (PASP) >60 mm Hg, as estimated by Doppler echocardiography or measured by cardiac catheterization (14). Porcelain aorta was defined as an extensive circumferential calcification of the thoracic aorta, as assessed by computed tomography and/or fluoroscopy (14). Patient–prosthesis mismatch was defined as an indexed effective orifice area ≤0.85 cm^2/m^2 (18,19). One-year follow-up was available in 131 of 132 patients (99%) with moderate or severe MR.

Statistical analysis. Continuous variables are expressed as mean ± SD or as median (interquartile range) in cases of skewed distributions. Categorical variables are expressed as frequencies and percents. Differences between independent groups were tested using the Kruskal-Wallis test for 3 groups and the Wilcoxon rank sum test and *t* test for continuous variables. In cases in which the samples were paired, the Wilcoxon signed rank or paired *t* test was used. Categorical variables were compared using the chi-square test. Survival rates at 30 days and at 1 and 2 years were estimated and graphed using the Kaplan-Meier method. Variables included in the baseline characteristic and procedural tables were tested for association with 2-year survival rates and included in the model if they were univariately significant at 0.25 to estimate the risk-adjusted hazard ratio (HR). A Cox regression model was used to estimate HRs and 95% confidence intervals (CIs) to compare the patients with moderate or severe MR with those with mild or less MR for all-cause mortality. On the basis of Schoenfeld residual plots, the effect of the MR groupings appeared to

Abbreviations and Acronyms

CI = confidence interval
HR = hazard ratio
LVEDD = left ventricular end-diastolic diameter
LVEF = left ventricular ejection fraction
MR = mitral regurgitation
OR = odds ratio
PASP = pulmonary artery systolic pressure
TAVR = transcatheter aortic valve replacement

Table 1 Baseline Characteristics

	Mild or Less MR (n = 319)	Moderate MR (n = 89)	Severe MR (n = 43)	p Value
Age (yrs)	81 ± 9	82 ± 7	84 ± 8	0.03
Female	163 (51%)	52 (58%)	24 (56%)	0.44
Coronary artery disease	230 (73%)	66 (74%)	35 (81%)	0.46
Previous myocardial infarction	134 (42%)	47 (53%)	26 (61%)	0.03
Previous open-heart surgery	109 (34%)	37 (42%)	21 (49%)	0.11
Previous PCI	93 (29%)	20 (23%)	16 (37%)	0.20
Previous cerebrovascular accident	66 (21%)	19 (21%)	7 (17%)	0.81
COPD	93 (29%)	21 (24%)	11 (26%)	0.55
Diabetes	97 (30%)	21 (24%)	9 (21%)	0.24
Hypertension	252 (79%)	70 (79%)	27 (63%)	0.06
GFR <60 ml/min	194 (61%)	61 (69%)	30 (70%)	0.32
Pulmonary hypertension	42 (13%)	18 (20%)	15 (35%)	<0.01
Porcelain aorta	53 (17%)	27 (30%)	8 (19%)	0.02
Atrial fibrillation	96 (30%)	35 (39%)	29 (67%)	<0.01
NYHA functional class III or IV	283 (88%)	78 (88%)	41 (95%)	0.37
STS risk score (%)	7.5 (5.0–10.7)	8.1 (6.3–12.2)	9.7 (6.3–12.1)	0.02
Mean gradient (mm Hg)	43 ± 17	44 ± 16	43 ± 17	0.95
Aortic valve area (cm^2)	0.64 ± 0.17	0.60 ± 0.15	0.59 ± 0.14	0.02
LVEF (%)	60 (50–65)	57 (45–60)	50 (40–60)	<0.01

Values are mean ± SD, n (%), or median (interquartile range).

COPD = chronic obstructive pulmonary disease; GFR = glomerular filtration rate; LVEF = left ventricular ejection fraction; MR = mitral regurgitation; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; STS = Society of Thoracic Surgeons.