International Journal of Cardiology 204 (2016) 95–100

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Mitral regurgitation prior to transcatheter aortic valve implantation influences survival but not symptoms

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ARTICLE INFO

Article history:
Received 20 October 2014
Received in revised form 16 November 2015
Accepted 22 November 2015
Available online 23 November 2015

Keywords:
Aortic valve stenosis
Transcatheter aortic valve implantation
Mitral regurgitation

ABSTRACT

Background: Current data about the impact of concomitant mitral regurgitation (MR) on outcome in patients who undergo transcatheter aortic valve implantation (TAVI) are conflicting. Our purpose was to analyze the clinical course of MR and to assess the influence of MR on survival and clinical status after TAVI.
Methods: We included 375 consecutive patients who underwent TAVI. MR grade and NYHA class were determined before TAVI and at follow-up.
Results: In total 171 patients (46%) had MR grade ≥ 2 at baseline and of these 29% improved to MR grade ≤ 1 after TAVI. MR grade ≤ 1 at baseline was present in 204 patients (54%) and of these 17% worsened to grade ≥ 2 after TAVI. Improvement of MR was associated with absence of atrial fibrillation (OR: 2.35, 95%CI: 1.17–4.71, p = 0.02). Worsening of MR was associated with moderate or more aortic valve regurgitation after TAVI (OR: 4.2, CI: 1.83–9.49, p = 0.001). NYHA class improved at follow-up. Baseline MR grade did not determine the degree of clinical improvement (MR grade ≤ 1: NYHA ≥3 from 67% to 17%; MR grade ≥ 2: NYHA ≥3 from 69% to 14%). Although patients with MR grade ≥ 2 at baseline improved symptomatically, this degree of MR was associated with reduced two year survival compared with patients with MR grade ≤ 1(mortality 37% vs 26%; HR 1.99; 95% CI 1.27–3.13; p = 0.003).
Conclusion: In patients who undergo TAVI almost half have MR grade ≥ 2 prior to the procedure. TAVI had no influence on MR grade at follow-up. Although patients with MR grade ≥ 2 at baseline improved symptomatically after TAVI, concomitant MR at baseline significantly reduced two year survival.

1. Introduction

Mitral regurgitation (MR) is frequently present in patients with aortic valve stenosis; 13% to 75% of patients undergoing surgical aortic valve replacement (SAVR) or transcatheter aortic valve implantation (TAVI) has concomitant MR. [1–11] MR in TAVI patients is usually treated conservatively. MR is often functional and thought to be related to the hemodynamic changes in aortic stenosis. Intuitively, it is expected that this MR improves after treatment of the aortic stenosis. Nevertheless, both improvement and worsening of MR have been reported after TAVI. Data about survival of patients with significant MR prior to TAVI are conflicting [1,3,7,10,12]. The effect of MR grade on outcomes after TAVI and the influence of TAVI on MR have not been elucidated yet.

Therefore the aim of this study was to study the clinical effect of TAVI on MR and to identify determinants for improvement and worsening of MR and analyze the influence of MR on functional class and survival after TAVI.

2. Methods

2.1. Patient population and TAVI procedure

In this single-center study we included consecutive patients who underwent a TAVI procedure, either by transfemoral, transapical or transaortic approach, between October 2007 and December 2013. All patients had symptomatic severe AS and were declined for surgical aortic valve replacement by our multidisciplinary heart-team due to high age and other severe comorbidities. Patients who had undergone any form of mitral valve surgery in the medical history and patients without proper pre- and/or post-procedure transthoracic echocardiographic images of the mitral valve were excluded from the analysis. All patients gave written informed consent prior to the TAVI procedure and to data being collected and utilized as per the ethical guidelines of the institute. The transfemoral procedures were performed with the selfexpandable Medtronic CoreValve bioprosthesis (Medtronic

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http://dx.doi.org/10.1016/j.ijcard.2015.11.129
0167-5273/

Inc.; Minneapolis, MN) or the balloon expandable Edwards SAPIEN bioprosthesis (Edwards Lifesciences LLC; Irvine, CA); all transapical and transaortic procedures were performed with the Edwards Sapien bioprosthesis. The procedures have been described in detail previously [13–16].

Baseline characteristics including age, gender, relevant medical and surgical histories were systematically collected. New York Heart Association (NYHA) class was determined pre-procedurally and during follow-up. All patients were invited for a follow-up visit between 1 and 6 months after TAVI. Follow-up was obtained in 198 patients of the 325 surviving patients. Missing echocardiographic exams were mainly attributable to the distance between living area of the patients and our institution. If data of multiple visits between 1 and 6 months were available, the latest follow-up data were used for our analyses.

2.2. Echocardiography

Transthoracic echocardiography (TTE) was performed prior to the TAVI procedure and post-procedurally (1–7 days after the procedure, before discharge) and during follow-up with a GE Vivid Dimension machine (GE Healthcare, Horten, Norway), all with 2D images. All views were obtained according to the recommendations of the American Society of Echocardiography [17,18]. All echocardiographic analyzes were performed by qualified senior echocardiographers of our institution and the following parameters were reviewed retrospectively by two experienced investigators: MR grades and etiology, left ventricular ejection fraction (LVEF), left ventricular end systolic and diastolic volumes (LVESV and LVEDV) and left atrial volumes.

The MR grade was based on qualitative and quantitative data by color Doppler and continuous wave Doppler using color flow jet area in the left atrium, pulmonary vein flow (in case of no atrial fibrillation), vena contracta width, effective regurgitant orifice area (using the proximal isovelocity surface area method), regurgitant fraction and regurgitant volume. MR severity was scored from 0 to 4 (0: none, 1: trace, 2: mild, 3: moderate, 4: severe). Primary or degenerative etiology of MR was assumed when intrinsic lesions to components of the mitral valve apparatus were present. Secondary or functional etiology of MR was assumed when the anatomy of the mitral valve apparatus was intact and MR resulted from tethering and reduced closing forces [19].

Left ventricular (LV) function and left atrial volumes were measured using the biplane Simpson's method [20]. The severity of aortic valve regurgitation (AR) after TAVI was determined (including both central and paravalvular jets). We used color-flow Doppler to visually estimate severity of AR based on % left ventricular outflow tract diameter [18,19] and was graded as mild, moderate, severe.

2.3. Statistical analysis

All patients were divided into two groups: patients with baseline MR grade ≤ 1 and patients with a baseline MR grade ≥ 2. Categorical data are reported as percentages and continuous data as mean ± SD or as median (25th and 75th percentile). Comparison of categorical data was conducted with a Chi square, Fischer's exact or McNemar test, whichever was appropriate. An independent T-test test was performed for continuous data to detect significant differences presuming normality assumption. Non parametric tests were used for not normally

Table 1
Baseline characteristics.

	All patients (n = 375)	MR grade ≤ 1 (n = 204)	MR grade ≥ 2 (n = 171)	P-value
Age, yrs	80 ± 7	80 ± 8	81 ± 7	0.04
BMI, kg/m2	27.7 ± 5.3	28.1 ± 5.6	27.1 ± 5.0	0.07
BSA, m2	1.87 ± 0.21	1.88 ± 0.21	1.86 ± 0.20	0.2
Male gender, %	40	42	39	0.5
Clinical history				
Hypertension,%	59	60	57	0.5
Diabetes, %	30	32	28	0.4
AF (paroxismal and chronic), %	36	26	47	<0.001
Previous myocardial infarction,%	20	20	20	1
Previous PCI,%	31	30	32	0.8
Previous aortic valve procedure, %	2	1	2	0.7
CABG,%	17	17	16	0.9
CVA,%	14	9	21	0.002
COPD, %	33	31	35	0.5
NYHA class ≥ 3, %	68	67	69	0.7
NT-proBNP (median), ug/L	1760 711–4300	1129 525–2587	3315 1284-6926	<0.001
Creatinine,umol/L	104 68	97 ± 57	112 ± 78	0.03
EuroSCORE	18.9 ± 12	16.3 ± 10.5	22.2 ± 13.6	<0.001
STS score	5.4 ± 4.3	4.9 ± 3.9	6.0 ± 4.8	0.03
Preoperative variables				
AVA, cm2	0.76 ± 0.22	0.79 ± 0.23	0.74 ± 0.22	0.04
AVPG max, mm Hg	70 ± 23	72 ± 24	67 ± 22	0.06
AVPG mean, mm Hg	45 ± 16	46 ± 16	44 ± 15	0.2
LVEF, %	48 ± 13	51 ± 12	45 ± 14	<0.001
LVESV, ml	40 ± 25	35 ± 18	46 ± 30	<0.001
LVEDV, ml	75 ± 32	70 ± 27	80 ± 36	0.004
LAVI, ml/m^2	35 ± 15	31 ± 13	40 ± 15	<0.001
Procedure				0.2
Transfemoral (CoreValve), %	30	28	31	
Transfemoral (Edwards), %	37	34	40	
Transapical (Edwards), %	18	23	13	
Transaortal (Edwards), %	15	15	16	

Data are expressed as n (%), mean ± SD or median (25th–75th percentile). BMI, body mass index; BSA, body surface area; AF: atrial fibrillation; CAD, coronary artery disease; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; NYHA: New York Heart Association; STS, society of thoracic surgeons; AVA, aortic valve area; AVPG, aortic valve pressure gradient; LVEF, left ventricular ejection fraction; LVESV: left ventricular end-systolic volume; LVEDV: left ventricular end-diastolic volume; LAVI: left atrial volume indexed; MR, mitral regurgitation.