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Original article

The significance of pulmonary arterial hypertension pre- and post-transfemoral aortic valve implantation for severe aortic stenosis

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ABSTRACT

Background: Transcatheter aortic valve implantation (TAVI) has become the treatment of choice for the symptomatic patients with aortic stenosis (AS) and high surgical risk. Pulmonary hypertension (PHTN) has been shown to be associated with worse early and late outcomes after aortic valve surgery. Data regarding the effect of TAVI on PHTN are limited.

Methods and results: We evaluated the characteristics and outcome of the patients with various degrees of systolic PHTN referred for TAVI. PHTN was defined as systolic pulmonary arterial pressure (SPAP) ≥50 mmHg as assessed by echocardiography. The patients with SPAP decrease after TAVI to below 50 mmHg were compared to the patients with persistent PHTN following TAVI. Of the 122 patients included in the present study, 49 (40%) patients had elevated SPAP prior to TAVI. This group of patients presented with smaller aortic valve areas, greater degrees of mitral or tricuspid regurgitation, lower left ventricular ejection fraction, and more prevalent chronic obstructive pulmonary disease (COPD) (all $p < 0.05$). Following TAVI, 57% of the patients with prior PHTN experienced a reduction in SPAP to below 50 mmHg. Multivariable analysis identified COPD to be the most powerful predictor for PHTN presence post-TAVI (hazard ratio 3.9, 95% confidence interval 1.5–9.9, $p = 0.005$). Post-TAVI PHTN (SPAP ≥50 mmHg) was associated with a 3.4-fold, independent, 2-year mortality risk ($p = 0.04$).

Conclusions: Our data suggest that TAVI is associated with a significant reduction in pulmonary pressure in more than half of the patients with preprocedural PHTN. COPD identifies the patients with persistent PHTN after TAVI. Post-TAVI PHTN is associated with markedly worse outcome.

Introduction

Transcatheter aortic valve implantation (TAVI) has emerged as an excellent alternative to surgical aortic valve replacement (AVR) for the symptomatic patients with high-risk or inoperable aortic stenosis (AS) [1–4]. Pulmonary hypertension (PHTN) is the end result of a variety of diverse pathologic cardiac processes [5]. It has been shown to be associated with worse early and late outcomes after aortic valve surgery [6,7], and is an important determinant of surgical risk in the contemporary risk scores. In the patients with left-sided cardiac disease, PHTN is common and associated with increased morbidity and mortality. The chronic elevation in pulmonary artery pressure often leads to right ventricular pressure overload and subsequent right ventricular failure. In the patients with severe AS, PHTN is a common finding reflecting long-standing stenosis, unrelated to systolic ventricular function. Whether PHTN is a marker of irreversible myocardial damage is not known and data regarding the effect of TAVI on PHTN are limited. We aimed to identify predictors of persistent PHTN following TAVI, and to evaluate the long-term significance of PHTN presence after TAVI.

Methods

Study population and definitions

The study population comprised of 122 patients who underwent TAVI at Sheba Medical Center between 2009 and 2011 and

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who had echocardiographic data regarding pulmonary pressure at baseline. PHTN was defined as systolic pulmonary arterial pressure (SPAP) ≥50 mmHg as assessed by echocardiography. Kidney dysfunction was defined as admission estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m^2. The diagnosis of chronic obstructive pulmonary disease (COPD) was obtained from medical records and considered significant if severity was greater than mild according to spirometry results following the American Thoracic Society (ATS) criteria [8].

The patients were divided into two groups according to the baseline SPAP (≥50 mmHg and <50 mmHg). Follow-up echocardiographic examination was performed at an average of 6.5 months following the procedure. Clinical follow-up was performed at 2 years. Mortality data were obtained from the Israeli national population registry.

Echocardiographic assessment

Doppler tracings and two-dimensional images were obtained from parasternal long- and short-axis, apical four-chamber, and subcostal four-chamber views. TR was identified by color flow Doppler techniques. Continuous-wave Doppler measured maximum jet velocity. Right ventricular systolic pressure was estimated based on the modified Bernoulli equation and was considered equal to the SPAP in the absence of right ventricular outflow obstruction. SPAP was calculated by adding transtricuspid pressure gradient to mean right atrial pressure estimated from inferior vena cava diameter and motion during respiration as follows: if the caliber of inferior vena cava (IVC) was normal (1.5–2.5 cm), mean right atrial pressure was estimated to be 5 mmHg if there was complete collapse of the IVC during inspiration, whereas mean right atrial pressure was estimated to be 10 mmHg if IVC collapse was <50%. If IVC was dilated, mean right atrial pressure was estimated to be 15 mmHg, and if the IVC collapsed by <50% with inspiration, atrial pressure was estimated to be 20 mmHg. Left ventricular end-diastolic and end-systolic volumes were measured by biplane Simpson's method and the left ventricular ejection fraction (LVEF) was estimated. Aortic valve morphology was evaluated at the parasternal short-axis view. Left ventricular outflow tract diameter and aortic annulus, sinus and sino-tubular junction diameters were measured at the parasternal long-axis view. Continuous-wave Doppler recordings through the aortic valve were obtained and peak and mean transaortic pressure gradients were calculated. Aortic valve area was calculated by continuity equation.

Aortic regurgitation (AR) was evaluated by color Doppler echocardiography after optimizing gain and Nyquist limit. Specifically, routine measurements included semi-quantitative parameters of AR severity such as jet width, vena contracta, and assessment of pressure half-time and holodiastolic flow reversal in the descending aorta.

TAVI procedure

All the patients with severe AS treated by TAVI were assessed by a dedicated "Heart Team" and were considered inoperable or high-risk for conventional surgery. The decision between the two available valves was at the discretion of the heart team and was based on annular size, diameter of femoral arteries, degree of calcification, and dilation of the ascending aorta. TAVI was performed using general or local anesthesia. Temporary pacemaker was inserted in all the patients and balloon valvuloplasty was performed under rapid pacing. Valve implantation was performed subsequently, while postdilation was performed if necessary, in cases of significant angiographic, echocardiographic, or hemodynamically significant AR. Vascular access site closure was obtained by Prostar® (Abbott, Abbott Park, IL, USA). Postprocedure, all the patients were hospitalized in the intensive cardiac care unit for 48–72 h and were monitored for potential complications, including conduction disturbances.

Statistical analysis

Characteristics of study participants were compared using χ^2 test for categorical variables and also by Student's *t*-test or Wilcoxon rank tests, as appropriate for continuous variables. The Kruskal–Wallis test was used for comparison of non-normally distributed continuous variables. Study design is a landmark analysis following the post-TAVI echocardiography.

Multivariate logistic regression modeling was used to identify independent predictors associated with PHTN presence following TAVI. The following covariates were introduced into the model using the best subset method: age, severity grades (0 to +3) of MR, AR, and TR, LVEF, diagnosis of coronary artery disease (CAD), aortic valve area (in cm^2), and diagnosis of COPD (defined as disease severity > mild).

We performed a landmark analysis including only those patients who underwent at least one follow-up echocardiographic study, following hospital discharge. Kaplan–Meier survival analysis was used to construct the cumulative 2-year survival probability curves by PHTN presence on follow-up echocardiography, and the log-rank test was used to declare significance. Mortality outcome was explored for each group according to the Kaplan–Meier method and graphically presented. Cox proportional hazards method was used to evaluate the independent effects of post-TAVI PHTN on the 2-year all-cause mortality outcome. The following covariates were introduced into the model: age, presence of CAD, COPD, New York Heart Association functional class, LVEF, post-TAVI SPAP ≥50 mmHg, and presence of renal dysfunction. A separate regression model was constructed as above, with the exception that baseline pre-TAVI SPAP ≥50 mmHg was introduced, instead of post-TAVI PHTN values. Consistent results were obtained when SPAP results were introduced as continuous values in all the models.

A two-sided value of $p < 0.05$ was used for declaring statistical significance. All data analyses were performed using SPSS statistical software (IBM, Chicago, IL, USA), version 20.

Results

The study population consisted of 122 patients divided into two groups according to the baseline SPAP. SPAP was successfully assessed by a TR signal on echocardiography in all the patients. Seventy-three patients (60%) had baseline SPAP <50 mmHg and 49 patients (40%) had baseline SPAP ≥50 mmHg. Fig. 1 shows the flow chart of the patients in our study. Within 3 months postprocedure, 13 patients (17%) died in the SPAP <50 group, and 5 (10%) in the SPAP ≥50 group. These patients had no available echocardiography data at follow-up and were excluded from the final analysis. As shown in Table 1, baseline characteristics were similar between the groups, except that the SPAP ≥50 group had significantly higher EuroSCORE (33 vs. 26, $p = 0.01$) and higher percentage of COPD (49% vs. 27%, $p = 0.02$). A lower percentage of CAD was also observed in the SPAP ≥50 group (44% vs. 64%, $p = 0.03$). Baseline echocardiography (Table 2) was performed before TAVI showed that the SPAP ≥50 group had significantly lower LVEF (49% vs. 54%, $p = 0.03$), smaller aortic valve area (0.63 cm^2 vs. 0.72 cm^2, $p = 0.003$), more concomitant valvular abnormalities, such as moderate to severe MR (44% vs. 20%, $p = 0.03$) and TR (42% vs. 8%, $p < 0.001$). Procedural details are summarized in Table 3.