Heart, Lung and Circulation (2016) **25,** 68–74
1443-9506/04/$36.00
http://dx.doi.org/10.1016/j.hlc.2015.05.019

ORIGINAL ARTICLE

Diabetes Mellitus Impairs Left Ventricular Mass Regression after Surgical or Transcatheter Aortic Valve Replacement for Severe Aortic Stenosis

Teruya Nakamura, MD, PhD [a], Koichi Toda, MD, PhD [a], Toru Kuratani, MD, PhD [a], Shigeru Miyagawa, MD, PhD [a], Yasushi Yoshikawa, MD [a], Satsuki Fukushima, MD, PhD [a], Shunsuke Saito, MD, PhD [a], Daisuke Yoshioka, MD [a], Noriyuki Kashiyama, MD [a], Takashi Daimon, PhD [b], Yoshiki Sawa, MD, PhD [a*]

[a]Department of Cardiovascular Surgery, Osaka University Graduate School of Medicine, Suita, Japan
[b]Department of Biostatistics, Hyogo College of Medicine, Nishinomiya, Japan

Received 22 March 2015; accepted 25 May 2015; online published-ahead-of-print 7 July 2015

Background It is well-documented that persistent myocardial hypertrophy in patients with aortic stenosis is related to suboptimal postoperative outcomes after aortic valve replacement. Although diabetes is known to potentially exacerbate myocardial hypertrophy, it has yet to be examined if it affects postoperative left ventricular mass regression (LVMR).

Methods A single-centre, retrospective analysis was performed on 183 consecutive patients who underwent either surgical or transcatheter aortic valve replacement between 2010 and May 2013. Patient demographics, postoperative outcomes and echocardiographic data were obtained preoperatively and a year after surgery.

Results There were 42 diabetic and 141 non-diabetic patients. Preoperative characteristics of diabetic patients were statistically similar to those of non-diabetic patients, except for higher prevalence of hyperlipidaemia ($p < 0.001$) and history of cerebrovascular disorder ($p=0.046$) in diabetic patients. Median value of postoperative LVMR of all patients was -36.5 g/m^2, and was significantly greater in the non-diabetics compared to the diabetics (-39.1 vs. -22.2 g/m^2, $p=0.008$). Univariate and multivariate analyses were performed on preoperative variables, and stepwise multiple regression analysis demonstrated that diabetes (standardised partial regression coefficient (SPRC)=-0.187, $p=0.018$), female gender (SPRC=0.245, $p=0.026$) and age (SPRC=0.203, $p=0.018$) were associated with poor postoperative LVMR.

Conclusions Patients with diabetes showed suboptimal postoperative LVMR, and the disease was a prognostic factor that was associated with poor LVMR. These findings suggest that diabetes may predispose the particular group of patients to worse postoperative outcomes.

Keywords Aortic valve stenosis • Aortic valve replacement • Diabetes mellitus • Myocardium • Hypertrophy • Left ventricular

*Corresponding author at: Department of Cardiovascular Surgery, Osaka University Graduate School of Medicine, 2-2 Yamada-oka, Suita 565-0871, Japan. Tel.: +81-6-6879-3160; fax: +81-6-6879-3163, Email: sawa@surg1.med.osaka-u.ac.jp

Introduction

In patients with aortic stenosis, the most crucial pathological determinant is a chronic pressure overload onto the left ventricle caused by the calcified, immobile aortic valve, leading to concentric hypertrophy and myocardial fibrosis [1]. Aortic valve replacement (AVR), either surgical or using a transcatheter approach, is the sole definitive treatment for aortic stenosis that results in immediate relief of mechanical obstruction [1]. Aortic valve replacement usually elicits a postoperative reverse remodelling of the hypertrophic myocardium, i.e., left ventricular mass regression (LVMR) [2,3]. It occurs early after surgery and continues up to 10 years [2]. However, persistent residual left ventricular hypertrophy is not uncommon despite successful AVR [4,5]. Suboptimal LVMR is known to be associated with late cardiac events and poor long-term outcomes [4,5]. From the physiological point-of-view, the majority of studies have focussed on patient-prosthesis mismatch, which is defined as the effective orifice area of a normally functioning prosthesis being too small for a patient's body size. Patients who are complicated with patient-prosthesis mismatch have reduced LVMR after AVR and worse exercise capacity compared with patients without mismatch [6,7]. Although afterload relief and subsequent LVMR are mostly attributed to prosthetic valve function, it has been relatively undetermined if various preoperative and/or perioperative patient factors affect poor post-AVR LVMR.

Diabetes is the most prevalent metabolic disorder that affects more than 300 million patients worldwide, and is well-known to increase the risk of various cardiovascular disorders and heart failure. It has been shown that diabetes exacerbates arterial stiffening and atherosclerotic disease [8,9], and also plays a role in accelerating myocardial remodelling and hypertrophy [10]. In addition, diabetes is a risk factor of progression of calcification and stenosis of the aortic valve [11,12]. Considering these findings, one could speculate that diabetes may alter the pathophysiological process of aortic stenosis, thereby worsening postoperative outcomes. In the present study, we investigate if diabetes is associated with postoperative myocardial remodelling and LVMR after surgical AVR (SAVR) or transcatheter AVR (TAVR) for aortic stenosis, mainly focussing on postoperative echocardiographic findings.

Materials and Methods

One-hundred-and-eighty-three consecutive patients who underwent SAVR or TAVR for aortic stenosis at Osaka University hospital between January 2010 and May 2013 were retrospectively analysed. Patients who underwent simultaneous operations for other valves, thoracic aorta and maze procedures were excluded from this study. All the data were retrospectively obtained from the medical records. The Institutional Review Board approved this study and patient consent was waived due to its retrospective nature. Definition of each preoperative comorbidity was as follows: hypertension, blood pressure >140/90 mmHg or current use of antihypertensive medication; hyperlipidaemia, total cholesterol level >220 mg/dl or triglyceride level >150 mg/dl or current use of lipid-lowering medication; diabetes mellitus, fasting plasma glucose level >126 mg/dl, plasma glucose level (at any time) >200 mg/dl, or current use of anti-diabetic medication including insulin; left ventricular dysfunction, left ventricular ejection fraction < 50%. Creatinine clearance was calculated by the Cockcroft-Gault formula [13].

Surgical AVR was performed using standard cardiopulmonary bypass with bicaval and aortic cannulation under tepid temperature. Antegrade and retrograde blood cardioplegia was administered every 20 to 30 minutes to maintain cardiac arrest. All prosthetic valves were implanted in a supra-annular position, using multiple non-everting, interrupted 2-0 braided sutures with pledgets. Types of prosthetic valves were selected based on surgeon's preference. In most cases, a bioprosthetic valve was used unless patients desired otherwise. Transcatheter AVR was performed using either the Medtronic CoreValve or the Edwards Sapien XT prosthesis, which has been described in detail elsewhere [14]. Vascular access options for device placement were the trans-femoral, trans-subclavian and trans-aortic route. Cardiopulmonary bypass was used for patients with severe left ventricular dysfunction.

Standard two-dimensional transthoracic echocardiography was performed preoperatively and postoperatively, according to guidelines of the American Society of Echocardiography [15]. As postoperative LVMR occurs within one year after AVR and left ventricular mass tends to become stable thereafter [4], echocardiographic data was collected preoperatively and 12 months after surgery. Pressure gradient across the aortic valve was calculated using a simplified Bernoulli equation. Left ventricular internal diameter, left ventricular posterior wall thickness, interventricular wall thickness and left ventricular ejection fraction were measured by standard M-mode study. Left ventricular mass was calculated by a formula reported by Devereux and colleague [16]. Then each calculated value was indexed to body surface area (g/m^2). Left ventricular mass regression was accessed by subtracting preoperative from postoperative indexed left ventricular mass (LVMI).

Statistical analyses were performed using JMP® 10 (SAS Institute Inc., Cary, NC). Since all the continuous variables did not fit a standard normal distribution, these are summarised as medians with minimums and maximums. The continuous variables were compared using the Mann-Whitney *U* test. Categorical variables are expressed as frequencies with proportions, and were compared using a chi-square test. In order to examine preoperative potential risk factors of poor postoperative LVMR, univariate analyses were performed using a Mann-Whitney *U* test and a linear correlation analysis for the categorical and the continuous factors, respectively. Preoperative and postoperative echocardiographic data were compared using Wilcoxon signed-rank test. A multiple linear regression model was used to select preoperative risk factors of LVMR. Factors with *p* values less