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Original article

Adverse effects of left ventricular electrical dyssynchrony on cardiac reverse remodeling and prognosis after aortic valve surgery

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ABSTRACT

Background: Electrical dyssynchrony (ED) is one of the important contributing mechanisms in the progression of heart failure. We hypothesized that ED would interfere with cardiac reverse remodeling and affect prognosis after aortic valve surgery.
Methods: A total of 411 consecutive patients (233 males, mean age 65 ± 11 years) who underwent aortic valve surgery were retrospectively analyzed. The patients were divided into two groups according to the presence of ED [Group 1: no ED ($n = 382$, 93%), Group 2: ED ($n = 29$, 7%)]. ED was defined as either left ventricular bundle branch block, or electrical pacing rhythm. Cardiac reverse remodeling was assessed at 1 year after surgery by the changes in left ventricular ejection fraction (LVEF), LV end-systolic volume (LVESV), and left atrial volume index (LAVI). The primary endpoint was a composite of hospitalization for heart failure, and all-cause mortality.
Results: At 1 year after surgery, group 2 showed lower LVEF (58 ± 15% vs. 64 ± 9%, $p = 0.044$), and higher LAVI (42 ± 18 ml/m^2 vs. 33 ± 13 ml/m^2, $p = 0.018$) than group 1. However, LVESV values (55 ± 38 ml vs. 42 ± 24 ml, $p = 0.076$) were not significantly different. In particular, in patients with reduced preoperative LVEF, the LVEF was markedly increased in group 1 but not in group 2 after 1 year. During a median follow-up of 39 months, group 2 showed a worse clinical outcome than group 1 (20.7% vs. 7.6%, $p = 0.031$). After adjusting for confounding factors in the multivariate analyses, age [hazard ratio (HR) 1.11, 95% confidence interval (CI) 1.06–1.16, $p < 0.001$] and the presence of ED (HR 2.43, 95% CI 1.01–5.89, $p = 0.046$) were found to be independent predictors of clinical outcomes.
Conclusions: ED after aortic valve surgery negatively affected cardiac remodeling and prognosis.

Introduction

Electrical dyssynchrony (ED) might occur in the course of left ventricular (LV) remodeling owing to severe aortic valve disease. Progressive increased myocardial stiffness and LV filling pressure might lead to ischemia that could then become predisposed to subendocardial fibrosis and permanent conduction disorder [1]. Moreover, because of the close proximity of atrioventricular (AV) conduction system to the aortic valvular complex [2], aortic valve surgery may result in conduction disturbance. Procedure-induced left bundle branch block (LBBB) in aortic valve surgery occurs in about less than 5% of cases [3] and the incidence of permanent pacemaker implantation (PPI) following aortic valve surgery has been found to range from 3.0% to 11.8% [4].

ED is an important contributing mechanism in the progression of heart failure and of LV remodeling. LBBB deteriorates both diastolic and systolic LV functions and constitutes a risk factor for the development and progression of cardiovascular disease [5]. The hemodynamic and mechanical disadvantages of right ventricular (RV) apical pacing are similar to those of LBBB [6]. RV apical pacing induces dyssynchrony, which leads to increased sympathetic activation, causes abnormalities in myocardial perfusion, and worsened hemodynamic parameters and myocardial remodeling [6–8]. However, evidence for the clinical impact of ED after aortic

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valve surgery remains scarce. Therefore, the aim of this study was to investigate LV and left atrial (LA) reverse remodeling and effect on clinical outcomes in patients with or without ED, after aortic valve surgery.

Materials and methods

Study patients

A cohort of consecutive patients undergoing surgical aortic valve replacement (SAVR) with or without coronary artery bypass graft (CABG) from April 2010 to February 2015 at Severance Cardiovascular Hospital (Yonsei University College of Medicine, Seoul, Republic of Korea) was assembled. The inclusion criteria were patients undergoing aortic valve surgery owing to severe aortic stenosis or severe aortic regurgitation defined as current guidelines criteria [9,10] with or without CABG. Patients who had concomitant mitral or tricuspid valve surgery, previous valvuloplasty or valve replacement, or complex congenital heart disease were excluded. Patients who had surgical intervention on the aorta were not excluded.

ED was defined as the presence of either LBBB, or electrical pacing rhythm. Patients with ED undergoing aortic valve surgery included: pre-existing LBBB ($n = 5$), pre-existing PPI ($n = 6$), post-SAVR LBBB ($n = 10$), and post-SAVR PPI ($n = 8$). The patients were divided into two groups according to the presence of ED [Group 1: no ED ($n = 382$, 93%), Group 2: ED ($n = 29$, 7%)]. All patients' medical records written by the physicians were carefully reviewed by two cardiologists. The institutional review board of Yonsei University College of Medicine approved the present study, which was conducted in compliance with the Declaration of Helsinki.

Electrocardiogram assessment

Electrocardiograms (ECGs) before aortic valve surgery, within 14 days, and 1 year after aortic valve surgery were assessed. According to the established guidelines, LBBB was defined as a post-procedural V1-negative QRS complex $\geq$120 ms with absent Q-waves and a notched or slurred R-wave in the left lateral leads (I, aVL, V5, V6). Right bundle branch block (RBBB) was defined as a post-procedural QRS complex $\geq$120 ms with a triphasic QRS complex in V1 together with a dominant S wave in leads I and V6 [11]. The indications for PPI were in accordance with the American College of Cardiology/American Heart Association guideline [12]. PPI was indicated for third degree and advanced second-degree atrioventricular block (AVB) at any anatomical level associated with postoperative AVB that was not expected to resolve after cardiac surgery.

Echocardiographic assessment

All subjects underwent comprehensive transthoracic echocardiography (TTE), reflecting left-sided chamber size and geometry, systolic and diastolic function of the right and left ventricles, and valvular hemodynamics, using commercially available equipment. Preoperative was TTE performed $\leq$3 months before surgery. Postoperative TTE was performed at 12 months after aortic valve surgery. LV volume and LV ejection fraction (LVEF) were calculated using the apical 4- and 2-chamber views (biplane Simpson's method). LV mass (LVM) was calculated according to the Devereux formula. LVM was indexed to body surface area. Calculation of relative wall thickness (RWT) was assessed by the formula (2 × diastolic posterior wall thickness)/LV end-diastolic diameter. RWT was used to categorize LV hypertrophy. LA volume was determined from 2 imaging planes by ellipsoid model and was indexed to the body surface area [left atrial volume index (LAVI)] [13]. Right ventricular systolic pressure (RVSP) was derived from the tricuspid regurgitation velocity and an estimate of the right atrial pressure based on the dimension of inferior vena cava. LV diastolic function was assessed by pulsed wave Doppler echocardiography of mitral inflow velocity and tissue Doppler echocardiography of mitral septal annular velocity. From the apical window, a 1–2 mm pulsed Doppler sample volume was placed at the mitral valve tip and mitral flow velocities from 5 to 10 cardiac cycles were recorded. The mitral inflow velocities were traced and the following variables were obtained: peak velocity of early diastolic filling (E), and late filling (A), and deceleration time of the E wave velocity. Early diastolic mitral annulus velocity (E'), late diastolic mitral annulus velocity (A'), and peak systolic mitral annulus velocity (S') were measured by Doppler tissue imaging at the septal corner of mitral annulus. To estimate LV filling pressures, the ratio of E/E' was calculated. For purposes of the principal analysis, a patient was classified as being a responder to aortic valve surgery if the LV end-systolic volume (LVESV) decreased by more than 15% [14,15], and there was a net increase in LVEF of 10% or more, and net decrease in LAVI of 10 ml/m^2 or more at 1 year follow-up compared with baseline [16,17]. ΔLVEF was defined as the differences between baseline and 1-year follow-up values. ΔLVESV was defined as the extent of reduction in LVESV between baseline and 1-year follow-up relative to baseline LVESV. ΔLAVI was defined as the extent of reduction in LAVI baseline and 1-year follow-up relative to baseline LAVI. Preoperative, and postoperative echocardiogram were analyzed by two experienced echocardiographers who were unaware of each patient's clinical data.

Follow-up

Follow-up information was obtained via review of the medical records. The primary end-point was a composite of mortality and hospitalization due to heart failure. The clinical management of the patients was determined independently by their personal cardiologists.

Statistical analysis

Data are presented as mean ± standard deviation or percentage unless otherwise specified. Non-normally distributed values are expressed as median and interquartile range (IQR). Continuous variables were compared with Student's t test for normally distributed values. The Mann–Whitney U test was used to compare non-normal distributions between groups. Categorical variables were compared with the chi-square test or Fisher's exact test. A paired t-test was used to compare parameters before versus after aortic valve surgery within each group. The Kaplan–Meier method was used for cumulative survival analysis and the log-rank test was used to assess the statistical significance of differences between the two groups according to the presence of ED. A two-sided p-value less than 0.05 was considered statistically significant.

Results

Baseline demographic data

The baseline clinical characteristics are shown in Table 1. The mean age of all 411 patients was 65 ± 11 years. Compared with group 1, the mean age was higher (69 ± 8 vs. 64 ± 11, $p < 0.001$) in group 2. The prevalence of diabetes and dyslipidemia were higher in group 2. The distribution of aortic valve dysfunction was not significantly different between the two groups. The prevalence of valvular dysfunction requiring surgery, combined significant mitral regurgitation, and infective endocarditis were comparable between the two groups. The surgical procedure included isolated

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