# The effect of postoperative medical treatment on left ventricular mass regression after aortic valve replacement

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**Objective:** The study objective was to analyze factors associated with left ventricular mass regression in patients undergoing aortic valve replacement with a newer bioprosthesis, the Trifecta valve pericardial bioprosthesis (St Jude Medical Inc, St Paul, Minn).

**Methods:** A total of 444 patients underwent aortic valve replacement with the Trifecta bioprosthesis from 2007 to 2009 at 6 US institutions. The clinical and echocardiographic data of 200 of these patients who had left ventricular hypertrophy and follow-up studies 1 year postoperatively were reviewed and compared to analyze factors affecting left ventricular mass regression.

**Results:** Mean (standard deviation) age of the 200 study patients was 73 (9) years, 66% were men, and 92% had pure or predominant aortic valve stenosis. Complete left ventricular mass regression was observed in 102 patients (51%) by 1 year postoperatively. In univariate analysis, male sex, implantation of larger valves, larger left ventricular end-diastolic volume, and beta-blocker or calcium-channel blocker treatment at dismissal were significantly associated with complete mass regression. In the multivariate model, odds ratios (95% confidence intervals) indicated that male sex (3.38 [1.39-8.26]) and beta-blocker or calcium-channel blocker treatment at dismissal (3.41 [1.40-8.34]) were associated with increased probability of complete left ventricular mass regression. Patients with higher preoperative systolic blood pressure were less likely to have complete left ventricular mass regression (0.98 [0.97-0.99]).

**Conclusions:** Among patients with left ventricular hypertrophy, postoperative treatment with beta-blockers or calcium-channel blockers may enhance mass regression. This highlights the need for close medical follow-up after operation. Labeled valve size was not predictive of left ventricular mass regression. (J Thorac Cardiovasc Surg 2015;149:781-6)

See related commentary on pages 787-8.

Left ventricular (LV) hypertrophy negatively influences postoperative survival after aortic valve replacement (AVR).[1] The extent of LV mass regression after AVR appears to be dependent on both transvalvular pressure gradients[2,3] and aortic valve (AV) area after replacement.[4]

Newer bioprostheses may have better hemodynamic profiles than older ones, which may lead to more complete LV mass regression in patients undergoing AVR. As reported by Wendt and colleagues,[5] AVR with bovine pericardial prostheses results in relatively low transvalvular gradients and increased AV areas. The Trifecta valve pericardial bioprosthesis (St Jude Medical Inc, St Paul, Minn) was implanted in 1014 patients between 2007 and 2009 at 31 centers worldwide. The initial results were promising; for patients with 19- and 29-mm prostheses, average mean gradients at hospital dismissal were 9.3 and 4.1 mm Hg, respectively, and effective orifice area (EOA) ranged from 1.58 to 2.50 $cm^2$.[6] In the current study, we analyzed determinants of LV mass regression in patients undergoing AVR with this new pericardial bioprosthesis.

## MATERIALS AND METHODS

To fulfill regulatory requirements of clinically evaluating the Trifecta valve, patients from 6 centers with the highest enrollment (Mayo Clinic, Rochester, Minn; Hospital of the University of Pennsylvania, Philadelphia, Pa; Minneapolis Heart Institute, Minneapolis, Minn; Mission Health and Hospitals, Asheville, NC; Vanderbilt Medical Center, Nashville, Tenn; and Intermountain Medical Center, Salt Lake City, Utah) were chosen

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**Abbreviations and Acronyms**

AV = aortic valve
AVR = aortic valve replacement
CI = confidence interval
EOA = effective orifice area
LV = left ventricular
OR = odds ratio
SD = standard deviation

(n = 444) as a subset of patients from the 31 centers in the initial investigation device exemption study (n = 1014) for long-term follow-up. In addition to initial consent to participate in the study, all subjects signed consent for follow-up visits, clinical evaluation, and echocardiography. Institutional review board approval was obtained at each participating site. Details of bioprosthetic AV implantation and definition of adverse events have been published.[6] Briefly, early adverse events were those that occurred before 30 days postimplantation, and late events occurred after 30 days.

For the entire group of patients, we examined clinical data to determine hemodynamic outcomes, valve gradients, and survival during a follow-up period of 5 years. We also analyzed determinants of LV mass regression. Among the 444 available patients, 405 had sufficient echocardiographic information to calculate LV mass, as follows:

$$\text{LV mass (in grams)} = \big(0.832\times 1.04\big[\{\text{interventricular septal thickness} + \text{LV end} - \text{diastolic dimension (in millimeters)} + \text{LV posterior wall thickness}\}^3 - (\text{LV end} - \text{diastolic dimension})^3\big]\big)/1000 + 0.6 \text{ g}.$$ [7]

LV mass index (in grams/meters squared) was calculated by dividing LV mass by body surface area. LV hypertrophy was defined as an LV mass index greater than 95 g/m$^2$ for women and greater than 115 g/m$^2$ for men.[8] Postoperative predismissal echocardiograms and all subsequent echocardiograms were read in a central core laboratory, and we used data from the predismissal echocardiogram for baseline data on LV hypertrophy.

Continuous variables are presented as mean (standard deviation [SD]), and categoric variables are presented as number of patients (percentage). All *P* values for comparisons between groups are based on the 2-sample *t* test, chi-square test, or Fisher exact test. No adjustments for multiple comparisons were made. We analyzed LV mass regression by 2 methods. First, we categorized patients with LV hypertrophy as having complete or incomplete regression of hypertrophy 1 year postoperatively on the basis of the cutoff values given earlier. In a second analysis, we used the absolute change in LV hypertrophy from the initial echocardiogram to the 1-year time point. For both end points, we performed univariate and multivariate analyses on clinical variables. All variables with a *P* value less than .2 in the univariate analysis were included in the multivariate analysis. In the multivariate analysis, $P < .05$ was considered significant. The Kaplan–Meier method was used to estimate survival for patients who had complete LV mass regression compared with those who did not. However, because data at 1 year were required to compose the groups, only deaths after 1 year were included. St Jude Medical Inc was involved in the collection of data and provided statistical support.

## RESULTS

The mean (SD) age of all 444 patients was 73.5 (8.9) years. Demographics and preoperative findings for these patients are detailed in Table 1. Implanted AV sizes ranged from 19 to 29 mm, with 31.5% of patients (n = 140) receiving a 23-mm valve. Total duration of follow-up was 1333.5 patient-years.

### Hemodynamic Performance

The mean (SD) initial AV gradient was 7.4 (3.3) mm Hg. The gradient increased slightly to 9.4 (4.6) mm Hg at 3 years and 9.8 (5.0) mm Hg at 5 years. Mean (SD) initial EOA was 1.95 (0.37) cm$^2$, compared with 1.60 (0.37) cm$^2$ at 3 years and 1.58 (0.37) cm$^2$ at 5 years postoperatively. Initial indexed EOA was 0.98 (0.18) cm$^2$/m$^2$, compared with 0.80 (0.17) cm$^2$/m$^2$ at 3 years and 0.80 (0.18) cm$^2$/m$^2$ at 5 years postoperatively.

Most patients (n = 441, 99.3%) had no or trivial aortic insufficiency at dismissal. At 3 years (258 patients at risk), 66.3% of patients (n = 171) had no aortic regurgitation, 19.8% of patients (n = 51) had trivial regurgitation, and 11.2% of patients (n = 29) had mild regurgitation. At 5 years (34 patients at risk), 50% of patients (n = 17) had no regurgitation, 29.4% of patients (n = 10) had trivial regurgitation, 14.7% of patients (n = 5) had mild regurgitation, and 5.9% of patients (n = 2) had moderate regurgitation.

### Adverse Events and Survival Among All Patients

Adverse events after AVR are shown in Table 2. At 3 years, cumulative freedom from embolism, endocarditis, nonstructural dysfunction, and structural valve deterioration was 95.4%, 99.1%, 99.2%, and 99.7%, respectively. The same measures at 5 years (30 patients at risk) were 94.9%, 99.1%, 99.2%, and 99.7%, respectively. Seven patients required reoperation for replacement of the prosthesis; 1 of these events occurred early and was due to partial obstruction of the left main coronary artery. The 6 late explantations were due to endocarditis (n = 2), structural valve deterioration (n = 1), and nonstructural dysfunction (n = 3). Freedom from AV reoperation 3 years postoperatively was 98.6%. At 3 years, cumulative freedom from overall mortality was 93.2%, and freedom from valve-related mortality was 99.5%. No valve thrombosis, minor paravalvular leak, or clinically significant hemolysis occurred.

### Left Ventricular Mass Regression

The average initial LV mass index for all 405 patients with data available (including those who did not have LV hypertrophy) was 113.6 g/m$^2$. By 1 year postoperatively, the LV mass index had decreased to 102.6 g/m$^2$ with little further decrease during the subsequent 4 years (5-year average, 101.7 g/m$^2$). Thus, the 1-year follow-up time point was chosen for our analysis to identify determinants of LV mass regression.

A total of 200 patients who had LV hypertrophy at the time of operation and sufficient echocardiographic data to allow determination of LV mass index 1 year postoperatively were analyzed further. These patients had a mean (SD) age of 73 (9) years, and 132 (66%) were men. Ninety-two percent (n = 184) had pure or predominant AV stenosis.

We compared the patient subsets of approximately 50% each who had complete (n = 102) and incomplete (n = 98)