

# Comparison of Exercise Echocardiography in Patients with 18mm ATS-AP Aortic Prosthesis

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There have been various arguments concerning the patient-prosthesis mismatch (PPM) after aortic valve replacement (AVR) for small valves. The objective of this study was to evaluate the postoperative hemodynamics in patients.

**Methods:** The subjects were 6 patients [6 females aged 64 (17~74) years, with a median body surface area (BSA) of 1.37 (1.29~1.51) m<sup>2</sup>] who underwent AVR at our facility using the 18-mm ATS-AP and tolerated exercise loading. We estimated pressure gradient (PG), ejection fraction (EF), left ventricular mass index (LVMI) at pre-operation and post-operation. Exercise echocardiography on an ergometer was performed before and 29.0 ± 14.4 months after surgery. We estimated PG and effective orifice area index (EOAI) at rest and at exercise. We compared echo data between pre-operation and post-operation, between at rest and at exercise.

**Results:** The effective orifice area index (EOAI) at rest was 0.92 (0.75~1.06) cm<sup>2</sup>/m<sup>2</sup>. There was a significant change in the LVMI between pre-operation and post-operation [158.5 (104.0~222.2) g/m<sup>2</sup> versus 102.4 (92.3~146.4) g/m<sup>2</sup>; P < 0.05]. However, there was no significant change in the EOAI [0.92 (0.75~1.06) cm<sup>2</sup>/m<sup>2</sup> versus 0.84 (0.78~0.91) cm<sup>2</sup>/m<sup>2</sup>; P > 0.05] and mean PG [11.0 (6.6~16.0) mmHg versus 14.0 (6.3~16.0) mmHg; P > 0.05], on maximal exercise.

**Conclusion:** In patients whose BSA were 1.37 (1.29~1.51) m<sup>2</sup>, the 18-mm ATS-AP was suggested to be a prosthetic valve that improves myocardial remodeling and provides stable hemodynamics even during exercise.

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**Keywords:** Aortic valve replacement; PPM; Exercise echocardiography

## Introduction

There have been various arguments concerning the patient-prosthesis mismatch (PPM) after aortic valve replacement (AVR) for small valves.<sup>1-7</sup> Some facilities are using relatively large artificial valves by performing aortic ring enlargement to avoid PPM. However, the addition of ring enlargement as well as AVR increases the complexity of the surgical procedure. According to catalogue specifications, the ATS-AP prosthesis provides a wider valve area than the standard ATS prosthesis of the same size. For example, the 18-mm ATS-AP has the same effective valve area as the 21-mm standard ATS. The objective of this study was to evaluate the postoperative hemodynamics in patients who underwent AVR using the 18-mm ATS-AP<sup>®</sup> (ATS Medical, Inc. Minneapolis, Minnesota) for a small valve ring.

## Objective

The valve function of the 18-mm ATS-AP prosthesis, with which better hemodynamics can be expected, was evaluated in the intermediate postoperative period by exercise echocardiography.

## Patients and Methods

### patients

The subjects were 6 patients who underwent AVR at our facility using the 18-mm ATS-AP and tolerated exercise loading [6 females aged 64 (17~74) years, with a median body surface area (BSA) of 1.37 (1.29~1.51) m<sup>2</sup>]. The patient characteristics are shown in Table 1. The surgical procedures were AVR alone in 4,

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**Table 1.** patient characteristics

	age	disease	NYHA	BSA	Concomitant procedure
case 1	61	AR	2	1.51	(-)
case 2	66	AR	3	1.46	(-)
case 3	70	AR MR IE	3	1.29	MVP
case 4	74	AR MSR	2	1.29	MVR
case 5	55	AS	3	1.34	(-)
case 6	17	ASR	3	1.40	(-)

AR: aortic valve regurgitation

IE: infective endocarditis

MR: mitral valve regurgitation

MSR: mitral valve stenosis and regurgitation

AS: aortic valve stenosis

ASR: aortic valve stenosis and regurgitation

MVP: mitral valve plasty

MVR: mitral valve replacement

AVR + mitral valve plasty (MVP) in 1, and AVR + mitral valve replacement (MVR) in 1. Two patients were in NYHA class II and four patients were in NYHA class III at pre-operation. There was no history of angina pectoris or myocardial infarction after the operation. In addition, normal coronary arteries had been documented in all subjects by preoperative coronary angiography.

### Surgical technique

Patients underwent cardiopulmonary bypass through the ascending aortic and right atrial cannulation. Active cooling was not routinely employed. Myocardial protection was achieved by LV venting, and the administration of cold crystalloid cardioplegic solution (St. Thomas solution) antegradely through the aortic root and by direct coronary cannulation. ATS-AP prostheses were implanted using everting mattress sutures.

### Exercise stress protocol

Exercise echocardiography on an ergometer was performed before and 29.0 ± 14.4 months after surgery under monitoring of the blood pressure, ECG, and oxygen saturation. The blood pressure and heart rate were measured noninvasively every minute using a sphygmomanometer cuff fixed over an arm. Exercise loading was started at 25 W and increased by 10-25 W every 3 minutes. During cycling exercise, patients were seated. Exercise was discontinued on the appearance of symptoms (dyspnea, muscular fatigue, etc.), and echocardiography was immediately performed. The pressure gradient (PG) between the left ventricle and aorta and effective orifice area index (EOAI) were evaluated before and after exercising.

### Doppler measurements and calculations

An experienced echocardiologist performed all tests. Echocardiography was carried out using a Toshiba Power-vision 8000 ultrasound system with a 2.5-MHz transducer (Toshiba, Japan) with facilities for continuous- and pulsed-wave Doppler. The left ventricular end-systolic dimension (LVDs) and end-diastolic dimension (LVDd) and thickness of the left ventricular posterior wall (LVPW) and interventricular septum (IVS) were assessed in the short axis of a parasternal view by multiple M-mode measurements with the calculation of fractional shortening. The left ventricular mass (LVM) was calculated as:

$$LVM = 1.04 \times (LVDd + IVS + LVPW)^3 - LVDd^3 - 13.6 \text{ (g)}$$

$$LVMI = LVM/BSA \text{ (g/m}^2\text{)}$$

Parasternal long-axis views were obtained and the early-systolic diameter (D) of the left ventricular outflow tract (LVOT) was measured just below the prosthetic valve using an inner-edge-to-inner-edge method. For each patient, an average of three diameter measurements was used. The LVOT cross-sectional area (CSA) was calculated as:

$$CSA = D^2 \text{ (cm}^2\text{)}$$

The flow velocity across the valve was obtained by means of continuous-wave Doppler after interrogation from multiple windows. Care was taken to orientate the transducer so that the angle between the Doppler cursor and LVOT was as close to 0° as possible, and to obtain the highest possible velocity signal. The peak velocity was measured, averaging from three velocity envelopes, and mean velocity was calculated by online averaging of the instantaneous velocities measured throughout the velocity complexes. Measurements were made in triplicate in each stage to ensure reproducibility. The modified Bernoulli equation was used to calculate the PG across the prosthesis as follows:

$$PG = 4 (V_{cw}^2 - V_{pw}^2) \text{ (mmHg)}$$

where PG is the pressure drop, and  $V_{cw}$  and  $V_{pw}$  are the velocities (peak or mean) across the valve (using continuous-wave Doppler) and in the LVOT (using pulsed-wave Doppler), respectively. The mean pressure drop was calculated by applying the modified Bernoulli equation at multiple instantaneous velocities throughout the velocity profile. The average of all such instantaneous pressure gradients represents the mean. In practice, this is done by online computer software during planimetry of the velocity waveform. The velocity ratio (VR), the ratio of the mean subaortic to mean transaortic velocity, gives an approximate guide to orifice behavior, independent of measurements of the LVOT diameter. The prosthetic valve effective orifice area index (EOAI) was calculated using the modified continuity equation as follows:

$$EOAI = CSA \times VR/BSA \text{ (cm}^2\text{/m}^2\text{)}$$

This simplified equation showed a marked correlation with the original continuity equation.

### Statistical analysis

Parameters were calculated for each patient at rest and during maximal exercise, and the data are presented as the median. The effect of exercise on the median resting Doppler measurements and the extent of the difference on exercise were compared using a paired nonparametric test (Wilcoxon test). A P-value of 0.05 was considered significant. The statistical program Statview (SAS Institute, Inc., version 5.0) was used to perform analyses.

## Results

Six patients who underwent aortic valve replacement using an 18 mm ATS-AP prosthesis were studied. The median body surface area was 1.37 (1.29~1.51) m<sup>2</sup>. Patients underwent echocardiography at rest and during exercise 29.0 ± 14.4 months after aortic valve replacement. Five patients were in NYHA class I and one patient was in NYHA class II at exercise echocardiography test. Exercise was well tolerated up to 45 ± 10 W. All patients showed good left ventricular function, and no impairment of regional myocardial contractility with exercise could be detected in any patient. All patients completed the symptom-limited exercise protocol postoperatively.

It was possible to calculate the EOAI and LVMI for all six patients receiving an 18 mm ATS-AP prosthesis. The echo data at pre-operation and post-operation are shown in Table 2. The EOAI at rest was 0.92 (0.75~1.06) cm<sup>2</sup>/m<sup>2</sup> at 29.0 ± 14.4 months after the operation. There was a significant change in the LVMI between pre-operation and post-operation [158.5 (104.0~222.2) g/m<sup>2</sup> versus 102.4 (92.3~146.4) g/m<sup>2</sup>; P < 0.05]. The changes in LVMI are illustrated in Figure. 1.

**Table 2.** Echo data at pre operation and post operation

	Pre operation	Post operation	p value
LVDd(mm)	47(40~54)	42(34~43)	0.15
LVDs(mm)	28(21~39)	23(18~27)	0.1
IVS(mm)	12(9~13)	11(8~12)	0.2
LVPW(mm)	10(9~15)	10(9~11)	0.58
EF(%)	73(60~82)	76(67~80)	0.43
LVMI(g/m <sup>2</sup> )	158.5(104.0~222.2)	102.4(92.3~146.4)	<0.05

LVDd: left ventricular end-diastolic dimension

LVDs: left ventricular end-systolic dimension

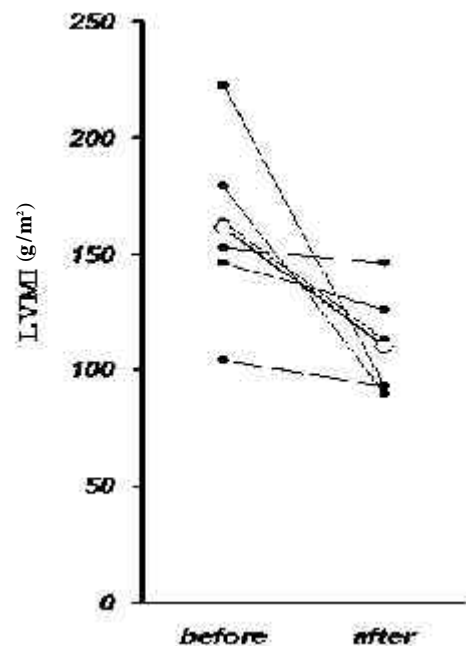
IVS: inter ventricular septum

LVPW: left ventricular posterior wall

EF: ejection fraction LVMI: left ventricular mass index

On peak exercise, the increase in the HR was 42%, from a resting HR of 72.5 (64~80) to 107 (87~120) beats per min (P < 0.001). With exercise, there was a highly significant increase in the mean blood pressure. The resting mean blood pressure of 97.5 (92.5~110) mmHg increased to 145 (117~182) mmHg on maximal exercise (P < 0.05).

The Hemodynamic data at rest and exercise are shown in Table 3. The changes in the mean and peak gradients are illustrated in Figures. 2 and 3. The peak pressure gradient (pPG) increased from 20.5 (13.8~37.0) mmHg at rest to 26.0 (14.6~42.0) mmHg with exercise (P > 0.05). The mean pressure gradient (mPG) increased from 11.0 (6.6~16.0) mmHg at rest to 14.0 (6.3~16.0) mmHg with exercise (P > 0.05). It was possible to calculate the EOAI for all six patients receiving an 18 mm ATS-AP prosthesis. The changes in the EOAI are illustrated in Figure. 4. There was no significant change in the EOAI on maximal exercise [EOAI:0.92 (0.75~1.06) cm<sup>2</sup>/m<sup>2</sup> at rest versus 0.84 (0.78~0.91) cm<sup>2</sup>/m<sup>2</sup> at exercise; P > 0.05].



**Figure 1.** Changes in LVMI, pre-versus postoperation

**Table 3.** Hemodynamic data at rest and exercise

	rest	exercise	p value
PG peak (mmHg)	20.5 (13.8~37.0)	26.0 (14.6~42.0)	0.10
PG mean (mmHg)	11.0 (6.6~16.0)	14.0 (6.3~16.0)	0.44
EOAI (cm <sup>2</sup> /m <sup>2</sup> )	0.92 (0.75~1.06)	0.84 (0.78~0.91)	0.43

PG: pressure gradient

EOAI: effective orifice area index

Changes in mPG on resting and exercise

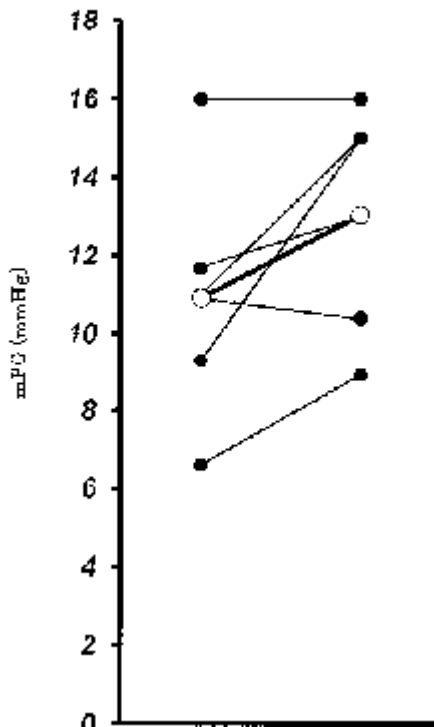


Figure 2. Changes in mPG on resting and exercise

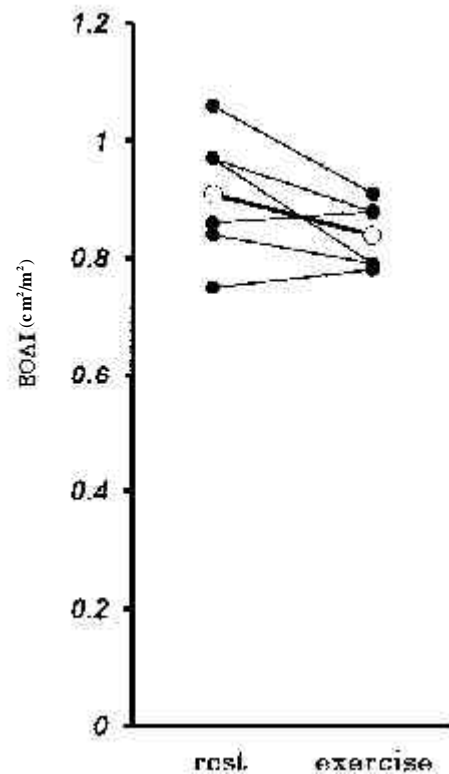


Figure 4. Changes in EOAI on resting and exercise

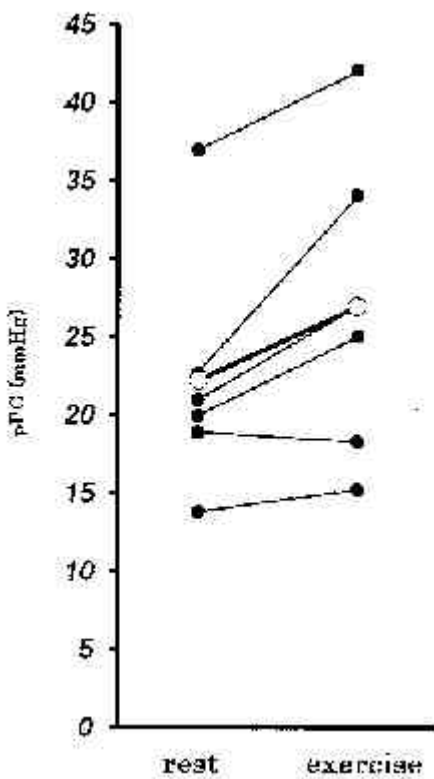


Figure 3. Changes in pPG on resting and exercise

### Discussion

The ATS-AP mechanical valve has been clinically applied for more than 10 years, showing good hemodynamic performance and satisfactory middle and long-term results.<sup>8</sup> However, small aortic valves have been reported to cause hemodynamic problems particularly when they are implanted in patients with a large body surface area, and it has been suggested that the implantation of a prosthesis considered small in relation to the physique should be avoided, because a sustained pressure gradient means persistent loading on the left ventricle, which may delay reverse remodeling of the left ventricle or, inversely, promote ventricular hypertrophy, leading to continued oversteering of the myocardium.<sup>1,7</sup> Exercise can be performed only with considerable cooperation by patients and after checking various conditions such as the absence of angina pectoris or restriction of the motion range of the knee. In addition, exercise-associated artifacts, etc., interfere with appropriate evaluation of the wall motion by Doppler echocardiography. However, exercise echocardiography is a relatively noninvasive examination that can be performed even at the outpatient clinic without using drugs. Also, as exercise loading can be performed relatively easily for exercise echocardiography, it is useful for the objective evaluation of valve functions in patients with masked symptoms.<sup>9-13</sup> Accordingly, 6 patients with an 18 mm ATS-AP mechanical aortic prosthesis were chosen and studied. Several studies have shown that transvalvular gradients are determined by the valve EOA, whether at rest or during exercise.<sup>14</sup> Other studies<sup>15,16</sup>

have revealed that an increase in cardiac output (for example, due to exercise or drug use) may increase the prosthetic valve EOA. Philippe Pibarot and colleagues<sup>14</sup> showed that the EOA of a bioprosthesis valve can increase *in vivo* during exercise. However, some studies<sup>17</sup> have shown that, in the case of mechanical valves, the EOA remained unchanged during maximal exercise despite a significant increase in the gradient. In this study, the EOAI measured in a middle postoperative period was 0.92 (0.75~1.06)cm<sup>2</sup>/m<sup>2</sup>, exceeding 0.85cm<sup>2</sup>/m<sup>2</sup>, and the pPG and mPG were 20.5 (13.8~37.0) mmHg and 11.0 (6.6~16.0) mmHg. In one patient, the pPG exceeded 35 mmHg after surgery. The pressure gradient is often overestimated by echocardiography. In this patient, no symptom was observed, and the LVMI improved, so the pressure gradient may have been overestimated. The LVMI decreased significantly at post-operation. In this study, the subjects were relatively small, with a mean BSA of 1.37 (1.29~1.51) m<sup>2</sup>, and these results suggest that patient-prosthesis mismatch could be avoided.

The hemodynamics were also evaluated by echocardiography before and after exercise. While there was no significant difference, the pressure gradient increased, and the EOAI slightly decreased, after exercise. The gradient is considered to have increased with an elevation in the cardiac output due to exercise. One cause of the decrease in the EOAI may have been an error of measurement in consideration of the report<sup>11</sup> that the EOA does not change in a mechanical valve even at the maximum exercise load. At any rate, a median EOAI (0.92cm<sup>2</sup>/m<sup>2</sup>) could be secured 0.85 cm<sup>2</sup>/m<sup>2</sup> even after exercise. A study<sup>18</sup> suggested that an EOAI of 0.85cm<sup>2</sup>/m<sup>2</sup> or greater should be maintained to avoid PPM. In this study a median EOAI of 0.85cm<sup>2</sup>/m<sup>2</sup> or greater could be achieved. Although the EOAI was less than 0.85cm<sup>2</sup>/m<sup>2</sup> in 2 patients, both patients showed improvements in the LVMI and no symptom in daily living, so that the hemodynamics are considered to have been improved. The HR and BP increased significantly during exercise. According to a report by Sheffield et al. on exercise intensity, the HR of 107 (87~112) bpm in the subjects of this study aged 64 (17~74) years corresponds to mild to moderate exercise. Therefore, the exercise intensity in this study is considered to have been equal to or higher than that of mild exertion the subjects are considered to undergo in their daily living (climbing up a slope, walking, taking a bath, etc.).

According to several studies,<sup>1,3</sup> we can permit EOAI to 0.7cm<sup>2</sup>/m<sup>2</sup>. And there were rarely problems in the case of moderate PPM with senior people because of their low activity. There was not a problem by cardiac function evaluation in an echocardiogram even in this case of a young woman of high activity, too. An 18-mm ATS-AP prosthesis was suggested to be useful to avoid patient-prosthesis mismatch in AVR for small valves, improve postoperative myocardial remodeling, and provide stable hemodynamics even during exercise.

## Study limitations

This study involved a relatively small number of patients.

We therefore need to examine more patients. Also, one of the major limitations of continuous-wave Doppler assessment of pressure gradients is its overestimation. To obtain accurate values, measurement of the left ventricle-aorta pressure gradient by catheterization may have been necessary, but catheterization is an invasive procedure. Echocardiography is considered to be a practical examination that can be performed readily in the outpatient clinic.

## Conclusion

In patients whose BSA were 1.37 (1.29~1.51) m<sup>2</sup>, the 18-mm ATS-AP was suggested to be a prosthetic valve that improves myocardial remodeling and provides stable hemodynamics even during exercise.

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