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Prosthesis-Patient Mismatch after Mitral Valve Replacement: Comparison of Different Methods of Effective Orifice Area Calculation

In-Jeong Cho[1], Geu-Ru Hong[1], Seung Hyun Lee[2], Sak Lee[2], Byung-Chul Chang[2], Chi Young Shim[1], Hyuk-Jae Chang[1], Jong-Won Ha[1], and Namsik Chung[1]

Divisions of [1]Cardiology and [2]Cardiovascular Surgery, Severance Cardiovascular Hospital, Yonsei University College of Medicine, Seoul, Korea.

Purpose: The incidence of prosthesis-patient mismatch (PPM) after mitral valve replacement (MVR) has been reported to vary. The purpose of the current study was to investigate incidence of PPM according to the different methods of calculating effective orifice area (EOA), including the continuity equation (CE), pressure half time (PHT) method and use of reference EOA, and to compare these with various echocardiographic variables.

Materials and Methods: We retrospectively reviewed 166 individuals who received isolated MVR due to rheumatic mitral stenosis and had postoperative echocardiography performed between 12 and 60 months after MVR. EOA was determined by CE (EOA_{CE}) and PHT using Doppler echocardiography. Reference EOA was determined from the literature or values offered by the manufacturer. Indexed EOA was used to define PPM as present if ≤1.2 cm^2/m^2.

Results: Prevalence of PPM was different depending on the methods used to calculate EOA, ranging from 7% in PHT method to 49% in referred EOA method to 62% in CE methods. The intraclass correlation coefficient was low between the methods. PPM was associated with raised trans-prosthetic pressure, only when calculated by CE (p=0.021). Indexed EOA_{CE} was the only predictor of postoperative systolic pulmonary artery (PA) pressure, even after adjusting for age, preoperative systolic PA pressure and postoperative left atrial volume index (p<0.001).

Conclusion: Prevalence of mitral PPM varied according to the methods used to calculate EOA in patients with mitral stenosis after MVR. Among the various methods used to define PPM, EOA_{CE} was the only predictor of postoperative hemodynamic parameters.

Key Words: Mitral valve, heart valve prosthesis

INTRODUCTION

Prosthesis-patient mismatch (PPM) can be considered after insertion into the patient when the effective orifice area (EOA) is of the prosthesis valve and is less than that of a normal human valve, which results in an increased postoperative transvalvular gradient.[1,2]

Previous studies reported that PPM after aortic valve replacement is associated with worse hemodynamics, decreased regression of left ventricular (LV) hypertrophy, more cardiac events and higher mortality.[3-6] However, PPM after mitral valve replacement (MVR) has not been widely investigated, and its incidence has been reported to vary.[7-10] In addition, studies on the clinical impact of PPM following MVR on survival have shown conflicting results, although two recent trials showed that PPM in the mitral position independently affects long-term survival.[7,8] The most important reason for the discrepancy among the previous studies might be that the methods used to define PPM were different. Three different techniques have been used to calculate EOA, including the continuity equation (CE),[7] pressure half time (PHT) method,[10,11] and reference EOA

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Corresponding author: Dr. Geu-Ru Hong, Division of Cardiology, Severance Cardiovascular Hospital, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea.
Tel: 82-2-2228-8443, Fax: 82-2-2227-7732, E-mail: grhong@yuhs.ac

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(EOA_R).[8,12-15] However, differences among the methods of calculating PPM after MVR have not yet been clarified.

Dumesnil and Pibarot[16] have addressed that indexed EOA derived from *in vivo* postoperative measures is the only parameter that can consistently be correlated with postoperative gradients as well as clinical outcomes in defining PPM. Therefore, it is emphasized that the indexed EOA, not geometric specifications of the prosthesis, should be used to define PPM.[17] However, data showing correlation between indexed EOA from postoperative echocardiography and clinical outcomes have been investigated mainly in patients with aortic prosthesis, and clinical evidences supporting the use of calculated EOA using CE for defining PPM in mitral prosthesis are scarce.

We hypothesized that EOA derived from *in vivo* postoperative measure using CE would be most valid compared with other parameters including PHT method and reference EOA for the evaluation of mitral PPM. Therefore, we investigated the incidence of PPM in the mitral position using different methods of EOA determination, including calculation by CE, calculation by PHT and use of reference EOA, and compared them with various echocardiographic variables in patients with mitral stenosis after MVR.

MATERIALS AND METHODS

Patient population

We retrospectively analyzed the data of patients who underwent isolated MVR due to rheumatic mitral stenosis at Severance Cardiovascular Hospital from January 2004 to December 2012. Patients with >2+ mitral valve regurgitation, >1+ aortic valve regurgitation and/or >mild aortic stenosis on preoperative and postoperative echocardiography, and patients with cardiomyopathy or coronary artery disease requiring concurrent bypass surgery were excluded. This study was approved by the Institutional Review Board of Yonsei University, Severance Hospital, Seoul, Korea.

Echocardiographic measurement

Clinical and echocardiographic assessment was performed prior to MVR and 12–60 months after operation. The echocardiographic images of the included patients were reanalyzed by 2 experienced echocardiographers who were unaware of the patient's clinical data. LV internal diameter, septal thickness, and LV posterior wall thickness were measured at end-diastole. LV mass was calculated using the formula developed by Devereux, et al.,[18] and LV mass was indexed for the body surface area. The left atrial volume was calculated from the parasternal long-axis view and apical four-chamber view using the prolate ellipse method[19] and was indexed for the body surface area. The severity of tricuspid regurgitation (TR) was assessed using color flow imaging and regurgitant jet area.[20] The calculated systolic pulmonary artery (PA) pressure was defined as: 4×(maximum velocity of TR jet)^2+right atrial pressure. Right atrial pressure was estimated by the inferior vena cava diameter and its response to inspiration.[10,11] Doppler color flow mapping was used to assess the competency of the prosthetic valves.

EOA calculation and definition of PPM

Mitral valve EOA, calculated by CE (EOA_{CE}), was determined using the stroke volume measured in the LV outflow tract divided by the integral of the mitral valve trans-prosthetic velocity during diastole. Mitral valve EOA, calculated by PHT (EOA_{PHT}), was calculated using the formula 220/PHT.[21] Three cardiac cycles for patients in sinus rhythm and five for patients in atrial fibrillation were recorded, and the results were averaged for every patient. EOA_R was determined from the literature or values offered by the manufacturer. EOA_{CE}, EOA_{PHT}, and EOA_R were indexed for the body surface area ($EOAI_{CE}$, $EOAI_{PHT}$, and $EOAI_R$, respectively). Indexed EOA was used to define PPM as not significant if >1.2 cm^2/m^2, moderate if >0.9 cm^2/m^2 and ≤1.2 cm^2/m^2, and severe if ≤0.9 cm^2/m^2.[7]

Statistical analysis

The distributions of all relevant variables are reported as percentages or as mean±SD. The groups were compared using chi-square statistics for categorical variables and Student's t-test for continuous variables. Correlation between the variables was assessed with the Pearson correlation test. Intraclass correlation coefficient (ICC) for a consistency was used to measure and compare agreement between EOA_{CE} and EOA_{PHT} and between EOA_{CE} and EOA_R. Good correlation was defined as an ICC >0.8. To determine independent predictors of postoperative systolic PA pressure, linear relationships were checked with univariate linear regression analysis. Variables that had statistical significance in univariate analysis and EOA values were entered in the multiple linear regression model. A p value <0.05 was considered statistically significant.

RESULTS

Among the eligible 185 patients who underwent MVR due to mitral stenosis, 167 patients received postoperative echocardiography between 12 and 60 months after MVR. After excluding one patient who showed paravalvular leakage on postoperative echocardiography, the remaining 166 patients (age 56±11 years) with a median follow-up time of 16 months comprised the study population. Preoperative and postoperative variables of the studied populations are shown in Table 1. Of the 166 patients included in this study, there were 45 men and 121 women with a mean age of 56±11 years. Prevalence of hypertension and diabetes were 10% and 9%, respectively. Maze procedure and TV repair were performed in 42 (25%) and 66 (40%) patients, respectively, and atrial fibrillation during postoperative echocardiography was shown in 71 patients (43%).

Table 1. Characteristics of the Studied Population

Variable	Value (n=166)
Age at operation (yrs)	56±11
Gender	
Female	121 (73%)
Male	45 (27%)
Body surface area (m^2)	1.58±0.25
Hypertension	17 (10%)
Diabetes mellitus	15 (9%)
Preoperative atrial fibrillation	102 (61%)
Maze procedure	42 (25%)
Tricuspid valve repair	66 (40%)
Atrial fibrillation at follow-up	71 (43%)
Type of prosthesis	
Mechanical prosthesis	129 (78%)
Bioprosthesis	37 (22%)
Prosthesis implanted	
St. Jude Mechanical	64 (39%)
ATS	29 (17%)
On-X	25 (15%)
Carpentier Edwards Perimount	16 (10%)
St. Jude Medical Epic	12 (7%)
St. Jude Medical Biocor	7 (4%)
Edwards MIRA	7 (4%)
SORIN	4 (2%)
Hancock II	2 (1%)
Prosthesis size (mm)	
25	22 (13%)
27	76 (46%)
29	62 (37%)
31	6 (4%)
MV EOA_R (cm^2)	2.0±0.5
MV $EOAI_R$ (cm^2/m^2)	1.3±0.3
Preoperative hemodynamics	
Systolic blood pressure, mm Hg	117±15
Diastolic blood pressure, mm Hg	74±10
Heart rate, bpm	73±16
Preoperative echocardiography	
LVEF (%)	62±9
LVMI (g/m^2)	90±21
LAVI (mL/m^2)	92±47
TR grade≥moderate	50 (33%)
Systolic PA pressure (mm Hg)	41±14
Mitral valve area by 2-dimensional planimetry (cm^2)	0.9±0.2
Postoperative hemodynamics	
Systolic blood pressure, mm Hg	119±15
Diastolic blood pressure, mm Hg	74±11
Heart rate, bpm	71±11
Postoperative echocardiography	
LVEF (%)	64±6
LVMI (g/m^2)	113±28
LAVI (mL/m^2)	60±33

Table 1. Characteristics of the Studied Population (Continued)

Variable	Value (n=166)
TR grade≥moderate	17 (10%)
Systolic PA pressure (mm Hg)	27±7
Mean diastolic trans-prosthetic gradient (mm Hg)	3.5±1.2
MV EOA_{CE} (cm^2)	1.8±0.5
MV EOA_{PHT} (cm^2)	2.6±0.5
MV $EOAI_{CE}$ (cm^2/m^2)	1.2±0.3
MV $EOAI_{PHT}$ (cm^2/m^2)	1.7±0.4

MV, mitral valve; EOA_R, referred effective orifice area; $EOAI_R$, referred effective orifice area index; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; LAVI, left atrial volume index; TR, tricuspid regurgitation; PA, pulmonary artery; 2D, 2-dimensional; EOA_{CE}, measured effective orifice area by continuity equation; $EOAI_{CE}$, measured effective orifice area index by continuity equation; EOA_{PHT}, measured effective orifice area by pressure half time; $EOAI_{PHT}$, measured effective orifice area index by pressure half time.
St. Jude Mechanical (St. Jude Medical, Minneapolis, MN, USA); ATS (ATS Medical, Minneapolis, MN, USA); On-X (MCRI, Austin, TX, USA); Carpentier Edwards Perimount (Edwards Lifesciences, Irvine, CA, USA); St. Jude Medical Epic (St. Jude Medical, Minneapolis, MN, USA); St. Jude Medical Biocor (St. Jude Medical, Minneapolis, MN, USA); Edwards MIRA (Edwards Lifesciences, Irvine, CA, USA); SORIN (SORIN-Biomedica, Saluggia, Italy); Hancock II (Medtronic, Inc., Minneapolis, MN, USA).

Fig. 1 shows the prevalence of mitral valve PPM according to the methods used to calculate EOA. Prevalence ranged from 7% in PHT method to 49% in referred EOA method to 62% in CE method. There were 63 patients without PPM (38%), 80 patients with moderate PPM (48%) and 23 patients with severe PPM (14%), when $EOAI_{CE}$ was used to define PPM. In contrast, the prevalence of moderate and severe PPM was relatively very low [8 patients (5%) and 3 patients (2%), respectively] according to $EOAI_{PHT}$. There were 85 patients without PPM (51%), 73 patients with moderate PPM (44%) and 8 patients with severe PPM (5%) according to $EOAI_R$.

Comparison of characteristics according to the method of PPM calculation is shown in Table 2. When PPM was defined by $EOAI_{CE}$, the prevalence of males was higher, body surface area was greater and trans-prosthetic pressure and postoperative systolic PA pressure were higher in the PPM group. When PPM was defined by $EOAI_{PHT}$, age at operation and prevalence of atrial fibrillation at follow-up were higher and left atrial volume index (LAVI) was larger in the PPM group. When we used $EOAI_R$, prevalence of atrial fibrillation at follow-up and postoperative LV ejection fraction was higher in the PPM group. There were no significant differences in prevalence of moderate or greater TR at preoperative echocardiography between the groups in all three methods. However, there was a tendency of high occurrence of moderate or greater TR at postoperative echocardiography in PPM group, only when PPM was defined according to CE (p=0.069).

Correlations between $EOAI_{CE}$ and $EOAI_{PHT}$, between $EOAI_{CE}$ and $EOAI_R$, and between $EOAI_{PHT}$ and $EOAI_R$ are demonstrated in Fig. 2. All the agreements between $EOAI_{CE}$ and $EOAI_{PHT}$, between $EOAI_{CE}$ and $EOAI_R$, and between $EOAI_{PHT}$ and $EOAI_R$ were poor [0.430, 95% confidence interval (CI) 0.226–0.580; 0.320,

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95% CI 0.077–0.500; and 0.362, 95% CI 0.133–0.530, respectively]. When the patients were divided into two groups according to the presence of PPM using various methods, the results of correlation were similar. CE methods poorly correlated with referred method (ICC=0.249) and PHT method (ICC=0.228) in defining PPM. Correlation between referred and PHT method was also poor (ICC=0.306).

Fig. 3 shows the correlation between indexed EOAs and postoperative systolic PA pressure. Among the indexed EOAs, $EOAI_{CE}$ showed significant correlation with postoperative systolic PA pressure (r=-0.384, p<0.001). In contrast, there were no significant correlations between $EOAI_{PHT}$ and postoperative systolic PA pressure (r=-0.089, p=0.254) or between $EOAI_R$ and postoperative systolic PA pressure (r=-0.110, p=0.158). Linear regression analysis was performed to identify the predictors of postoperative systolic PA pressure as a dependent variable (Table 2). On multivariate regression, age, mitral valve $EOAI_{CE}$, and postoperative LAVI were found to be independent predictor of postoperative systolic PA pressure (p=0.002, p<0.001, and p=0.001, respectively) (Table 3). On the contrary, $EOAI_{PHT}$ and $EOAI_R$ were not predictors for postoperative systolic PA pressure.

Fig. 4 compares of postoperative systolic PA pressure among the patients without PPM (n=63), with moderate PPM (n=80) and with severe PPM (n=23) according to $EOAI_{CE}$. Systolic PA pressure was statistically different between the patients without PPM and with moderate PPM (25±6 mm Hg vs. 28±6 mm Hg, p=0.007), as well as between patients with moderate and severe PPM (28±6 mm Hg vs. 33±11 mm Hg, p=0.037).

DISCUSSION

The principal findings of the present study are that 1) the incidence of PPM after MVR in patients with mitral stenosis was variable according to the different methods of determining EOA, and 2) among the EOAs assessed by 3 different methods, including the CE method, PHT method and use of reference values, only the $EOAI_{CE}$ was found to be independently associated with the postoperative systolic PA pressure.

Conflicting data on PPM after MVR

Since first described in 1978,[1] PPM after MVR has been suggested to correlate with poor clinical outcomes including persistent pulmonary hypertension and late functional TR.[4,9] However, some authors have insisted that PPM did not affect survival after MVR,[10,15] although several recent trials suggested that mitral PPM independently affects long-term survival.[7,8] In addition, the overall incidence of PPM (<1.3 to <1.2 cm^2/m^2) after MVR has been shown to vary, ranging from 3.7% to 85.9%.[7,8,10-15] The incidence of moderate PPM has also been reported to vary, ranging from 37.4% to 69.5%, and the incidence of severe PPM ranged from 8.7% to 16.4%.[22]

Explanations for discrepancy

There may be several explanations concerning the conflicting data on the clinical effect of PPM after MVR. First, different valve types and patients groups were employed in the studies. Especially, patients suffering PPM have sometimes additional risk factors, including hypertension and diabetes, which could also affect long-term survival. Second, when evaluating the impact of PPM after MVR, it is also important to consider pathophysiological status of patients. In the current study, minimize those problems, we included only patients with rheumatic mitral stenosis and analyzed postoperative echocardiography 12 to 60 months after MVR, thus avoiding dynamic changes of hemodynamic status at early postoperative period and the late development of prosthetic valve malfunction which might be

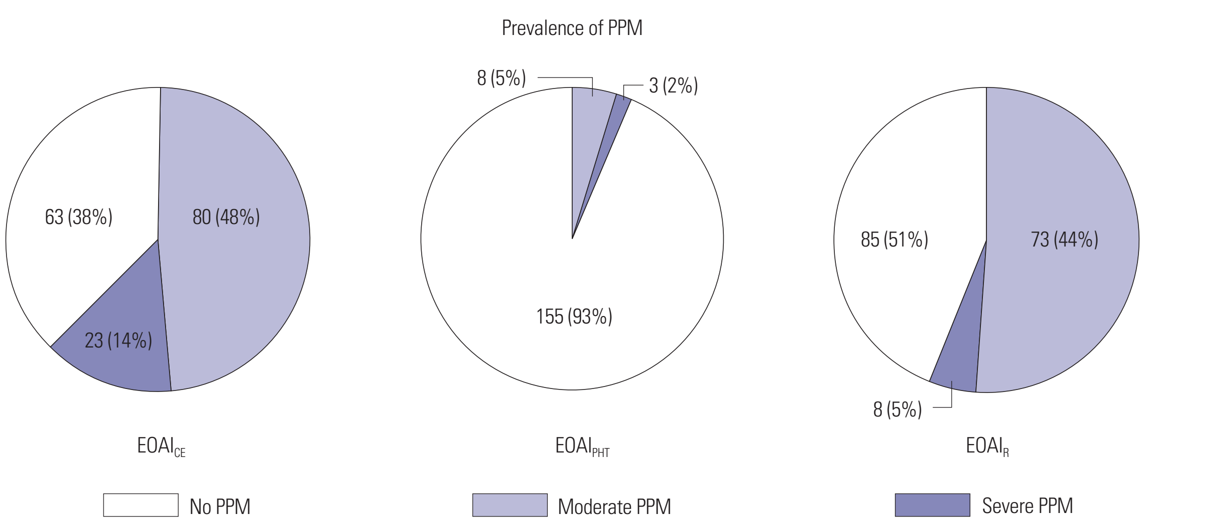

Fig. 1. Prevalence of PPM according to the methods used to calculate effective orifice area. PPM, prosthesis-patient mismatch; $EOAI_{CE}$, measured effective orifice area index by continuity equation; $EOAI_{PHT}$, measured effective orifice area index by pressure half time; $EOAI_R$, referred effective orifice area index.

associated with pannus formation. Consequently, we found that PPM determined by CE showed significant correlation with various postoperative hemodynamic parameters.

Methods to determine effective orifice area

The most important reason for discrepancy among the previous studies might be that the methods used to define PPM were different. In previous studies, three different methods have

Table 2. Characteristics of the Study Population According to the Method of Prosthesis-Patient Mismatch Determination

Variable	EOA_{CE}			EOA_{PHT}			EOA_{R}		
	No PPM (n=63)	PPM (n=103)	*p* value	No PPM (n=155)	PPM (n=11)	*p* value	No PPM (n=85)	PPM (n=81)	*p* value
Age at operation (yrs)	56±11	56±11	0.810	56±11	64±9	0.016	55±11	57±11	0.211
Gender			0.048			0.475			0.108
Female	51 (81%)	70 (68%)		114 (74%)	7 (64%)		66 (78%)	55 (68%)	
Male	12 (19%)	33 (32%)		41 (26%)	4 (36%)		19 (22%)	26 (32%)	
Body surface area (m^2)	1.53±0.15	1.60±0.14	0.001	1.57±0.15	1.63±0.15	0.209	1.55±0.15	1.61±0.14	0.211
Hypertension	6 (10%)	11 (11%)	0.517	13 (8%)	4 (36%)	0.016	8 (9%)	9 (11%)	0.718
Diabetes mellitus	5 (8%)	10 (10%)	0.465	14 (9%)	1 (6%)	0.659	7 (8%)	8 (10%)	0.712
Preoperative atrial fibrillation	40 (63%)	62 (60%)	0.399	91 (59%)	11 (100%)	0.004	45 (54%)	57 (70%)	0.021
Maze procedure	19 (30%)	23 (22%)	0.895	41 (26%)	1 (6%)	0.090	23 (27%)	19 (23%)	0.130
Tricuspid valve repair	27 (43%)	39 (38%)	0.524	61 (39%)	5 (45%)	0.690	29 (34%)	37 (46%)	0.128
Atrial fibrillation at follow-up	26 (41%)	45 (44%)	0.443	62 (40%)	9 (82%)	0.007	29 (34%)	42 (52%)	0.016
Type of prosthesis			0.242			0.001			0.008
Mechanical prosthesis	52 (83%)	77 (75%)		125 (81%)	4 (36%)		73 (86%)	56 (69%)	
Bioprosthesis	11 (17%)	26 (25%)		30 (19%)	7 (64%)		12 (14%)	25 (31%)	
Prosthesis size (mm)			0.484			0.307			0.356
25	6 (10%)	16 (16%)		21 (14%)	1 (9%)		8 (9%)	14 (17%)	
27	27 (43%)	49 (48%)		68 (44%)	8 (73%)		38 (45%)	38 (47%)	
29	27 (43%)	35 (34%)		60 (34%)	2 (18%)		35 (41%)	37 (46%)	
31	3 (5%)	3 (5%)		6 (4%)	0 (0%)		4 (5%)	2 (2%)	
Mitral valve EOA_R (cm^2)	2.1±0.5	2.0±0.5	0.339	2.1±0.5	1.7±0.3	0.016	2.4±0.5	1.6±0.2	<0.001
Mitral valve $EOAI_R$ (cm^2/m^2)	1.4±0.4	1.3±0.3	0.034	1.3±0.3	1.0±0.2	0.004	1.6±0.3	1.0±0.1	<0.001
Preoperative echocardiography									
LVEF (%)	62±9	62±9	0.762	64±6	62±5	0.389	62±8	62±9	0.585
LVMI (g/m^2)	87±23	92±20	0.145	89±20	113±21	0.122	91±22	89±20	0.585
LAVI (mL/m^2)	110±31	114±26	0.444	89±43	135±71	0.057	92±43	93±50	0.868
TR grade≥moderate	22 (35%)	28 (27%)	0.292	48 (31%)	2 (18%)	0.372	25 (29%)	25 (31%)	0.838
Systolic PA pressure (mm Hg)	43±14	40±14	0.169	41±14	40±9	0.832	39±11	43±16	0.051
Mitral valve area by 2D planimetry (cm^2)	0.9±0.2	0.9±0.2	0.236	0.9±0.2	0.8±0.2	0.158	0.9±0.2	0.9±0.2	0.264
Postoperative echocardiography									
LVEF (%)	64±6	63±6	0.245	64±6	62±5	0.389	62±6	65±6	0.013
LVMI (g/m^2)	103±56	86±39	0.131	111±27	131±39	0.122	114±29	112±27	0.626
LAVI (mL/m^2)	66±42	57±24	0.089	59±31	85±43	0.008	58±30	63±35	0.380
TR grade≥moderate	3 (5%)	14 (14%)	0.069	15 (10%)	2 (18%)	0.369	9 (11%)	8 (10%)	0.880
Mean diastolic trans-prosthetic gradient (mm Hg)	3.2±1.1	3.7±1.2	0.021	3.4±1.2	3.4±1.5	0.844	3.4±1.3	3.4±1.0	0.915
Systolic PA pressure (mm Hg)	25±6	29±8	0.001	27±7	29±9	0.381	27±7	28±8	0.440
MV EOA_{CE} (cm^2)	2.2±0.4	1.6±0.2	<0.001	1.8±0.5	1.6±0.3	0.120	1.8±0.5	1.8±0.5	0.520
MV EOA_{PHT} (cm^2)	2.8±0.5	2.6±0.5	0.014	2.7±0.4	1.7±0.3	<0.001	2.7±0.5	2.6±0.5	0.114
MV $EOAI_{CE}$ (cm^2/m^2)	1.5±0.2	1.0±0.1	<0.001	1.2±0.3	1.0±0.2	0.029	1.2±0.3	1.1±0.3	0.093
MV $EOAI_{PHT}$ (cm^2/m^2)	1.8±0.4	1.6±0.3	<0.001	1.8±0.3	1.1±0.2	<0.001	1.8±0.4	1.6±0.3	0.007

MV, mitral valve; EOA_R, referred effective orifice area; $EOAI_R$, referred effective orifice area index; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; LAVI, left atrial volume index; TR, tricuspid regurgitation; PA, pulmonary artery; 2D, 2-dimensional; EOA_{CE}, measured effective orifice area by continuity equation; $EOAI_{CE}$, measured effective orifice area index by continuity equation; EOA_{PHT}, measured effective orifice area by pressure half time; $EOAI_{PHT}$, measured effective orifice area index by pressure half time.

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been used to calculate EOA, including the CE method,[7] PHT method,[10,11] and reference EOA.[8,12-15]

We compared the three methods and found that agreement among $EOAI_{CE}$, $EOAI_{PHT}$, and EOA_R was poor, and the prevalence of PPM varied according to the calculation method, ranging from 7% in the PHT method to 49% in the reference EOA method to 62% in the CE method. This finding explains the discrepant prevalence of PPM and conflicting data about the prognosis of PPM in the various studies. Long-term survival data of patients with PPM defined by EOA_{CE} has not yet been reported, and further studies with EOA_{CE} might be necessary to clarify the clinical impact of PPM.

Interestingly, it has been reported in the previous reports[9,23] that prevalence of PPM was relatively high when CE was used to define PPM , ranging from 42% to 71%. We also found similar results of high prevalence of PPM, especially in moderate PPM. Possible explanation is that in bileaflet valves, the smaller central orifice has a higher velocity than the larger outside orifice, which may lead to underestimation of EOA_{CE}.[17] Patients who underwent MVR with bileaflet mechanical heart valve were 78% in the current study, and therefore, there is a chance that EOA_{CE} might be underestimated in part. Therefore, further research and overall agreement are required to establish the allowable range of EOA_{CE} for the definition of PPM, although CE methods might be the most appropriate method to determine EOA. In addition, clinical implication of moderate PPM in mitral position is not clear, since moderate PPM did not show statistically significant result of poor survival, contrast to severe PPM, which showed poor long-term survival.[7] Nevertheless, we demonstrated that even patients with moderate PPM showed raised systolic PA pressure compared to those without PPM, suggesting clinical significance of moderate PPM. Therefore, the clinical impact of moderate PPM and EOA range for the diagnosis of PPM might need further investigation.

Among the three methods, mentioned above EOA_{PHT} is not recommended for calculating EOA of the mitral prosthesis because of the influence of chronotropic conditions and atrioventricular compliance.[24] Nevertheless, some studies still use PHT method to define EOA.[10,11] In the current study, as anticipated, EOA calculation via the PHT method was found to be not associated with postoperative hemodynamic parameters and largely overestimated the EOA compared to other methods. Therefore, we should try not to use PHT to calculate EOA in mitral prosthesis.

Pulmonary artery pressure after MVR

A rise in PA pressure can result from elevation of pulmonary blood flow, pulmonary venous pressure and/or vascular resis-

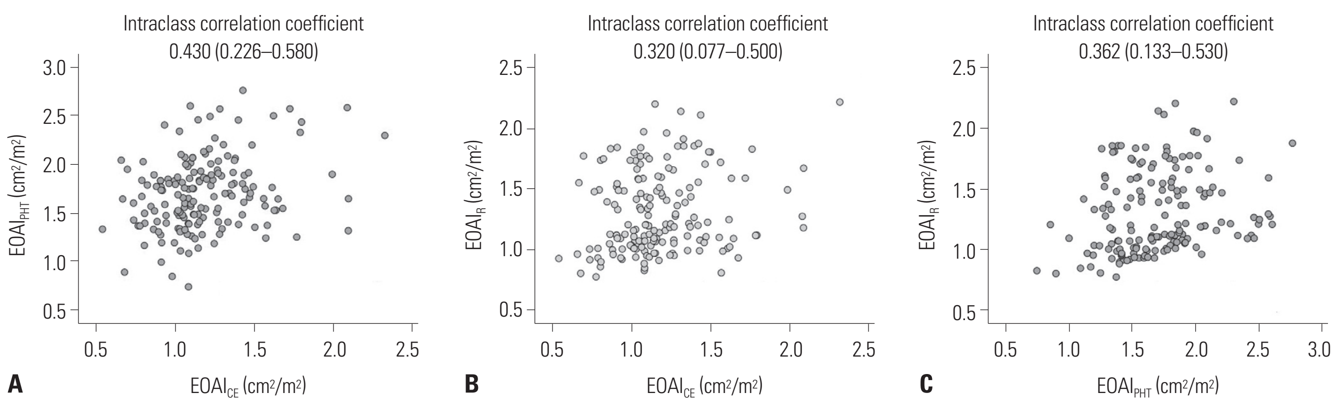

Fig. 2. Correlation between $EOAI_{CE}$ and $EOAI_{PHT}$ (A), between $EOAI_{CE}$ and $EOAI_R$ (B) and between $EOAI_{PHT}$ and $EOAI_R$ (C). $EOAI_{CE}$, measured effective orifice area index by continuity equation; $EOAI_{PHT}$, measured effective orifice area index by pressure half time; $EOAI_R$, referred effective orifice area index.

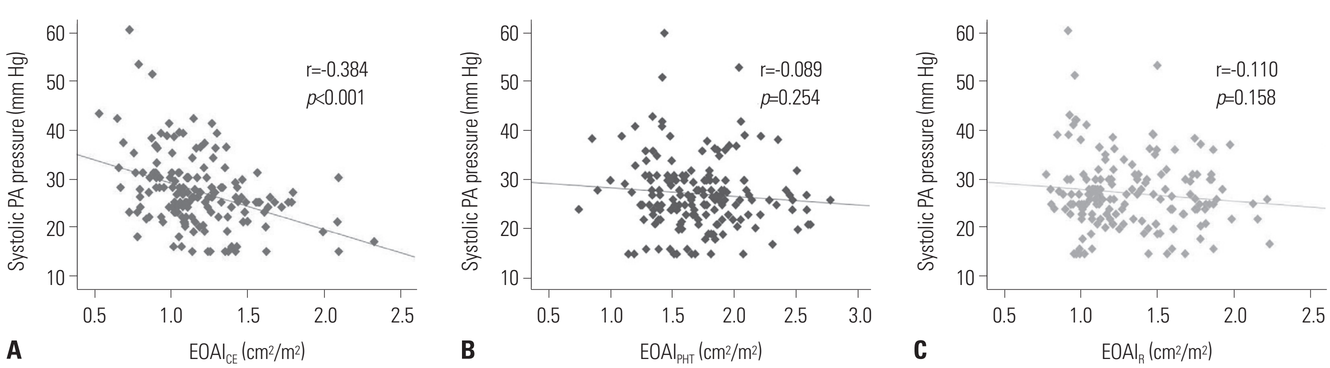

Fig. 3. Correlations between effective orifice area index and postoperative systolic PA pressure. (A) Effective orifice area index by continuity equation, (B) effective orifice area index by pressure half time, and (C) referred effective orifice area index. PA, pulmonary artery; $EOAI_{CE}$, measured effective orifice area index by continuity equation; $EOAI_{PHT}$, measured effective orifice area index by pressure half time; $EOAI_R$, referred effective orifice area index.

tance,[9] and pulmonary hypertension is an important risk factor for morbidity and mortality in patients with various cardiovascular diseases.[25-27] Pulmonary hypertension is frequently observed in patients with mitral stenosis. Since increased PA pressure is associated with poor functional capacity and a dismal prognosis in patients with severe mitral valve disease, normalization of PA pressure constitutes a crucial goal of MVR.[28-30]

The development of late TR after MVR is an important complication of the surgery, since it is associated with a severe impairment of exercise capacity and a poor symptomatic outcomes.[31] However, the pathogenesis of this condition remains poorly understood, and treatment for the patients with late TR is clinically difficult to decide. Recently, it has been reported that mitral PPM is associated with the persistence of TR and pulmonary hypertension following MVR.[23] Our study also demonstrated similar results, showing a tendency of high prevalence in moderate or greater TR in PPM group, defined by CE. In addition, PPM calculated by $EOAI_{CE}$ showed higher trans-prosthetic pressure, and $EOAI_{CE}$ was the only parameter which showed independent correlation with postoperative systolic PA pressure. Systolic PA pressure has been known to be influenced by many factors including age, diastolic dysfunction and cardiopulmonary disease,[32] as well as trans-prosthetic pressure. Since we enrolled homogenous, relatively young patient population of pure mitral stenosis, we can speculate that systolic PA pressure might be influenced mainly by trans-prosthetic gradient in the studied population. Therefore, the use of $EOAI_{CE}$ rather than $EOAI_{PHT}$ and $EOAI_{R}$ may be appropriate for identifying PPM in the mitral position, since hemodynamic variables, including trans-prosthetic pressure and systolic PA pressure, showed significant correlation with EOA, only when it is calculated by using CE.

Unfortunately, however, most previous studies on PPM after MVR used $EOAI_{R}$ to define PPM. $EOAI_{CE}$ was used to define PPM in only two studies, and both demonstrated clinical significance of PPM after MVR, including association with persistent pulmonary hypertension and late TR.[9,23] Therefore, further larger studies to define PPM using EOAICE are needed to clarify clinical significance and implications of PPM after MVR.

Limitations

The results of the study were based on retrospective analysis; however, we carefully reviewed patient medical records and echocardiography. As our findings are based upon an observational cohort of patients with rheumatic mitral stenosis, they may not necessarily be generalizable to all patients with mitral regurgitation. We compared indexed EOA to systolic PA pressure, not clinical outcome, since the studied group was at relatively low risk for cardiovascular events, as indicated by the low prevalence of combined co-morbidities such as hypertension and diabetes. In addition, functional data, such as maximum exercise capacity and maximum oxygen consumption, which would be more helpful for identifying the clinical implication of mitral PPM, were not included. Prevalence of pulmonary hypertension (systolic PA pressure >40 mm Hg) was relatively low, and therefore, further investigation into the clinical significance of the results of the current study is needed. Patients with atrial fibrillation were included in the study population, although five cardiac cycles were recorded and these results were averaged. We used linear regression analysis to determine independent predictors of systolic PA pressure, although we cannot conclude that there is no association just because the linear re-

Table 3. Multivariate Regression Analysis for the Predictors of Systolic PA Pressure after Mitral Valve Replacement

Variable	β coefficient	95% CI	*p* value
Model 1			
Age at operation	0.23	0.06 to 0.26	0.002
Preoperative systolic PA pressure	0.09	-0.02 to 0.12	0.179
Postoperative LAVI	0.25	0.02 to 0.09	0.001
Mitral valve $EOAI_{CE}$	-0.37	-12.2 to -5.8	<0.001
Model 2			
Age at operation	0.28	0.08 to 0.30	0.001
Preoperative systolic PA pressure	0.07	-0.04 to 0.11	0.324
Postoperative LAVI	0.23	0.02 to 0.09	0.006
Mitral valve $EOAI_{PHT}$	-0.04	-3.68 to 1.95	0.543
Model 3			
Age at operation	0.27	0.07 to 0.29	0.001
Preoperative systolic PA pressure	0.06	-0.04 to 0.11	0.402
Postoperative LAVI	0.23	0.02 to 0.09	0.004
Mitral valve $EOAI_{R}$	-0.05	-4.28 to 2.00	0.474

CI, confidence interval; PA, pulmonary artery; $EOAI_{CE}$, measured effective orifice area index by continuity equation; LAVI, left atrial volume index; $EOAI_{PHT}$, measured effective orifice area index by pressure half time; $EOAI_{R}$, referred effective orifice area index.

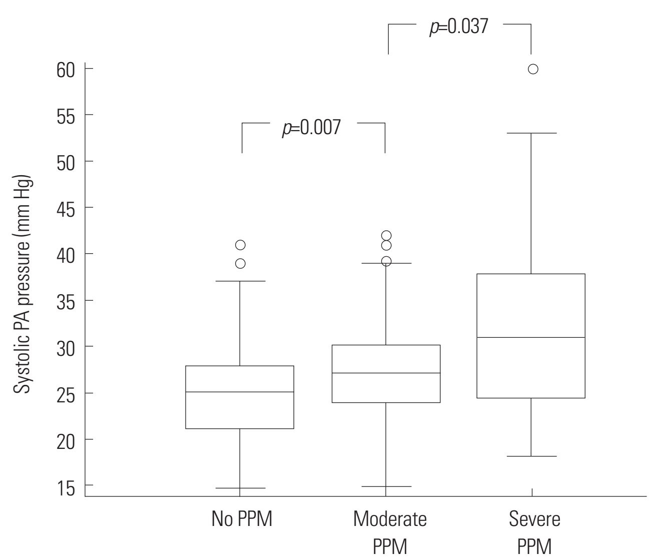

Fig. 4. Comparison of postoperative systolic PA pressure among patients without PPM (n=63) to those with moderate PPM (n=80) and with severe PPM (n=23), defined using the continuity equation. Vertical bars represent range, boxes represent inter-quartile range, and horizontal lines represent the median. PPM, prosthesis-patient mismatch; PA, pulmonary artery.

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gression is not significant. Nevertheless, the association with $EOAI_{PHT}$ and $EOAI_R$ is unlikely, since there were no significant differences in systolic PA pressure between the groups, and the multivariate regression analysis showed that $EOAI_{PHT}$ and $EOAI_R$ were not predictors of systolic PA pressure.

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