The frequency of prosthesis-patient mismatch after mechanical mitral valve replacement and its effect on postoperative systolic pulmonary arterial pressure

Mekanik mitral kapak değişimi sonrası gelişen protez kapak-hasta uyumsuzluğu ve sistolik pulmoner arter basıncı üzerine etkisi

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Objectives: We investigated the frequency of prosthesis-patient mismatch (PPM) after mechanical mitral valve replacement (MVR), its effect on postoperative systolic pulmonary arterial pressure (PAP), and the relationship of indexed effective orifice area (EOA) with systolic PAP and hemodynamic variables of the prosthetic valve.

Study design: The study included 100 patients (27 men, 73 women; mean age 51±11 years) with a normally functioning mechanical mitral valve prosthesis. Prosthetic mitral EOA, indexed EOA, and net atrioventricular compliance (Cn) were estimated by Doppler echocardiography. Prosthesis-patient mismatch was defined as an indexed EOA 0.1.2 cm²/m² and Cn, 84 ml/mmHg, and pulmonary hypertension (PHT) was defined as systolic PAP ≥40 mmHg. Results: The frequencies of PPM and postoperative persistent PHT were 33% and 31%, respectively. Postoperative persistent PHT was seen in 79% and 8% in patients with and without PPM, respectively (p<0.001). The frequency of low Cn was significantly higher in patients with PPM (60% vs. 31%; p<0.001). Postoperative systolic PAP was significantly higher in patients with PPM (42.0±6.6 mmHg vs. 29.9±6.0 mmHg, p<0.0001) and in 41 patients having a low Cn, compared to 59 patients having a high Cn (37.2±8.8 mmHg vs. 31.6±7.4 mmHg, p<0.001). Postoperative systolic PAP was significantly correlated with indexed EOA (r=-0.535, p<0.001) and Cn (r=-0.422, p<0.001), whereas prosthetic valve size was not correlated with systolic PAP (r=0.022, p=0.829) and indexed EOA (r=0.008, p=0.93). In multivariate regression analysis, indexed EOA, age, mean transprosthetic gradient, and Cn were independent factors affecting systolic PAP.

Conclusion: Prosthesis-patient mismatch after MVR is associated with persistent PHT. Use of a prosthetic valve that is compatible with the body surface area may significantly reduce the incidence of PPM, and thus the frequency of persistent PHT.

Key words: Echocardiography, Doppler; heart valve prosthesis implantation/adverse effects; hypertension, pulmonary/etiology; mitral valve/surgery; prosthesis fitting.
Prosthesis-patient mismatch (PPM) is caused by the effective orifice area (EOA), which is provided by prosthetic valve due to incompatibility of the small EOA in relation to the body surface area (BSA). Due to the small nature of EOA of the prosthetic valve used for mitral valve replacement (MVR) and despite a normally functioning mitral valve, the transvalvular gradient was found to be relatively high similar to mild-moderate mitral stenosis.[11] PPM in the mitral position is known to prevent regression of left atrial pressure and pulmonary artery hypertension (PHT).[12,13] On the other hand, PHT increases cardiovascular morbidity and mortality by causing right ventricular dysfunction. As a result, restoration of normal PAP is the objective of MVR.[14,15]

Net atrioventricular compliance is one of the important determinants of PAP in patients with mitral stenosis.[10] Net atrioventricular compliance (C_n) is the ratio of the volume change between the left atrium and left ventricle (LV) during diastole to the change in transmural pressure gradient, and reflects the post-capillary resistance. C_n was found to be an independent determinant of left ventricular pressure and PAP in patients with mitral stenosis.[11]

The incidence of PPM in the mitral position has been reported by literature studies to vary between 8.6% and 71%. Variation in the prosthetic valve size and type may have led to data variation. Considering the higher rate of mechanical prosthesis use in turkey compared to Europe and the USA, we aimed at investigating (i) the incidence of post mechanical MVR development of PPM, (ii) relationship of index EOA with prosthetic size and mean gradient, and (iii) the effect of PPM and C_n on postoperative systolic PAP.

**PATIENTS AND METHODS**

Patient selection. We retrospectively evaluated the hospital data of 346 patients who underwent mechanical MVR in our hospital between January 2003 and September 2007. The following were considered as the study exclusion criteria: prosthetic valve dysfunction (separation, thrombus on the valve, pannus and endocarditis), history of surgery due to natural valve endocarditis, history of coronary artery bypass graft (CABG) surgery, prosthetic aortic or tricuspid valve, tricuspid valve plasty, more than mild aortic stenosis or regurgitation, ejection fraction (EF) <50%, cardiomyopathy, chronic obstructive pulmonary disease, congenital heart diseases, surgery within the past six months, age less than 18 years, unavailability of preoperative echocardiographic data and inability to perform echocardiographic measurements due to chest structure. A total of 100 patients (27 men, 73 women; mean age 51±11; range 26-84) who respected these criteria, and performed their preoperative echocardiographic and PAP measurement were included in the study.

**Echocardiographic measurements.** Echocardiographic analysis was performed by two experienced cardiologists (AT and OK) who were blinded for the patient’s clinical condition in the left lying position using the Acuson Sequoia C256 device (Siemens Medical Systems, Mountain View, CA, USA), and the 2.5-3.5 MHz transducer. Standard M-mode measurements were made according to recommendations of the American Society of Echocardiography.[16] Evaluation of left ventricular regional wall movement was carefully made based on the 17 segment model. EF was determined in the double-plane apical view (2 chamber view and 4 chamber view), using the modified Simpson’s method. Normal left ventricular systolic function was defined as normal left ventricular end diastolic and end systolic dimensions, absence of important regional contraction abnormality, and EF >50%.[17]

Prosthetic mitral valve and aortic and tricuspid regurgitation were evaluated by color Doppler in the apical four-chamber view. The tricuspid regurgitation peak flow rate was obtained using the continuous wave Doppler technique, while the right ventricular-right atrial peak pressure gradient was estimated by the modified Bernoulli equation. The systolic PAP was obtained by adding the right atrial pressure to this value.[14] Right atrial pressure was estimated by the largest diameter of the inferior vena cava (IVC) from the subcostal view and the degree of inspiratory collapse.[15] Pulmonary hypertension was defined as a systolic PAP >40 mmHg.[16]

The prosthetic mitral EOA was estimated by dividing the prosthetic mitral valve diastolic flow of the left ventricular outflow path by the velocity-time integral, using the continuity equation.[17] The index EOA was calculated by dividing the EOA by BSA. PPM was defined as an index EOA ≤1.2 cm²/m².[6,17,18] Patients were divided into two groups as those with PPM and those without PPM, according to the value of index EOA.

Net atrioventricular compliance was calculated from the mitral flow profile in the Doppler echocardiography in accordance with that postulated by Flachskampf et al, by the following equation: C_n=1.270 (EOA/E-wave curve).[10] In this equation EOA is the mitral valve EOA estimated from the continuity equation (cm²) while E-wave curve is the down curve of the E-wave velocity obtained from the mitral Doppler flow signal (cm²/sec.). The result was expressed as mmHg. A low C_n was considered as ≤4 mmHg.[19]

Concomitant monitoring of heart beat was performed during echocardiographic analysis. Measurements were
repeated three times and the mean values were obtained.

Statistical analysis. Study data were expressed as mean±standard deviation. The Students t-test was used for comparison of continuous variables, while the Chi-square test and the Fisher’s exact tests were used for categorical analyses. The Person’s correlation coefficient was used for correlation analyses. Correlation coefficients of 0-0.25, 0.25-0.50, 0.50-0.75 and 0.75-1 were defined as low/weak, moderated, strong and very strong respectively.

Comparison of more than one continuous variable was performed using the ANOVA test. On the other hand, the Bonferroni method was used for intergroup comparison, while the linear regression analysis was used for multivariable analysis. Results were evaluated with a confidence interval of 95% and a statistical significance value of p<0.05. The SPSS (Windows 15.0) program was used for all statistical analyses.

RESULTS

Clinical, preoperative characteristics, group intraoperative data of the patients are shown in Table 1. There was no significant difference between the groups with regards to gender (p>0.05). The mean age of the group with prosthesis-patient mismatch (p=0.014), body mass index (p=0.001), and mean values for BSA (p=0.003) were found to be significantly higher. No significant difference was found between the two groups with regards to preoperative mitral valve pathologies, rhythm, frequency of PHT, size of prosthesis used, and the Maze procedure (p>0.05). The frequency of applying the ≤27 valve (81.8% in the PPM group and 85.1% in the non-PPM group) was found to be similar in both groups.

Echocardiographic characteristics. Pre- and postoperative (mean 35 months) echocardiographic characteristics of the patients are shown in Table 2. Although the EF values of both groups were within normal limits, the PPM group values were found to be higher (p=0.013). The mitral
valve EOA, index EOA and the \( C_n \) values were found to be significantly low in the PPM group (\( p<0.0001 \)), whereas the mean prosthetic transvalvular gradient and the systolic PAP values were found to be significantly high (\( p<0.0001 \)).

The effect of prosthesis-patient mismatch on systolic pulmonary artery pressure. A relationship was found between the index EOA and the postoperative systolic PAP (\( r=-0.535, p<0.001 \)) (Figure 1), \( C_n \) (\( r=0.498, p<0.001 \)) and the mean prosthetic transvalvular gradient (\( r=-0.360, p<0.001 \)), whereas no relationship was identified between the index EOA and valvular size (\( r=0.008, p=0.93 \)). There was no relationship between prosthetic valve size and the postoperative systolic PAP (\( r=0.022, p=0.829 \)).

The incidence of persistent PHT in the PPM group before and after surgery was found to be 82% and 79%, respectively. In the non-PPM group, the incidence was found to be 94% and 8% respectively. Changes in the incidence of PHT after surgery, was found to be significant between the groups (\( p<0.001 \)). PHT was
predictable with a sensitivity of 84% and specificity of 91% when the index EOA was ≤1.2 cm²/m².

The effect of net atrioventricular compliance on systolic pulmonary artery pressure. A moderate relationship (r=-0.422, p<0.001) was found between postoperative systolic PAP and Cn (Figure 2). The postoperative systolic PAP of a 41 year-old patient with low Cn (≤4 ml/mmHg) was found to be 37.2±8.8 mmHg, whereas that of a 59 year-old patient with high Cn was found to be 31.6±7.4 mmHg (p<0.001) (Table 3). The mean Cn of 69 patients with postoperative PHT was 6.3±2.8 ml/mmHg, whereas the mean Cn of 31 patients with postoperative PHT was found to be 3.8±1.5 ml/mmHg (p=0.0001). Evaluation of the groups in respect of low Cn values demonstrated that the incidence of low Cn in the group with PPM (n=20, 60%) was significantly higher than in the group without PPM (n=21, 31%) (p<0.001). The distribution of postoperative systolic PAP values and the frequency of PHT between the groups with respect to low and high Cn values is shown in Table 4.

Independent variables of pulmonary artery pressure. In the univariate analysis, a relationship was found between postoperative systolic PAP and age (r=0.47, p<0.001), index EOA (r=-0.53, p<0.001), Cn (r=-0.42, p<0.001), the mean prosthetic transvalvular gradient (r=0.43, p<0.001) and postoperative atrial fibrillation. On the other hand, the multivariate analysis demonstrated that index EOA, age, mean prosthetic transvalvular gradient and Cn, were independent variables affecting postoperative systolic PAP (Table 5).

**DISCUSSION**

Increase in pulmonary artery pressure is known to be caused by pulmonary blood flow, pulmonary venous pressure and/or pulmonary vascular resistance. Pulmonary hypertension is an important risk factor of cardiovascular diseases morbidity and mortality. As a result, the main objective of MVR should be normalization of PAP. However, regression of PAP after surgery differs from one patient to the other and it is generally not complete. Development of PPM following mitral valve replacement is suggested to lead to persistent PHT, similar to mitral stenosis. PHT is thought to be

### Table 3. Distribution of pre- and post operative systolic pulmonary artery pressure values in patients with a low and high net atrioventricular compliance (Cn).

<table>
<thead>
<tr>
<th>Cn ≤4 ml/mmHg (n=41)</th>
<th>Cn &gt;4 ml/mmHg (n=41)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary artery pressure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before surgery</td>
<td>50.7±11.5</td>
<td>52.8±15.3</td>
</tr>
<tr>
<td>After surgery</td>
<td>37.2±8.8</td>
<td>31.6±7.4</td>
</tr>
<tr>
<td>Difference</td>
<td>-13.5±13.4</td>
<td>-21.8±17.5</td>
</tr>
</tbody>
</table>

### Table 4. Distribution of postoperative systolic pulmonary artery pressure values and frequency of pulmonary hypertension between the groups with respect to low and high net atrioventricular compliance (Cn) values

<table>
<thead>
<tr>
<th>Post operative:</th>
<th>PPM (+) (n=33)</th>
<th>PPM (+) (n=33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary artery pressure (mmHg) (Mean±SD)</td>
<td>Cn ≤4 ml/mmHg (n=20)</td>
<td>Cn &gt;4 ml/mmHg (n=13)</td>
</tr>
<tr>
<td>44.0±3.8</td>
<td>38.8±8.8</td>
<td>30.6±7.1</td>
</tr>
<tr>
<td>Frequency of pulmonary hypertension (n, %)</td>
<td>19 (95%)</td>
<td>7 (53.8%)</td>
</tr>
</tbody>
</table>
Argano et al. [6] postoperatively. On the other hand, Totaro and Argano [12] conducted in patients with PPM (66% preoperatively and 69% to 19%, whereas no significant change was reported in patients who underwent implantation of mechanical prosthesis (85.1%). In our study, we did not also demonstrate any relationship of valve size with index EOA, and of valve size with postoperative systolic PAP.

Table 5. Independent variables affecting postoperative pulmonary artery pressure

<table>
<thead>
<tr>
<th>Variable</th>
<th>β</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.434</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Index effective orifice area (cm²/m²)</td>
<td>-0.315</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean gradient (mmHg)</td>
<td>0.281</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Net atrioventricular compliance (ml/mmHg)</td>
<td>-0.162</td>
<td>0.041</td>
</tr>
</tbody>
</table>

PPM has been shown to be associated with decreased hemodynamics, inadequate regression of LV hypertrophy, increases in the incidence of cardiac events and high mortality rate, after aortic valve replacement.[24] However, the clinical and hemodynamic effects of the incidence of PPM in the mitral position is not fully understood and results of studies conducted in this respect have been controversial.[6,12] Li et al.[6] demonstrated the presence of PPM in the mitral position (84% rate of mechanical prosthesis use) defined as an index EOA ≤1.2 cm²/m² in 28 of the 40 patients (71%), whereas Totaro and Argano[12] observed the presence of PPM in the mitral position (completely bioprosthesia) only in eight of the 92 patients (8.6%). The incidence of PPM in our study was 33%. Unlike in the studies mentioned, our study included only patients who underwent implantation of mechanical prosthesis. These differences of PPM incidence may have been due to patient characteristics and the prosthetic valve used (mechanical or bioprosthesia).

Data concerning changes in PAP following mitral valve replacement are also controversial. In the study conducted by Zielenski et al.[23] to investigated the values of PAP obtained through catheterization before MVR and one year later, the PHT of seven of the 14 patients (50%) who registered preoperative PHT (systolic PAP ≤40 mmHg) was reported to persist after surgery. Li et al.[6] reported a 54% (30 out of 56 patients) incidence of PHT (systolic PAP ≤40 mmHg) following MVR; the incidence of PHT in non-PPM patients was reported to regress after surgery from 69% to 19%, whereas no significant change was reported in patients with PPM (66% preoperatively and 68% postoperatively). On the other hand, Totaro and Argano[12] reported a 47% one-month post MVR incidence of PHT. The incidence of postoperative PHT in our study was lower (31%) than in these other studies. In the PPM group, the post MVR mean systolic PAP was found to be 7.3±8.4 mmHg, compared to the group preoperative values, whereas in the non-PPM group this decrease was 22±7.9 mmHg (p<0.001).

The relationship between PPM and the valve size used is not clear. Lam et al.[25] did not find any relationship between index EOA and postoperative PAP. They demonstrated that index EOA was not a predicting factor for postoperative persistent PHT, whereas use of the ≤27 valve and increased mean prosthetic transvalvular gradient were found to be predictive for PHT. Results of the said study were compared to those of Lit et al.[8] who demonstrated that there was a relationship between index EOA and systolic PAP, and this difference was attributed to various factors. Primarily, the ≤27 prosthesis size which was used in the study by Li et al. at a rate of 52% (n=29) was reported to be higher than current standards; the incidence of ≤27 prosthesis valve size use in patients with PPM (66%) was found to be significantly higher compared to that of non-PPM patients (19%). Secondly, it was suggested that regression of postoperative PHT would be delayed by the high rate of small-sized prosthetic valve use. Authors have concluded that the relationship between index EOA and systolic PAP would be strengthened by the high rate of postoperative persistent PHT in patients with PPM. Although the frequency of ≤27 prosthesis valve size use in our study was higher (84%) than that of the study by Li et al.[8], no significant difference was found in this respect between patients with PPM (8.9%) and those without PPM (85.1%). In our study, we did not also demonstrate any relationship of valve size with index EOA, and of valve size with postoperative systolic PAP.

Pibarot et al.[20] reported a strong relationship of index EOA with prosthetic transvalvular gradient measure at rest and during exercise. However, Dumesnil et al.[17] and Li et al.[8] demonstrated that the relationship of index EOA with prosthetic transvalvular gradient in patients with prosthetic mitral valve was weaker than that observed in patients with prosthetic aortic valve. Similarly, we also demonstrated a moderate relationship (r=0.36) between index EOA and mean prosthetic transvalvular gradient in our study. Compared to the aortic valve, hemodynamics of the mitral valve is more sensitive to chronotropic effects; as a result, different gradients may be observed during various heart rates over the mitral valve, for similar index EOA values. Consequently, the weak relationship between index EOA and mean prosthetic transmitral gradient values, compared to prosthetic aortic valve is an expected result.

Atrial compliance (Cₐ) is the measure of the left atrial reservoir function.[27,28] In other words, Cₐ measures the extent of absorption of the increased left atrial volume due to enlargement of the left atrium and as a result the extend by which pulmonary arteries are protected from increased pressure due to this increased pressure.
volume. Decreased left atrial compliance leads to increases in left atrial pressure due to increased flow during exercise; this pressure would completely be conveyed to the pulmonary artery and as a result lead to the development of symptoms and limitation of exercise capacity.[20] Net atrioventricular compliance is theoretically affected by atrial and ventricular compliance. Any abnormality of Cn would give information about the normal function of any of these chambers, in the presence of normal function of the other chamber. LV function and LV compliance are usually normal in isolated mitral stenosis. As a result, Cn is usually considered to be completely equal to Ca under conditions regarded as clinically associated with mitral stenosis, and hence abnormal Cn indicates abnormal Ca.[20] Left atrial remodeling and hyper trophy which occur in chronic mitral valve disease frequently lead to a decrease in Cn. Passive pressure in the left atrium and the relieve in PAP which arises as a consequence is not complete in the presence of PPM. As a result PPM has been suggested to be possibly associated with low Cn.[21] Li et al.[21] reported that Cn was moderately related with index EOA and systolic PAP. They demonstrated that postoperative PAP was significantly higher in the patient group with low Cn compared to the patient group with high Cn.[2] In our study, we also demonstrated a moderate relationship of Cn with index EOA and systolic PAP. We demonstrated a significantly higher postoperative systolic PAP in patients with low Cn compared to those with high Cn. We observed that low Cn very mildly affected systolic PAP in the absence of PPM; however, in the presence of low Cn with concomitant PPM, systolic PAP was greatly affected by Cn.

In this study, we demonstrated that age, index EOA, Cn and mean prosthetic transvalvular gradient were independent predictors of postoperative systolic PAP. We suggest that differences in literature study results are due to the variation in patient characteristics and the characteristics of valve used. More data is required to better understand the effect of PPM on hemodynamic and clinical outcomes, and the incidence of PHT following PPM. In conclusion, we demonstrated that PPM and persistent PHT were frequently encountered after mechanical MVR, and that there was a relationship between postoperative systolic PAP and PPM. We did not demonstrate any relationship of postoperative systolic PAP with prosthetic valve size and index EOA. On the other hand, we observed that Cn would provide valuable information about postoperative persistent PHT in patients with PPM following MVR. Age, index EOA, mean prosthetic transvalvular gradient and Cn were shown to be independent predictors of postoperative systolic PMT following MVR. Our study demonstrated that selection of a prosthetic valve before surgery that is consistent with body surface area would greatly prevent PPM, and as a result reduce the frequency of postoperative PHT.

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