KASTAMONU MEDICAL JOURNAL

Original Article

DOI: 10.51271/KMJ-0178

Kastamonu Med J. 2025;5(1):25-29

The effect of Fat-free Mass Index and other predictive factors on the severity of patient prosthesis mismatch in patients with isolated mechanical aortic valve replacement

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Cite this article as: Yılmaz Ü, İndelen C, Erden B, Taşpınar Y, Ergenç Güven E, Sunar H. The effect of Fat-free Mass Index and other predictive factors on the severity of patient prosthesis mismatch in patients with isolated mechanical aortic valve replacement. *Kastamonu Med J.* 2025;5(1):25-29.

Received: 15.10.2024 ◆ **Accepted**: 05.12.2024 ◆ **Published**: 04.03.2025

ABSTRACT

Aims: The development of patient prosthesis mismatch (PPM) in patients undergoing aortic valve replacement (AVR) is an important problem in terms of functional capacity and cardiac events in the postoperative period. Increasing the severity of PPM will increase the transvalvular gradient and retard cardiac recovery. The aim of this study was to determine the relationship between PPM severity and Fat-free Mass Index (FFMI) and other predictive factors in patients who underwent AVR.

Methods: A total of 73 patients, who underwent isolated mechanical AVR between September-2017 and February-2020 and developed PPM in the postoperative period, were included in the study. Preoperative data, operation data, and postoperative follow-up of the included cases were reviewed. Body surface area and body-mass index (BMI) were calculated using the height and weight measurements of the patients. Echocardiography examinations of the cases were evaluated preoperatively and at the first, sixth and twelfth months after surgery. Preoperative body fat ratios were measured using the bioimpedance method and FFMIs were calculated. According to the severity of PPM, patients were divided into 3 groups as mild, moderate, and severe. FFMI and other predictive factors were analyzed by comparing 3 groups among themselves

Results: The effects of preoperative diagnosis, age, gender, BMI, FFMI, aortic cross clamp, cardiopulmonary bypass duration on PPM severity were evaluated statistically and no significant effect was observed. It was determined that the size of the prosthetic valve implanted in the patient was closely related to the severity of PPM.

Conclusion: It was seen that the size of the prosthesis to be selected was the most important parameter in terms of PPM severity. Severe PPM has been shown to have a worse prognosis than moderate and mild PPM in many studies. Reducing the severity of PPM may reduce the need for reoperation and the number of cardiac events that may occur. More extensive studies are needed to identify predictive factors associated with PPM severity. In this study, no statistically significant effect of fat free mass index on the severity of patient prosthesis mismatch in patients with isolated mechanical AVR was detected.

Keywords: Aortic valve replacement, Fat-free Mass Index, patient prosthesis mismatch

INTRODUCTION

Patient-prosthesis mismatch (PPM) is defined as the inadequacy of the implanted prosthesis size in proportion to the patient body surface area (BSA). Although many studies have been conducted on this definition, PPM results are still controversial. PPM is seen in 30-60% of patients undergoing aortic valve replacement (AVR) and causes a high transvalvular gradient.[1] High transvalvular gradient increases left ventricular workload and delays left ventricular mass (LVM) regression. Diastolic dysfunction caused by high gradient limits functional capacity and causes cardiovascular events.[2]

The purpose of AVR is to provide regression of left ventricular hypertrophy, but this regression varies from patient to patient. In cases where the severity of PPM is advanced, left ventricular regression is less common than in other groups; mortality and cardiac reoperations are higher than in mild and moderate PPM.[3]

Although there are studies showing that aortic root dilator surgical strategy reduces the incidence or severity of PPM, it is argued that it should be applied to the right patient group because it increases perioperative risks. Mild and moderate PPM are tolerable and have no effect on long-term survival.

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Many studies have demonstrated that avoiding advanced PPM should be the primary surgical approach.[4]

The relationship between PPM and many variables has been investigated. A significant interaction with age was observed. Severe PPM was associated with increased overall mortality in the patient group under 70 years of age, while it was observed that it had no significant effect on survival in the older age group. Severe PPM has been shown to increase mortality by approximately 1.8 times in patients under 70 years of age. Severe PPM has been shown to have a significant effect on survival in the patient group with a body-mass index (BMI) below 30 kg/m^2, while it has no significant effect in obese patients with a BMI above 30 kg/m^2.[5]

The concept of BMI, which uses height and body weight values to interpret the body's working principles practically, has been used for a long time. Recently new indexes have been developed that also calculate fat rates and lean body mass. Fat-free Mass Index (FFMI) includes the components of all tissues except fat.[6]

Metabolically active fat-free mass (FFM) has been shown to be positively associated with stroke volume and cardiac output.[7]

LVM has been shown to be independently determined by lean mass and not by any other measure of body size or composition. It has been suggested that it may be more appropriate to index LVM to FFM rather than body measurements that include fat mass.[8]

The percentage of fat in the body, the distribution of fat, and therefore BMI are important risk factors for cardiovascular diseases. Calculating the percentage of fat in the body is important for the prevention and treatment of obesity-related diseases. Since BMI is not determined by body fat percentage or lean body mass, it cannot determine differences in body composition that occur according to gender or age.[9]

Prognosis in cardiac patients is closely related to many parameters such as age, gender, and New York Heart Association (NYHA) profile classification. For example, obesity is considered to be a strong predictor of poor prognosis in heart failure patients. However, since BMI is related to water retention, no significant relationship has been demonstrated. FFMI is a parameter independent of water retention in the body, and its decreased levels have been shown to be closely related to cardiac diseases.[10]

METHODS

Ethics

The study was carried out with the permission of the Kartal Koşuyolu High Specialization Training and Research Hospital Clinical Researches Ethics Committee (Date: 23.02.2021, Decision No: 2021/4/478). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patient Selection

Our study included 73 cases that underwent isolated mechanical AVR between September 2017 and February 2020. During this period, a total of 485 AVRs were performed in our hospital and PPM was observed in 81 of them. 8 of these patients were not included in the study because they died during our follow-up. During our study, preoperative FFMI values of patients who underwent AVR surgery were measured and recorded. Patients who underwent combined other valve and coronary artery bypass surgeries other than aortic valve, major vascular surgery, patients with low ejection fraction (EF<50%), patients with more than 15% weight change after surgery, patients who underwent surgery under emergency conditions, and patients who had previously undergone surgery and developed complications were excluded from the study.

Preoperative data, operational data, and postoperative follow-up of the included cases were examined. BSA and BMI were calculated using the patients' height and weight measurements. Echocardiography (ECHO) examinations of the cases were evaluated before and at 1, 6, and 12 months after surgery.

Parameters Analyzed and Methods of Measurement

Body fat ratios of the patients were measured by bioimpedance method in the postoperative period and FFM was calculated with the formula below. This measurement was made at the end of the first postoperative year at the earliest, when the ventricular remodeling process is considered to be completed.

- Fat-free mass=body weightx[1-(% body fat)/100)]

FFMI was calculated and evaluated by dividing the individual's FFM by the square of their height.[11]

The patients' LVM were calculated with the ''Devereux and Reishek'' formula and their Left Ventricular Mass Indexes (LVMI) were calculated by dividing by BSA.

- LVM (gr)=1.04x(LVEDD+IVS+PWD)^3-13.6
- LVMI (gr/m^2)=LVM/BSA

During the operation, the type and number of implanted prosthetic valves, cardiopulmonary bypass (CPB) and aortic cross-clamp (ACC) times were recorded. Echocardiography examined aortic root diameter, aortic valve morphology, systolic gradient, mean gradient, degree of insufficiency and/or stenosis, left ventricular end-systolic and end-diastolic diameters, ejection fraction, and interventricular septum thickness.

All cases were divided into three groups as mild, moderate and severe according to the degrees of PPM classification specified previously according to Effective Orifice Area Index (IEOA). Patient ages, genders, preoperative diagnoses, ACC duration, CPB duration, prosthetic valve size, BMI, and the effects of FFMI on PPM degrees and changes in LVM over time were examined in three separate groups.

Statistical Analysis

The study is a prospective, cross-sectional study and the NCSS (number cruncher statistical system) 2007 (Kaysville, Utah, USA) program was used for statistical analyses. Descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum) were used while evaluating the study data. Skewness test, Kolmogorov-Smirnov test, and histogram graphics were used as criteria for compliance with normal distribution in numerical data. Chi-square and Fischer tests were applied between independent groups in categorical data and the relationship between dependent groups was examined with the McNemar test. Student-t test was applied to compare means between independent groups that were normally distributed in continuous variables. Mann-Whitney U test was used to compare independent group medians in a distribution that did not show normal distribution in continuous variables. The relationship between variables was examined with Spearman correlation analysis for nonparametric variables and Pearson correlation analysis for parametric variables. The differences in the results of the factors affecting the severity of HPKU were examined by Kaplan-Meier analysis. A p-value of <0.05 was accepted as statistically significant.

RESULTS

A total of 73 patients-45 male and 28 female-were included in the study. The follow-up period for the patients was 18±8 months. Among them, 56 had preoperative diagnoses of aortic regurgitation (AR), 11 had aortic stenosis (AS), and 6 had both conditions (AS+AR).

In the postoperative period, the indexed effective orifice area (iEOA) was calculated by dividing the effective orifice areas (EOAs) from the 12-month follow-up echocardiography by the body surface areas (BSAs). Patients were categorized into three groups based on the severity of PPM: mild, moderate, and severe.

The effects of preoperative diagnosis, age, gender, BMI, FFMI, ACC time, and CPB duration on PPM severity were statistically evaluated. No statistically significant difference was found in the compatibility of these values between the groups (**Table 1**).

When we examined the valve sizes of the patients, a size 17 valve was used in one patient, and it was noted that this patient had advanced PPM. A size 19 valve was used in twelve patients, with advanced PPM observed in half of them and moderate PPM in the other half. Moderate PPM was noted in twenty-four of the thirty-one patients who received the most commonly used size 21 valve. Advanced PPM was observed in only four of the eighteen patients who received a size 23 valve. No advanced PPM was seen in any patient who received size 25 or 27 valves (**Table 2**).

Table 2. PPM severity according to valve size

Valve size (mm)	Mild PPM	Moderate PPM	Severe PPM	Number of patients
17	0	0	1	1
19	0	6	6	12
21	2	24	5	31
23	2	12	4	18
25	6	3	0	9
27	1	1	0	2
Total	11	46	16	73

PPM: Prosthesis-patient mismatch

When the mean transvalvular gradients of patients with PPM were examined, it was seen that there was a statistically significant difference between the gradient values in all groups according to the Freidman analysis (p<0.001).

The median values of the measurements from the preoperative period to the 12th postoperative month tended to decrease in the months when the transvalvular gradient was measured.

In all patient groups, the median value of the mean gradient measurements was higher in patients with severe PPM (p<0.001) (**Table 3**).

Table 1. Demographic data analysis according to PPM severity

		PPM												
		Mild				Moderate				Severe				
		Mean±SD	Median	Min	Max	Mean±SD	Median	Min	Max	Mean±SD	Median	Min	Max	p
Age		55.09±5.36	57	43	61	52.33±7.5	54.5	35	62	53.36±7.5	56.5	40	62	0.46
CPB		104.73±33.47	105	51	169	118.81±64.2	100.5	50	424	132.29±49.41	119.5	55	245	0.24
ACC		77.27±25.41	74	33	120	82.73±39.5	75	28	270	105.43±44.89	97	34	208	0.08
BMI		26.75±2.88	26.5	22.2	31.9	27.52±3.47	26.85	20.6	36.3	28.19±5.5	28	17.8	35.9	0.65
FFMI		19.7±1.04	19.8	17.6	21	19.53±1.33	19.4	16.4	22.7	20.06±1.94	20.4	17.1	22.7	0.49
		n	%			n	%			n	%			
Gender	Female	3	10.7			17	60.7			8	28.6			
	Male	8	17.8			31	68.9			6	13.3			
Diagnosis	AS	7	12.5			37	66.1			12	21.4			
	AR	2	20			7	70			1	10			
	AS+AR	2	28.6			4	57.1			1	14.3			

PPM: Prosthesis-patient mismatch, SD: Standard deviation, Min: Minimum, Max: Maximum, CPB: Cardiopulmonary bypass, ACC: Aortic cross-clamp, BMI: Body-mass index, FFMI: Fat-free Mass Index, AS: Aortic stenosis, AR: Aortic regurgitation

Table 3. Transvalvular gradient change

PPM severity	Pre-op mean GR	Post-op 1 mean GR	Post-op 6 mean GR	Post-op 12 mean GR	p-value
Mild	52 (33-77)	15.00 (9-29)	15.00 (8-27)	12.00 (7-25)	<0.001
Moderate	51 (32-100)	17.50 (5-38)	15.00 (7-38)	14.50 (7-31)	<0.001
Severe	65 (33-88)	26.50 (8-40)	24.00 (8-37)	23.00 (9-45)	<0.001

PPM: Prosthesis-patient mismatch, GR: Gradiyent

When the distribution of LVMI measurements by months was examined with the ANOVA test, the LVMI measurement averages were higher in the pre-op and post-op 1st month, especially in the groups with mild and moderate PPM. In the 6th and 12th months postoperatively, it was observed that the mean LVMI measurements were higher in the group with severe PPM (**Figure**).

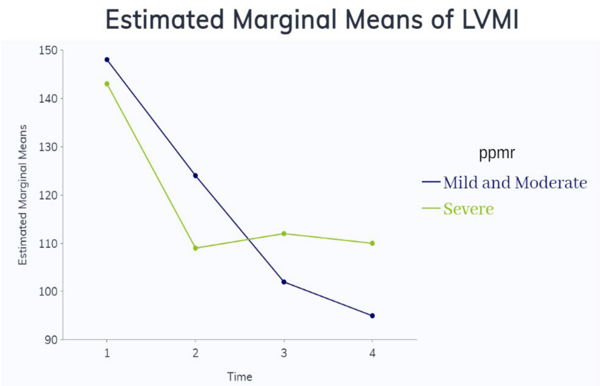

Figure. LVMI change according to PPM

LVMI: Left Ventricular Mass Indexes, PPM: Prosthesis-patient mismatch

DISCUSSION

The formula used to determine the severity of patient-prosthetic valve mismatch is BSA and IEOA. It is necessary to know the hemodynamic changes that occur when mild, moderate or advanced PPM develops and the effects of this condition on quality of life. It is known that the severity of PPM affects the patient's mortality and morbidity.[12]

In this study, the parameters that we think can affect the severity of PPM were investigated. The effects of age, gender, preoperative diagnosis (AS or AR), ACC-CPB duration, and BMI as well as FFMI on the severity of PPM were evaluated. It was determined that none of the investigated factors had a significant effect on the severity of PPM. However, it was statistically shown that the implanted prosthesis size was the most effective factor on the severity of PPM.

Moon et al.[13] observed that PPM had a negative effect on survival and need for reoperation in younger patients but minimal effects in older patients in 1400 patients who underwent mechanical and bioprosthetic valve replacement. In addition, they showed that PPM was insignificant in terms of cardiac events and survival in patients with low BMI, but significant in patients with average or higher BMI.

PPM after AVR is associated with medium and long-term mortality. Conflicting results have been reported regarding perioperative mortality. 58 articles were analyzed and their data were reviewed by Dayan et al.[14] The effect of PPM on mortality was observed to be higher in patients under the age of 70. While severe PPM was associated with both perioperative and overall mortality, moderate PPM did not increase the risk of overall mortality but was only closely associated with perioperative mortality. It was emphasized that investigating predictive factors for PPM could be useful for identifying patients at high risk.

Fuster et al.[15] showed that in patients with moderate and advanced PPM in terms of postoperative cardiac events and mortality, non-compliance affected mortality in the group with high preoperative left ventricular hypertrophy, but not in patients with low hypertrophy. It was shown that PPM remained at acceptable levels in patients who underwent AVR without progression of hypertrophy.

Florath et al.[16] measured the EOA of 533 patients using echocardiographic methods in their study. A high degree of consistency was observed between the estimated IEOAs of the prostheses and the postoperatively measured IEOAs. It was observed that there was a close relationship between the preoperative diagnosis of AS and the severity of PPM.

Head et al.[17] reviewed data from 348 studies on PPM in their review. PPM was found to be associated with a statistically significant increase in all-cause mortality. The effects of increasing PPM severity on cardiac events and mortality lead surgeons to prevent or reduce the severity of PPM. The first step in this strategy was to calculate the minimum prosthetic valve EOA required before surgery to avoid PPM. In cases where PPM is thought to be unpreventable, root expansion surgery can be performed by considering the risk-benefit ratio, thus at least reducing the severity of PPM. These procedures have been shown to be effective in reducing PPM rates and severity, but it should be noted that prolonging ACC and CPM times will increase perioperative risk.

Adverse outcomes have been reported in patients undergoing cardiac surgery with low FFMI and high-fat content secondary to malnutrition. In a study of 325 cardiac surgery patients, perioperative FFMI and fat content were closely associated with increased postoperative morbidity and infection rates. It has been advocated that the body composition of patients scheduled for cardiac surgery should be determined.[18] In our study, we investigated the effects of body compositions and FFMI ratios on PPM severity and could not determine a statistically significant effect.

Sarcopenia may be used as a marker of cardiac muscle loss and dysfunction in aging and chronic disease with subsequent increased rates of treatment and cardiac surgery. An adverse prognostic relationship between FFMI and congestive heart therapy has been reported. A clinical trial of perioperative FFMIs in 135 patients undergoing coronary artery bypass grafting (CABG) and valve replacement was conducted. Those with low FFMI were shown to have a higher probability of cardiac events and a longer hospital stay compared with those with high FFMI.[19]

Garatti et al.[20] observed that increased BMI was associated with higher postoperative gradient and increased FFM severity. In our study, no statistically significant effect of BMI was found between groups compared according to FFM severity.

Kulik et al.[21] showed that LVMI regression increased with increasing IEOA in patients who underwent AVR and argued that this regression was less common in patients with PPM. In our study, regression was higher in patients with mild and moderate PPM, while regression in advanced PPM was observed to be limited.

Limitations

The main limitations of our study were that it was a single-center, retrospective study and that the postoperative functional capacities of our patients were not included in the study. Given the higher number of patients but heterogeneous groups of patients in the literature, we think that our relatively small but selected group of patients was an advantage of our study.

CONCLUSION

The PPM that occurs in patients who have undergone mechanical AVR is a significant risk factor for postoperative cardiac events and the need for reoperation. Numerous studies emphasize the importance of identifying predictive factors, aside from the valve formulation, that are related to the severity of PPM in predicting quality of life and the likelihood of experiencing a cardiac event. In our study, we classified patients into three groups based on the severity of PPM: mild, moderate, and severe. We compared these groups in terms of predictive factors. Since body composition can vary in patients with similar BSAs, the concept of FFMI has gained importance and is now recognized as an indicator of LVM and cardiac hemodynamics. We examined FFMI alongside age, gender, ACC time, CPB duration, preoperative diagnosis, and BMI, believing that calculating FFMI in addition to BSA could help guide valve selection to reduce the severity of PPM. However, we did not find a significant effect of these measurements on PPM severity.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Kartal Koşuyolu High Specialization Training and Research Hospital Clinical Researches Ethics Committee (Date: 23.02.2021, Decision No: 2021/4/478).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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