Moderate Patient-Prosthesis Mismatch Has No Negative Effect on Patients' Functional Status After Aortic Valve Replacement With CarboMedics Prosthesis

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Abstract

Background: Patient-prosthesis mismatch (PPM) after aortic valve replacement (AVR) is the subject of continuing debate in the cardiac surgery field.

Objectives: The aim of this study was to evaluate the frequency and severity of patient-prosthesis mismatch (PPM) and the functional status of patients undergoing aortic valve replacement (AVR) using a CarboMedics prosthesis in the mid-term follow up.

Patients and Methods: We retrospectively studied 66 consecutive patients who were referred to AVR with a CarboMedics prosthesis at the Rajaie cardiovascular medical and research center, a university referral hospital in Tehran, Iran. The severity of PPM as well as clinical and echocardiographic parameters and the patients' New York heat association (NYHA) functional classification status, operative data and postoperative complications, and mortality in a mid-term (4 - 5 months) follow up period was assessed. Severe PPM was defined as the effective orifice area (EOA) indexed to the patient's body surface area (BSA) < 0.65 cm^2/m^2 and moderate PPM was defined as the indexed effective orifice area (IEOA) between 0.65 and 0.85 cm^2/m^2.

Results: Of the 66 studied patients, 39 were male and 27 were female. The mean age of the patients was 43 ± 17 with a range of 6 - 76 years. Implanted sizes of the CarboMedics AV prosthesis in 22 patients were 19 and 21 mm, and in 44 patients were 23 and 25 mm. Eleven patients had moderate PPM (IEOA < 0.85 cm^2/m^2) and 55 of them did not have PPM (IEOA ≥ 0.85 cm^2/m^2). There were no statistically significant differences between the two groups in the echocardiographic trans-aortic pressure gradients (35.6 ± 19 vs. 23.2 ± 16 mmHg; P = 0.061) and the mean NYHA functional classification (1.10 ± 0.3 vs. 1.01 ± 0.10; P = 0.074) after AVR in the mid-term follow up.

Conclusions: Moderate PPM has no negative effect on echocardiographic trans-aortic pressure gradients or the patients' NYHA functional status after AVR with a CarboMedics prosthesis in the mid-term follow up.

Keywords: Aortic Valve, Heart Valve Prosthesis, Echocardiography, Follow-Up Studies

1. Background

Patient-prosthesis mismatch (PPM) after aortic valve replacement (AVR) is the subject of continuing debate in the cardiac surgery field (1). Most evidence agrees that morbidity and mortality increases in the presence of severe PPM, defined as an indexed effective orifice area (IEOA) < 0.65 cm^2/m^2 body surface area (BSA), after AVR operation (1, 2). For example, two recent meta-analyses by Head et al. (2) (on 34 observational studies) and Urso et al. (3) (on 22 cohort studies) concluded that severe PPM was associated with increased mortality after long-term follow up. However, Head et al. reported that patients with moderate PPM (IEOA between 0.65 and 0.85 cm^2/m^2 BSA) didn't show any increase in 30-day or mid-term overall mortality after AVR, but Urso et al. reported a slight increase in overall mortality (hazard ratio = 1.19, 95% CI: 1.07 - 1.33) after AVR (2, 3). Jamieson et al. in a 15-year study of 3343 AVR patients concluded that PPM is not a predictor of overall standard unadjusted mortality up to 15 years after AVR, regardless of the category of IEOA (1). In this study he found that PPM has no effect on survival adjusted for the covariates [IEOA, age, and ejection fraction (EF)] except for severe PPM when adjusted for ejection fraction (EF) more than 50%. Jamieson included the prosthesis type as one of predictors of overall mortality after AVR (1).

Different conditions linked with an adverse outcome in the presence of PPM in patients after AVR have not been well-defined. There are patient-related parameters, such as aortic valve annulus diameter, left ventricular hypertrophy, age, gender, and body size, as well as the prosthesis type, that influence the outcome in the pres-

ence of PPM (1-4). Most cardiac surgeons use a St-Jude mechanical prosthesis for AVR operation and the majority of studies on PPM after AVR involved the St-Jude prosthesis. However, some surgeons prefer to use the CarboMedics mechanical prosthesis for AVR. For example, Carrier et al. at the Montreal heart institute in 2006 used the CarboMedics valve as the mechanical valve of choice for a period of 15 years (1988 - 2004) (5). They followed 1597 isolated AVR patients using CarboMedics prostheses and found the mean 5-, 10-, and 15-years survival rates were $83 \pm 1\%$, $70 \pm 2\%$, and $62 \pm 3\%$; respectively. These patients had a mean trans-aortic gradient of 29 ± 14, 20 ± 8, 18 ± 7, 16 ± 7, 12 ± 5, and 11 ± 5 mmHg with 19, 21, 23, 25, 27, and 29 mm CarboMedics prostheses, respectively (P = 0.001). They noticed moderate PPM only in AVR using 19 mm prostheses (5).

2. Objectives

There is very limited evidence regarding incidence and pattern of PPM following AVR operation with the CarboMedics prosthesis. We aimed to evaluate the frequency and severity of PPM as well as other clinical parameters and mortality in a mid-term follow up period for patients who were referred to AVR using the CarboMedics prosthesis in a referral university hospital in Tehran, Iran.

3. Patients and Methods

3.1. Study Participants

Between March 2010 and March 2011, 66 patients were referred to Rajaie cardiovascular medical and research center, a tertiary care center for cardiovascular patients in Tehran, Iran, for AVR. Standard or top hat CarboMedics valves were used for isolated severe aortic stenosis (AS) or - aortic insufficiency (AI) or both. We performed this retrospective study using available data in the medical records. The frequency and severity of PPM as well as clinical and echocardiographic parameters and the patients' NYHA functional status, operative data, postoperative complications, and mortality in a mid-term (4-5 months) follow up period were assessed. Severe PPM was defined as EOA indexed to the patient's BSA < 0.65 cm^2/m^2 and moderate PPM was defined as IEOA between 0.65 and 0.85 cm^2/m^2 (6).

3.2. Statistical Analysis

The data were analyzed using IBM SPSS statistics 22 for windows (IBM Inc. Armonk, NY, USA). The one sample Kolmogorov-Smirnov test was applied to investigate the fitness of interval data to normal distribution. Data were described as the mean ± standard deviation (SD). Subgroup analysis was performed via chi-square or Fischer's exact test for nominal, Mann-Whitney U for ordinal, and Student's t-test for interval data. A P value ≤ 0.05 was considered statistically significant.

4. Results

4.1. Background Data

Of the 66 studied patients, 39 were male and 27 were female. The mean age of the patients was 43 ± 17 with a range of 6 - 76 years. Eleven patients underwent redo operations with a history of previous aortic or mitral valve replacement surgeries or both. Thirty six patients had concomitant procedures, mostly operations on mitral or tricuspid valves, coronary artery bypass grafts, septal myomectomy, or ascending aorta repair. The preoperative characteristics of the 66 patients are illustrated in Table 1. Thirteen patients received the top hat CarboMedics AV prosthesis and 53 patients underwent AVR using the standard CarboMedics prosthesis. Table 2 shows the different implanted sizes of the CarboMedics AV prosthesis; most (n = 44) were 23 and 25 mm.

4.2. Assessment of the Functional Status

The pressure gradients were higher and IEOA was lower in smaller prostheses. We also divided patients regarding whether they had moderate PPM (IEOA < 0.85 cm^2/m^2) or not (IEOA ≥ 0.85 cm^2/m^2). Eleven patients had moderate PPM and Table 3 shows their hemodynamic profiles and compares them with those who did not have PPM. As Tables 1 and 2 shows, there were no statistically significant differences between the two groups regarding echocardiographic and clinical parameters. Twenty three patients had a NYHA functional class III or IV in the preoperative period and this number was reduced to only three patients after AVR. As shown in Figure 1 and 2 the NYHA functional classification statuses of the patients after AVR were mostly I and II and there were no significant differences in the functional status regarding the trans-aortic pressure gradient or IEOA. Reduction in the mean pressure gradients (comparing preoperative and postoperative values) were statistically significant in two valve size subgroups (P < 0.05).

Table 1. Preoperative Characteristics of 66 Studied Patients Undergoing Aortic Valve Replacement[a]

Variable	Mean [a]	Range
BSA, m^2	1.6 ± 0.2	0.78 - 2.12
Annulus size, mm	22.2 ± 3	15 - 30
LVESD, mm	39.4 ± 10	14 - 64
LVEDD, mm	54.7 ± 12	26 - 80
AV Mean Gradient, mmHg	57.4 ± 23	4 - 145
PAP, mmHg	38.0 ± 15	13 - 110
Pre-op LVEF, %	47.7 ± 11	30 - 65
Pre-op NYHA class	2.4 ± 0.7	2 - 4

Abbreviations: AV, aortic valve; BSA, body surface area; LVESD, left ventricular end systolic dimension; LVEDD, left ventricular end diastolic dimension; LVEF, left ventricular ejection fraction; NYHA= new york heart association; PAP, pulmonary artery pressure.
[a]Values are presented as mean ± SD.

Table 2. Echocardiographic Parameters of Implanted Prosthetic Valves According to Prosthesis Size[a]

Parameters	Implanted Prosthetic Valve Size, mm		P Value
	19 - 21 (n = 22)	23 - 25 (n = 44)	
Pre-op TVPG, mmHg	74.9 ± 24	48.2 ± 20	.015
Early post-op PG, mmHg	34.3 ± 14	24.7 ± 16	.028
Mid-term F/U TVPG, mmHg	36.9 ± 12	22.5 ± 10	.001
Mean gradient reduction	12 (54)	21 (48)	.794
Mean EOA	1.45 ± 0.15	1.78 ± 0.20	.001
Mean BSA	1.61 ± 0.18	1.70 ± 0.24	.126
Mean IEOA	0.90 ± 0.12	1.07 ± 0.21	.001
Valve type			.848
Top hat	4 (31)	9 (69)	
Standard	17 (32)	36 (68)	

Abbreviations: BSA, body surface area; EOA, effective orifice area; F/U, follow up; IEOA, indexed effective orifice area; TVPG, trans-valve mean pressure gradient.
[a]Values are presented as mean ± SD or No. (%).

Table 3. Patients' Hemodynamic Profiles According to Indexed Effective Orifice Area (IEOA) of Aortic Prosthetic Valve[a]

Parameters	IEOA < 0.85 cm^2/m^2 (n = 11)	IEOA ≥ 0.85 cm^2/m^2 (n = 55)	P Value
Post-op NYHA	1.10 ± 0.3	1.01 ± 0.10	.074
Pre-op TVPG, mmHg	58 ± 25	57.3 ± 23	.945
Early Post-op TVPG, mmHg	32.1 ± 12	26.8 ± 16	.331
Mid-term F/U TVPG, mmHg	35.6 ± 19	25.2 ± 16	.061
PG reduction during F/U	5 (45)	31 (56)	.740

Abbreviations: F/U, follow up; IEOA, indexed effective orifice area; NYHA, New York heart association; TVPG, trans-valve mean pressure gradient.
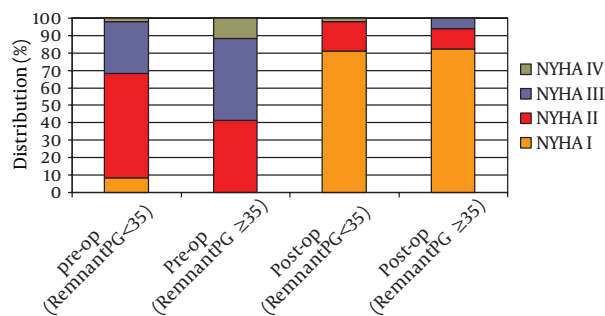[a]Values are presented as mean ± SD or No. (%).

Figure 1. Comparison of NYHA Functional Status Based on Postoperative Residual Trans-Aortic Gradient

Figure 2. Comparison of NYHA Functional Status Based on IEOA

The mean pre-operative AV pressure gradient (PG) in patients who underwent AVR with top hat valves was 82.4 ± 53 mmHg and in those who underwent AVR with standard CarboMedics prostheses was 51.0 ± 38 mmHg (P = 0.025). The mean postoperative PG in top hat prostheses was 27.5 ± 17.2 mmHg and in standard prostheses was 28.9 ± 13.9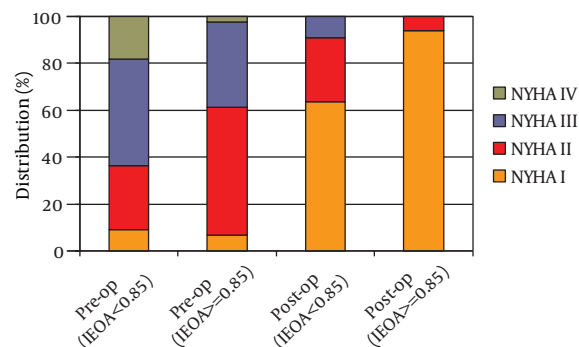 mmHg (P = 0.796). These findings were 28.9 ± 14.1 and 27.3 ± 12.2 mmHg, in top hat and standard prostheses, respectively after mid-term follow up period (P = 0.806). All of the patients who received top hat valves and 92.5% of those who received standard prostheses had a NYHA functional class I postoperatively. Implanted prosthetic valve sizes for the two valve types are listed in Table 2.

4.3. Complications

We faced five major postoperative complications (three cases of bleeding, one case of a cerebral vascular accident, and one case of mediastinitis). There was one case of postoperative mortality. She was a 58-year-old woman with NYHA class III-IV and LVEF 30 - 35% presented with sever AI; she underwent AVR and CABG and died due to myocardial failure. There were three cases of postoperative IEOA < 0.75 cm²/m² (moderate PPM). All of them underwent AVR with CarboMedics prostheses of sizes 19 and 21 mm; none of them faced any postoperative morbidity or mortality. These patients' NYHA functional classes were II-III in the preoperative period and improved to functional class I in the postoperative period.

5. Discussion

Hanayama (7) defined PPM as low as IEOA < 0.60 cm²/m², while Milano (8) considered a cut-off point of IEOA < 0.90 cm²/m² for PPM after AVR. In the present study, we defined severe PPM as IEOA < 0.65 cm²/m² and moderate PPM as 0.65 < IEOA < 0.85 cm²/m². The frequency of PPM (IEOA < 0.60 cm²/m²) varies widely from 17% (in our study) to 63.6% in numerous studies of patients undergoing AVR with different prosthetic valve types (9-12).

Regarding echocardiographic assessment, there was no statistically significant differences between patients with or without moderate PPM after AVR in the trans-aortic Doppler study on pressure gradients (35.6 ± 9 vs. 23.2 ± 16 mmHg, respectively; P = 0.211). However, there are some reports that show a poor correlation between PPM after AVR and pressure gradients measured by Doppler studies and the Doppler mean and peak gradients were slightly more than catheter gradients due to the "pressure recovery" phenomenon. So, evaluated the patients' clinical and NYHA functional class status in a follow up period after 4 - 5 months and compared them by pressure gradients of prosthetic valves measured by Doppler studies (13, 14). We found noteworthy improvements in the NYHA functional class of the patients, mostly from III-IV to I-II, after the follow up period.

Even in three cases of moderate to severe PPM (IEOA < 0.75 cm²/m²) that underwent AVR with CarboMedics (two top hat and one standard) prostheses of sizes 19 and 21 mm, none of them faced any postoperative morbidity or mortality. These patients' NYHA functional classes were II-III in the preoperative period and improved to functional class I in the postoperative period. We did not have any cases of severe PPM in our 66 studied patients.

Most researchers noticed that increased morbidity and especially mortality in AVR patients who experienced PPM are mainly related to concomitant co-morbidities such as low LVEF, small aortic valve annulus size (especially in older females), and concomitant coronary artery bypass grafting (CABG) surgery (1, 3-8, 15, 16). Jamieson et al. reported that the predictors of overall (unadjusted) mortality after mechanical prostheses and bioprostheses AVT were age, NYHA functional class III/IV, concomitant CABG, prosthesis type, preoperative congestive heart failure (CHF), diabetes mellitus, renal failure, chronic obstructive pulmonary disease (COPD), and PPM. A 15-year survival rate adjusted for the covariates (effective orifice area index, age, basal mass index, and ejection fraction) determined no negative effect except for severe PPM (IEOA < 0.65 cm²/m²) when adjusted for EF > 50% (1).

In our study the mean aortic pressure gradients in the 19 and 21 mm prostheses were slightly higher than in the 23 and 25 mm CarboMedics prostheses (Table 2); however, similar to Carrier's study, the mean trans-aortic gradients were higher with the smaller CarboMedics prostheses, though patients still showed acceptable hemodynamic performance and clinical functional status (5).

Price et al. observed the effect of age on the influence of PPM on outcomes after AVR. He found that in patients with an age of < 70 years and normal LVEF, the presence of PPM did not meaningfully alter the survival rate. However, in patients < 70 years with left ventricule (LV) dysfunction, PPM was related to reduced survival. In patients aged ≥ 70 years, the presence of PPM had no influence on mortality, regardless of LV function (14). Considering the mean age of 43 ± 17 years in our patients with a mean LVEF of 47.7 ± 11%, we found similar results. We faced no mortality and presence of PPM had no effect on postoperative functional status.

Although we found no effect of moderate PPM on the NYHA functional classification of our (middle-aged) patients using CarboMedics prostheses for AVR, Hernandez-Vaquero et al. (9) reported moderate PPM (in St. Jude prostheses) as an independent predictor of cardiac events and an advanced functional class (NYHA III-IV) in young and middle-aged patients undergoing AVR as a predictor for severe AS in the mid-term follow up.

5.1. Limitations

In this study the patients' data was collected retrospectively in a single hospital. Center-specific data may lead to bias, so all findings and inferences should be made with caution. PPM is predominantly risky in patients with low preoperative LVEF. The small number of patients involved in the study, and the low number of patients in the valve size 19 - 21 mm subgroup and the moderate PPM subgroup may be responsible for some of the non-significant statistical differences. In our study, most of the patients had a good LVEF and therefore the results can be generalized to this category of patients.

Acknowledgments

Footnote

Authors' Contribution: Alireza Alizadeh Ghavidel conducted the study and performed surgeries and follow up with the patients. Rasoul Azarfarin contributed to patients' management, statistical analysis, writing the paper, and journal submission. Azin Alizadehasl followed up with the patients and performed echocardiographic studies. Ali Sadeghpour Tabaei performed surgeries and followed up with the patients And Zia Totonchi contributed to patients' management and writing the paper.

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