석사 학위 논문

조직판막을 이용한 승모판막 치환술의 임상적 결과 비교

A comparison of clinical outcomes in patients undergoing bioprosthetic mitral valve replacement: Carpentier-Edwards Magna Mitral Ease valve versus Perimount Plus valve

울산대학교 대학원

의학과

류승우

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이 논문을 석사학위 논문으로 제출함

2020년 10월

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연구 목적

Carpentier-Edwards Magna Mitral Ease 판막은 Perimount Plus 판막에 비해 낮은 측면상으로 디자인 되었고, ThermaFix 가공처리를 하여 석회화를 막고자 하였다. 본 연구는 승모판막 치환술에서 Magna Mitral Ease 판막과 Perimount Plus 판막의 임상적 그리고 혈역학적 결과를 비교하고자 한다.

연구 방법

2015년 1월부터 2019년 8월까지 서울아산병원에서 조직판막을 이용한 승모판막 치환술을 시행받은 환자 284명 중 170명(Perimount Plus 판막 군 93명, Magna Mitral Ease 판막 군 77명)을 대상으로 하였다. 후향성연구로 임상적, 혈역학적 자료를 검토하였다. 혈역학적 평가는 심장초음파로 하였고, 좌심실 심박출률, 좌심실 유출로 혈류 가속, 평균 압력 기울기 등을 측정 하였다.

연구 결과

두 군 간에 나이, 성별, 체표면적, 좌심실 내경, 대동맥판막-승모판막 각도 등을

포함한 혈역학적으로 영향을 줄 수 있는 변수들은 유의한 차이가 없었다. 수술 후 좌심실 유출로 혈류 가속은 Perimount Plus 판막 군 9명에서 확인되었으나 Magna Mitral Ease 판막 군에서는 확인되지 않아 유의한 차이가 있었다 (p=0.004). 조기 사망은 Perimount Plus 판막 군 8명 (8.6%), Magna Mitral Ease 판막 군 2명 (2.6%) 보고되었다 (p=0.115). 그 외 판막 관련 합병증은 두 군간에 유의한 차이가 없었다.

결론

Magna Mitral Ease 판막의 낮은 측면상 디자인은 Perimount Plus 승모판막에 비해 좌심실 유출로 혈류 가속의 발생률을 낮춰준다. 하지만 임상적 결과에는 유의한 차이가 없었다. 따라서 구조적인 부분에 대한 추가 연구 및 임상결과에 대한 장기적인 추적 관찰이 필요하다.

차례

Glossary of abbreviations

MVR, mitral valve replacement

LVOT, left ventricular outflow tract

LVOTO, left ventricular outflow tract obstruction

Introduction

Although uncommon, left ventricular outflow tract obstruction (LVOTO) during bioprosthetic mitral valve replacement (MVR) is a serious complication.[1,3] There are various factors that cause LVOTO after MVR, including the profile of the valve, aorto-mitral angle, small left ventricular cavity size, and left ventricular hypertrophy.[3,5] To improve hemodynamic performance with respect to these issues, the design of prosthetic valves has been modified. In 2010, Edwards Lifesciences proposed a modified model, the Magna Mitral Ease, with a lower profile and treated with the ThermaFix process. The Magna Mitral Ease valve protrudes less into the left ventricular outflow tract (LVOT) than its predecessor, the Perimount Plus mitral valve (Fig 1).[2] It is also predicted to have less structural valve deterioration because of the ThermaFix process, which reduces the risk of calcification. Although in vitro testing of the new bioprosthetic valves has demonstrated improved hemodynamic characteristics, few studies have compared the clinical outcomes of these bioprosthetic valves. Hence, this study aimed to compare the clinical and hemodynamic outcomes between the Magna Mitral Ease valve and the Perimount Plus mitral valve.

Methods

Patients who underwent bioprosthetic MVR with the Perimount Plus mitral valve or the Magna Mitral Ease valve at Asan Medical Center between January 2015 and August 2019 were enrolled in this study. The Magna Mitral Ease valve has been used from July 2017 at Asan Medical Center. There were no exclusion criteria with regard to patient characteristics or type of surgery. Patients who underwent redo cardiac surgery or concomitant surgical procedures were also included. A retrospective review of medical records was performed to obtain the perioperative, operative, and follow-up data of the patients. We compared preoperative clinical characteristics, operative data, and the postoperative hemodynamic and clinical outcomes of patients. Follow-up data were obtained till December 31, 2019. This study was approved by the Institutional Review Board of Asan Medical Center (2020-0627). Informed consent from the patients was not required because of the retrospective nature of the study.

All patients underwent transthoracic two-dimensional and Doppler echocardiographic evaluation preoperatively and before discharge from the hospital, except for 4 patients who died in-hospital before postoperative echocardiography could be performed. Postoperatively, standard echocardiographic measurements of prosthetic valves were evaluated, including left ventricular ejection fraction, LVOT flow acceleration, mean pressure gradients, and mitral valve area. LVOT flow acceleration was identified on Doppler echocardiography to confirm the presence or absence of LVOTO (Fig 2). The aorto-mitral angle was manually measured using the end-diastole parasternal long axis view of two-dimensional echocardiography. [4]

We aimed to compare the hemodynamic and clinical outcomes between the Magna Mitral Ease valve and the Perimount Plus mitral valve. Early mortality and complications were defined as occurring within 30 days post-operatively. Early complications included low cardiac output

syndrome requiring mechanical circulatory support, in-hospital stroke, postoperative bleeding requiring exploration, new-onset dialysis, wound infection, and pacemaker insertion. Valve-related complications included structural valve deterioration, infective endocarditis, paravalvular leak (> mild), valve thrombosis, hemorrhage, thromboembolic infarct, stroke, and reoperation.

Statistical Analysis

Continuous variables are reported as mean ± standard deviation. Categorical variables are presented as percentages and frequencies. The comparison between the groups was performed using the Student t-test or the Mann-Whitney U-test for continuous variables, and the chi-square test or the Fisher exact test for categorical variables, as appropriate. A p-value < 0.05 was considered statistically significant. Analyses were performed using the Statistical Package for the Social Sciences (SPSS Software for Windows version 21; IBM Corp., Armonk, NY, USA).

Results

Between January 2015 and August 2019, 284 patients underwent bioprosthetic MVR at Asan Medical Center. Among these patients, 170 who received either the Perimount Plus mitral valve (Group 1, n = 93) or the Magna Mitral Ease valve (Group 2, n = 77) were enrolled. The baseline characteristics of each group of patients are detailed in Table 1. The mean age of each group was 72.2 years and 70.8 years, respectively. Body mass index and body surface area were not significantly different between the two groups. The other variables were also not significantly different between the two groups, except for hemoglobin and total bilirubin levels. The etiology of mitral valve disease, in order of frequency, included rheumatic heart disease, degenerative change, infective endocarditis, functional, and others (cleft mitral valve, pannus or paravalvular leak of prosthetic valve, and prosthetic valve failure) in both groups (Table 1).

Preoperative echocardiographic data are shown in Table 2. Mean left ventricular ejection fractions were 55.46 % and 57.18% in Group 1 and Group 2, respectively. Both end-systolic and end-diastolic left ventricular internal dimensions were not significantly different. Both groups did not significantly differ in end-systolic volume and end-diastolic volume either. Underlying mitral valve pathologies were not different between the two groups: mitral stenosis, mitral regurgitation, and both were present in 23%, 43%, and 20% of patients in Group 1; and in 15%, 42%, and 17% of patients in Group 2, respectively. The mean aorto-mitral angle was comparable between both groups (121.4 vs. 120.9, p = 0.798).

The operative data are summarized in Table 3. Concomitant procedures included aortic valve replacement, coronary artery bypass grafting, tricuspid valve surgery, ascending aorta replacement, and maze procedure, without significant between-group differences. The mini-thoracotomy approach was used as per the surgeons' preference in 35 patients. Emergency

surgery was performed mainly due to cardiogenic shock or infective endocarditis. The mean cardiopulmonary bypass time was 171 ± 72 min in Group 1 and 170 ± 53 min in Group 2 ($p = 0.932$). The mean aortic cross-clamp time was 119 ± 45 min in Group 1 and 119 ± 42 min in Group 2 ($p = 0.967$). Group 1 used a 25 mm prosthetic mitral valve more frequently than group 2 ($p = 0.038$), but there was no difference in frequency of use among other-sizes of prosthetic mitral valves.

Early mortality was reported in 8 (8.6%) and 2 (2.6%) patients in Group 1 and Group 2, respectively ($p = 0.115$). The causes of mortality included low cardiac output syndrome, intracerebral hemorrhage, left ventricular rupture, pneumonia, acute respiratory distress syndrome, and metastatic infection. There were no significant differences in risk between the groups with respect to early complications including low cardiac output syndrome requiring mechanical cardiac support, early stroke, postoperative bleeding requiring exploration, new-onset dialysis, wound infection, and permanent pacemaker insertion (Table 4).

On postoperative echocardiographic data, LVOT flow acceleration was identified only in Group 1 (9.7% vs. 0%, $p = 0.004$) (Table 5). Among patients who underwent double valve replacement, there was no statistically significant difference in the rate of LVOT flow acceleration ($p = 0.126$) (Table 6). Other echocardiographic variables, including left ventricular ejection fraction, mitral valve area, and mitral valve mean pressure gradient, were not significantly different between the groups.

The mean follow-up period was 26.6 months and 17.4 months in Group 1 and Group 2, respectively ($p < 0.001$). With respect to long-term outcomes, there were no significant differences in the rates of late mortality and valve-related complications (Table 7). One patient who underwent double valve replacement with ascending aorta replacement had extremely

early structural degenerative findings in the prosthetic mitral valve, indicated by mitral stenosis on follow-up echocardiography at 8 months after surgery, and he underwent reoperation for MVR. The other reoperations were caused by prosthetic valve endocarditis. Hemorrhagic events causing intramuscular hematoma occurred in two patients in Group 2. Two patients had thromboembolic events: one patient underwent below-knee amputation due to left posterior tibial artery infarction, and the other patient was diagnosed with spleen infarction on abdominal computed tomography.

Discussion

To our knowledge, the present study is the first to compare the Mitral Magna Ease valve with the Perimount Plus valve. The primary goal of our study was to compare clinical and hemodynamic outcomes. The low-profile design of the Mitral Magna Ease valve protrudes less into the LVOT. Although LVOT flow acceleration was observed only in 9 patients with the Perimount Plus mitral valve, there was no clinically significant LVOTO. With respect to durability, it has been predicted to have less structural valve deterioration due to the ThermaFix process, but this is uncertain because the follow-up period was not enough to cause structural degeneration.

LVOTO is an uncommon complication of MVR. There are several case reports of LVOTO following MVR in the literature. Risk factors that predispose to LVOT narrowing can be classified as either patient-related or prosthetic-related.[7] Patient-related factors include small LVOT, septal hypertrophy, or sigmoid-shaped septum. Small left ventricular cavity size, which is common in patients with mitral stenosis and in the elderly, also increases the risk of obstruction. With respect to prosthetic-related factors, LVOTO more frequently occurs with insertion of small, high-profile prosthetic valves. High-profile valves may protrude into and obstruct the LVOT. Insertion of small prosthetic valves also contributes to prosthetic projection into the LVOT by narrowing the aorto-mitral angle. In addition, based on our experience, the correct orientation of bioprostheses during implantation is critical.

The low-profile design is effective for patients with small ventricle sizes undergoing multiple valve procedures or reoperations. Multiple valve procedures or reoperations in patients with degenerative disease or mitral annular calcification cause restrictions on prosthesis size.[2] In our study, we expected significant hemodynamic differences between the groups in patients with

double valve replacement. However, there were no significant between-group differences in hemodynamic performance, including LVOT flow acceleration ($p = 0.126$).

Of the 9 patients with postoperative LVOT flow acceleration, 2 patients showed disappearance of LVOT flow acceleration on follow-up echocardiography. Perioperatively, the low intravascular volume state and the inotropic effects of vasopressors may provoke LVOTO in susceptible patients. Most of these patients recover with fluid loading, beta-blockade, and time, as the ventricle recovers. [6,8]

The current study has limitations: It is a single-center, retrospective study with a relatively short follow-up period. Moreover, the mean follow-up period was different between the groups. The type of valve implanted was as per the surgeons' preference, and was not randomized.

Conclusion

This is the first report to compare clinical outcomes between Mitral Magna Ease valve and the Perimount Plus valve. The Mitral Magna Ease valve's low-profile design contributed to less protrusion into the LVOT and created less LVOT flow acceleration than the Perimount Plus mitral valve. However, clinical outcomes were not significantly different between the two groups during the intermediate period. Therefore, further studies on bioprosthetic valve structure and function are necessary to determine the efficacy of this modified model.

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Figures legends

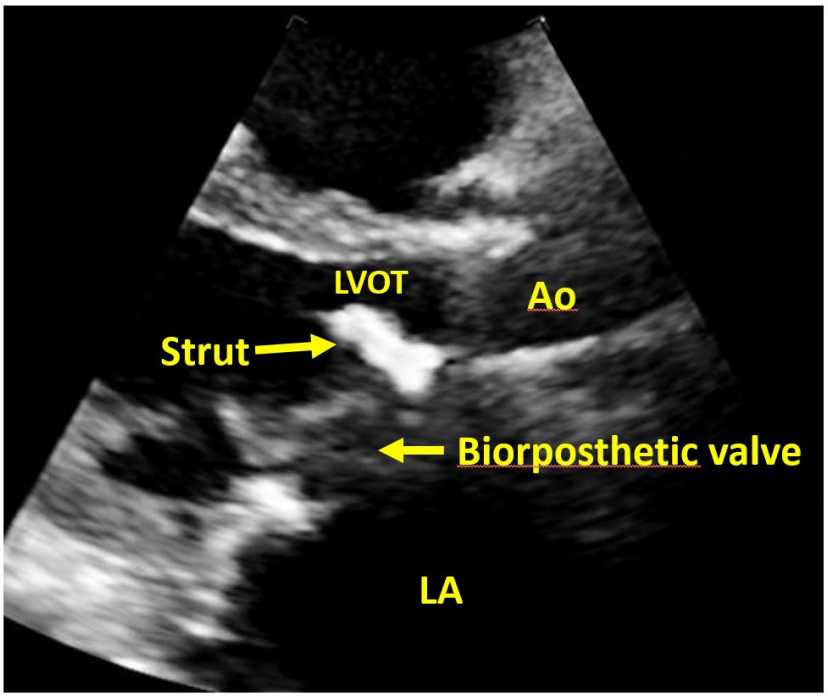
Fig 1. A. Magna Mitral Ease valve. B. Perimount Plus valve.

A

B

Fig 2. A. Echocardiographic image showing protrusion of bioprosthetic valve into LVOT following mitral valve replacement. B. This resulted in LVOT flow acceleration on Doppler echocardiography. Ao, aorta; LVOT, Left ventricular outflow tract; LA, left atrium.

A



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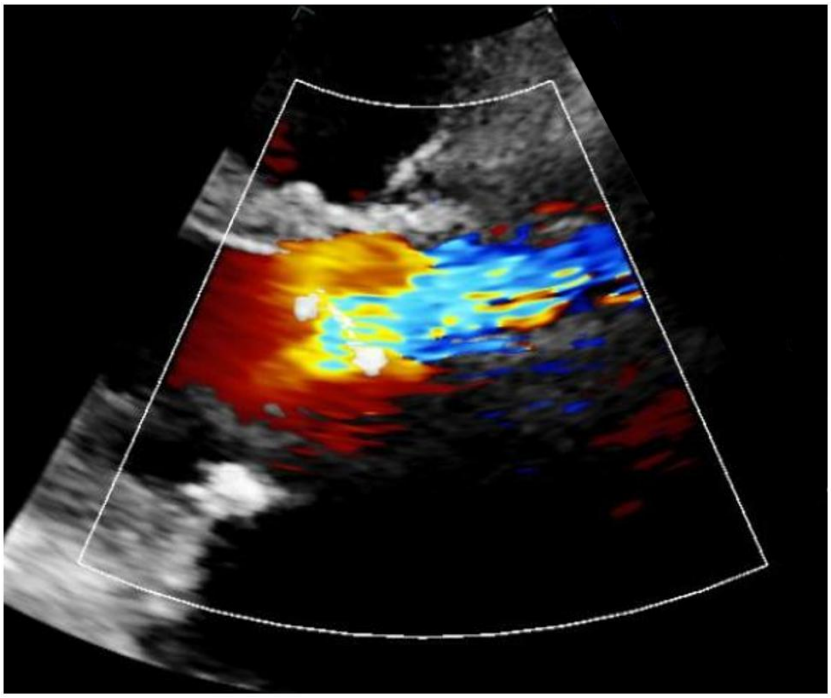

Tables

Table 1. Demographic Data

Variable	Perimount (n = 93)	Magna Ease (n = 77)	P value
Age, years	72.2 ± 6.8	70.8 ± 9.4	0.261
Female gender	63 (67.7)	46 (59.7)	0.279
BMI	23.2 ± 3.1	22.6 ± 3.0	0.251
BSA, m^2	1.5 ± 0.1	1.5 ± 0.1	0.756
Hypertension	47 (50.5)	35 (45.5)	0.509
Diabetes mellitus	28 (30.1)	17 (22.1)	0.238
Dyslipidemia	30 (32.3)	21 (27.3)	0.480
Congestive heart failure	8 (8.6)	6 (7.8)	0.848
CKD	10 (10.8)	6 (7.8)	0.511
Hemodialysis	5 (5.4)	1 (1.3)	0.225
COPD	12 (12.9)	9 (11.7)	0.811
History of CVA	19 (20.4)	13 (16.9)	0.556
Coronary artery disease	17 (18.3)	12 (15.6)	0.642
Previous PCI	8 (8.6)	8 (10.4)	0.691
Atrial fibrillation	50 (53.8)	45 (58.4)	0.541
Hemoglobin, mg/dL	11.8 ± 1.8	11.0 ± 2.0	0.010

Creatinine, mg/dL	1.2 ± 1.2	1.0 ± 0.7	0.192
Total bilirubin, mg/dL	1.0 ± 1.0	0.7 ± 0.3	0.010
NYHA class 3 or 4	36 (38.7)	24 (31.2)	0.306
Previous cardiac surgery	22 (23.7)	16 (20.8)	0.654
Etiology			
Rheumatic heart disease	41 (44.1)	40 (51.9)	0.307
Degenerative disease	23 (24.7)	21 (27.3)	0.706
Infective endocarditis	15 (16.1)	6 (7.8)	0.100
Functional	5 (5.4)	2 (2.6)	0.458
Etc	9 (9.7)	8 (10.4)	0.878

BMI, body mass index; BSA, body surface area; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVA, cerebral vascular accident; PCI, percutaneous coronary intervention; NYHA, New York Heart Association classification

Table 2. Preoperative Echocardiographic Data

Variable	Perimount (n = 93)	Magna Ease (n = 77)	P value
LV ejection fraction, %	55.4 ± 12.4	57.1 ± 10.7	0.344
LVIDs, mm	36.3 ± 9.1	37.1 ± 9.1	0.588
LVIDd, mm	53.8 ± 8.8	53.7 ± 8.9	0.938
ESV, ml	53.4 ± 33.5	55.5 ± 33.9	0.685
EDV, ml	119.7 ± 60.3	125.5 ± 54.3	0.517
LA size, mm	54.9 ± 11.0	54.3 ± 9.2	0.741
Mitral Stenosis	23 (24.7)	15 (19.5)	0.413
Mitral Regurgitation	43 (46.2)	42 (54.5)	0.281
Mitral Stenosis and Regurgitation	20 (21.5)	17 (22.1)	0.928
Peak TRPG, mmHg	43.7 ± 16.6	44.3 ± 17.3	0.833
TR ≥ moderate	34 (36.6)	31 (40.3)	0.621
Aorto-mitral angle	121.4 ± 9.8	120.9 ± 17.0	0.798

LV; left ventricular; LVIDs, left ventricular internal diameter end systole; LVIDd, left ventricular internal diameter end diastole; ESV, end-systolic volume; EDV, end-diastolic volume; LA, left atrium; TRPG, tricuspid regurgitation peak gradient; TR, tricuspid regurgitation

Table 3. Operative Data

Variable	Perimount (n = 93)	Magna Ease (n = 77)	P value
Concomitant cardiac surgery			
AVR	40 (43.0)	31 (40.3)	0.717
CABG	7 (7.5)	5 (6.5)	0.793
TVR	5 (5.4)	2 (2.6)	0.458
TVP	32 (34.4)	35 (45.5)	0.142
Ascending aorta replacement	5 (5.4)	1 (1.3)	0.223
Maze operation	42 (45.2)	40 (51.9)	0.378
Redo surgery	22 (23.7)	16 (20.8)	0.654
Minimally invasive surgery	15 (16.1)	20 (26.0)	0.114
Emergency surgery	12 (12.9)	6 (7.8)	0.281
Procedural Time			
CPB time, minutes	171.3 ± 72.1	170.4 ± 53.0	0.932
ACC time, minutes	119.0 ± 45.2	119.3 ± 42.5	0.967
Prosthetic mitral valve size (mm)			
25	24 (25.8)	10 (13.0)	0.038
27	28 (30.1)	24 (31.2)	0.881
29	33 (35.3)	28 (36.4)	0.905

31	5 (5.4)	10 (13.0)	0.082
33	3 (3.2)	5 (6.5)	0.470

AVR, aortic valve replacement; CABG, coronary artery bypass grafting; TVR, tricuspid valve replacement; TVP, tricuspid valve repair; CPB, cardiopulmonary bypass time; ACC, aortic cross-clamp time

Table 4. Early Outcomes

Variable	Perimount (n = 93)	Magna Ease (n = 77)	P value
Early death	8 (8.6)	2 (2.6)	0.115
Early complications			
LCOS requiring MCS	5 (5.4)	3 (3.9)	0.730
Stroke	9 (9.7)	4 (5.2)	0.274
Bleeding	5 (5.4)	5 (6.5)	0.757
New-onset dialysis	8 (8.6)	7 (9.1)	0.911
Wound infection	1 (1.1)	0 (0.0)	< 1
PPM implantation	5 (5.4)	1 (1.3)	0.223

LCOS, low cardiac output syndrome; MCS, mechanical cardiac support; PPM, permanent pacemaker

Table 5. Postoperative Echocardiographic Data

Variable	Perimount (n = 93)	Magna Ease (n = 77)	P value
LV ejection fraction, %	52.2 ± 11.7	50.6 ± 14.1	0.438
LVOT flow acceleration	9 (9.7%)	0 (0%)	0.004
Mitral valve area, cm^2	2.8 ± 0.4	2.7 ± 0.4	0.711
MVPG mean, mmHg	5.5 ± 1.9	5.6 ± 1.7	0.638

LV, left ventricular; LVOT, left ventricular outflow tract; MVPG, mitral valve pressure gradient

Table 6. Postoperative Echocardiographic Data of DVR patients

Variable	Perimount (n = 40)	Magna Ease (n = 31)	P value
LV ejection fraction, %	51.3 ± 11.8	50.9 ± 14.3	0.914
AVPG mean, mmHg	14.1 ± 5.4	14.3 ± 4.1	0.877
LVOT flow acceleration	4 (10.0%)	0 (0%)	0.126
Mitral valve area, cm^2	2.7 ± 0.3	2.7 ± 0.5	0.914
MVPG mean, mmHg	5.7 ± 1.9	5.8 ± 1.4	0.848

LV, left ventricular; AVPG, aortic valve pressure gradient; LVOT, left ventricular outflow tract; MVPG, mitral valve pressure gradient

Table 7. Late Outcomes

Variable	Perimount (n = 93)	Magna Ease (n = 77)	P value
Late death	16 (17.2%)	8 (10.4%)	0.204
Mean follow-up time, months	26.6 ± 17.5	17.4 ± 8.7	< 0.001
Valve-related complications			
Structural valve deterioration	1 (1.1%)	0 (0%)	<1
Infective endocarditis	4 (4.3%)	2 (2.6%)	0.690
Paravalvular leak, > mild	0 (0%)	2 (2.6%)	0.204
Valve Thrombosis	2 (2.2%)	0 (0%)	0.501
Hemorrhage	0 (0%)	2 (2.6%)	0.204
Thromboembolic Infarct	1 (1.1%)	1 (1.3%)	<1
Stroke	14 (15.1%)	10 (13.0%)	0.700
Reoperation	4 (4.3%)	2 (2.6%)	0.690

ABSTRACT

Background: The Carpentier-Edwards Magna Mitral Ease valve has a low-profile design and uses the ThermaFix process for enhanced calcium removal. We compared the clinical and hemodynamic outcomes of the Magna Mitral Ease valve with those of the Perimount Plus mitral valve.

Methods: A total of 170 patients underwent bioprosthetic mitral valve replacement between January 2015 and August 2019, with implantation of either the Perimount Plus mitral valve (Group 1, n = 93) or the Magna Mitral Ease valve (Group 2, n = 77). We retrospectively reviewed the clinical and hemodynamic data. Hemodynamic performance, including the left ventricular ejection fraction, left ventricular outflow tract (LVOT) flow acceleration, mean pressure gradients, and mitral valve area, was evaluated by echocardiography.

Results: The groups did not differ among the variables known to affect hemodynamic measurements, including age, sex, body surface area, left ventricular inner dimension, and aorto-mitral annular angle. Postoperatively, LVOT flow acceleration was observed in 9 patients in Group 1 and none in Group 2 ($p = 0.004$). Early mortality was reported in 8 (8.6%) patients in Group 1 and 2 (2.6%) patients in Group 2 ($p = 0.115$). There was no significant difference in the incidence of major valve-related complications.

Conclusion: The Mitral Magna Ease valve's low-profile design resulted in less LVOT flow acceleration when compared with the Perimount Plus mitral valve. However, there were no significant differences in clinical outcomes. Further studies should be performed to determine the efficacy of this modified model.

Keywords: Mitral valve, replacement, Bioprothesis, Hemodynamics.