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Article

Outcomes of Different Mitral Valve Approaches Combined with Aortic Valve Replacement in Patients with Degenerative Valve Disease

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Abstract

Introduction: The objective of this cohort study was to analyze the long-term relative survival of degenerative valve disease (DVD) patients who underwent mitral valve repair (MVP) or replacement and aortic valve replacement (AVR). **Methods**: A total of 146 patients underwent double valve replacement (DVR) or MVP+AVR at four institutions between 2016 and 2022. Kaplan–Meier method was applied to analyze survival rate. The potential predictors of mortality were investigated by Cox regression. **Results**: Of 146 patients, 62 underwent MVP+AVR, and 84 underwent DVR. The thirty-day mortality rate was 4.76% in the DVR cohort and 1.61% in the MVP+AVR cohort. At baseline, there were differences in age (63.39 $\pm$ 8.01 *vs*. 58.46 $\pm$ 9.92, $p = 0.012$), proportions of male patients (51.61% *vs*. 72.62, $p = 0.014$), smoking history (45.16% *vs*. 28.57%, $p = 0.039$). More biological valves were applied in the MVP+AVR cohort (77.42% *vs*. 47.62%, $p < 0.001$). There was no significant difference in mortality between the cohorts (1339.5 [Interquartile range (IQR), 1021.25–1876.75] *vs*. 1026.00 [IQR, 679.50–1674.00], $p = 0.252$). The overall mortality rate was 16.67% for DVR and 6.45% for MVP+AVR. Mechanical valve replacement (hazard ratio (HR) = 3.7, 95% confidence interval (CI): 1.0–12.0, $p = 0.029$) was increased the risk of postoperative mortality. **Conclusion**: Although the superiority of MVP+AVR was not verified with statistical significance in our cohort, we believe that MVP+AVR should be the preferred strategy for treating most DVD patient because it is associated with higher survival rates during follow-up.

Keywords

heart valve disease; morbidity; mortality

Introduction

The proportion of valvular disease cases with degenerative etiology has increased gradually [1,2]. However, multiple valve disease less frequently develops in patients with degenerative valve disease (DVD). According to the 2017 and 2021 guidelines published by the European Society of Cardiology and the European Association for Cardio-Thoracic Surgery, more data about multiple valve disease are needed, in terms of its natural history and the outcomes of its treatment to better define the indications for intervention [3,4]. According to the American Heart Association and American College of Cardiology 2014 guidelines, there is a paucity of data on the natural history of mixed valve disease [5]. Thus, more clinical data about multiple-valve disease are needed.

With improvements in surgical techniques and outcomes, mitral valve repair (MVP) is a low-risk procedure that provides excellent long-term durability of repair in mitral valve disease. However, the technique of MVP for the treatment of multiple valve disease in patients with DVD should be the focus of further research. To understand whether DVD patients benefit from MVP+aortic valve replacement (AVR), we used a four-center database to identify patients who underwent MVP+AVR and those who underwent double valve replacement (DVR). In particular, the survival of patients who underwent different surgical procedures is also considered.

Methods

Patient Population

965 patients underwent simultaneous aortic and mitral valve surgery at four centers between 2016 and 2022. Manual chart review was performed by four cardiac surgeons. The exclusion criteria included concomitant coronary artery bypass grafting, congenital heart disease, aortic dissection,

Table 1. Baseline characteristics of patients with MVP+AVR or DVR.

	MVP+AVR (n = 62)	DVR (n = 84)	*p* value
Age, years	63.39 ± 8.01	58.46 ± 9.92	0.012
Age ≥70 years	18 (29.03)	8 (9.53)	0.004
Gender, men, n (%)	32 (51.61)	61 (72.62)	0.014
BMI (kg/m^2)	25.08 ± 4.21	24.18 ± 3.79	0.264
BSA (m^2)	1.74 ± 0.24	1.73 ± 0.18	0.766
History of alcohol, n (%)	11 (17.74)	14 (16.67)	0.518
History of smoking, n (%)	28 (45.16)	24 (28.57)	0.039
Hypertension, n (%)	30 (48.39)	38 (45.24)	0.739
Diabetes mellitus, n (%)	6 (9.67)	8 (9.52)	0.975
AF, n (%)	24 (38.71)	34 (40.48)	0.829
eGFR (mL/min/1.73 m^2)	81.42 ± 17.09	82.59 ± 20.93	0.180
AV disease			
Stenosis	8 (12.90)	12 (14.29)	0.810
Regurgitation	42 (67.74)	58 (69.05)	0.867
Mixed lesion	12 (19.35)	14 (16.67)	0.675
MV disease			
Regurgitation	62 (100.00)	83 (98.81)	1.000
Mixed lesion	0 (0.00)	1 (1.19)	-
LAD (mm)	48.45 ± 6.02	50.60 ± 7.09	0.128
LVESD (mm)	46.82 ± 7.88	43.89 ± 9.42	0.118
LVEDD (mm)	65.61 ± 7.08	62.97 ± 9.75	0.162
EF (%)	53.30 ± 9.02	55.82 ± 9.08	0.180
BNP (pg/mL)	1335.00 (587.14, 2762.00)	1108.00 (319.21, 4980.00)	0.727
EuroSCORE II	1.87 (1.18, 4.01)	1.41 (0.99, 2.08)	0.020

Continuous variables reported as mean (SD) or median (25%, 75%). Categorical variables reported as n (%). AF, Atrial fibrillation; AV, Aortic valve; AVR, Aortic valve replacement; BMI, Body Mass Index; BNP, B-type natriuretic peptide; BSA, body surface area; EF, eject fraction; DVR, Double valve replacement; eGFR, estimated glomerular filtration rate. eGFR was calculated using the Chronic Kidney Disease Epidemiology collaboration equation (https://www.kidney.org/professionals/KDOQI/gfr_calculator); EuroSCORE II, European System for Cardiac Operative Risk Evaluation II; LAD, Left atrial dimension; LVEDD, Left ventricular end diastolic dimension; LVESD, Left ventricular end systolic dimension; MVP, Mitral valve repair.

rheumatic heart disease, infectious endocarditis, and tricuspid regurgitation. Of these, 146 DVD patients who underwent primary simultaneous AVR, and either MVR (n = 84) or MVP (n = 62) were included.

Outcomes and Covariates

Information about survival and deaths were obtained through telephone interviews or outpatient chart review. To assess other covariates associated with overall survival, we considered age, history of smoking, alcohol, hypertension, diabetes mellitus, atrial fibrillation (AF), perioperative B-type natriuretic peptide (BNP), EuroSCORE II, and estimated glomerular filtration rate (eGFR). Perioperative echocardiographic data was also collected.

Operative Techniques and Follow-Up

Following a standard median sternotomy, surgical procedures were performed under cardiopulmonary bypass at 34 °C and cold blood cardioplegia arrest. At all 4 centers, the mitral and aortic valves were exposed using similar methods, a right atriotomy to the atrial septum and a 'hockey-stick' incision in the ascending aorta, respectively. Decisions to repair were made intraoperatively following transoesophageal echocardiogram and exploration and inspection of the mitral valve. During MVR, the posterior leaflet preservation technique or the no leaflet preservation technique was performed. For MVP, surgical techniques included neochorade, edge-to-edge repair, commissurotomy, leaflet patch augmentation, resection of the leaflet, suture of the cleft of the anterior leaflet, and a supporting annuloplasty ring. Then, the aortic valve was re-

Table 2. Surgical details and mortality.

	MVP+AVR (n = 62)	DVR (n = 84)	*p* value
Mechanical aortic valve, n (%)	14 (22.58)	44 (52.38)	<0.001
Biological aortic valve, n (%)	48 (77.42)	40 (47.62)	<0.001
Mechanical mitral valve, n (%)	-	44 (52.38)	-
Biological mitral valve, n (%)	-	40 (47.62)	-
Cox Maze IV, n (%)	13 (20.97)	20 (23.81)	0.842
LAA amputated	28 (45.16)	30 (35.71)	0.305
MV techniques			
Annuloplasty+neochordae, n (%)	49 (79.03)	-	-
Annuloplasty+edge-to-edge repair, n (%)	6 (9.68)	-	-
Annuloplasty+leaflet patch augmentation, n (%)	1 (1.61)	-	-
Annuloplasty+resection of leaflet, n (%)	4 (6.45)	-	-
Annuloplasty+suture of indentation of anterior leaflet, n (%)	2 (3.23)	-	-
Posterior leaflet preservation, n (%)	-	67 (79.76)	-
No leaflet preservation, n (%)	-	17 (20.24)	-
CPB duration (min)	132.91 ± 26.81	184.43 ± 63.72	<0.001
Clamping time (min)	98.00 ± 17.87	112.01 ± 23.49	0.004
30-Day mortality rate, n (%)	1 (1.61)	4 (4.76)	0.395

Categorical variables reported as n (%).

LAA, Left atrial appendage; MV, Mitral valve; CPB, Cardiopulmonary bypass.

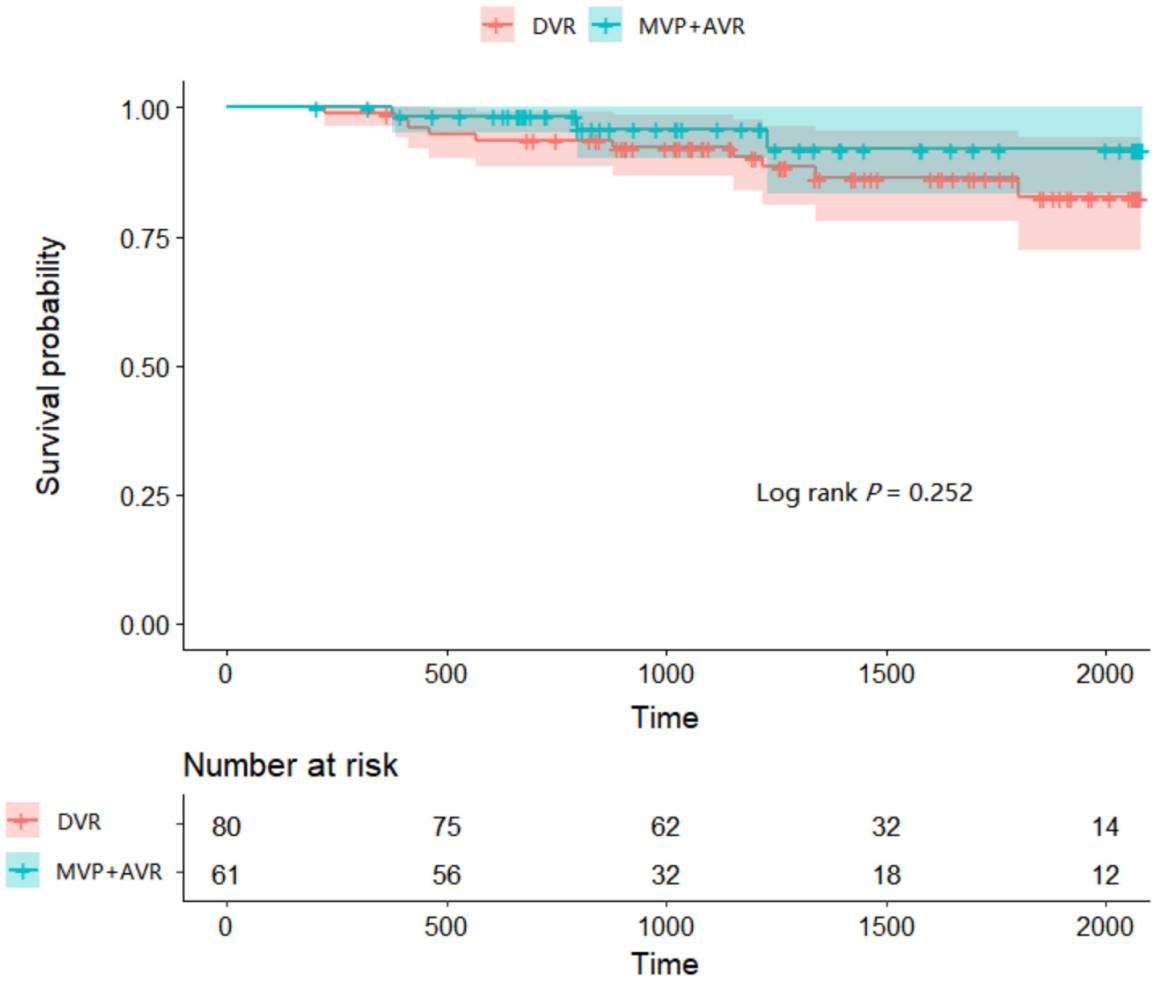

Fig. 1. Kaplan-Meier curves depicting for MVP+AVR and DVR.

placed. The aorta was closed after the deairing maneuvers. The enlarged left atrial appendage was routinely amputated. For patients with symptomatic AF, the biatrial Cox-Maze IV procedure was performed according to the guidelines [6]. The early and late mortality were defined according to the "Guidelines for Reporting Mortality and Morbidity After Cardiac Valve Interventions" [7].

Statistical Analysis

Statistical methods were described in previous study [8,9]. Statistical analysis was performed by using R software (version 4.1.2; R Foundation for Statistical Computing, Beijing, China).

Baseline Characteristics

Table 1 shows characteristics of the patients in two group. The MVP+AVR patients were older than the DVR patients (63.39 ± 8.01 *vs.* 58.46 ± 9.92, $p = 0.012$). Patients aged ≥70 years was more in the MVP+AVR group than in DVR group (29.03% *vs.* 9.53%, $p = 0.004$). Conversely, 72.62% of the patients in the DVR group were male. Patients who underwent MVP+AVR were more likely to have a history of smoking (45.16% *vs.* 28.57%, $p = 0.039$). There was no differences in the preoperative prevalence of AF when comparing both groups: they were 38.71% and 40.48%, respectively. There was a significant difference in EuroSCORE II between two groups (1.87% [Interquartile range (IQR) 1.18 to 4.01] *vs.* 1.41% [IQR 0.99 to 2.08], $p = 0.020$).

Surgical Details

Surgery details are listed in Table 2. The MVP+AVR group had a higher rate of biological valve prosthesis use than the DVR group (77.42% *vs.* 47.62%, $p < 0.001$). In terms of the Cox Maze IV procedure, there was no statistically significant difference between the MVP+AVR group and the DVR group (20.97% *vs.* 23.81%, $p = 0.842$). The 30-day mortality rate was 4.76% (4/84) in the DVR group and 1.61% (1/62) in the MVP+AVR group.

Survival for MVP+AVR and DVR Patients

The median duration of follow-up after hospital discharge was 1221 (IQR, 838.00–1828.50) days, with a maximum of 2083 days. There was no significant difference in mortality between the cohorts (1339.5 [IQR, 1021.25–1876.75] *vs.* 1026.00 [IQR, 679.50–1674.00], $p = 0.252$). Fig. 1 shows Kaplan–Meier survival curves.

At the end of the postoperative follow-up period, three patients in the MVP+AVR group had died. The causes of death were as follows: infection (n = 1) and cancer (n = 2). Ten patients in the DVR group died. The causes of death were as follows: heart failure (n = 1), sudden cardiac death (n = 2), stroke (n = 4) and unknown causes (n = 3). In Fig. 2, at the end of the last observed event, the unadjusted survival rate in the MVP+AVR group was 92.1% (95% confidence interval (CI): 0.835–1.000). When adjusting for age ≥70 years, history of smoking, Cox Maze IV procedure, and mechanical valve implantation, the survival rate in the MVP+AVR group was 100%. The unadjusted survival rate in the group with DVR was 82.7% (95% CI: 0.726–0.943). When adjusting for age ≥70 years, history of smoking, Cox Maze IV procedure, mechanical valve implantation, the survival rate in the DVR group increased to 93.4% (95% CI: 0.817–1.000).

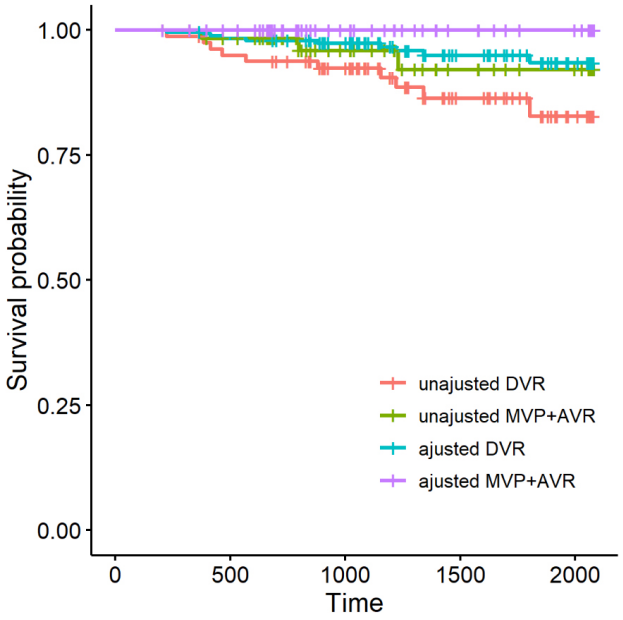

Fig. 2. Adjusted and unadjusted survival curves in MVP+AVR and DVR groups.

Table 3. HRs for survival analysis.

Variable	HR (95% CI)	*p* value
Mechanical valve	3.7 (1.00–12.00)	0.029
Perioperative LAD >50 mm	2.1 (0.69–6.50)	0.187
Age of 70 years or older	1.4 (0.39–5.20)	0.591
Cox Maze IV	0.6 (0.13–2.70)	0.508
MVP+AVR	0.46 (0.13–1.70)	0.262

$\alpha = 0.05$ for CI. HR, Hazard ratios; AVR, Aortic valve replacement; CI, Confidence interval; MVP, Mitral valve repair; LAD, Left atrial dimension.

The final model is shown in Table 3. Mechanical valve replacement (Hazard ratios (HR) = 3.700, 95% CI: 1.00–12.00, $p = 0.029$) was associated with a higher risk of long-term mortality. However, Cox Maze IV (HR = 0.610, 95% CI: 0.13–2.70, $p = 0.508$), perioperative left atrial dimension (LAD) >50 mm (HR = 2.100, 95% CI: 0.69–6.50, $p = 0.187$), and age of 70 years or older (HR = 1.400, 95% CI: 0.39–5.20, $p = 0.591$) were not significantly associated

with a higher risk of long-term mortality. Relative to DVR, MVP+AVR was associated with a lower mortality rate (HR = 0.464, 95% CI: 0.13–1.70, $p = 0.262$), adjusting for age $\geq$70 years, Cox Maze IV procedure, perioperative LAD $>$50 mm, and mechanical valve replacement.

Discussion

Although survival in the MVP+AVR was numerically higher, Kaplan-Meier (KM) analysis did not show statistical significance, probably due to the small sample size. Thus, we believe that it is necessary to verify the superiority of MVP+AVR in the treatment of DVD patients with larger sample size.

Hamamoto *et al*. [10] previously demonstrated that the survival rate 15 years after surgery was similar between MVP+AVR and DVR. However, only 37 out of 379 patients had degenerative heart disease. Similarly, Leavitt *et al*. [11] claimed that MVP+AVR was associated with significantly lower in-hospital mortality and higher survival rates than DVR. However, the etiology of the valve disease was not described. Thus, the results of MVP+AVR in DVD patients are still unclear [11]. Recently, the opinion that MVP+AVR may be a feasible option for DVD patients have been demonstrated. Coutinho *et al*. [12] demonstrated that MVP can be the procedure of choice whenever feasible in nonrheumatic patients undergoing AVR. These results can build enthusiasm for surgery in these patients. However, these clinical data from patients who underwent coronary artery bypass grafting or tricuspid valve surgery were enrolled, which may have led to some heterogeneity of the data [13,14]. Recently, Egger *et al*. [15] demonstrated that both DVR and MVP+AVR are reasonable options for DVD patients. In that analysis, 72 out of 89 cases with degenerative etiologies were included. However, the proportion of patients with other valve etiologies, such as rheumatic, endocarditis, and stenosis, were mixed in the final analysis. Although most etiologies are degenerative, selection bias cannot be eliminated sufficiently. In this study, we focused on the role of MVP+AVR in a cohort of isolated DVD patients. Our results found herein are compatible with and extend these results.

In our study, MVP+AVR was much more commonly performed in DVD patients with valve regurgitation, which is consistent with the proportion of patients with mitral regurgitation in the MVP+AVR cohort (Table 1). A previous study indicated that multiple-valve regurgitation in patients with DVD is a typical example of a frequent yet understudied scenario [16]. According to the 2017 AHA/ACC focused update of the 2014 AHA/ACC guidelines, if valve regurgitation is severe, MVP or replacement is a Class I recommendation (level B evidence) for patients with chronic severe primary mitral regurgitation undergoing AVR. If aortic regurgitation is severe and primary mitral regurgitation is moderate, MVP+AVR is considered reasonable (Class IIa, level of evidence C) [17]. Thus, MVP for the treatment of mitral regurgitation has been established as the gold standard of surgical care for patients with DVD [18]. Furthermore, compared with that in the DVR cohort, the 30-day mortality rate in the MVP+AVR group was 1.61%, coinciding with previously reported 30-day mortality rates [12,14,15]. It should be noted that the long-term mortality rate of patients who underwent MVP+AVR in our cohort was lower (4.92%). It indicated that reoperation and mortality in the mitral valve after a good repair should be lower than after bioprosthetic valve replacement in the long-term.

Limitations

There are some limitations in our study. First, after exclusion, our sample size was small. Our results could not be generalizable to the overall population. Second, it should be noted that as a multiple-center study, the experience of the center and the surgeon plays a significant role in the long-term outcomes.

Conclusion

Although the superiority of MVP+AVR was not verified, we believe that whenever feasible, MVP+AVR is the procedure of choice for treating DVD patients because it is associated with reduced mortality and higher survival rates during the follow-up period.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

YJ-Writing, Data collection, Statistics and Draft. MC-Design, Reviewing. YJ, MC, WZ, XP and QS-Data collection, HL and JL-Statistics. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

This study was reviewed and approved by the Institutional Review Board of Bengbu Medical College (reference

number: 2024[103]). All participants provided written informed consent, and the ethics committee approved the procedures.

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Conflict of Interest

The authors declare no conflict of interest.

References

[1] Soler-Soler J, Galve E. Worldwide perspective of valve disease. Heart (British Cardiac Society). 2000; 83: 721–725.

[2] Coffey S, Roberts-Thomson R, Brown A, Carapetis J, Chen M, Enriquez-Sarano M, *et al*. Global epidemiology of valvular heart disease. Nature Reviews. Cardiology. 2021; 18: 853–864.

[3] Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, *et al*. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. European Heart Journal. 2017; 38: 2739–2791.

[4] Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, *et al*. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. European Heart Journal. 2022; 43: 561–632.

[5] Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, 3rd, Guyton RA, *et al*. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Journal of the American College of Cardiology. 2014; 63: e57–e185.

[6] Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, *et al*. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. European Journal of Cardio-Thoracic Surgery. 2016; 50: e1–e88.

[7] Akins CW, Miller DC, Turina MI, Kouchoukos NT, Blackstone EH, Grunkemeier GL, *et al*. Guidelines for reporting mortality and morbidity after cardiac valve interventions. The Annals of Thoracic Surgery. 2008; 85: 1490–1495.

[8] Ghali WA, Quan H, Brant R, van Melle G, Norris CM, Faris PD, *et al*. Comparison of 2 methods for calculating adjusted survival curves from proportional hazards models. JAMA. 2001; 286: 1494–1497.

[9] Fiedler AG, Bhambhani V, Laikhter E, Picard MH, Wasfy MM, Tolis G, *et al*. Aortic valve replacement associated with survival in severe regurgitation and low ejection fraction. Heart (British Cardiac Society). 2018; 104: 835–840.

[10] Hamamoto M, Bando K, Kobayashi J, Satoh T, Sasako Y, Niwaya K, *et al*. Durability and outcome of aortic valve replacement with mitral valve repair versus double valve replacement. The Annals of Thoracic Surgery. 2003; 75: 28–33; discussion 33–34.

[11] Leavitt BJ, Baribeau YR, DiScipio AW, Ross CS, Quinn RD, Olmstead EM, *et al*. Outcomes of patients undergoing concomitant aortic and mitral valve surgery in northern new England. Circulation. 2009; 120: S155–S162.

[12] Coutinho GF, Martínez Cereijo JM, Correia PM, Lopes CS, López LR, Muñoz DD, *et al*. Long-term results after concomitant mitral and aortic valve surgery: repair or replacement? European Journal of Cardio-thoracic Surgery: Official Journal of the European Association for Cardio-thoracic Surgery. 2018; 54: 1085–1092.

[13] Gillinov AM, Blackstone EH, Cosgrove DM, 3rd, White J, Kerr P, Marullo A, *et al*. Mitral valve repair with aortic valve replacement is superior to double valve replacement. The Journal of Thoracic and Cardiovascular Surgery. 2003; 125: 1372–1387.

[14] Kilic A, Grimm JC, Magruder JT, Sciortino CM, Whitman GJR, Baumgartner WA, *et al*. Trends, clinical outcomes, and cost implications of mitral valve repair versus replacement, concomitant with aortic valve replacement. The Journal of Thoracic and Cardiovascular Surgery. 2015; 149: 1614–1619.

[15] Egger ML, Gahl B, Koechlin L, Schömig L, Matt P, Reuthebuch O, *et al*. Outcome of patients with double valve surgery between 2009 and 2018 at University Hospital Basel, Switzerland. Journal of Cardiothoracic Surgery. 2022; 17: 152.

[16] Unger P, Lancellotti P, Amzulescu M, David-Cojocariu A, de Cannière D. Pathophysiology and management of combined aortic and mitral regurgitation. Archives of Cardiovascular Diseases. 2019; 112: 430–440.

[17] Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, 3rd, Fleisher LA, *et al*. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2017; 135: e1159–e1195.

[18] Smith A, Argáez C. Experiences and Perspectives of Treatments for Heart Valve Disease: A Rapid Qualitative Review [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health. 2020.