

Research Article

Left Ventricular Recovery after Transapical Transcatheter Aortic Valve Implantation Compared with Conventional Aortic Valve Replacement in Patients with Aortic Regurgitation and Reduced Ejection Fraction

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Background and Aim of the Study. To evaluate differences in left ventricular recovery after transapical transcatheter aortic valve implantation and conventional aortic valve replacement in patients with aortic regurgitation and reduced left ventricular ejection fraction. **Methods.** All patients with reduced left ventricular ejection fraction who underwent aortic valve surgery for AR at our institution between January 2015 and November 2021 were retrospectively reviewed. Generalized estimating equations were used to compare left ventricular recovery and remodeling outcomes between the patient groups. **Results.** A total of 87 cases were included in this study, 36 patients for TA-TAVI and 51 patients for C-AVR. Transapical transcatheter aortic valve implantation was associated with better and faster recovery of left ventricular ejection fraction and left ventricular end-diastolic dimension (adjusted $\beta = 0.002$, 95% CI: 0.000 to 0.003, and $p = 0.046$; adjusted $\beta = 0.330$, 95% CI: 0.185 to 0.474, and $p < 0.001$, respectively) within the first 3 months postoperatively compared with left ventricular ejection fraction, with the same improvement in New York Heart Association function class (adjusted $\beta = 0.381$, 95% CI: -0.349 to 1.111, and $p = 0.306$). **Conclusions.** This study highlights patients who underwent transapical transcatheter aortic valve implantation for aortic regurgitation with reduced left ventricular ejection fraction. However, future randomized controlled prospective clinical trials with longer follow-up durations are required.

1. Introduction

In patients with severe aortic regurgitation (AR), some eventually develop severe left ventricular (LV) dysfunction due to gradual LV volume overload and have a poor prognosis after conservative treatment. According to the latest American College of Cardiology/American Heart Association guidelines for the surgical management of patients with AR, surgery is recommended for patients with asymptomatic LV dysfunction, i.e., patients with a left ventricular ejection fraction (LVEF) less than 50%, with a Class I recommendation [1]. However, the treatment of patients with severe AR and reduced LVEF remains controversial, with studies showing mixed outcomes after

conventional aortic valve replacement (C-AVR) for this group of patients [2–4]. In recent years, with the development of minimally invasive valve technology, transapical transcatheter aortic valve implantation (TA-TAVI) has evolved as an alternative surgical option, particularly for high-risk patients who are not candidates for C-AVR under extracorporeal circulation with anoxic cardiac arrest. Jennifer et al. reported similar early clinical outcomes after TA-TAVI and C-AVR in high-risk patients [5]. Improvements in LV mechanics and remodeling after surgical relief of AR and LV overload may have a positive impact on the early prognosis of patients [6]. C-AVR can cause myocardial ischemia-reperfusion injury, while TA-TAVI can also cause myocardial suture and puncture injury at the apex.

Therefore, further research is needed to determine whether TA-TAVI leads to better LV functional recovery and remodeling in patients with severe AR and reduced LVEF. The aims of this retrospective study were to (1) evaluate early LV functional recovery, as estimated by LVEF, LV remodeling, as estimated by left ventricular end-diastolic internal diameter (LVEDD), and cardiac function, estimated by the New York Heart Association (NYHA) functional class, in patients with severe AR and reduced LVEF undergoing TA-TAVI and (2) to analyze potential differences between LV function recovery and remodeling in patients undergoing TA-TAVI and C-AVR.

2. Materials and Methods

2.1. Study Patients and Data Collection. This was a retrospective analysis of a prospectively collected sample database. Eighty-seven consecutive patients with severe AR and reduced LVEF (defined as EF <50% in this study) underwent TA-TAVI or C-AVR at our institution between January 2015 and November 2021. The exclusion criteria were as follows: (1) patients with greater than moderate aortic stenosis, active endocarditis, or any other concomitant cardiac surgical procedures (e.g., mitral valve repair or replacement, coronary artery bypass, or radiofrequency ablation of atrial fibrillation) and (2) patients with acute AR due to aortic dissection, infective endocarditis, or iatrogenic causes. Patient characteristics, laboratory values, echocardiographic results, and in-hospital and follow-up outcomes were extracted from the hospital electronic medical records. A team of five surgeons was involved in both procedures, and a team of six cardiac sonographers was involved in the evaluation of functional LVEF. Patients undergoing TA-TAVI were deemed to be too high-risk or contraindicated for C-AVR and were indicated for patients who were not candidates for transfemoral TAVI in conditions such as pure aortic regurgitation without annulus or leaflet calcification, peripheral vascular disease, challenging vascular anatomy, the presence of previously implanted arterial grafts, or high coronary artery risk. Transthoracic echocardiography examinations were routinely performed during preoperative examination and postoperative follow-up. Echocardiographic measurements for this study included LVEF, which was calculated using the Simpson method and LVEDD, which was detected by M-mode. These measurements were obtained at baseline, 7 days, and 3 months after both procedures. The grading of the severity of AR was based on the American Society of Echocardiography recommendations. The European System for Cardiac Operative Risk Evaluation (EuroScore) was calculated online using an official website (<https://www.euroscore.org>). Surgical risk was predicted according to additive EuroScore values, with low risk defined as additive EuroScore ≤ 4 , moderate risk defined as additive EuroScore 4-5, and high-risk defined as additive EuroScore ≥ 6 . This study was approved by the Ethics Committee of Union Hospital, Fujian Medical University and adhered to the tenets of the Declaration of Helsinki (Ethics approval number: 2022KY023). The need to obtain individual patient consent was waived because of the retrospective nature of the present study.

2.2. Surgical Procedures and Postsurgical Treatment. The decision to perform TA-TAVI and SAVR was made by a multidisciplinary “heart team” that included interventional cardiologists, cardiac surgeons, and imaging specialists. Patients who had an unfavorable transfemoral approach were at high surgical risk, defined as an additive EuroScore ≥ 6 , and were considered eligible for TA-TAVI. The “heart team” also considered other factors in the patient/family financial situation to determine which procedure to use. The key steps of TA-TAVI and C-AVR procedures have been described in detail elsewhere [7]. Briefly, TA-TAVI was performed using the J-Valve system (JieCheng Medical Technology Co., Ltd., Suzhou, China) via the left ventricular apex through anterolateral minithoracotomy in the fifth or sixth intercostal space. C-AVR procedures were performed through a standard midline sternotomy or upper partial sternotomy under general anesthesia, with cardiopulmonary bypass and mild systemic hypothermia. Postoperative care was similar in both the groups. Warfarin therapy was generally recommended for 3 months in patients with a mechanical biological and for life in patients with a mechanical valve. Various types of drugs, such as angiotensin-converting enzyme inhibitors, β -adrenoceptor blockers, and aldosterone antagonists, are routinely used to reverse myocardial remodeling after surgery. Warfarin was given orally for 3 months to prevent valve thrombosis after surgery, unless there was a specific contraindication.

2.3. Statistical Analysis. Continuous variables were expressed as the median or mean \pm standard deviation and were evaluated using Student's *t*-test. Categorical variables are presented as counts or percentages and were evaluated using Fisher's exact test. Non-normally distributed variables are reported as the median (interquartile range [IQR]) and were evaluated using the Wilcoxon signed-rank test.

Data may have been missing at 3 months because the patients died before the follow-up visit. To present a complete case analysis and assess any potential impact of missing information due to case death on the analysis, we performed generalized estimating equations (GEEs) to analyze LV function recovery and remodeling over time and to assess whether LV functional recovery and remodeling differed between the TA-TAVI and C-AVR groups. To compare changes in LVEF and LVEDD over time in the TA-TAVI and C-AVR groups, we included an interaction term (group \times time) in the GEE models. Crude and adjusted β coefficients with 95% confidence intervals (CIs) were reported to estimate the strength of the association between surgical strategy and LV functional recovery and remodeling outcomes. Statistical significance was defined as a two-sided *p* value of <0.05 was considered statistically significant. The statistical software used throughout the analysis was SPSS v.26.0 (IBM SPSS Inc., Armonk, NY) and R 4.0.1.

3. Results

A total of 87 cases were included in this study; 36 patients for TA-TAVI and 51 patients for C-AVR. A stented biological valve was implanted in 27 patients (52.9%) and a mechanical

valve in 24 patients (47.1%) in the C-AVR group. None of the patients crossed over from TA-TAVI to C-AVR. TA-TAVI patients demonstrated a similar incidence of hospital mortality as C-AVR patients (TA-TAVR, 5.6%; C-AVR, 15.7%; $p = 0.144$).

3.1. Baseline Characteristics. Baseline characteristics and comorbidities are shown in Table 1. The preoperative baseline characteristics were similar between the two patient groups, except for some characteristics of patients in the TA-TAVI group, including the older age of the patients in this group (73 (71–75.25) years vs. 64 (55.5–67) years, $p < 0.001$), the higher proportion of comorbid hypertensive disease (50.0% vs 25.5%, $p = 0.034$), the lower incidence rate in bicuspid aortic valve (8.3% vs 29.4%, $p = 0.034$), and the higher additive EuroScore (7 (6–9) vs 4 (2–5.5), $p < 0.001$). Two patients in the TA-AVR group and 3 patients in the SAVR group had a history of prior cardiac surgery. Out of these five patients, two in the TA-AVR group and two in the SAVR group had undergone conventional mitral mechanical valve replacement via an open sternotomy approach, and one had undergone ligation of patent ductus arteriosus via a left posterior sternotomy approach.

3.2. Comparison of Changes in EF and LVEDD Recovery between Two Groups. Table 2 and Figures 1(a) and 1(b) show the results of the groups at baseline, 1 week, and 3 months regarding LVEF and LVEDD over time. Table 3 shows that surgical strategy (TA-TAVI or C-AVR) had a significant influence on LV functional recovery and remodeling using GEE analysis. Following adjustment of baseline clinical characteristics, LVEF at 1 week and 3 months increased over baseline ($p < 0.001$ and $p < 0.001$, respectively) in the TA-TAVI group and showed greater improvement within the first 3 months postoperatively (adjusted β for treatment effect 0.002, 95% CI: 0.000 to 0.003, $p = 0.046$) compared with the C-AVR group. LVEDD at 1 week and 3 months decreased over baseline ($p < 0.001$ and $p < 0.001$, respectively) in the TA-TAVI group but showed greater decreases within the first 3 months postoperatively (adjusted $\beta = 0.330$, 95% CI: 0.185 to 0.474, $p < 0.001$) compared with the C-AVR group after covariate adjustment.

3.3. Change in NYHA Functional Class. Analysis showed that improvements in NYHA functional class over time from baseline were significant in both TA-TAVI and C-AVR groups ($\beta = 0.266$, 95% CI 0.187 to 0.345, and $p < 0.001$; $\beta = 0.421$, 95% CI 0.301 to 0.541, and $p < 0.001$, respectively) (as shown in Figure 1(c)). However, there was no significant between-group difference in changes in NYHA functional class within the first 3 months postoperatively between TA-TAVI and C-AVR groups after covariate adjustment (adjusted $\beta = 0.381$, 95% CI -0.349 to 1.111, and $p = 0.306$) (as shown in Table 3).

4. Discussion

In this study, we compared LV function recovery and remodeling after TA-TAVI with C-AVR in patients with AR and reduced LVEF. The most important finding of this study is that TA-TAVI was associated with better and faster recovery of LVEF and LVEDD within the first 3 months postoperatively compared with C-AVR, with the same improvement in NYHA function class.

LVEF is regarded as the most validated and commonly used echocardiographic method to assess LV systolic function and is the critical parameter used for cardiac surgical decision-making and assessment of prognosis [8]. AR leads to progressive LV enlargement and reduced LVEF over time. Previous studies have shown that reduced LVEF and enlarged LV are important prognostic indicators in aortic valve surgery [9]. Preoperative LV dysfunction (EF $< 60\%$) had a detrimental effect on overall survival after correction for chronic severe AR [10].

Patients with pure AR are more likely to be unable to undergo TAVI via the femoral approach due to the lack of effective anchor points resulting from factors such as frequent lack of valve calcification, so this study focuses on the comparison between transapical TAVI and conventional aortic valve replacement in patients with AR and reduced EF.

Studies on LV functional recovery and remodeling in patients with AR after TA-TAVI are scarce. D'Onofrio et al. discovered that LVEF improvements were not significant in 30 patients who underwent TA-TAVI [11]. In their study, patients had a preoperative EF of $57.0 \pm 10.3\%$; a finding which is higher than that in our study population. We found a significant improvement in LVEF after TA-TAVI in patients with preoperative LVEF less than 50%. This is consistent with several previous studies on transcatheter aortic valve implantation, which have reported that patients with poor preoperative LVEF are more likely to have significant LVEF improvement and that poor preoperative LVEF was an independent predictor of LVEF improvement [12–14].

Importantly, TA-TAVI remained a strong and independent predictor of LVEF recovery after adjusting for these baseline characteristics. Although TA-TAVI is also somewhat invasive, because it involves the opening of the chest wall and puncture and suture of the LV apex, ischemia/reperfusion injury, inflammatory response, myocardial infarction, surgical trauma, and oxidative stress associated with conventional open-heart surgery involving extracorporeal circulation are more likely to affect postoperative LVEF recovery due to myocardial cell contractile dysfunction [15, 16]. Patients with existing LV systolic dysfunction will be more severely affected in these aspects. By avoiding the effects of these factors, TA-TAVI can better protect and restore the myocardial function in high-risk patients. Another possible explanation for this difference is related to the effect of valve type on recovery of left ventricular function after surgery [17–19]. In our study, about 47.1% of patients in

TABLE 1: Comparison of patients' baseline demographic and clinical characteristics.

Variables ^a	Total sample (n = 87)	Patient groups		p value
		TA-TAVR (n = 36)	SAVR (n = 51)	
Age (yr)	68.0 (62.0–72.5)	73.0 (71.0–75.3)	64.0 (55.5–67.0)	<0.001
Male (n)	32	24	27	0.290
BMI (kg/m ²)	21.65 (19.21–24.40)	22.24 (19.23–25.14)	21.48 (19.19–23.64)	0.278
Smoking history (n)	24	12	12	0.445
Diabetes (n)	13	8	5	0.195
Hypertension (n)	37	18	13	0.034
Peripheral vascular disease	6	3	3	0.657
NYHA class (n)				
II	21	9	8	0.185
III	56	21	39	
IV	10	6	4	
AF (n)	13	7	6	0.494
Renal insufficiency (n)	8	5	3	0.203
Dialysis (n)	3	2	1	0.365
COPD (n)	9	5	2	0.092
Cancer history (n)	4	2	2	0.720
Lung cancer		2	1	
Thyroid cancer		0	1	
Stroke history (n)	28	5	4	0.952
CAD (n)	22	12	10	0.230
Prior MI (n)	5	3	2	0.383
Liver dysfunction (n)	8	5	3	0.203
Prior cardiac surgery (n)	5	2	3	0.949
LVEF (%)	43.70 (41.65–45.85)	43.35 (41.48–45.68)	44.40 (42.25–46.15)	0.278
LVEDD (mm)	70.70 (68.05–75.30)	69.95 (68.30–74.95)	70.80 (67.65–75.55)	0.945
BAV (n)	18	3	15	0.034
Additive Euroscore	6 (3–7)	7 (6–9)	4 (2–5.5)	<0.001

BMI, body mass index; NYHA, New York heart association; AF, atrial fibrillation; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; MI, myocardial infarction; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic dimension; BAV, bicuspid aortic valve. ^aNon-normally distributed variables are presented as median (interquartile range (IQR)) and categorical data as numbers.

TABLE 2: Changes in LVEF and LVEDD over time.

Variables ^a	Baseline	1 week	3 months	p value *	
				1 week vs baseline	3 months vs baseline
<i>No</i>					
Total	87	77	77		
TA-TAVR	36	34	34		
C-AVR	51	43	43		
<i>LVEF (%)</i>					
Total	43.70 (41.65–45.85)	46.20 (43.20–48.80)	53.4 (50.70–56.20)	<0.001	<0.001
TA-TAVR	43.35 (41.48–45.68)	48.65 (45.53–52.78)	54.55 (53.40–56.95)	<0.001	<0.001
C-AVR	44.40 (42.25–46.15)	45 (42.25–47.05)	52.7 (48.90–54.40)	0.630	<0.001
<i>LVEDD (mm)</i>					
Total	70.70 (68.05–75.30)	63.40 (58.40–67.30)	59.40 (55.80–63.70)	<0.001	<0.001
TA-TAVR	69.95 (68.30–74.95)	60.90 (55.42–65.48)	56.40 (53.10–60.00)	<0.001	<0.001
C-AVR	70.80 (67.65–75.55)	65.50 (60.45–68.20)	62.20 (58.60–66.35)	<0.001	<0.001

TA-TAVI, transcatheter aortic valve implantation; C-AVR, conventional aortic valve replacement; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic dimension. *Generalized estimating equation models were used. ^aNon-normally distributed variables are presented as median (interquartile range (IQR)) and categorical data as numbers.

the C-AVR group used mechanical valves. The valves used in TA-TAVI have a larger effective orifice area, better coronary flow, and lower transvalvular gradient than those used in C-AVR. Better valve hemodynamic performance associated with TA-TAVI may contribute to a better recovery of LV function in high-risk patients with severe AR and reduced

LVEF. However, few studies have been reported in this area, and the explanation of superiority is speculative and needs to be confirmed in future studies.

Chaliki et al. reported that patients with significantly reduced LV function experienced LV reverse remodeling after AVR surgery [14]. Other studies have shown that the

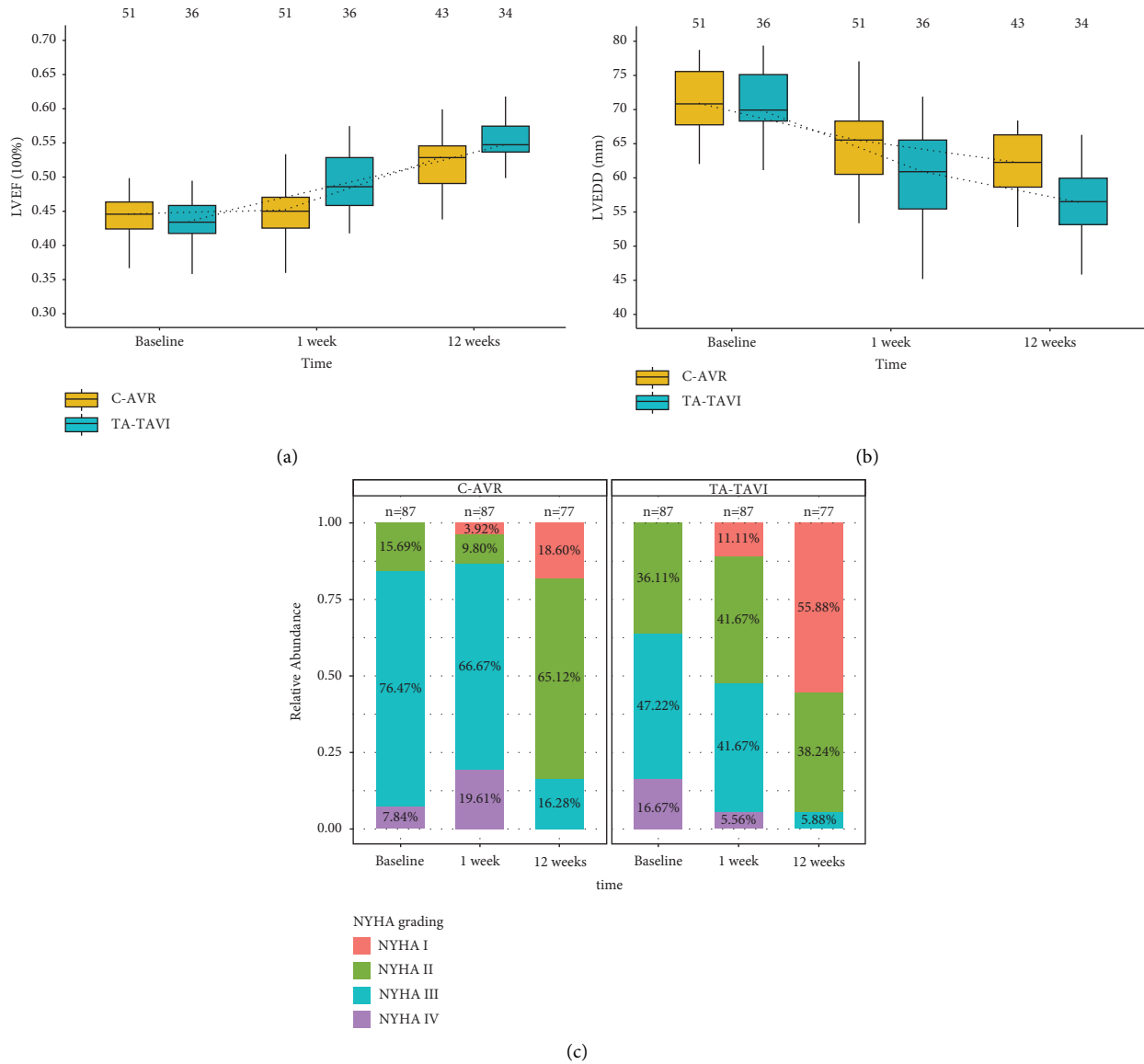


FIGURE 1: LVEF, LVEDD, and NYHA grading of the two groups at baseline and follow-up. (a) Median (interquartile range) of LVEF of the two groups at baseline and follow-up. (b) Median (interquartile range) of LVEDD of the two groups at baseline and follow-up. (c) Comparison of the proportion of patients in the different subclasses of NYHA function of the two groups at baseline and follow-up. TA-TAVI, transcatheter aortic valve implantation; C-AVR, conventional aortic valve replacement; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic dimension; and NYHA, New York heart association.

TABLE 3: The effect of surgical strategy (TA-TAVI of C-AVR) on LVEF, LVEDD, and NYHA class using GEE models.

Variables	Crude		Adjusted	
	β (95% CI)	<i>p</i> value	β (95% CI)	<i>p</i> value
<i>LVEF</i>				
Surgical strategy ^a	0.002 (0.000 to 0.003)	0.038	0.002 (0.000 to 0.003)	0.046
<i>LVEDD</i>				
Surgical strategy ^b	0.326 (0.182 to 0.470)	<0.001	0.330 (0.185 to 0.474)	<0.001

TABLE 3: Continued.

Variables	Crude		Adjusted	
	β (95% CI)	<i>p</i> value	β (95% CI)	<i>p</i> value
<i>NYHA class</i>				
Surgical strategy ^c	0.468 (−0.124 to 1.060)	0.120	0.381 (−0.349 to 1.111)	0.306

TA-TAVI, transapical transcatheter aortic valve implantation; C-AVR, conventional aortic valve replacement; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic dimension; NYHA, New York Heart Association; GEE, generalized estimating equations; CI, confidence interval. ^aBaseline covariates in the final adjusted GEE model: age, sex, body mass index, smoking history, diabetes, hypertension, peripheral vascular disease, NYHA class, atrial fibrillation, renal insufficiency, dialysis, cancer history, stroke history, coronary artery disease, prior myocardial infarction, liver dysfunction, prior cardiac surgery, LVEDD, bicuspid aortic valve, and additive EuroScore. ^bBaseline covariates in the final adjusted GEE model: age, sex, body mass index, smoking history, diabetes, hypertension, peripheral vascular disease, NYHA class, atrial fibrillation, renal insufficiency, dialysis, cancer history, stroke history, coronary artery disease, prior myocardial infarction, liver dysfunction, prior cardiac surgery, LVEF, bicuspid aortic valve, and additive EuroScore. ^cBaseline covariates in the final adjusted GEE model: age, sex, body mass index, smoking history, diabetes, hypertension, peripheral vascular disease, atrial fibrillation, renal insufficiency, dialysis, cancer history, stroke history, coronary artery disease, prior myocardial infarction, liver dysfunction, prior cardiac surgery, LVEF, LVEDD, bicuspid aortic valve, and additive EuroScore.

improvement of LVEF after AR is not only related to the reduction of pressure and volume load but also to LV remodeling. Our study demonstrated that LV reverse remodeling may occur in parallel with improvement in LV systolic function in both the TA-TAVI and C-AVR groups of patients. In one study, Zhang et al. reported that preoperative LVEF influences the early recovery of LVEDD after aortic valve replacement in patients with chronic severe aortic regurgitation [20]. Therefore, the observation that LVEDD recovered better and faster than C-AVR within 3 months after TA-TAVI in our study population seems encouraging. Our findings add to the limited literature on postoperative LV reverse remodeling in this subgroup of patients.

It is worth emphasizing that the evaluation of LV function by Doppler echocardiography at rest may not reflect the status of valvular hemodynamics and cardiac function in patients' daily activities. Therefore, in our study, we further observed improvements in the NYHA functional class during follow-up. There was no significant difference between TA-TAVI and C-AVR in the improvement of the postoperative NYHA functional class in this subgroup of patients.

No clinical trials have been conducted to determine the optimal surgical treatment for AR with reduced EF. Our results may be helpful for clinicians in selecting the surgical modalities for this subgroup of patients. Considering that most ARs lack calcium anchoring, TA-TAVR is the most mature alternative approach when the transfemoral approach is not feasible and is more likely to be an option for high-risk AR patients. Understanding the impact of different techniques on LV functional recovery will help inform treatment decisions. Baseline LV systolic dysfunction has also been associated with mortality after C-AVR and TA-TAVR; moreover, patients with poor recovery of left ventricular function generally have a higher risk of postoperative clinical events, including a higher mortality rate and a tendency for heart failure-related hospitalization. In patients with AR and low LV systolic function, the heart team must decide whether to assign the patient to TA-TAVR or C-AVR, thus requiring preoperative risk assessment. At our center, we used the EuroScore system to quantify risk, which may overestimate the risk of surgery based on relevant

studies [21]. The more reliable EuroScore II or Society of Thoracic Surgeons (STS) score can be applied in future studies.

The present analysis has some limitations. First, it was a single-center retrospective study with a small sample size. Our findings may not be generalizable to subgroups of patients treated in other institutions. Second, echocardiographic data were obtained from a single-center using a standardized echocardiographic data collection protocol. LVEF is a simple measure of global systolic function that is unsatisfactory in terms of reliability and accuracy. Future studies may provide more insight into the field by using more sensitive parameters, such as global longitudinal strain and strain rate [22, 23], to understand the pathology and assess the likely benefit to be gained from TA-TAVI. Third, we included patients with coronary artery disease to maximize the sample size. Some studies have shown that a history of myocardial infarction can cause LV dysfunction. It is necessary to exclude patients with coronary artery disease in future studies assessing the recovery of LV function after TA-TAVI to prevent this confusion in patients with isolated severe AR with reduced LVEF. Future studies should further investigate the effects of factors such as frailty, obesity, and chronic obstructive pulmonary disease [24, 25].

5. Conclusions

This study highlights a subgroup of patients with chronic AR with reduced LVEF who had better and faster recovery of LVEF and LVEDD within the first 3 months postoperatively than those with C-AVR, with the same improvement in NYHA function class. However, future randomized controlled prospective clinical trials with a longer follow-up duration comparing the impact of TA-TAVI and C-AVR on LV functional recovery and remodeling are needed in patients with AR and reduced LVEF.

Data Availability

All data generated or analyzed during this study are included in this published article.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Zhiqin Lin conceptualized/designed the study, drafted the article, approved the article, and provided the statistics. Xiaofu Dai critically revised the article, approved the article, provided the statistics, secured the funding, and collected the data. Liangwan Chen critically revised the article, approved the article, provided the statistics, secured the funding, and collected the data. Zhiqin Lin and Zheng Xu contributed equally to this study and share first authorship.

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