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Article

Clinical Outcomes of Systemic Tricuspid Valve Replacement in Adult Patients With Congenitally Corrected Transposition of Great Arteries

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Abstract

Background: Congenitally corrected transposition of great arteries (ccTGA), a rare congenital heart disease, is generally asymptomatic during infancy and childhood but can lead to dysfunction of the morphologic right ventricle (mRV) and severe insufficiency of the systemic tricuspid valve (sTV) in adulthood if left untreated. This study aims to evaluate clinical outcomes of systemic tricuspid valve replacement (sTVR) in adult patients with ccTGA. **Methods:** A total of 18 patients who underwent sTVR at Guangdong Provincial People's Hospital between Jun 2009 and Sept 2024 were enrolled in this retrospective analysis. Comprehensive clinical data spanning perioperative evaluation through postoperative follow-up were analyzed. All patients experienced a smooth surgery and recovery, and had a median follow-up duration of 35.7 (17.0, 78.1) months. **Results:** The cohort comprised 12 males and 6 females, with a mean age of 34.5 ± 12.9 years, median height of 165.0 (157.3, 170.0) cm, and mean weight of 55.9 ± 14.0 kg. 13 patients were implanted with an On-X mechanical valve and the remaining received a St Jude Regent (SJR) mechanical valve. Three patients with the On-X developed newly occurring third-degree atrioventricular block (AVB) and accepted permanent pacemaker implantation. One patient underwent heart transplantation owing to heart failure at 63.5 months and two patients with SJR underwent redo tricuspid replacement as a result of prosthetic thrombosis at 63.4 and 131.6 months after the surgery. The remaining patients had no adverse events during follow-up. Mid-term follow-up of echocardiography revealed a significant decrease in right atrial diameter (RAD) (p = 0.034), mRV ejection fraction (mRVEF) (p = 0.018) and morphologic mitral regurgitation index (MRI) at 3 years post-surgery (p = 0.045) and a steady promotion of aortic flow velocity (AFV) ($p < 0.05$). **Conclusions:** sTVR is an effective option to address the severe left-sided atrioventricular regurgitation for ccTGA with preserved mRVEF but fails to prevent deterioration of systemic ventricular dysfunction. The On-X mechanical valve suggests a potential trend to avoid prosthetic thrombosis but there was an underlying trend toward third-degree AVB and the necessity for permanent cardiac pacing rather than the SJR.

Keywords: congenitally corrected transposition of great arteries; systemic tricuspid valve replacement; clinical outcomes; adult patients; On-X; St Jude Regent

1. Introduction

Congenitally corrected transposition of great arteries (ccTGA) is a rare congenital cardiac malformation with an incidence of 1 in 33,000 live births, constituting 0.5% of all the congenital heart defects [1]. It features both ventriculo-arterial and atrioventricular discordance, where the morphologic right ventricle (mRV) functions as the systemic ventricle while the tricuspid valve serves as the left-sided atrioventricular valve. Patients without major associated lesions, such as large ventricular septal defects, critical left ventricular outflow tract obstruction, Ebstein anomaly or third-degree atrioventricular block (AVB), are generally asymptomatic for years or decades and may not present with left-sided ventricular failure until adolescence or later. Surgical therapies for ccTGA include expectant management, anatomical repair, physiological repair, Fontan palliation, primary heart transplantation, or implantable cardiac electronic device therapy in rare circumstances [2]. The treatment of ccTGA in adults is challenging, with more limited options compared with pediatric patients [3]. Despite the gloomy long-term outcomes, physiological repair remains the optimal choice for symptomatic or asymptomatic adult patients with progressive systemic ventricular dysfunction without correction of discordant connections, where mRV

remains the systemic pumping chamber [4,5,6]. Isolated systemic tricuspid valve replacement (sTVR), as a major option of physiological repair, and is generally adopted in the presence of severe tricuspid regurgitation (TR), progressive mRV dilation and preserved mRV ejection fraction (mRVEF) >40% [6]. In this study, we aimed to evaluate the clinical outcomes of sTVR in a single-center cohort of ccTGA patients to analyze the possible mechanisms.

2. Materials and Methods

2.1 Study Population and Design

This study retrospectively analyzed the clinical data of 18 adult patients diagnosed with ccTGA who underwent sTVR at Guangdong Provincial People's Hospital between June 2009 and September 2024. Comprehensive perioperative and follow-up data were systematically collected and analyzed, including baseline characteristics, surgical details, postoperative courses, echocardiogram and electrocardiogram measurements, and mid-term follow-up results. A self-control design was adopted to compare involved items before and after surgery and to evaluate the efficacy of surgery. Follow-up was discontinued upon the occurrence of an endpoint event, such as death, reoperation or heart transplantation. Patients investigated had to meet the following selection criteria: (1) aged over 18 years old; (2) with severe systemic TR and preserved or mildly impaired systemic ventricular systolic function (mRVEF ≥40%); (3) isolated ccTGA not accompanied by other major malformations such as functionally univentricular heart, severe pulmonary stenosis or double outlet right ventricle. The study was approved by the Ethics Committee of Guangdong Provincial People's Hospital (Grant number: GDREC2019324H).

2.2 Surgical Methods

All patients underwent surgery via median sternotomy, under standardized general anesthesia with double-lumen endotracheal intubation to deliver double-lung ventilation. Arrested-heart valve surgeries were carried out under mild hypothermic cardiopulmonary bypass (CPB) (28–32 ℃) in all patients, which was realized by administration of Del Nido or histidine-tryptophan-ketoglutarate (HTK) cardioplegia (Dr. Franz Köhler Chemie GmbH, Bensheim, HE, GER). Concomitant procedures included closure of patent foramen ovale, atrial septal defect, and ventricular septal defect. Types of prosthetic devices were On-X (Artivion, Inc., Kennesaw, GA, USA) and St. Jude Regent (SJR) (Abbott Laboratories, Chicago, IL, USA) mechanical valves and Assurity MRI PM1272/1282/2722 (Abbott Laboratories, Chicago, IL, USA) permanent pacemakers.

2.3 Data Collection and Follow-Up

The study evaluated comprehensive outcome measures across multiple domains:

(1) baseline characteristics: including gender, age, height, weight, body mass index (BMI), body surface area (BSA), accompanying lesions, imaging data, and New York Heart Association (NYHA) classification;

(2) surgical details: including operation duration, CPB duration, aortic cross-clamp (ACC) duration, management of coexisting lesions, and types of mechanical valve;

(3) postoperative courses: including intensive care unit (ICU) length of stay, mechanical ventilation time (MVT), hospitalization duration, thoracic drainage duration (TDD), adverse events such as re-thoracotomy and pacemaker implantation;

(4) echocardiographic measurements: including mRVEF, including cardiac chamber dimensions, valvular flow velocities, status of morphologic mitral valve. Mitral regurgitant index (MRI) was defined as the ratio between mitral regurgitant area (MRA) and BSA.

The 18 patients were followed for a median of 35.7 (17.0, 78.1) months, which was conducted by phone interview and retrieval of information from the hospital database.

2.4 Statistical Analysis

Statistical analyses and graphing were performed using IBM SPSS Statistics 28.0 (IBM Corp., Armonk, NY, USA) and GraphPad Prism 9.5 (Dotmatics, San Diego, CA, USA).

For quantitative variables, normality was assessed using the Shapiro-Wilk test. Data conforming to a normal distribution were presented as the mean ± standard deviation ($\bar{x} \pm s$), and the intergroup comparison was conducted using the paired sample *t*-test. For the non-normally distributed variables, data were expressed as a median and interquartile range (IQR), and differences between the groups were assessed using the Mann-Whitney U test. Categorical data were presented as frequencies and percentages. A p-value < 0.05 was considered statistically significant.

3. Results

In terms of baseline characteristics, the Mcgoon ratio and Nakata index of the cohort were both within normal range, indicating good development of pulmonary vasculature. Electrocardiograms revealed three patients with atrial fibrillation and one patient with third-degree AVB. Four individuals were classified as moderate or severe pulmonary arterial hypertension according to the pulmonary arterial pressure (PAP) estimated by echocardiography. Cardiac function was evaluated at a median level of NYHA class III (Table 1).

At surgery, there was a median operation duration of 251.0 (238.8, 360.0) minutes, a CPB duration of 140.5 (112.8, 205.8) minutes, and an ACC duration of 72.5 (59.3, 113.0) minutes. 13 patients were implanted with an On-X 29/33 mm, while 5 patients' valves were replaced with SJR 25/27 mm. Every patient experienced routine postoperative

Table 1. Baseline characteristics.

Variable	n = 18
Female gender	6 (33.3)
Age (year)	34.5 ± 12.9
Height (cm)	165.0 (157.3, 170.0)
Weight (kg)	55.6 ± 13.3
BMI (kg/m^2)	20.8 ± 3.5
BSA (m^2)	1.55 ± 0.22
Smoke	6 (33.3)
Hyperlipidemia	3 (16.7)
McGoon ratio	2.71 ± 0.61
Nakata index (mm^2/m^2)	601.50 ± 278.18
Dextrocardia	6 (33.3)
Situs inversus	2 (11.1)
Atrial fibrillation	3 (16.7)
Third-degree AVB	1 (5.6)
Previous heart surgery	2 (11.1)
Moderate/severe PAH	4 (22.2)
PAP (mmHg)	32.5 (22.5, 41.0)
SpO_2 (%)	99.5 (98.0, 100.0)
NYHA classification	3.0 (2.0, 3.0)

Abbreviation: BMI, body mass index; BSA, body surface area; AVB, atrioventricular block; PAH, pulmonary arterial hypertension; PAP, pulmonary arterial pressure; SpO_2, peripheral capillary oxygen saturation; NYHA, New York Heart Association.

Table 2. Surgical details, postoperative courses and follow-up outcomes.

Parameters	n = 18
Surgical details	
Operation duration (min)	251.0 (238.8, 360.0)
CPB duration (min)	140.5 (112.8, 205.8)
ACC duration (min)	72.5 (59.3, 113.0)
On-X prosthetic valve	13 (72.2)
Preservation of TV	13 (72.2)
Preservation of ASD/PFO	5 (27.8)
Postoperative courses	
ICU stay (h)	44.3 (39.4, 74.3)
MVD (h)	14.0 (6.5, 21.2)
TDD (h)	82.3 (56.4, 98.0)
Hospitalization (h)	148.4 (134.3, 238.5)
Re-thoracotomy	2 (11.1)
ECMO	1 (5.6)
Implantation of pacemaker	4 (22.2)
Follow-up outcomes	
Free of endpoint events	15 (83.3)
Heart failure	1 (5.6)
Dysfunction of prosthetic valve	2 (11.1)

Abbreviations: CPB, cardiopulmonary bypass; ACC, aortic cross-clamp; TV, tricuspid valvuloplasty; ASD, atrial septal defect; PFO, patent foramen ovale; ICU, intensive care unit; MVD, mechanical ventilation duration; TDD, thoracic drainage duration; ECMO, extracorporeal membrane oxygenation.

care, with a median ICU stay of 44.3 (39.4, 74.3) hours, mechanical ventilation duration (MVD) of 14.0 (6.5, 21.2) hours, and hospitalization length of 148.4 (134.3, 238.5) hours. Two patients underwent re-thoracotomy for constantly increased thoracic drainage, one received extracorporeal membrane oxygenation as a result of low cardiac output syndrome, and four were implanted with a permanent pacemaker, with three newly occurring and one previously existing complete AVB. At follow-up, one case of heart transplantation due to heart failure and two cases of re-operation due to thrombosis of a prosthetic valve were observed (Tables 2,3).

Mid-term follow-up using echocardiography showed a significant decrease in right atrial diameter (RAD) (p = 0.034), mRVEF (p = 0.018) and MRI at 3 years post-surgery (p = 0.045) and a steady promotion of aortic flow velocity (AFV) ($p < 0.05$). Notably, several items presented no statistical significance ($p > 0.05$) but could be regarded as remarkable variation, including mRVEF (p = 0.068), mRV end-diastolic diameter (mRVEDD) (p = 0.056), morphologic left ventricular end-diastolic diameter (mLVEDD) (p = 0.061), and MRA (p = 0.053) 3 years postoperatively. No significance between pre- and postoperative electrocardiography was observed ($p > 0.05$) except for QRS complex (QRS) width 6 months post-surgery ($p < 0.001$) (Table 4, Figs. 1,2).

4. Discussion

This study evaluated the early and mid-term outcomes of sTVR for isolated ccTGA in adult patients. Postoperative results confirmed the surgery efficacy in terms of correcting severe TR and enlarged size of heart, while 3-year follow-up revealed the progressive reduction of mRVEF. Types of prosthetic valves might have an influence on the postoperative outcomes as well.

Optimal surgical management of patients with ccTGA and associated lesions remains controversial. Physiological repair has been a valid option for decades, but concerns about the long-term mRV dysfunction and systemic tricuspid valve insufficiency promoted the advent of anatomic repair, which restores the morphological left ventricle (mLV) into the systemic circulation via double switch operation [7,8]. Although several research studies report better short-term outcomes of anatomic repair, long-term survival rates were not always superior to those of physiological repair, especially for older patients or those with ccTGA and pulmonary stenosis [5,9,10,11]. Tricuspid replacement is a representative procedure of physiological repair and has proven successful in correcting tricuspid regurgitation and resulting in good outcomes [4,12].

Table 3. Partial outcomes of the cohort.

No.	Age (y)	Associated lesion	Dextrocardia	Surgical option	Prosthetic valve type	Preservation of TV	Permanent pacemaker	Newly occurring third-degree AVB	Follow-up (month)	Status
1	40.0	VSD	N	sTVR+VSD	On-X 33 mm	N	N	N	17.0	Survival
2	41.3	N	Y	sTVR	On-X 33 mm	Y	Y	Y	24.0	Survival
3	23.6	PFO+mMR	N	sTVR+PFO	On-X 33 mm	Y	N	N	10.5	Survival
4	25.8	mMR	Y	sTVR	On-X 33 mm	Y	N	N	10.5	Survival
5	45.2	mMR	N	sTVR	On-X 33 mm	Y	Y	Y	11.0	Survival
6	27.1	mMR	N	sTVR	On-X 33 mm	Y	N	N	17.0	Survival
7	59.9	ASD+mMR	N	sTVR+ASD	On-X 29 mm	Y	N	N	28.5	Survival
8	50.0	mMR	N	sTVR	On-X 33 mm	N	N	N	35.0	Survival
9	28.1	ASD+VSD	N	sTVR+VSD	On-X 33 mm	Y	N	N	36.3	Survival
10	20.7	mMR	N	sTVR	On-X 33 mm	Y	N	N	48.6	Survival
11	55.8	mMR	N	sTVR	On-X 33 mm	N	N	N	34.0	Survival
12	19.9	VSD	Y	sTVR+VSD	On-X 33 mm	Y	Y	Y	54.3	Survival
13	42.8	PFO+mMR	N	sTVR+PFO	St Jude 25 mm	Y	N	N	63.4	Thrombosis
14	19.0	PFO+mMR	N	sTVR+PFO	St Jude 25 mm	Y	N	N	103.0	Survival
15	40.0	mMR	Y	sTVR	St Jude 27 mm	Y	N	N	126.5	Survival
16	33.2	ASD+VSD	Y	sTVR+VSD	St Jude 27 mm	N	N	N	131.6	Thrombosis
17	30.0	mMR	N	sTVR	On-X 33 mm	Y	N	N	96.7	Survival
18	18.8	mMR	Y	sTVR	St Jude 25 mm	N	Y	N	63.5	HF

Abbreviations: N, no; Y, yes; VSD, ventricular septal defect; sTVR, systemic tricuspid valve replacement; PFO, patent foramen ovale; mMR, morphologic mitral regurgitation; ASD, atrial septal defect; HF, heart failure.

Table 4. Pre- and postoperative echocardiographic and electrocardiographic measurements.

Measurements	Pre-surgery	Discharge	*p*-value	6-month follow-up	*p*-value	Latest follow-up	*p*-value
mRVEF (%)	55.2 ± 9.5	50.6 ± 13.4	0.240	47.2 ± 13.7	0.068	45.3 ± 11.8	0.018*
mRVEDD (mm)	61.1 ± 10.5	58.1 ± 10.7	0.410	56.5 ± 6.2	0.218	52.5 ± 12.5	0.056
mRVESD (mm)	44.7 ± 11.1	43.1 ± 11.5	0.678	43.2 ± 7.7	0.720	38.4 ± 13.0	0.187
LAD (mm)	54.8 ± 13.4	48.7 ± 17.7	0.260	50.3 ± 8.9	0.349	46.6 ± 16.5	0.155
mLVEDD (mm)	45.5 ± 11.2	50.3 ± 12.5	0.251	52.0 ± 7.8	0.116	53.8 ± 11.1	0.061
RAD (mm)	41.5 (37.5, 46.0)	41.3 ± 7.5	0.822	44.9 ± 12.9	0.752	38.0 (35.8, 39.5)	0.034*
AAO (mm)	27.1 ± 3.8	26.4 ± 5.1	0.699	24.7 ± 3.1	0.194	25.7 ± 3.3	0.446
MPA (mm)	24.9 ± 5.7	23.9 ± 4.1	0.582	22.4 ± 4.0	0.232	22.0 ± 2.9	0.083
PFV (m/s)	1.04 (0.79, 2.73)	1.04 (0.79, 2.73)	0.390	0.99 (0.80, 1.20)	1.000	0.87 (0.83, 1.20)	0.770
AFV (m/s)	0.84 ± 0.22	1.00 (0.82, 1.30)	0.014*	1.00 (0.95, 1.20)	0.006*	1.08 ± 0.25	0.004*
TFV (m/s)	0.74 (0.65, 0.91)	0.85 (0.67, 1.50)	0.105	0.77 (0.60, 0.80)	0.689	0.94 ± 0.35	0.187
MFV (m/s)	0.67 (0.60, 0.85)	0.66 ± 0.20	0.193	0.63 (0.57, 1.10)	0.524	0.67 (0.55, 0.75)	0.540
MRA (cm^2)	1.75 ± 1.70	1.61 ± 1.36	0.782	0 (0, 1.70)	0.091	0 (0, 1.45)	0.053
MRI (cm^2/m^2)	1.19 ± 1.15	1.09 ± 0.92	0.772	0 (0, 1.02)	0.082	0 (0, 0.96)	0.045*
P wave (ms)	75.8 ± 30.4	85.0 (76.5, 92.0)	0.348	92.6 ± 16.9	0.076	88.1 ± 26.8	0.284
QRS (ms)	109.6 ± 26.3	102.0 (92.0, 113.5)	0.885	157.1 ± 30.4	<0.001*	109.7 ± 17.3	0.987
PR (ms)	166.6 ± 32.3	171.6 ± 39.3	0.690	163.6 ± 22.5	0.799	165.5 ± 24.4	0.922
QTc (ms)	437.0 (427.0, 465.0)	445.8 ± 36.4	0.759	429.8 ± 28.5	0.238	441.7 ± 30.1	0.556

Note: * indicates $p < 0.05$. Abbreviations: mRVEF, morphologic right ventricular ejection fraction; mRVEDD, morphologic right ventricular end-diastolic diameter; mRVESD, morphologic right ventricular end-systolic diameter; LAD, left atrial diameter; mLVEDD, morphologic left ventricular end-diastolic diameter; RAD, right atrial diameter; AAO, ascending aorta; MPA, main pulmonary artery; PFV, pulmonary flow velocity; AFV, aortic flow velocity; TFV, tricuspid flow velocity; MFV, mitral flow velocity; MRA, mitral regurgitant area; MRI, mitral regurgitant index; QRS, QRS complex; PR, PR interval; QTc, corrected QT interval.

Postoperative echocardiography revealed a considerable shrink of mRV but an enlargement of mLV at end-diastole, confirming that resolving TR can effectively reduce the preload of the systemic ventricle. A remarkable acceleration of blood flow velocity at the aortic valve indicated sufficient blood flow for systemic circulation. The

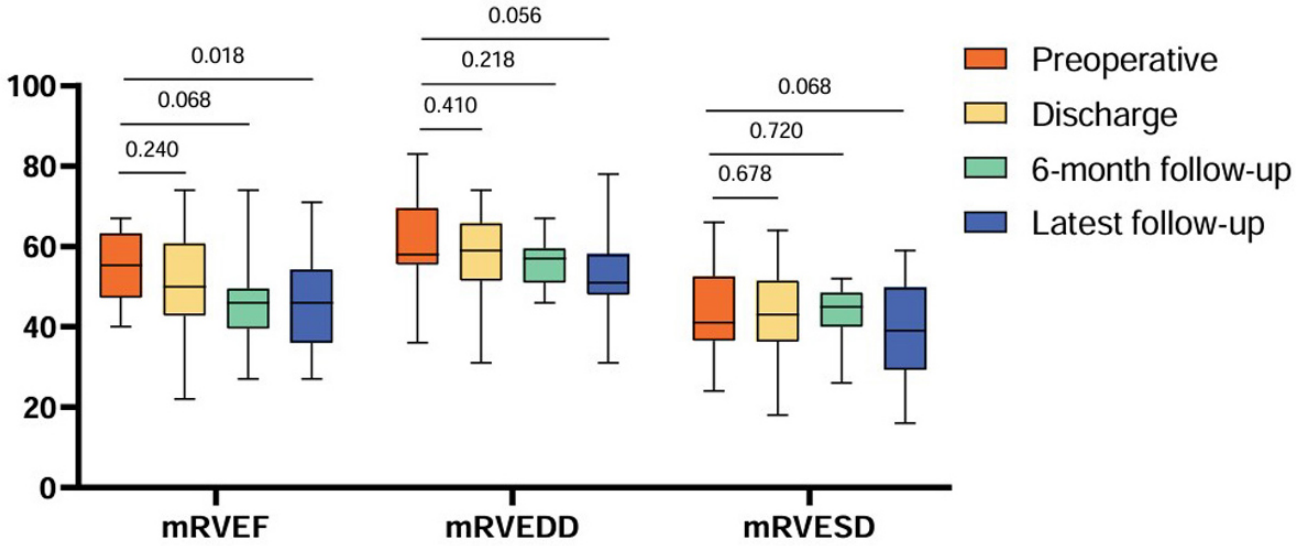

Fig. 1. Pre- and postoperative echocardiographic measurements of mRV. mRVEF at 3-year follow-up showed a significant reduction compared with pre-surgery. mRVEF at 6-month follow-up, mRVEDD and mRVESD at 3-year follow-up could also be supposed a remarkable decrease.

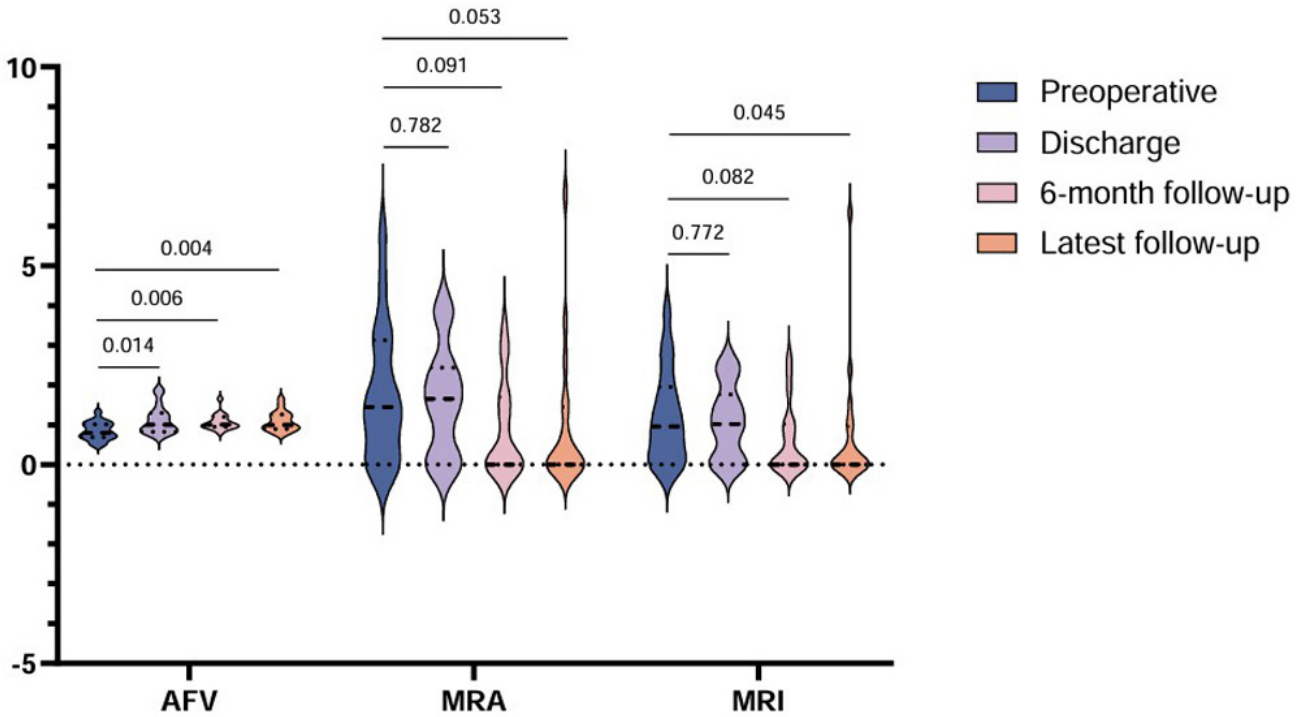

Fig. 2. Pre- and postoperative echocardiographic measurements of mitral and aortic valves. AFV presented a steady increase after surgery. Mitral valve regurgitation witnessed a considerable amelioration without being addressed.

underlying mechanism lies in the effective management of severe systemic TR, which augments forward blood flow during systole and elevates the velocity at the aortic annulus. Although not addressed during the surgery, mitral valve regurgitation at mid-term follow-up presented a significant reduction in comparison with the preoperative condition, especially in terms of MRI. It is supposed that diminishment of abnormal flow within systemic circulation ameliorated the pulmonary congestion, improved the overall function of the right-sided ventricle and morphological mitral valve, thus reducing the size of the right atrium. The constant decrease in mRVEF during the follow-up indicated that isolated sTVR for ccTGA with severe TR doesn't prevent the deterioration of mRV function. A consistent finding from previous research supported this discovery and indicated the discouraging long-term results [4,5]. It is be-

lieved that the inherent vulnerability of mRV as a systemic ventricle might account for the progressive deterioration of mRVEF. Major causes for the dysfunction include ventricular remodeling such as myocardial hypertrophy, reduced compliance and heart enlargement, as a result of inappropriate systemic pressure load applied to the mRV, and insufficient blood supply delivered by the small right coronary artery [13]. Secondary systemic TR also contributes to the excessive volume load for mRV without prompt intervention [2]. Isolated sTVR only ameliorates the tricuspid reflux, with other inherent risk factors left untreated. The tendency might predict a worse outcome as the follow-up continues.

On-X and SJR prostheses are both common bileaflet mechanical heart valves with decades of proven clinical practice [14]. Previous studies have revealed an equal performance between the two products in the mitral position regarding long-term outcomes and adverse events rate [15,16]. On-X valve yielded better hemodynamic performance such as flow velocity fields, pressure gradient, effective orifice area and turbulent shear stresses confirmed by *in-vitro* assessment, and had been recommended a low-density anticoagulation therapy that allows patients after 3 months from implantation to be managed at an international normalized ratio level of 1.5 to 2.0 that is closer to unmedicated level, in contrast to the SJR with a potential risk of valvular thrombosis [14,17,18,19]. Probable reasons might be the tactful designs of the On-X valve that avoid major turbulence, which include intra–supranuclear valve position, pannus overgrowth protection, larger orifice length, flexible pivot, bigger leaflet angle and two-point closing geometry, as well as less thrombotic material of pure pyrolytic carbon compared with silicon-alloyed ones of SJR [15]. This helped explain the outcome that two out of five cases fitted with a SJR valve presented with thrombosis due to inadequate anticoagulation while all the On-X prostheses worked within ideal conditions. However, three patients who developed newly occurring third-degree AVB exclusively received implantation of the On-X valve. It is thought that the oversized sewing ring in the systemic tricuspid position could contribute to suppression of the atrioventricular node or other conduction tissues.

According to the guidelines issued by the European Society of Cardiology in 2020, patients with PAP >50 mmHg, atrial fibrillation, and NYHA class III to IV are a highly predisposed population to late mortality [20]. However, no adverse event was observed to be associated with these risk factors in the cohort. It is suggested that a longer follow-up should be carried out to recognize the potential risk and take prompt preventive measures.

Major limitations included inadequate sample size and length of the follow-up period. The small cohort scale weakened the reliability of conclusions and failed to group participants to be able to seek the relationship between mechanical valve types and incidence of AVB and thrombosis. A 3-year follow-up might omit upcoming postoperative events that are vital to this study.

Limitation

As a single-center study on a rare congenital heart disease, the limited sample is the major deficiency of this research, which probably leads to coincidences of the results and unreliability of our conclusion. A lack of an adequate follow-up period might result in the missed possible adverse events, including deaths, thrombosis, or reoperations. A multi-center, prospective study is warranted to eliminate these biases and provide strong evidence to support or withdraw the current conclusions.

5. Conclusions

Isolated sTVR is an effective option to address the severe left-sided atrioventricular regurgitation, enlarged size of cardiac chambers and insufficiency of forward blood in the systemic circulation. But the dysfunction of mRV deteriorates as the patients have a longer survival period. In this circumstance, the On-X mechanical valve presents a potential trend to avoid thrombosis of the prosthesis but a greater tendency to bring complete AVB, resulting in the need for permanent pacemaker implantation compared to SJR.

Availability of Data and Materials

The data involved in this study are available from the corresponding author upon reasonable request.

Author Contributions

The interpretation of data for the work and reviewing the initial manuscript, SW and XL; Conceptualization, YF and HY; methodology, HY and YF; software and analysis, YF and XW; investigation, HX, JT, ZY, ZL and JL; data resources, XW and YH; writing—original draft preparation, YF; writing—review and editing, HY; visualization, YF and HY; supervision, SW and XL; funding acquisition, HY. All authors participated in revising the manuscript. All authors reviewed the results and approved the final version of the manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was carried out in accordance with the guidelines of the Declaration of Helsinki and was approved by the Ethics Committee of Guangdong Provincial People's Hospital (Grant number: GDREC2019324H). All patients included in the study were informed about the operation, perioperative procedures, and written consents of study participants were taken.

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Conflicts of Interest

The authors declare no conflicts of interest.

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