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Serial assessment of postoperative ventricular mechanics in young children with tetralogy of Fallot: Comparison of transannular patch and valve-sparing repair

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Abstract

Background: Little is known about the early time course of biventricular function and mechanics after tetralogy of Fallot (TOF) repair. We sought to evaluate and describe the evolution of the right ventricle (RV) after TOF repair in young infants and children using conventional echocardiographic parameters and global longitudinal strain (GLS).

Methods: A retrospective review was performed of all patients with TOF and pulmonary stenosis who underwent repair from January 2002 to September 2015 and had at least 3 serial postsurgical echocardiograms spanning from infancy to early childhood (<8 years). Student's t test was performed to compare patients who underwent valve sparing (VS) versus transannular patch (TAP) repair. ANOVA was used to track measures of ventricular systolic function over time.

Results: We analyzed 151 echocardiograms performed on 42 patients. Pulmonary regurgitation (PR, moderate or severe) and the RV to left ventricular (LV) basal dimension ratio were higher in TAP patients ($P < .04$ at all-time points). Along with a significant increase in RV basal diameter *Z*-score in the TAP group ($P < .001$), there was an improvement in RV and LV GLS over time in both groups ($P < .001$). The LV GLS at last follow-up was lower in patients who underwent reoperation than those who did not ($P = .050$). LV GLS at the last follow-up echocardiogram was lower in patients with significant PR than those without ($P < .001$).

Conclusions: Ventricular function appeared improve over time from the initial postoperative period in TOF patients. TAP repair was associated with a progressively higher RV/LV ratio in young children. GLS and RV/LV basal diameter ratio may be useful when following young children after TOF repair. Further research is necessary to understand the trajectory of ventricular functional and volumetric changes in young children in order to provide the most effective lifetime management of patients with TOF.

KEYWORDS

pulmonary regurgitation, right ventricle, speckle-tracking strain, tetralogy of Fallot repair

1 | INTRODUCTION

There has been substantial research on the implications and impact of right ventricular (RV) dilation and dysfunction due to pulmonary regurgitation (PR) in patients with repaired tetralogy of Fallot (TOF), with most studies focusing on young adults. Although pulmonary valve replacement (PVR) facilitates some degree of reverse RV remodeling, RV function does not completely normalize.[1,2] Controversy remains regarding the appropriate timing of PVR given the mixed data regarding long-term morbidity and mortality.[2,3] Ideally, deciding when to implant a pulmonary valve in patients with PR will be based on a global understanding of how RV function and remodeling evolve after repair, and whether there is a critical transition point. However, very little is known about the longitudinal early time course of biventricular function, mechanics, and volumes after repair. In a recent study using serial cardiac magnetic resonance imaging (CMR), Lindsey et al. reported moderate or severe RV dilation and impaired RV or left ventricular (LV) systolic function in preadolescent TOF patients who had undergone surgical repair.[4] Otherwise, studies in young children have typically included only 1 or 2 time points,[5] and to the best of our knowledge, there have been no previous echocardiographic studies looking at serial ventricular function and dimensions after TOF repair in infants and very young children.

As the deleterious effects of long-standing PR following transannular patch (TAP) repair became clear, surgeons renewed efforts to preserve the pulmonary valve in patients undergoing surgery for TOF.[6,7] While such valve-sparing (VS) approaches may result in preserved valve function acutely, the longer-term implications remain unclear.[8] In particular, it is not known whether VS TOF repair alters the time course or extent of adverse volumetric and functional changes in the RV.

In an effort to gain insight into the impact of PR on the RV in the short- to mid-term after TAP and VS repair of TOF, the present study aimed to evaluate the evolution of the RV after TOF repair in infants and young children using speckle-tracking echocardiography (STE) and other routine echocardiographic parameters.

2 | METHODS

2.1 | Study population

We retrospectively reviewed all patients with a diagnosis of TOF in the echocardiographic database at Lucile Packard Children's Hospital Stanford between January 2002 and September 2015. Of the 1580 patients, we only included patients who underwent complete repair at our institution for TOF with pulmonary stenosis at <12 months of age. We excluded patients with fewer than 3 serial follow up echocardiograms at our center spanning at least 3 years. Additionally, patients with pulmonary valve atresia, major aortopulmonary collaterals, double-outlet RV, and/or who underwent placement of a RV to pulmonary artery conduit at the time of initial surgery were excluded, as were patients with inadequate or missing echocardiographic images. We also collected anthropometric and clinical data. The study was approved by the Stanford University Institutional Review Board, with a waiver of informed consent.

2.2 | Surgical groups

Surgical repairs were categorized TAP or VS. VS procedures included those in which the annulus was not transected or a limited transannular incision was performed and an effort was made to preserve or restore leaflet function.

2.3 | Echocardiographic data

Clinically obtained echocardiographic images were reviewed from the immediate postoperative period (0-14 days; ECHO1), early postrepair (4-6 months; ECHO2), 2-4 years after repair (ECHO3), and 5-7 years after repair (ECHO4). Echocardiograms were grouped into one of these 4 periods, which were analyzed as discrete evaluation points. Ultrasound equipment used for the echocardiographic studies was either the Siemens Sequoia C512 (Siemens Medical Solutions USA, Inc., Mountain View, CA) or the Philips iE33 (Philips Medical Systems, Bothell, WA). Commercially available standard ultrasound system and software were used to measure routine echocardiographic functional indices and strain data. All offline measurements were made using Syngo US workplace version 3.5 (Siemens Medical Solutions).

PR was qualitatively assessed by color flow mapping and jet size and graded as none, trivial, mild, moderate, or severe: moderate PR was defined as retrograde diastolic flow in the main pulmonary artery at level of bifurcation and severe PR as retrograde diastolic flow reversal in the branch pulmonary arteries (1 cm distal to the bifurcation).[9,10]

RV size was measured from RV basal diameter measurements made at end-diastole from the apical 4-chamber view. RV enlargement was defined as the RV basal diameter *Z*-score > 2.[11] RV function was assessed using FAC and 2D TAPSE. RV basal dimensions and TAPSE *Z*-scores were from obtained from published data.[11] The left ventricular ejection fraction (LV EF) was measured using the 5/6 area × length method.[12]

RV function was also evaluated using STE strain analysis. Endocardial borders were visually identified and manually traced from the apical 4-chamber view to ensure appropriate tracking. Global and segmental longitudinal peak systolic strain (GLS) data for the right and LV were collected using Syngo Velocity Vector Imaging (VVI) software (Siemens Medical Solutions USA, Inc., version 2.0). The average frame rate was 40 Hz. RV global longitudinal myocardial deformation was calculated using the full RV myocardium method. RV free wall GLS (RV FW GLS) was also calculated by averaging peak systolic strains of the 3 RV free wall regional segments: basal, mid-ventricular, and apical. LV GLS was calculated as the average of the 6 segments of the myocardium (Figure 1).

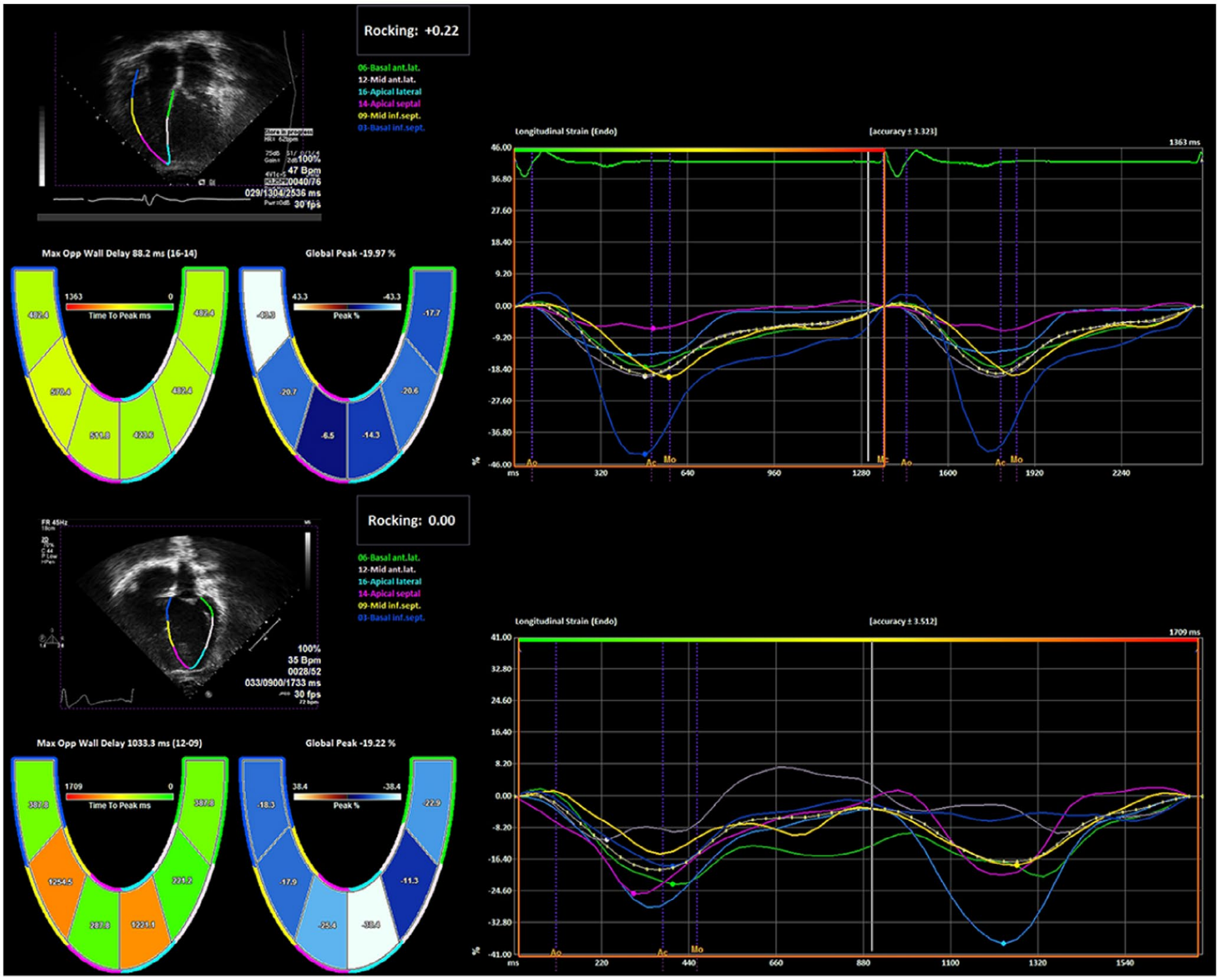

FIGURE 1 Global longitudinal right and LV strain measurement after TOF repair. The ventricular endocardium is manually traced and the VVI software analysis calculates myocardial velocity. Each color-coded curve graphically represents segmental strain. The global longitudinal strain represents the peak average of the segments

2.4 | Statistical analysis

Continuous data are presented as mean ± standard deviation. Student's t test was performed to compare the echocardiographic markers between both the surgical groups. Discrete variables were analyzed by the chi-square or Fischer's exact test. ANOVA was performed to assess changes in parameters over time. We also compared RV volume and functional parameters by categorizing patients with and without significant (moderate/severe) PR at each time point. Because the immediate postrepair values were markedly abnormal for some parameters, serial changes were analyzed relative to both ECHO1 (immediate) and ECHO2 (early postrepair). Differences were considered significant at $P \leq .05$, but were adjusted for multiple comparisons over time using the Bonferroni correction. Data analysis was performed using the SAS Enterprise Guide 5.1 (SAS, Cary, NC), Microsoft Excel Version 15.24 (Redmond, WA), and Graphpad Prism Version 7.0.

3 | RESULTS

3.1 | Patient population

We analyzed 151 echocardiograms performed on 42 patients who met inclusion criteria, who were 60% male and nearly evenly distributed between VS (45%) and TAP (55%) repair. The mean age at surgery was 2.1 ± 1.1 months and did not differ between the 2 surgical groups. Patient and surgical characteristics are listed in Table 1. RV outflow tract (RVOT) procedures performed in patients who underwent a VS repair included infundibular myectomy in 19 (89%), pulmonary valvotomy in 8 (42%), patch augmentation of the

TABLE 1 Comparison of patient characteristics and conventional echocardiographic indices after VS or TAP repair

Group	ECHO1 <3 months VS (n = 17)	ECHO1 <3 months TAP (n = 21)	P	ECHO2 4-6 months VS (n = 14)	ECHO2 4-6 months TAP (n = 18)	P	ECHO3 2-4 years VS (n = 19)	ECHO3 2-4 years TAP (n = 23)	P	ECHO4 5-7 years VS (n = 18)	ECHO4 5-7 years TAP (n = 20)	P
Age (months)	2.7 ± 1.1**,***	2.1 ± 0.9**,***	.07	5.3 ± 2.3**,***	5.5 ± 1.6**,***	.83	39.1 ± 8.3***	35.7 ± 6.9***	.15	72.2 ± 8.6	70.4 ± 12.7	.62
BSA (m2)	0.27 ± 0.05**,***	0.25 ± 0.04*, **, ***	.106	0.3 ± 0.05**,***	0.34 ± 0.13**,***	.57	0.60 ± 0.07***	0.56 ± 0.05	.023	0.83 ± 0.08	0.76 ± 0.1	.034
PR ≥moderate (%)	21*, **, ***	95	<.001	33**,***	94	<.001	45	95	<.001	42	95	<.001
FAC (%)	42.7 ± 5.4	44.5 ± 5.5	.33	44.8 ± 3.6	47.5 ± 2.9	.038	47.3 ± 7.4	47.6 ± 5.5	.89	46.3 ± 6.9	45.0 ± 5.6	.52
TAPSE (mm)	6.1 ± 1.6*, **, ***	6.4 ± 2.2	.66	9.3 ± 2.7**,***	10.6 ± 2.5	.18	12.3 ± 2.9	11.8 ± 2.9	.58	12.0 ± 2.6	14.1 ± 3.9	.089
TAPSE *Z*-score	−3.7 ± 0.97	−3.5 ± 1.5	.63	−2.4 ± 1.9***	−1.6 ± 1.6**,***	.27	−3.8 ± 2.3	−3.7 ± 2.9	.95	−4.7 ± 1.9	−3.6 ± 2.3	.098
TV *Z*-score	0.59 ± 1.0	0.52 ± 1.1	.83	1.4 ± 1.5	1.3 ± 1.2	.81	1.0 ± 1.3	1.4 ± 1.3	.39	0.3 ± 1.3	1.6 ± 1.6	.016
Maximum RVOT velocity (m/s)	2.1 ± 0.6*	1.8 ± 0.4	.036	2.2 ± 0.6	1.9 ± 0.4	.21	1.9 ± 0.8	2.1 ± 0.8	.79	1.7 ± 0.5	2.0 ± 0.6	.16
RV basal *Z*-score	0.62 ± 1.2	0.77 ± 0.9*, **, ***	.60	1.1 ± 1.0	1.9 ± 0.7	.009	1.7 ± 1.3	2.2 ± 0.9	.085	1.6 ± 1.2	2.1 ± 0.9	.085
RV:LV basal ratio	0.85 ± 0.1	0.95 ± 0.13**	.025	0.9 ± 0.2	1.0 ± 0.1	.025	0.92 ± 0.2	1.1 ± 0.2	.039	0.9 ± 0.2	1.1 ± 0.18	.002
LV EF (%)	59.1 ± 5.4*	63.4 ± 5.5	.027	62.4 ± 4.8	61.7 ± 2.7	.63	61.5 ± 2.9	61.4 ± 4.0	.86	62.5 ± 4.1	62.9 ± 3.9	.74

Abbreviations: RVOT, right ventricular outflow tract; TV, tricuspid valve annulus.
Note. Data presented as mean ± SD.
*$P < .05$ vs ECHO2.
**$P < .05$ vs ECHO3.
***$P < .05$ vs ECHO4.

main pulmonary artery in 7 (37%), and a subvalvar RVOT patch in 4 (21%).

3.2 | Echocardiographic data

3.2.1 | Conventional measures

Moderate or severe PR was present in ~95% of the TAP group at all time points, and was higher compared to the VS patients at all time points ($P < .001$). However, the proportion of VS patients with moderate or greater PR increased significantly over time, from 21% early postrepair to >40% at the 2-4 and 5-7-year time points (did not reach statistical significance). There was also an increase in RV size (basal dimension *Z*-score) on the last echocardiogram compared to the first in the TAP group ($P < .001$, Figure 2A) and was also higher in the TAP group than the VS group at all time points. The absolute RV:LV basal dimension ratio was also higher in the TAP group at all points ($P < .039$ for all, Figure 2B) as well as over time in the TAP group ($P = .012$). Although, the LV EF was lower in the VS group in the early postoperative period ($P < .03$), there was no significant difference in the conventional measures of RV and LV systolic function such as FAC and LV EF at later time points. The LV EF improved over time in the VS group ($P < .02$); no changes were noted over time using these conventional measures in the TAP group. However, TAPSE *Z*-scores decreased from early postintervention to the last follow-up time point in both groups ($P < .003$), Figure 2D). There were no time-related changes in LV EF in either group except in the immediate postoperative period.

Comparison of patients based on severity of PR at each time point (moderate to severe versus none-mild) showed higher absolute RV:LV basal dimension ratio at all points (Table 2) in patients with significant PR, as well as an increase from the first to the last echocardiogram in that cohort ($P = .045$). The TAPSE *Z*-score was lower at the last echocardiogram than in the early postoperative period in patients with both moderate to severe PR and no significant PR ($P < .001$ and $P = .035$); however, there was no difference between the 2 groups at the last time point. Both the FAC and TAPSE *Z*-scores were lower in patients with no significant PR in the early postoperative period than in those with moderate to severe PR ($P < .001$ and $P = .03$, respectively). The RV GLS improved over time in patients with and without significant PR ($P < .001$), and there was no difference between the 2 groups at the time of the last echocardiogram. Although the LV GLS improved over time in the patients with moderate-severe PR, it was significantly lower than in patients with no significant PR at the time of the last echocardiogram ($P < .001$).

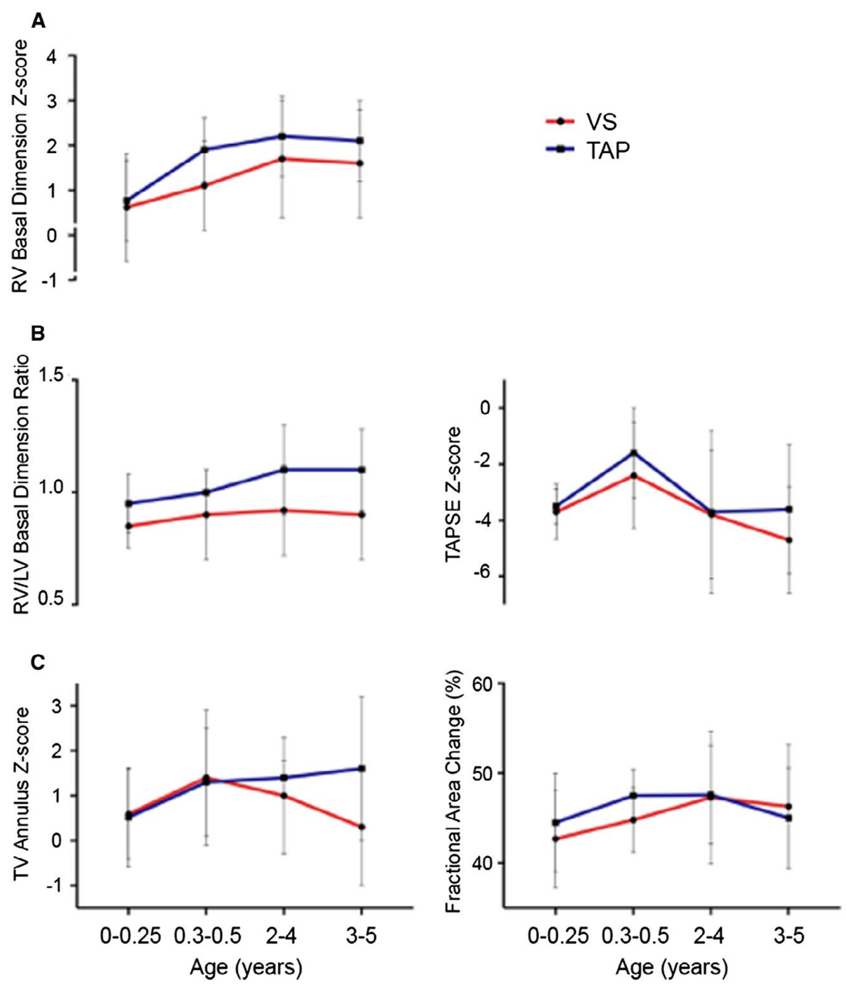

FIGURE 2 Ventricular size and functional measures – valve sparing versus transannular patch repairs. A, The RV basal *Z*-score shows an increase over time in the TAP group. B, The maximal RV/LV basal diameter size ratio measured in the apical 4 chamber view shows an increase over time in the TAP group and is also higher compared to the VS group at the last follow-up echo ($P = .002$). C, The tricuspid valve annulus *Z*-scores were higher in the TAP group vs the VS group by the last time point ($P = .016$); however, there was no statistically significant change over time in both the groups. D, The TAPSE *Z*-scores were lower in both the TAP and VS groups by the last time point. There were no statistically significant differences in the TAPSE *Z*-scores between the 2 groups at any time point. E, The FAC % did not significantly change over time in both groups; it was lower in the VS group compared to the TAP group in the immediate postoperative period

TABLE 2 Ventricular functional and size parameters based on PR severity

Group	ECHO1 <3 months None-mild (n = 14)	ECHO1 <3 months Moderate-severe PR (n = 23)	P	ECHO2 4-6 months None-mild (n = 11)	ECHO2 4-6 months Moderate-severe PR (n = 21)	P	ECHO3 2-4 years None-mild (n = 12)	ECHO3 2-4 years Moderate-severe PR (n = 30)	P	ECHO4 5-7 years None-mild (n = 12)	ECHO4 5-7 years Moderate-severe PR (n = 26)	P
LV EF (%)	58.7 ± 5.8*,**,***	63.2 ± 5.2	.02	62.0 ± 5.1	62.1 ± 2.9	.94	61.1 ± 2.5	61.6 ± 3.9	.69	64.0 ± 4.1	62.1 ± 3.8	.18
FAC (%)	43.1 ± 6.1	44.1 ± 5.1*,**	.61	43.6 ± 3.1	47.9 ± 2.6	<.001	45.3 ± 4.8	48.4 ± 6.8	.15	46.7 ± 5.1	44.9 ± 6.8	.44
TAPSE Z-score	−3.6 ± 1.0	−3.5 ± 1.5*	.79	−2.9 ± 1.8***	−1.4 ±1.6**,***	.03	−3.5 ± 1.8	−3.8 ± 2.9	.75	−4.5 ± 2.0	−3.9 ± 2.3	.45
RV Basal Z-score	0.64 ± 1.3	0.8 ± 0.9*,**,***	.95	0.95 ± 1.1	1.9 ± 0.71	.008	1.3 ± 1.5	2.3 ± 0.77	.049	1.5 ± 1.2	2.0 ± 0.99	.18
RV:LV ratio	0.82 ± 0.11	0.96 ± 0.13**,***	.002	0.85 ± 0.15	1.04 ± 0.12	<.001	0.83 ± 0.2	1.1 ± 0.18	<.001	0.91 ± 0.15	1.1 ± 0.19	.02
RV GLS(%)	−7.7 ± 2.7*,**,***	−11.3 ± 4.9*,**,***	.006	−11.1± 4.4**,***	−14.3 ± 4.3***	.057	−17.9 ± 5.9	−16.2 ± 4.3	.29	−19.6 ± 4.9	−17.5 ± 4.4	.22
LV GLS (%)	−9.3 ± 3.1*,**,***	−10.3 ± 5.1*,**,***	.50	−13.6 ± 2.7***	−14.9 ± 5.3	.34	−16.7 ± 4.1	−14.5 ± 4.1	.14	−19.7 ± 1.9	−15.4 ± 5.5	<.001

Note. Data presented as mean ± SD.
*P < .04 vs ECHO2.
**P < .04 vs ECHO3.
***P < .04 vs ECHO4.

TABLE 3 Global and segmental ventricular strain after VS or TAP TOF repair

Group	ECHO1 <3 months VS (n = 17)	ECHO1 <3 months TAP (n = 21)	P	ECHO2 4-6 months VS (n = 14)	ECHO2 4-6 months TAP (n = 18)	P	ECHO3 2-4 years VS (n = 19)	ECHO3 2-4 years TAP (n = 23)	P	ECHO4 5-7 years VS (n = 18)	ECHO4 5-7 years TAP (n = 20)	P
RV FW (%)	−8.7 ± 5.4	−10.9 ± 4.9	.2	−10.2 ± 4.7	−15.6 ± 4.9	.005	−18.4 ± 6.6	−19.3 ± 4.9	.64	−20.4 ± 6.7	−21.2 ± 6.1	.72
RV FW_B (%)	−11.9 ± 6.9	−13.2 ± 6.3	.55	−14.0 ± 9.4	−23.1± 7.9	.007	−28.1 ± 12.9**	−29.0 ± 9.9	.78	−30.2 ± 9.5	−32.3 ± 10.2	.53
RV FW_MV (%)	−7.7 ± 8.9	−11.3 ± 7.3	.18	−8.8 ± 6.7	−13.7 ± 6.5	.05	−14.6 ± 10.1	−16.5 ± 6.1	.47	−17.4 ± 9.5	−20.0 ± 8.2	.36
RV FW_A (%)	−6.7 ± 10.8	−8.3 ± 7.3	.58	−7.9 ± 7.8	−10.0 ± 6.9	.42	−12.6 ± 11.8	−12.2 ± 9.5	.91	−13.7 ± 13.3	−11.3 ± 10.4	.52
RV GLS (%)	−9.1 ± 4.3	−10.6 ± 4.7	.30	−10.2 ± 3.9**,***	−15.4 ± 3.7	<.001	−16.8 ± 5.8	−16.6 ± 3.9	.86	−18.4 ± 4.4	−17.9 ± 4.7	.76
LV GLS (%)	−9.4 ± 3.4	−10.2 ± 5.0	.62	−11.9 ± 3.3	−16.4 ± 4.5	.006	−15.9 ± 4.2	−14.5 ± 4.2	.29	−18.0 ± 4.5	−15.5 ± 5.4	.13

Abbreviations: A, apex; B, basal; FW, free wall; GLS, global longitudinal strain; MV, midventricular; TAP, transannular patch repair; VS, valve-sparing repair.
Note. Data presented as mean ± SD.

TABLE 4 Details of patients who underwent RVOT re-intervention according to original repair type

Age at initial repair (days)	Age at reintervention (years)	Procedure	Indication
Transannular patch repair			
8	1.2	LPA augmentation	LPA stenosis
70	3.2	Surgical PVR, LPA augmentation	PR, proximal LPA stenosis
108	3.3	Surgical PVR	PR, RV dilation
14	4.0	Surgical PVR, bilateral PA augmentation	RVOTO, PR
9	7.25	Surgical PVR, branch PA augmentation	PR, RV dilation
83	7.6	Surgical PVR	PR, RV dilation
82	9	Transcatheter PVR	RVOTO, PR, mild RV dilation
63	9.7	Surgical PVR	Free PR, RV dilation
Valve-sparing repair			
77	4.0	RVOT augmentation with TAP	RVOTO
11	7.6	Surgical PVR, LPA augmentation	PR, RV dilation, mildly depressed RV function

Abbreviations: LPA, left pulmonary artery; PA, pulmonary artery; PR, pulmonary regurgitation; PVR, pulmonary valve replacement; RV, right ventricular; RVOTO, right ventricular outflow tract obstruction; TAP, transannular patch.

3.3 | STE strain data

GLS values for both the RV and LV were remarkably low in the immediate postoperative period, although they improved significantly by the last follow-up echocardiogram at 5-7 years ($P < .001$ for VS group and $P = .004$ for TAP). RV GLS in the VS and TAP cohorts at the last time point (5-7 years postrepair) were −18.4 ± 4.4% and −17.9 ± 4.7%, respectively (Table 3), while LV GLS values were −18.0 ± 4.5% and −15.5 ± 5.4%. In the early postoperative period, there were significant differences in the RV and LV GLS, with higher values in the TAP cohort (Table 3, ECHO 2). There were no significant differences between TAP and VS groups in either the RV and LV GLS at the other time points. Additionally, GLS values for both groups were lower at all time points compared to published normal values (different software package – EchoPAC).[13,14] Across all time points, there was a significant decrement in regional longitudinal RV FW strain from base to mid to apex.

3.4 | Reintervention

As summarized in Table 4, surgical or transcatheter reintervention on the RVOT was performed in 10 patients (24%), 5.1 ± 2.5 years after repair, primarily for PR and RV dilation. Table 4 provides a summary of the patient characteristics, procedures, and indications for reintervention. The LV GLS prior to intervention was lower at the time of the last follow-up in patients who underwent reintervention (−13.2 ± 6.0%) compared to those who did not (−17.3 ± 4.6%, $P = .050$).

4 | DISCUSSION

The purpose of this study was to examine the evolution of RV size and function during early childhood after TOF repair. In this longitudinal analysis of patients who underwent TOF repair in early infancy with either TAP or VS techniques, we observed that significant PR was almost universal after TAP and significantly less common after VS repair, but that the prevalence of moderate-severe PR after VS repair increased over time. Dilation of the RV was not present immediately postoperatively, but mild enlargement was seen within 2-4 years after TAP repair. There was no significant RV dilation in patients who underwent a VS repair. Although there were no significant differences between TAP and VS patients in conventional measures of ventricular function such as RV FAC and LV EF, the GLS of both ventricles was lower than published normal values in both surgical groups at all time points,[13,14] suggesting that ventricular mechanics are abnormal immediately after repair in early infancy and do not normalize over time.

STE data showed that the systolic deformation of the RV and LV was significantly below normal in the immediate postoperative period. We postulate that this is likely secondary to exposure to a period of ischemia and cardiopulmonary bypass during surgical repair. The higher RV GLS values in the initial postoperative period in the TAP group (ECHO 2) compared to the VS group may have been due to volume loading related to the PR in this cohort. Although, no significant differences in RV or LV GLS were noted between TAP and VS groups at the other time points, both measures improved over time, regardless of the type of repair. However, strain values never normalized in comparison to published data in similarly aged normal children.[13,14] This finding supports other published data in both children and adults that showed decreased deformational parameters after TOF repair compared to normal controls.[5,15] Our data also suggest an abnormal and pronounced RV FW strain gradient from base to apex relative to published normal values, which may suggest mechanical adaptation to a dyskinetic outflow tract, although we did not assess the outflow tract in this study. The etiology for regional RV dysfunction in repaired TOF patients remains poorly understood. Analysis of our patients based on PR severity showed an increase in RV/LV size ratio and a decrease in LV systolic function (LV GLS) at the time of the last follow-up echocardiogram in patients with moderate to severe PR, suggestive of adverse RV-LV interaction.[16]

TAPSE values at the last echocardiographic time point in our study were comparable to recently published data in children from ages 5 to 8 years after TOF repair.[17,18] Additionally, there were no changes in the TAPSE *Z*-scores over time. Mercer-Rosa et al compared TAPSE values obtained on 2D echocardiography to RV EF measured by CMR[18] and found that TAPSE was reproducible but was only 49% sensitive and 54% specific in detecting RV dysfunction identified by CMR, and there was no association between TAPSE and RV output or mass. Koestenberger et al found only a modest correlation between TAPSE and RV EF by CMR (age range 0-28 years).[17] The poor ability of TAPSE to discriminate decreased RV function in repaired TOF could be attributable to the fact that it does not take into account the longitudinal contractile function of the dysfunctional RV outflow tract after surgery in this population and is thus not a true measure of global systolic function.

The etiology of the abnormal ventricular mechanics in our population is likely complex and multifactorial. At the molecular level, Jeewa et al studied the genotype of 180 patients after TOF repair to identify at risk patients before significant RV remodeling occurred. They found that children with a lower number of functioning alleles of hypoxia-inducible factor *HIF1A*, which regulates the myocardial response to hypoxia and hemodynamic load, were more likely to develop RV dilation and dysfunction, implying that genetic modifiers also likely play a role in RV adaptation and are thus important to identify in order to risk stratify and determine timing of intervention.[19]

The effect of chronic PR on the progression of RV enlargement and dysfunction has been documented in prior studies.[20,21] There have been multiple investigations to determine the optimal timing for PVR in patients with TOF, given that RV and LV dysfunction are associated with impaired clinical status and adverse outcomes.[22] However, there are limited data regarding the progression and evolution of ventricular mechanics in very young patients after repair. Knowledge of the state of the RV starting in infancy is important, and our results suggest that GLS and the RV:LV basal diameter ratio may serve as useful parameters when following young children after TOF repair.

5 | LIMITATIONS

This was a single-center retrospective study with a relatively small number of patients meeting inclusion criteria. We did not have age, gender, and BSA-matched controls in our study. STE deformation analysis has limitations related to image quality, operator experience, and inter- and intra-vendor variability. CMR is the gold standard for quantitative assessment or RV function and size, and such data would have provided an important point of reference for our findings. Additionally, given the referral structure of our center and our preference for early primary repair even in acyanotic TOF,[8] the study population may not be representative of other centers.

6 | CONCLUSIONS

In the face of PR after TAP, and progressively VS, repair, RV enlargement is evident within the first few years following surgery. The RV:LV basal dimension ratio, which is a simple and quick tool, helps track RV enlargement over time in young patients. Although conventional measures of RV function were stable over the time period studied, RV and LV GLS were abnormally low after TOF repair in early infancy. Although, both RV and LV GLS improved over time in our cohort, they were lower than published normal values. Additionally, the LV GLS was significantly lower in children with significant PR compared to those without although there was no difference in LV EF. GLS and RV:LV basal diameter ratio can be valuable, additional clinical tools when serially following young children post TOF repair. In order to understand the time course of ventricular change after TOF repair, and ultimately to determine the optimal timing of PVR, it will be important to extend longitudinal studies such as this one into older childhood, and to integrate the findings with both CMR-derived and biological data.

CONFLICT OF INTERESTS

The authors declare that they have no conflicts of interest with the contents of this article.

AUTHOR CONTRIBUTIONS

Helped conceive the study, reviewed and analyzed data, and drafted the manuscript: Annavajjhala
Helped conceive the study, reviewed and analyzed data, and reviewed and revised and approved the manuscript: Punn
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