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Tricuspid Annular Plane Systolic Excursion in the Assessment of Right Ventricular Function in Children and Adolescents after Repair of Tetralogy of Fallot

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Abstract

Background—Assessing right ventricular (RV) performance is essential for patients with tetralogy of Fallot (TOF). The aim of this study was to investigate the reliability and validity of tricuspid annular plane systolic excursion (TAPSE) against cardiac magnetic resonance imaging measures and cardiopulmonary exercise testing.

Methods—A retrospective study was performed in 125 outpatients with repaired TOF with available protocol-driven echocardiography, cardiac magnetic resonance imaging, and exercise stress testing obtained as part of a cross-sectional study. TAPSE was measured on the two-dimensional apical four-chamber view on echocardiography by two readers. Multivariate linear regression was used to examine the association between TAPSE and measures of RV function and exercise capacity.

Results—The mean age was 12.6 ± 3.3 years, 41 patients (33%) were female, and 104 (83%) were white. TAPSE averaged 1.6 ± 0.37 cm, with an interreader intraclass correlation coefficient of 0.78 ($n = 18$). TAPSE was significantly associated with cardiac magnetic resonance–based RV stroke volume after adjustment for gender and body surface area ($\beta = 13.8$; 95% confidence interval, 2.25–25.30; $P = .02$). TAPSE was not associated with cardiac magnetic resonance–based RV ejection fraction ($P = .77$). On exercise testing, TAPSE was not associated with peak oxygen consumption, percentage of predicted oxygen consumption, oxygen pulse, or the ventilatory equivalent for carbon dioxide in patients with maximal exercise stress testing ($n = 73$ [58%]).

Conclusions—TAPSE is reproducibly measured by echocardiography in patients with TOF. It is not associated with RV ejection fraction or exercise performance, and its association with RV

stroke volume may be confounded by body size. On the basis of these results, TAPSE is not representative of global RV performance in patients with TOF.

Keywords

Tricuspid annular plane systolic excursion; Echocardiography; Exercise; Magnetic resonance imaging; Tetralogy of Fallot

Quantification of right ventricular systolic performance is vital given the growing number of survivors with congenital heart disease, in particular those with involvement of the right heart, such as tetralogy of Fallot (TOF). Patients operated on for TOF experience pulmonary insufficiency, which results in RV dilation and ultimately RV failure.¹ Therefore, assessment of RV function is of paramount importance in the longitudinal follow-up of this patient population. The assessment of RV function by echocardiography in patients with TOF is challenging and currently is largely qualitative.²

Tricuspid annular plane systolic excursion (TAPSE) is a well-described echocardiographic measure of RV function in the adult population without congenital heart diseases.^{3,4} Representing the distance of the tricuspid valve annular descent toward the apex of the heart during systole, this measurement reflects the longitudinal component of RV contraction.⁵ In normal subjects as well as in patients with pulmonary hypertension and other cardiac diagnoses, TAPSE is associated with global measures of RV systolic function, including RV ejection fraction (RVEF).^{4,6} This likely reflects the fact that longitudinal RV shortening accounts for the majority of total RV contraction in normal subjects.⁷ Studies in pulmonary hypertension and heart failure have shown that lower TAPSE is associated with a higher risk for death.^{8,9} Therefore, this measure could similarly be of use in congenital heart disease, in particular because TAPSE depends neither on endocardial border definition nor on geometric assumptions.⁴ Studies have examined the use of TAPSE in TOF and other congenital heart diseases. Of note, those studies have produced mixed results regarding TAPSE and RVEF; in addition, none have examined its association with maximal exercise capacity.¹⁰⁻¹⁴ Therefore, further investigation is needed to determine the usefulness of TAPSE to assess RV function in congenital heart disease.

We sought to examine the reliability of the interpretation of TAPSE and to determine its validity against measures of RV function by cardiac magnetic resonance (CMR) and indices of exercise performance in a large cohort with TOF.

METHODS

Subjects

This was a retrospective study of participants in a cross-sectional protocol conducted at the Children's Hospital of Philadelphia (RO1-HL74731) that recruited 177 patients and performed echocardiography, CMR, and exercise stress testing (EST). The study sample for this analysis included subjects with surgically treated TOF aged 8 to 19 years who underwent transthoracic echocardiography, CMR, and EST within a maximum of 3 months of one another. TAPSE measurements were retrospectively obtained in this study sample.

The study was approved by the Children's Hospital of Philadelphia Institutional Review Board.

Echocardiography

Echocardiography was performed using a Phillips iE33 machine (Phillips Medical Systems, Andover, MA) using a standard protocol. Briefly, images were acquired with 3-MHz to 8-MHz transducers, suited for patient size and acoustic windows and digitally stored using syngo Dynamics version 3.0 (Siemens Healthcare, Ann Arbor, MI). Although TAPSE was originally measured using two-dimensional (2D) tricuspid annular displacement, TAPSE is currently more commonly measured using M-mode echocardiography, by placing the cursor through the tricuspid annulus and measuring the amount of longitudinal motion of the annulus at peak systole.^{4,15} Because M-mode imaging was not available in this study population, we performed offline TAPSE measurements using 2D apical four-chamber views. We identified the lateral annulus of the tricuspid valve and measured the distance at end-diastole and end-systole to a point on the screen that was the same for systole and diastole. We measured the maximal excursion and used the electrocardiographic tracing as a guide to ensure that all measurements were obtained at the same time in the cardiac cycle. The distance the annulus travels vertically should be the same whether the point measured is the apex of the heart or the apex of the sector. To corroborate the technique we used in this study, we repeated measurements in 12 patients, comparing the measurement of the annulus with a point on the screen to measurement of the annulus to the apex. We found that the measurements are essentially the same (correlation coefficient = 0.98; $P < .0001$; intraclass correlation coefficient [ICC] = 0.99; 95% confidence interval [CI], 0.96–1.02).

Measurements were performed by two trained readers blinded to clinical information and to CMR and EST results. The tricuspid valve annulus was identified at end-systole and end-diastole using electrocardiographic guidance, and the distance was measured as has been previously reported (Figure 1).⁴ The average of three TAPSE measurements was used for each patient. We randomly selected 10% of studies for blind reinterpretation by the same reader and 10% for interpretation by the second reader.

To assess the agreement of 2D TAPSE with M-mode measurements, we compared measurements performed using both techniques performed in a blinded fashion in 20 children without congenital heart disease.

CMR

CMR studies were performed using a 1.5-T Avanto magnetic resonance imaging scanner (Siemens Healthcare, Erlangen, Germany) with a six-channel phased-array body coil using a standard imaging protocol. The magnetic resonance imaging sequences included a steady-state free precession sequence through the cardiac apex. Sedation was used when appropriate according to patient age and ability to lie still for the scan. To assess RV end-systolic volume (RVESV) and RV end-diastolic volume (RVEDV), a cine magnetic resonance sequence in a short-axis view was used (echo time, 2.0 ms; repetition time, 4.5ms; flip angle, 75°–90°; matrix size, 196 × 196). RV stroke volume was calculated by subtracting RVESV from RVEDV. RVESV and RVEDV were indexed to body surface area

(BSA), and ventricular size was compared with published normative data.^{16,17} RVEF was calculated from RV stroke volume divided by RVEDV. RVEF < 50% was defined as abnormal on the basis of prior studies in normal children.^{16,17} Pulmonary insufficiency was graded as mild if the regurgitant fraction was < 20%, moderate if it was 20% to 40%, and severe if it was > 40%. RV regional wall motion abnormalities were assessed qualitatively by examining four-chamber and short-axis views on cine CMR and recorded as present or absent. The RV outflow tract was assessed on the sagittal RV outflow tract view.

EST

Patients exercised to maximal ability using an electronically braked cycle ergometer (SensorMedics, Yorba Linda, CA). Eighteen subjects who were <130 cm tall exercised on a treadmill (Series 2000; Marquette, Milwaukee, WI). Metabolic data were obtained throughout the study and for the first 2 min of recovery on a breath-by-breath basis using a metabolic cart (V29; SensorMedics), including oxygen consumption (\dot{V}_{O_2}), carbon dioxide production (\dot{V}_{CO_2}), maximum work (physical working capacity), oxygen pulse, respiratory exchange ratio, and the ventilatory equivalent of carbon dioxide ($\dot{V}E/\dot{V}_{CO_2}$). Anaerobic threshold was measured using the V-slope method. The predicted percentage of maximum \dot{V}_{O_2} ($\dot{V}_{O_2max\%}$) was calculated for each patient, according to normative values for age, gender, and body size.¹⁸ Exercise performance was defined by peak \dot{V}_{O_2} and $\dot{V}_{O_2max\%}$. Abnormal aerobic performance was defined as $\dot{V}_{O_2max\%} < 80$. Ventilatory efficiency was assessed by $\dot{V}E/\dot{V}_{CO_2}$ at the anaerobic threshold and by the slope of the $\dot{V}E/\dot{V}_{CO_2}$ relationship from initiation to peak exercise ($\dot{V}E/\dot{V}_{CO_2}$ slope). Maximal EST was defined as attaining a respiratory exchange ratio > 1.1.

Statistical Analysis

Continuous variables are presented as mean \pm SD or as medians with interquartile ranges, as appropriate. Categorical variables are described using counts and percentages. Reproducibility of TAPSE interpretations and the agreement of 2D TAPSE measurements with M-mode measurements are expressed using ICCs with 95% CIs. Student's *t* or Mann-Whitney *U* tests were used to compare continuous variables according to their distribution.

Multivariate linear regression was used to assess the association of TAPSE (the independent variable) with CMR and EST parameters of interest (the dependent variables). The final models included clinically relevant covariates that were significant ($P < .15$) on univariate analysis or thought to be confounders, defined as a covariate that resulted in a >15% change in the TAPSE β coefficient. Body size was accounted for as BSA in the multivariate model.¹⁹ Receiver operating characteristic curve analysis was used to test the ability of TAPSE to predict RV dysfunction (RVEF < 50%) by CMR.

Analyses of exercise covariates included only those with maximal EST (respiratory exchange ratio > 1.1). All analyses were performed using Stata version 11.0 (StataCorp LP, College Station, TX). Statistical significance was defined as $P < .05$.

RESULTS

Description of the Study Sample

A total of 177 individuals were recruited for the parent study. One hundred forty-one subjects completed all three studies of interest (echocardiography, CMR, and EST). Of these 141, 125 had interpretable TAPSE plus the other CMR and EST covariates of interest and therefore constituted the study sample. Most echocardiographic (70%) and CMR studies were performed within 2 weeks of each other, and all three studies were performed within 3 months of one another. There were no differences in age, gender, and race between those in the study sample ($n = 125$) and those excluded ($n = 52$). The time between echocardiography and CMR averaged 14 ± 25 days (range, 0–96 days). Half of the subjects underwent echocardiography and CMR on the same day ($n = 62$). Those with echocardiography and CMR performed within 2 weeks of each other were comparable in terms of RV volumes, RVEF, TAPSE, and peak V_{O_2} with those who had studies performed >2 weeks and <3 months apart.

The mean age was 12.5 ± 3.3 years (range, 8–19 years), and 41 patients (33%) were female. All age groups were represented (Figure 2). One hundred four (83%) were non-Hispanic white. Most subjects (76%) were repaired before 1 year of age and presented with pulmonary valve stenosis (79%), followed by atresia and absent pulmonary valve leaflets (15% and 6%, respectively). Surgical repair included a transannular patch in most subjects (67%) (Table 1). No subjects had undergone pulmonary valve replacement at the time of the study.

On CMR, there was significant pulmonary insufficiency and RV dilation. Pulmonary insufficiency was severe in 40% of the subjects (regurgitant fraction $> 40\%$) (Table 2). RV volumes were increased but RV function was preserved, with a mean RVEF of $61 \pm 8\%$. RV systolic dysfunction (RVEF $< 50\%$) was present in 10% of patients. Despite overall preserved RVEF, we found average TAPSE to be 1.6 ± 0.38 cm (range, 0.75–2.75 cm), lower than that of children without congenital heart disease. Moreover, TAPSE was decreased in each age group in our study compared with published normal values²⁰ (Table 3). Regional wall motion abnormalities of the right ventricle were noted in most subjects (89%). Most subjects had mild or less than mild tricuspid regurgitation (mean regurgitant fraction, $5.6 \pm 5\%$).

On EST, the overall cohort had decreased aerobic performance (mean $V_{O_2\max\%}$, $76 \pm 18.4\%$). Seventy-three subjects (58%) achieved maximum effort. In those, the peak V_{O_2} was 33.7 ± 7.9 mL/kg/min ($V_{O_2\max\%}$, $80 \pm 17\%$) compared with 29.3 ± 8.4 mL/kg/min ($V_{O_2\max\%}$, $70 \pm 18\%$) in subjects who achieved submaximal EST ($P < .001$).

Comparisons among TAPSE, CMR, and EST

TAPSE measurements showed excellent intrareader reliability and interreader reliability (intrareader 1 ICC = 0.85 [95% CI, 0.68–1]; intrareader 2 ICC = 0.66 [95% CI, 0.27–1]; interreader ICC = 0.78 [95% CI, 0.52–1]). In addition, we found excellent agreement between 2D and M-mode TAPSE measured in a sample of 20 patients without congenital

heart disease (ICC = 0.90, $P < .001$), confirming that measurements by these two different methods are essentially identical.

TAPSE was associated with stroke volume after adjustment for sex and BSA ($\beta = 13.8$; 95% CI, 2.25–25.30; $P = .02$; Table 4). There also appeared to be direct associations between TAPSE and RVEDV and RVESV. There was no significant association between TAPSE and RVEF (Figure 3). Similarly, subanalysis limited to patients with pulmonary valve stenosis demonstrated no association of TAPSE and RVEF ($\beta = -0.78$, $P = .72$).

The ability of TAPSE to discriminate those with systolic dysfunction (RVEF < 50%) from those with preserved RV function was no better than chance (c-statistic = 0.57; 95% CI, 0.39–0.75; Figure 4). Using a TAPSE value of 1.6 (the median in our study population), TAPSE had only 49% sensitivity and 54% specificity to detect abnormal RV function on CMR. There was no association among TAPSE, RV cardiac output, and RV mass after adjustment for sex and BSA.

TAPSE was not associated with any measures of exercise performance (peak V_{O_2} , $V_{O_2\max}$ %, oxygen pulse, or VE/V_{CO_2} slope) after adjustment for sex and BSA.

DISCUSSION

We have shown that TAPSE may be reproducibly measured from echocardiography in patients with TOF offline using 2D imaging. Higher TAPSE was associated with greater RV stroke volume on CMR after adjustment for sex and body size. There also appeared to be direct associations between TAPSE and RVEDV and RVESV. TAPSE was not associated with EF or any other CMR parameters. TAPSE did not predict maximal exercise performance in patients operated for TOF.

RVEF assessed by CMR is considered the gold standard measure of RV systolic function.^{21–23} RVEF and RV volumes from CMR are particularly useful in the follow-up of patients with TOF to assist in determining the timing for pulmonary valve replacement.^{23–25} Although RVEF by CMR offers a more robust measure of function than most echocardiographic indices, ejection fraction is load dependent and does not offer a measure of contractility. In addition, CMR is limited by cost, inconvenience, and potential requirement for sedation. Therefore, echocardiographic indices that predict RV function by CMR would be clinically useful.

Prior studies in normal and diseased hearts have demonstrated the reproducibility of TAPSE with high intrareader and interreader agreements, including recently in patients with TOF.^{8,9,12,26,27} We have confirmed the reliability of the measurement of TAPSE in TOF, but we failed to demonstrate an association of TAPSE and RVEF on CMR. These findings are in contrast to those of some studies but in agreement with the results of others.^{11,12,27} Van der Zwaan *et al.*²⁷ studied patients with heart failure and affected right and/or left ventricles and found a modest correlation of TAPSE with RVEF on CMR (correlation coefficient = 0.4). In TOF, Koestenberger *et al.*¹² found a modest correlation (correlation coefficient = 0.47) between TAPSE and RVEF measured on CMR. Their study included patients with a wide age range, so it is possible that they examined a different population

with TOF. However, a smaller study of TOF in an age group comparable with ours also found that TAPSE failed to predict RVEF on CMR.¹¹ In agreement with this smaller study, our data suggest that TAPSE is not discriminative, sensitive, or specific for identifying patients with TOF with reduced RVEFs.

There are some possible explanations for why TAPSE performed less well in our population with TOF than in other patients with pulmonary hypertension or congestive heart failure.^{8,9,28} The right ventricle in TOF poses a particular challenge in the assessment of systolic function because of its native complex shape and the fact that patients with TOF usually have RV outflow tract patches that can be hypocontractile. Although TAPSE measures the longitudinal motion of the RV body, ejection fraction calculated on CMR combines the RV body and outflow tract. Therefore, TAPSE may not represent global RV systolic function in patients with dysfunctional RV outflow tracts. Prior studies have shown that in the normal heart, RV infundibular and outflow tract contraction contributes only a minor degree (~13%) to the overall stroke volume generated by the right ventricle, so the RVEF is preserved in this young population, although TAPSE values are abnormal.^{29,30} To corroborate this hypothesis, a recent study by Puranik *et al.*³¹ found similar TAPSE (measured on CMR) in patients with TOF compared with those with dilated right ventricles from pulmonary regurgitation after pulmonary valvuloplasty. In patients without congenital heart disease or in those with congenital heart disease but normal RV outflow tracts, the contractility of the RV outflow tract may reflect RV function. However, such methods may be less useful in TOF given the dysfunctional outflow tract seen in this setting.³²

Patients with TOF have diminished regional longitudinal deformation properties of the RV free wall.^{14,33–35} It is possible that wall motion abnormalities (present in most patients in our study) could have contributed to the lack of association between TAPSE and RVEF and could explain abnormal TAPSE values.

In our study, the mean RVEF was normal at approximately 60%, yet TAPSE was lower than that of children without congenital heart disease.²⁰ In adults, TAPSE is consistently reported at >2.0 cm.^{7,36,37} These findings suggest that there is a difference in the RV contractile pattern of patients with TOF compared with non-congenital heart disease states, such as acquired valvular heart disease, cardiomyopathy, and pulmonary hypertension. Therefore, longitudinal contraction may not be the principal determinant of RVEF in patients with certain types of RV disease. Pettersen *et al.*¹⁰ demonstrated predominant circumferential over longitudinal free wall shortening in systemic right ventricles after the Senning operation for patients with D-transposition of the great arteries. Even though the right ventricles in patients with TOF (supporting the pulmonary circulation) and in those with D-transposition of the great arteries (supporting the systemic circulation) are pathophysiologically different, it is possible that the contractile pattern changes in certain disease states, including TOF. A recent study in patients with pulmonary hypertension also showed a better correlation between transverse wall motion and baseline RVEF than longitudinal wall motion.³⁸

We found borderline associations of TAPSE with RV volumes. Although higher TAPSE tracked with greater RVEDV, RVESV, and RV stroke volume, residual confounding by

body size could explain these findings, and the association of TAPSE with RV stroke volume should be interpreted with caution.

We found decreased exercise performance in our study patients overall. This is in keeping with other studies demonstrating that patients with TOF have exercise intolerance over time, with decreased peak V_{O_2} compared with healthy subjects.³⁹⁻⁴⁴ Because TAPSE was not an adequate indicator of RV systolic function in TOF (and RV function is an important determinant of exercise performance), it is not surprising that TAPSE did not track with measures of exercise performance, including VE/V_{CO_2} , as it does in other cardiac diseases.⁴⁵

Limitations

There were certain limitations to this study. We performed retrospective, offline measurements of TAPSE from 2D images on echocardiograms, and M-mode measurements were not possible. We applied a different technique from the standard 2D and M-mode methods. However, we found good agreement between readers, supporting at least the reliability of this technique. Moreover, we found a high correlation between 2D and M-mode measurements in a set of echocardiograms without congenital heart disease, supporting the use of this technique for offline TAPSE measurements when M-mode is not available. We also highlight that the technique used in this study must be taken into consideration when interpreting differences from normal values, acquired using standard methodology.

Our study population constitutes one of the largest cohorts of children and teenagers with TOF that has ever been studied with concurrent echocardiography, EST, and CMR, and this study was one of the first to examine the association of TAPSE with measures of exercise performance. Although it is possible that potentially “sicker” patients were not included in this sample if they had hardware (such as pulmonary artery stents) that precluded their undergoing CMR testing, we found that excluded patients were comparable with the study sample in terms of demographics and anthropometrics, making selection bias less likely. Because patients included in the study were not limited by original pulmonary valve anatomy, type of surgical repair, genetic status, place of follow-up, gender, race, or age at surgical repair, generalizability is a particular strength of this study.

A prolonged time interval between tests and resultant biologic variability could have biased our results toward the null hypothesis, such that there could have been associations we did not detect. However, tests were performed within a maximum of 3 months to avoid this type of bias. In addition, in the clinical setting, methods for the evaluation of RV function are typically performed non-simultaneously. Moreover, we believe that pulmonary regurgitation and ejection fraction are not factors that have major variability in stable patients with TOF.

Measurement error in CMR parameters could have occurred, biasing our results toward or away from the null; nonetheless, CMR studies were reviewed by a single experienced reader who was blinded to other test results, making systematic measurement error less likely.

Most subjects in the study had normal RVEFs, but that should not affect the ability of TAPSE to detect RV dysfunction. A greater number of patients with decreased RVEF would lead to greater precision of the c-statistic but would be unlikely to change the study results.

We were not able to compare TAPSE and RVEF according to regional wall dysfunction, because the number of patients without regional dysfunction was too small to allow a meaningful comparison. Likewise, we did not study the effect of tricuspid regurgitation, because it was present only in a small number of patients.

CONCLUSIONS

We demonstrated that TAPSE is a reliable measure by echocardiography in patients with TOF. TAPSE was not associated with RVEF or other CMR parameters. In addition, TAPSE was not associated with exercise performance. These findings suggest that longitudinal shortening is not the dominant contributor to global RV systolic function in TOF. In addition, TAPSE is not representative of global RV performance in TOF and may not be useful as a single measure of RV function in this patient population. Future studies should explore other novel measures of RV function in TOF.

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Abbreviations

BSA	Body surface area
CI	Confidence interval
CMR	Cardiac magnetic resonance
EST	Exercise stress testing
ICC	Intraclass correlation coefficient
RV	Right ventricular
RVEDV	Right ventricular end-diastolic volume
RVEF	Right ventricular ejection fraction
RVESV	Right ventricular end-systolic volume
TAPSE	Tricuspid annular plane systolic excursion
TOF	Tetralogy of Fallot
2D	Two-dimensional
V_{CO₂}	Carbon dioxide production
VE/V_{CO₂}	Ventilatory equivalent of carbon dioxide
V_{O₂}	Oxygen consumption

$V_{O_2\max\%}$ Predicted percentage of maximum oxygen consumption

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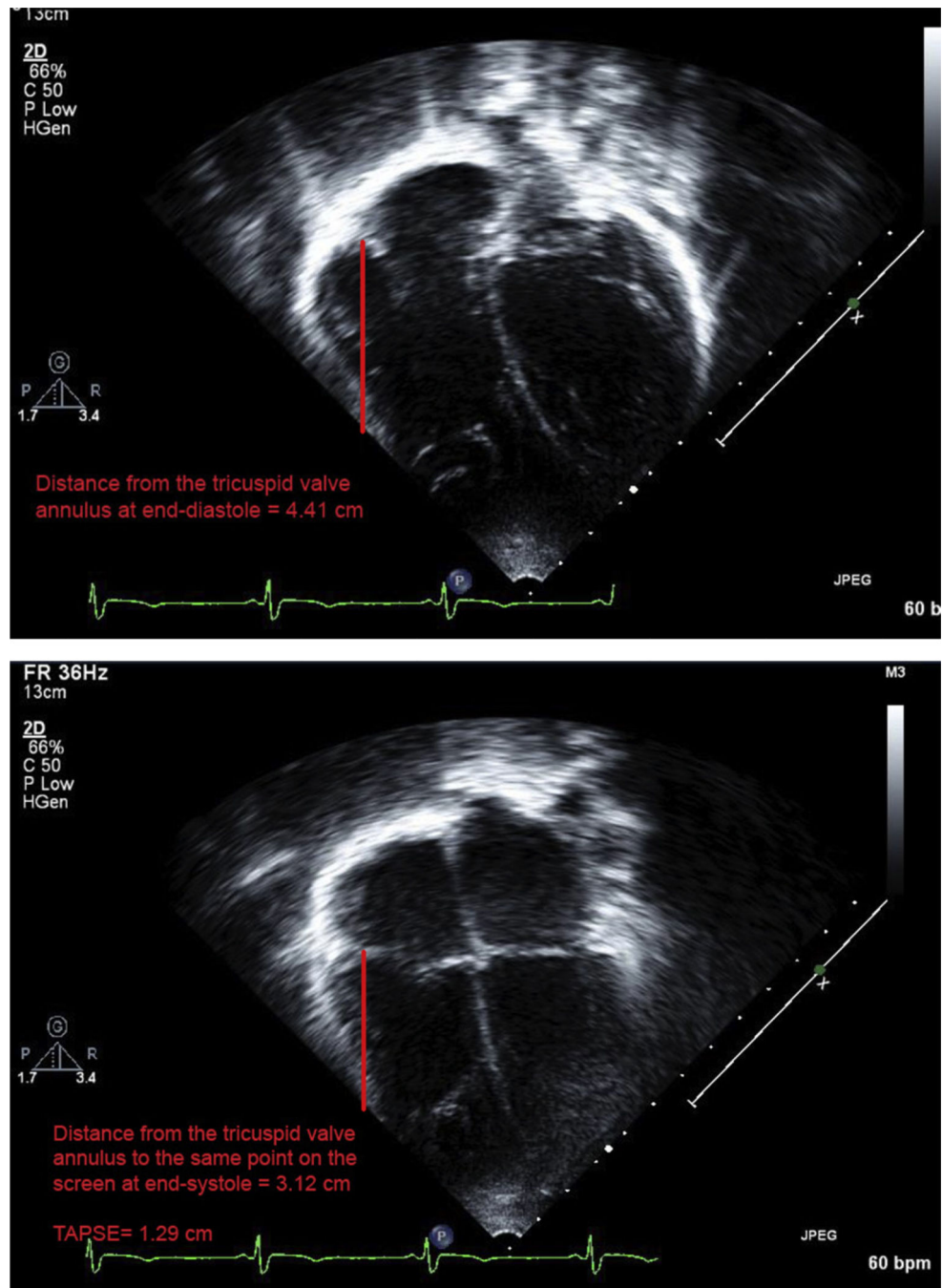


Figure 1. Example of TAPSE measurement by 2D echocardiography on apical four-chamber view from a study patient. (*Top*) Tricuspid valve annulus at end-diastole (distance to a point on the screen, 4.41 cm). (*Bottom*) Tricuspid valve annulus in end-systole (distance to the same point on the screen, 3.12 cm). TAPSE = 1.29 cm.

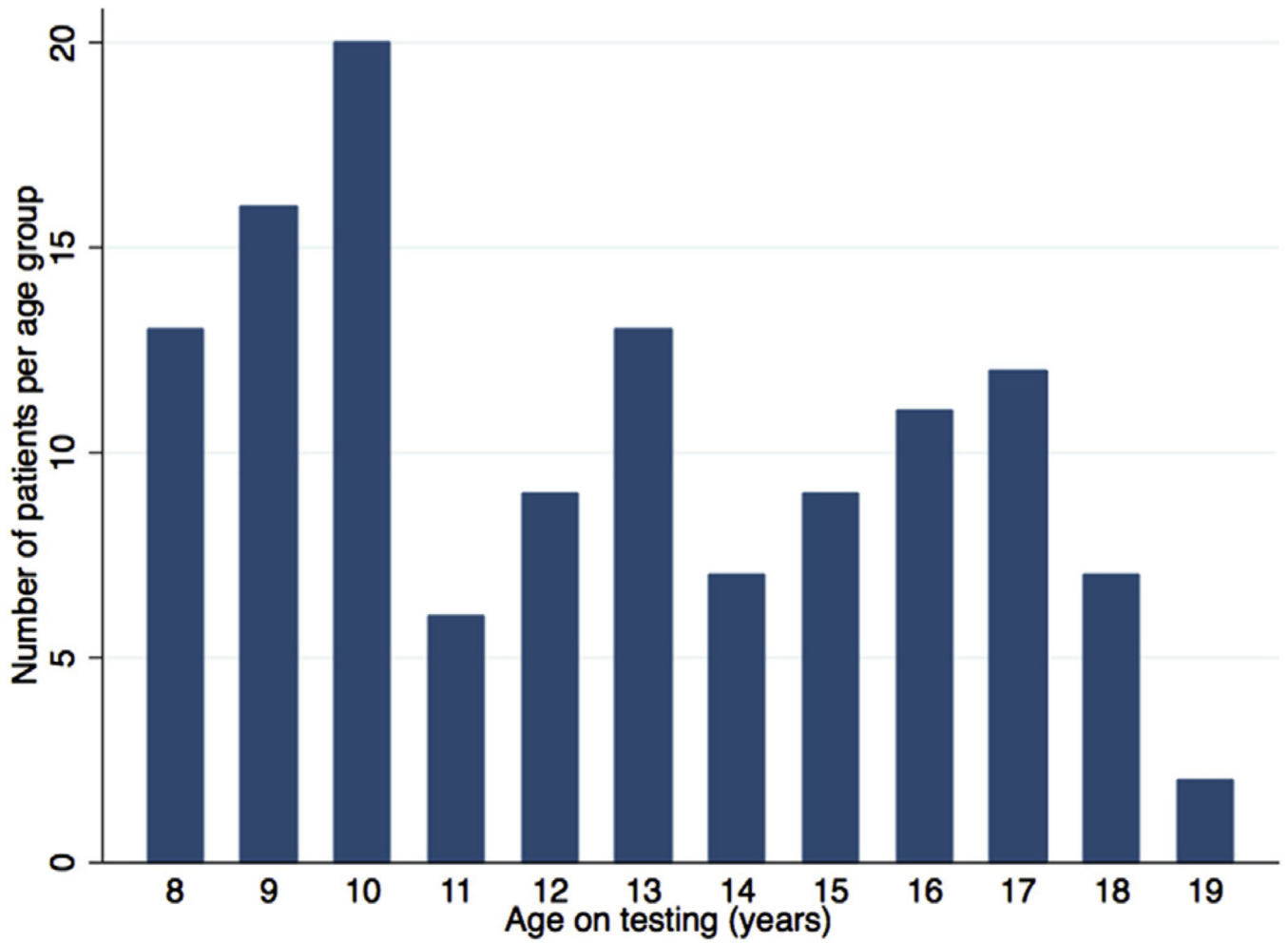


Figure 2.
Age distribution of the study cohort. The graph displays the number of patients per year of age.

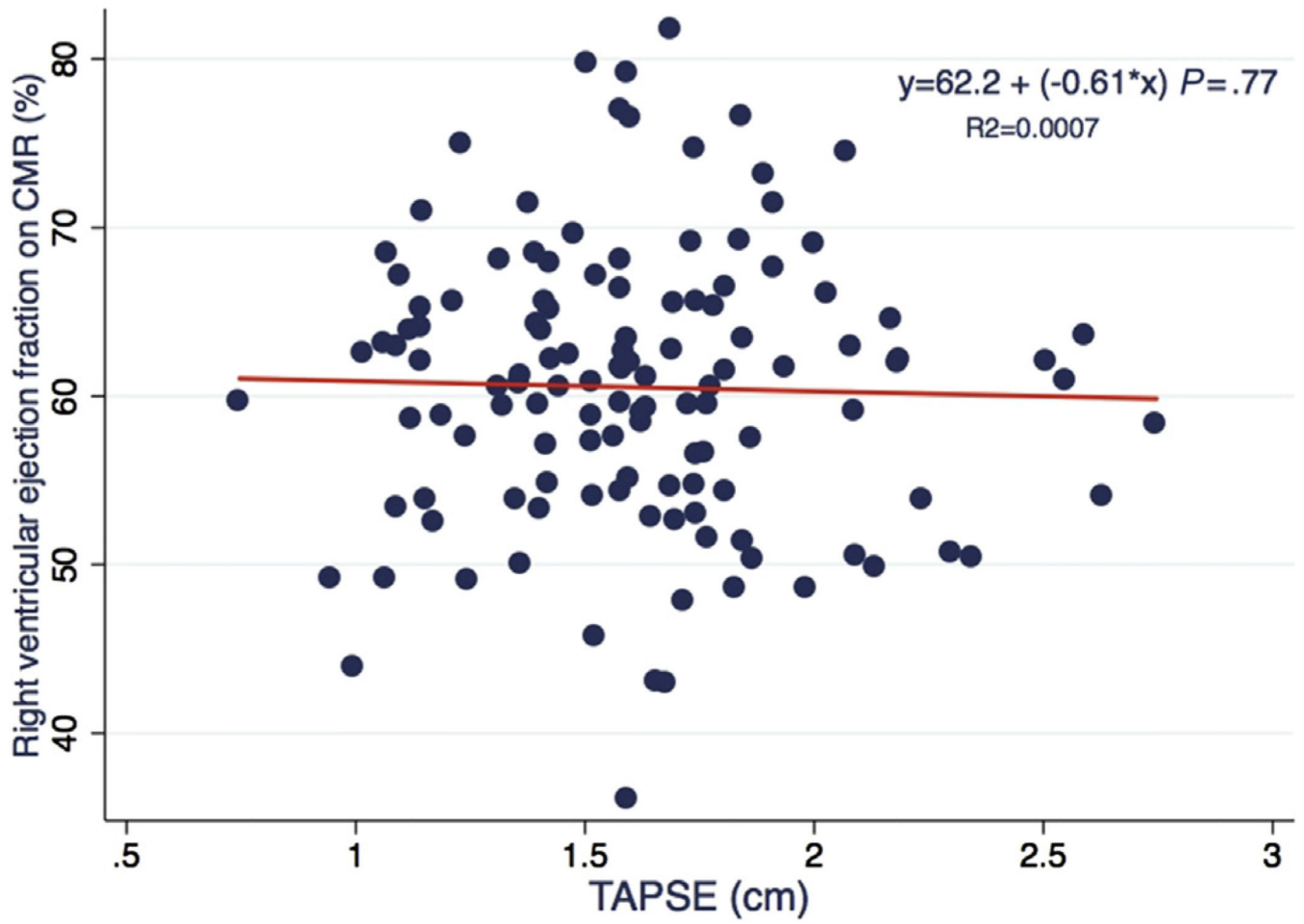


Figure 3. Scatterplot with linear regression line demonstrating the relationship of TAPSE and RVEF.

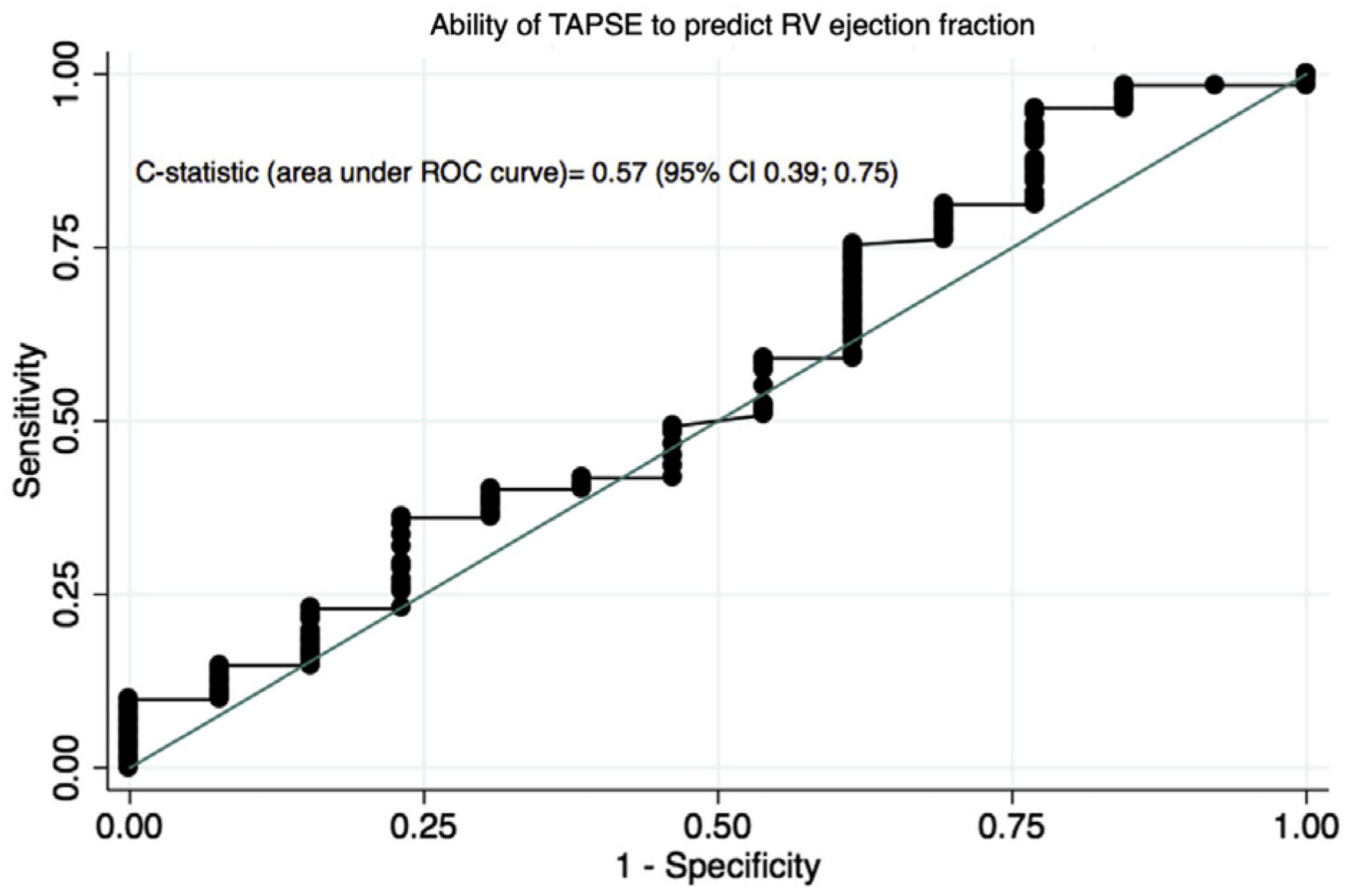


Figure 4. Receiver operating characteristic (ROC) curve displaying the ability of TAPSE to identify decreased RVEF (<50%) on CMR. C-statistic = 0.57 (95% CI, 0.39–0.75).

Table 1Patient characteristics ($n = 125$)

Variable	Value
Age (y)	12.5 \pm 3.2
Male	84 (67.2%)
Race/ethnicity	
Non-Hispanic white	104 (83%)
African American	15 (12%)
Asian	6 (5%)
Weight (kg)	42.8 \pm 15.7
Height (cm)	147 \pm 17.5
Ideal body weight (kg)	51.3 \pm 11
Body mass index (kg/m ²)	19.8 \pm 4.2
BSA (m ²)	1.31 \pm 0.3
Original pulmonary valve	
Stenosis	99 (79%)
Atresia	19 (15%)
Absent leaflets	7 (6%)
Age at surgical repair (mo)	4.4 (4.1–4.7)
Time elapsed since surgical repair (y)	7.5 (5.2–10.7)
Use of transannular patch	82 (66%)
TAPSE (cm)	1.6 \pm 0.38

Data are expressed as mean \pm SD, number (percentage), or median (interquartile range).

Table 2CMR and EST characteristics ($n = 125$)

Variable	Value		
CMR			
RVEF (%)	60.6 ± 8.3		
RVEF			
<50% ($n = 13$)	46 ± 4		
50% ($n = 112$)	62 ± 7		
RV cardiac output (L/min)	7.2 ± 2.5		
RV cardiac index (L/min/m ²)	5.5 ± 1.5		
RV stroke volume (mL)	92.8 ± 37		
RV stroke volume index (mL/m ²)	70.3 ± 19.3		
RVEDV (mL)	155.2 ± 63		
Indexed RVEDV (mL/m ²)	117.7 ± 34.4		
RVESV (mL)	62.4 ± 31.2		
Indexed RVESV (mL/m ²)	47 ± 20		
Pulmonary regurgitant fraction (%)	34.1 ± 16.73		
RV mass (g)	91 (67–127)		
RV mass (g/m ²)	76 (58–93)		
Pulmonary insufficiency*			
Mild or less	20 (16%)		
Moderate	49 (39%)		
Severe	50 (40%)		
Regional wall motion abnormalities [†]			
Yes	111 (89%)		
No	13 (10%)		
Left ventricular ejection fraction (%)	68.4 ± 7.1		
EST	Overall ($n = 125$)	RER > 1.1 ($n = 73$)	RER 1.1 ($n = 52$)
Peak V_{O_2} (mL/kg/min)	31.7 ± 8.41	33.5 ± 7.8	29.2 ± 8.4
V_{O_2} (L/min)	1.34 ± 0.56	1.56 ± 0.53	0.96 ± 0.38
V_{O_2} max%	76 ± 18.4	80 ± 18	70 ± 18
Maximum work (W)	114 ± 48.6	128.1 ± 50	84.3 ± 29
Oxygen pulse (mL/beat)	7.4 ± 3	8.58 ± 2.9	5.63 ± 2.1
RER	1.14 ± 0.13	1.22 ± 0.9	1.02 ± 0.07
VE/ V_{CO_2} at anaerobic threshold	39 ± 6.9	37.8 ± 6.61	42.3 ± 6.73
VE/ V_{CO_2} slope	37.9 ± 8.23	35.7 ± 6	41.6 ± 10.1
Measured anaerobic threshold	89 (68%)	65 (86%)	24 (48%)

RER, Respiratory exchange ratio.

Data are expressed as mean \pm SD, number (percentage), or median (interquartile range).

* Not assessed in six subjects.

† Not assessed in one subject.

Table 3

Comparison of TAPSE measurements with normal published values

Age (y)	Patients with TOF			Normal controls ²⁰			P
	n	Mean	SD	n	Mean	SD	
8	15	1.45	0.2720	23	1.97	0.1525	<.0001
9	17	1.48	0.3456	20	2.01	0.1425	<.0001
10	20	1.51	0.3518	27	2.05	0.13	<.0001
11	8	1.79	0.4137	25	2.1	0.1325	<.0001
12	10	1.45	0.2424	18	2.14	0.1475	<.0001
13	15	1.58	0.2554	20	2.2	0.1725	<.0001
14	9	1.60	0.4491	35	2.26	0.195	<.0001
15	9	1.74	0.3479	25	2.33	0.205	<.0001
16	11	1.72	0.5198	34	2.39	0.2	<.0001
17	12	1.93	0.4984	27	2.45	0.21	<.0001
18	7	1.62	0.1502	21	2.47	0.215	<.0001

Table 4

Associations among TAPSE, CMR, and EST adjusted for sex and BSA

Dependent variable	Parameter estimate (β)	SE	P
CMR			
RVEF	-0.61	2.1	.77
RV stroke volume	13.8	5.82	.02
RV cardiac output	0.31	0.46	.51
RVEDV	25.7	10.3	.01
RVESV	11.93	6.15	.055
RV mass	2.91	8.17	.72
Pulmonary regurgitation	7.72	4.2	.07
EST*			
Peak V_{O_2}	2.2	2.0	.28
Percentage predicted V_{O_2} [†]	8.15	4.96	.10
Oxygen pulse	0.72	0.48	.13
Maximum work	11.2	8.9	.21
VE/ V_{CO_2} slope	-1.14	1.69	.50

* Analysis limited to those with maximal tests (respiratory exchange ratio > 1.1).

[†] Age-matched and gender-matched normative data. 18,46