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RESEARCH ARTICLE

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Tricuspid annular plane systolic excursion in pulmonary hypertension—Moving beyond the sector plane

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Abstract

Tricuspid annular plane systolic excursion (TAPSE) is usually measured with M-mode using sector line, however, this may not align with the anatomical shortening of the right ventricular (RV). In this study, we compared the different methods to measure TAPSE using three different reference lines (sector line, anatomical line, and apico-annular line). We included 148 patients diagnosed with pulmonary arterial hypertension (PAH) who underwent TTE and right heart catheterization within 2 weeks of each other. TAPSE was measured by M-mode (sector, anatomical), 2D (sector, anatomical), or as tricuspid apico-annular displacement (TAAD). Agreement between measures was assessed using coefficient of variation (COV), Spearman's correlation, and Bland–Altman analysis. Receiver–operating characteristics and Kaplan–Meier analysis were used to explore associations with the combined outcome of death or lung transplantation at 5 years. There was a good concordance between anatomical and sector M-mode with a COV of $15.5 \pm 1.6\%$ and a bias of -0.6 ± 3.2 mm. In contrast, anatomical M-mode TAPSE and TAAD differed significantly with the mean difference of 3.3 ± 3.8 mm (COV $30.5 \pm 6.1\%$; $p < 0.0001$). Among the different 2D methods, anatomical 2D agreed well with anatomical M-mode TAPSE (COV of $11.8 \pm 2.0\%$; $r = 0.89$; $p < 0.0001$). Among the five methods, TADD had the strongest association with the combined endpoint of death or transplantation at 5 years (C-statistic 0.64, 95% confidence interval [CI] 0.57–0.71). We concluded that different measures of TAPSE are not interchangeable.

KEYWORDS
analytic variability, echocardiography, pulmonary Hypertension, TAPSE

INTRODUCTION

Tricuspid annular plane systolic excursion (TAPSE) is a simple and reproducible measure of right ventricular (RV) systolic function in transthoracic echocardiography (TTE).[1,2] According to the American Society of Echocardiography and the latest European Society of Cardiology guideline for pulmonary hypertension (PH), TAPSE is among the most feasible and reproducible metrics of RV longitudinal function in patients with PH.[1,2] Forfia et al. was one of the first to demonstrate its prognostic value in patients with pulmonary arterial hypertension (PAH).[3] Furthermore, the prognostic role of TAPSE to RV systolic pressure (RVSP) ratio is used clinically for noninvasive risk assessment of PAH patients.[4] Its value was also proven in patients with congenital heart disease and heart failure.[4,5]

TAPSE measures the longitudinal shortening of the RV, which is one of the important components of RV contraction along with the radial (transverse) and anteroposterior components.[6] Although mechanical studies have shown that a decrease in RV transverse shortening precedes a decrease in annular displacements,[7] the wide adoption of TAPSE in echocardiography can be explained by its simplicity, reproducibility, and association with outcome.[3–5]

M-mode with the cursor placed at the lateral wall of the tricuspid annulus (i.e., sector line, Figures 1a,b) is the standard method to measure TAPSE.[8] However, the sector line may not always align with the direction of the annular motion. Anatomical M-mode has been used as an alternative method to measure TAPSE, which allows to define a freely oriented line along the tricuspid annulus and thus enables to align the cursor with the direction of excursion (i.e., "anatomical" direction indicated as anatomical line in Figure 1a).[9] Here "anatomical" is defined by the axis with minimal Euclidean distance (the minimum distance between the two points) of the tricuspid annulus at end-diastole and end-systole. However, anatomical studies of the heart by Buckberg et al. have shown that the true anatomical direction of the annular motion follows the apico-annular line (Figure 1a) due to the existence of spiral apical

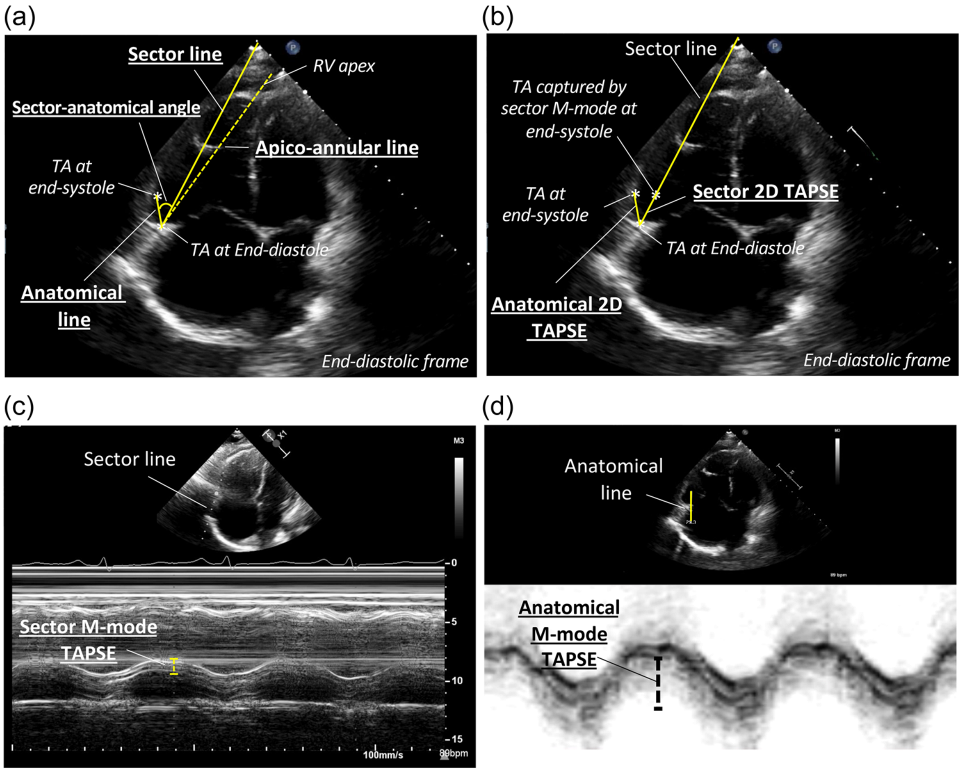

FIGURE 1 Definition of the reference lines and different methods to measure TAPSE. (a) Definition of the three different lines. Sector line connects the zero mark on the scale (transducer–skin interface) and the tricuspid annulus (TA) at end-systole (long yellow line). The asterisks show the TA at end-diastole and end-systole, and anatomical line is the line that connects the two asterisks (short yellow line). Apico-annular line connects the RV apex and TA (yellow dashed line). Sector-anatomical angle is defined as the angle between sector and anatomical line. (b) Sector 2D TAPSE was measured as the distance between the two asterisks on the sector line. Sector Anatomical 2D TAPSE was measured as the distance between the two asterisks on the anatomical line (i.e., the Euclidian distance between the TAs at end-systole and end-diastole). (c) Sector M-mode TAPSE measured using sector line (standard method). (d) Anatomical M-mode TAPSE measured by aligning the M-mode cursor to the anatomical line (yellow line). RV, right ventricular; TAPSE, Tricuspid annular plane systolic excursion.

loop[10,11]—which is measured as the change in the apico-annular distance (i.e, TAAD: tricuspid apico-annular displacement). TAAD has been more commonly measured in cardiac magnetic resonance and this measure may not be interchangeable with M-mode derived TAPSE.[12] Table 1 summarizes the concept of the different reference lines and their relationship with the tricuspid annular motion.

Another method used to measure TAPSE is based on 2D mode (Figure 1c). Methods using 2D could be useful when M-mode is unavailable[13–15] and has been used in research settings or as an extra-quality control measure. However, it has less spatial resolution than M-mode as the annular echo signals may not be well defined. Table 2 summarizes the concepts of these measures and compares the theoretical advantages of these methods.

To date, few studies have compared these different measures of tricuspid annular displacement in patients with PAH. This would be useful to quantify variability between anatomical and sector-based measures of M-mode and see whether they are interchangeable. In addition, this would offer validity to the 2D methods for research or to add extra quality control when M-mode TAPSE is suboptimal. Therefore, the first aim of this study is to compare the methods based on three different reference lines (sector line, anatomical line, and apico-annular line), and also show how the sector-anatomical angle influences the M-mode measurements. The second aim is to compare the measurements obtained by M-mode and 2D methods. The third aim is to explore the association between TAPSE or TAAD and the combined endpoint of death or transplantation at 5 years in an exploratory analysis.

METHODS

Study population

This study was approved by the Stanford University Institutional Review Board (IRB #14083, #20942) and all patients gave written informed consent. Patient cohorts from Stanford Adult Pulmonary Hypertension Program and Vera Moulton Wall Center for Pulmonary Vascular Disease Database[16] were retrospectively analyzed in this study. The inclusion criteria of both cohorts were diagnosis of PAH according to the guidelines at the time of diagnosis (mean pulmonary arterial pressure [mPAP] ≥25 mmHg and pulmonary arterial wedge pressure ≤15 mmHg measured by invasive right heart catheter [RHC]) and by ruling out other causes of PH. Patients with other etiologies of PH and patients with complex congenital heart diseases such as Eisenmenger syndrome

TABLE 1 Annular motion and reference lines.

Reference line	Measure	Method	Number of references
Sector line	Excursion towards the probe	M-mode/2D	1 (M-mode), 2 (2D)
Anatomical line	Euclidian distance	M-mode/2D	1 (for both)
Apico-annular line	Apico-annular shortening	2D	1

TABLE 2 Comparison of methods to assess different reference lines.

	Sector M-mode	Anatomical M-mode	TAAD
Temporal resolution	Highest	Lower	NA (2 phases)
Spatial resolution	Highest	Lower	Lower
Alignment motion	With sector line	with Euclidian distance	Apical annular
Easy tracking	If aligned with excursion	If aligned with excursion	If annuls well-defined
Susceptibility to			
Translation	Yes	Yes	Less
Apical foreshortening	No	No	yes
Apical aneurysm	No	No	Yes
View	Usually in RV-focused view- may be best in modified view (aligned)	Flexible to different views	Usually in RV focused view

Abbreviations: NA, not available; RV, right ventricular; TAAD, tricuspid apico-annular displacement.

and sinus venosus defect were excluded. For this study, we selected 148 patients from this cohort who had M-mode TAPSE measured with TTE and RHC performed within 2 weeks.

Echocardiographic assessment

Echocardiographic images were acquired using Hewlett Packard Sonos 5500 or Philips IE33 ultrasound systems. All the images were obtained according to the American Society of Echocardiography guidelines for chamber quantification[17] and the measurements were performed using the TomTec-Arena 2.51 (TomTec Imaging system). RV parameters were measured on the RV-focused apical four-chamber views in the research core laboratory by certified sonographers and verified by trained cardiologists (K.I., B.E.C). End-diastole (ED) and end-systole (ES) were defined by largest and smallest chamber size, respectively. Comprehensive measures of the right heart were performed, including RV areas, basal and mid-transverse dimensions, and right atrial volumes. Right heart dimensions were indexed using height for diameters and body surface area for areas. RV mid transverse diameter was measured by the method described by Kind et al.[18] RVFWS and RVFAC were measured using the same frame to ensure maximal consistency. RVFWS was measured using the length of line method from the tricuspid annulus to RV apex and calculated as (end-systolic—end-diastolic RV free wall length/end-diastolic RV free wall length).[16] Value of RVFWS is presented in absolute value for consistency with other RV functional parameters. Left ventricular diameters were measured in the parasternal long-axis views, and the LV ejection fraction was quantified using Simpson's method.

We measured TAPSE by M-mode (sector, anatomical), 2D (sector, anatomical), and TAAD, all of which were measured in the same RV-focused apical four-chamber view. Two blinded individuals measured the TAPSE values with different methods as show (Supporting Information S1: Table 1). Sector M-mode TAPSE was measured by the conventional M-mode tracing with the cursor at the lateral tricuspid valve annulus captured during the routine echocardiography examination (Figure 1b). Sector 2D TAPSE was measured as the difference in the distance between the zero mark (transducer-skin interface) and the lateral tricuspid annulus at ED and ES (Figure 1c).[19] Anatomical 2D TAPSE was measured by annotating the lateral tricuspid annulus at ED and ES with an asterisk and measuring the distance between the two asterisks (Figure 1c). Anatomical M-mode TAPSE was measured using TomTec post-processing tool 2D cardiopulmonary performance analysis and by aligning the M-mode cursor perpendicular to the tricuspid annular plane excursion plane (Figure 1d). TAAD was measured as the difference in the distance between the RV apex and the lateral tricuspid annulus at ED and ES. The sector-anatomical angle was measured as described in Figure 1a.

We collected demographic data (sex, date of birth, age, race, height, and weight) and clinical data (systolic and diastolic blood pressure, heart rate, etiology of PAH, comorbidities, medications, transplant, date of transplant, death, and date of death) using the hospital medical chart of each patient. The RHC parameters were obtained through the Stanford Adult Pulmonary Hypertension Program and Vera Moulton Wall Center for Pulmonary Vascular Disease Database which have all the RHC parameters for each patient who underwent RHC. Biological data (NT-proBNP, GFR, hemoglobin, Na, bilirubin) were collected using the lab results in the medical chart, and we chose the closest value to the echo date to be the most representative of the patient's condition during this time.

Statistical analysis

Statistical analyses were performed using GraphPad Prism 9 and MEDCALC v22.014 software. Descriptive statistics for continuous variables were summarized as mean ± standard deviation (SD) if they did not have significant deviation from normal distribution. Otherwise, data were presented as median and interquartile range (IQR). Categorical variables were summarized as a proportional number of subjects (%).

We calculated the coefficient of variation (COV) using the root square mean method to assess the variability of the different TAPSE measurement methods. For the comparison of the different methods of TAPSE, linear regression equations were used to assess the relationship between them with Spearman's correlation coefficient (r) and coefficient of determination (R^2). Bland–Altman analysis was conducted using GraphPad Prism 9 to assess the agreement between the two measurements (TAPSE measured by sector vs anatomical M-mode method, or anatomical M-mode TAPSE vs TAAD).

We performed a receiver operator characteristic (ROC) curve analysis with C-statistic and Kaplan–Meier survival analysis for outcome analysis. The outcome was death or transplant within 5 years. We used a logistic regression model with ROC curve and C-statistic to assess how each TAPSE method's model can predict outcomes. The C-statistic results were presented using a Forest plot showing central values and their confidence intervals for each TAPSE method. Kaplan–Meier survival analysis was performed to assess the differences between patients according to the tertile classification of anatomical M-mode TAPSE or TAAD.

RESULTS

Patient characteristics

A total of 424 patients were screened from the database with an initial diagnosis of PAH or mixed PAH from 1989 to 2021. Among them, 240 patients had RHC and TTE within 2 weeks, and 223 had a final diagnosis of PAH. We identified 148 cases who had TTE with M-mode TAPSE measured at the time of image acquisition and included in the analysis. Ninety-two patients did not have M-mode TAPSE measured as this was not a standard measurement at the time and thus was excluded from the analysis. Also, some were done as focused limited studies that were close to the RHC and thus lacked M-mode TAPSE measurement.

The patient characteristics are summarized in Table 3. Selected TTE parameters of the RV and the left ventricle (LV) metrics are summarized in Table 4. The majority of the patients were female (80%), mean age was 49.6 ± 14.4 years, and 55.4% ($n = 82$) were Caucasians. The majority had either idiopathic (46.6%) or connective tissue disease-associated (27.0%) PAH. The mPAP was 50.7 ± 14.3 mmHg, and pulmonary vascular resistance index (PVRi) was 22.1 ± 11.3 WU m^2; 31.1% of patients were in New York Heart Association (NYHA) class IV status, and 44.6% had NT-proBNP > 1100 pg/mL (severity criteria). The median and IQR range for the Registry to Evaluate Early and Long-term PAH Disease Management (REVEAL) Lite score was 8.0 [6.0–10.0], and 36.5% of the patients ($n = 54$) were treatment naïve at the time of TTE.

Comparing m-mode TAPSE and TAAD measures

First, we compared the methods based on three different reference lines (sector line, anatomical line, and apico-annular line, Figure 1a). As one of our aims was to investigate how the sector-anatomical angle would affect the TAPSE values measured by different methods, we selected the anatomical M-mode (which by definition would not be confounded by sector-anatomical angle) as the reference method of comparison. The COV between

TABLE 3 Patient characteristics of the pulmonary arterial hypertension cohort.

	Population ($n = 148$)
Demographics	
Age	49.6 (14.4)
Male	30 (20.0%)
White Race	82 (55.4%)
Etiology	
Idiopathic	69 (46.6%)
Connective tissue disease	40 (27.0%)
Drug and toxin	4 (2.7%)
Hereditary	2 (1.3%)
Simple repaired congenital	3 (2.0%)
Medications	
Treatment naive	54 (36.5%)
Biological markers	
NT-proBNP (pg/mL)	
<300	40 (27.0%)
300–1100	42 (28.4%)
≥1100	66 (44.6%)
GFR by CKD-EPI (mL/min/1.73m^2)	54.3 (20.1)
Sodium (mM)	137 (3.4)
Hemoglobin (g/dL)	13.2 (2.3)
Bilirubin (mg/dL)	0.93 (1.1)
RHC parameters	
mPAP (mmHg)	50.7 (14.3)
RAP (mmHg)	9.2 (5.6)
PAWP (mmHg)	11.1 (4.5)
CI (L/min/m^2)	2.1 (0.7)
PVRi (WU m^2)	22.1 (11.3)
NYHA status	
1	4 (2.7%)
2	35 (23.6%)
3	63 (42.6%)
4	46 (31.1%)
Reveal Lite 2.0 score	
≤5	37 (25.0%)
6–7	32 (21.6%)
≥8	79 (53.4%)

(Continues)

TABLE 3 (Continued)

	Population ($n = 148$)
Outcomes	
Death or transplant within 5 years	31 (21.1%)

Abbreviations: CDK-EPI, Chronic Kidney Disease Epidemiology Collaboration; CI, cardiac index; GFR, glomerular filtration rate; IV, intravenous; mPAP, mean pulmonary arterial pressure; NYHA, New York Heart Association; PAWP, pulmonary artery wedge pressure; PVRi, indexed pulmonary vascular resistance; RAP, right arterial pressure; RHC, right heart catheterization.

TABLE 4 Echocardiographic parameters of the pulmonary arterial hypertension cohort.

Metrics	PAH, $n = 148$ mean (SD)
RV dimensions	
Basal transverse diameter (diastole, mm/m)	54.9 (10.5)
Mid transverse diameter (diastole, mm/m)	48.2 (11.0)
RV areas (cm^2/m^2)	
RVEDAi (cm2/m2)	20.2 (6.0)
RVESAi (cm2/m2)	16.4 (5.8)
RA volume(ml/m2)	44.9 (28.1)
RV function	
RVFAC (%)	20.1 (6.6)
RVFWS in absolute value (%)	13.1 (4.6)
LV metrics	
LV internal diameter (mm)	40.0 (7.0)
LV internal diameter (mm/m)	23.2 (4.0)
LVEF Simpson (%)	65.8 (7.9)

Abbreviations: LV, left ventricle; LVEF, left ventricular ejection fraction; RA, right atrial; RV, right ventricular; RVEDAi, indexed right ventricular end-diastolic area; RVESAi, indexed right ventricular end-systolic area; RVFAC, right ventricular fractional area of change; RVFWS, right ventricular free-wall strain.

anatomical M-mode and sector M-mode TAPSE was in a lower range (15.5 ± 1.6%) compared to TAAD (30.5 ± 6.1%, Figure 2a). Accordingly, the correlation between anatomical M-mode and sector M-mode TAPSE was stronger ($r = 0.77$; $p < 0.001$) than that of anatomical M-mode TAPSE and TAAD ($r = 0.66$; $p < 0.0001$, Figure 2b). Bland–Altman analysis showed the mean difference between the anatomical M-mode and sector M-mode TAPSE was 0.58 ± 3.2 mm (Figure 2c) with no significant bias between the two measurements ($p = 0.30$), whereas anatomical M-mode TAPSE and TAAD differed significantly with the mean difference of 3.32 ± 3.8 mm ($p < 0.0001$; Figure 2d).

Sector-anatomical angle and its relationship with M-mode measures

Next, we sought to investigate the factor that determines the discrepancy between sector and anatomical M-mode TAPSE. The distribution of the sector-anatomical angle is shown in Figure 2e, where the median was 13.3°; the sector-anatomical angle was less than 15° in 82 patients (55%). Multiple linear regression analysis showed that the sector-anatomical angle was the most important factor among the other RV parameters (RVFAC, RV diameter, RVFWS) to explain the discrepancy between the two TAPSE measurements (Supporting Information S1: Table 2). While we observed a linear relationship between the sector-anatomical angle and the difference of TAPSE measures (ΔM-mode TAPSE) when the angle was below or equal to 15° ($r = 0.35$; $p < 0.001$), the correlation was lost when the angle was beyond 15° as ΔM-mode TAPSE was highly variable ($r = 0.12$; $p = 0.35$).

TAPSE measured by anatomical methods correlate better than that measured by sector methods

Next, we measured TAPSE with 2D methods and compared with M-mode TAPSE. The COV between anatomical M-mode TAPSE and anatomical 2D TAPSE was 11.8 ± 2.0%, whereas that between sector M-mode TAPSE and sector 2D TAPSE was 30.3 ± 2.0%. The correlation between TAPSEs measured by anatomical methods was stronger (Figure 3a; $r = 0.89$; $p < 0.0001$) compared to that measured by 2D methods (Figure 3b; $r = 0.45$; $p < 0.0001$).

Bland–Altman analysis showed the mean difference between the TAPSEs measured by anatomical methods was 0.66 ± 2.3 mm (Figure 3c) with no significant difference ($p = 0.41$), whereas TAPSEs measured by sector methods differed significantly with the mean difference of 1.5 ± 5.5 mm ($p = 0.04$; Figure 3d).

Comparison of TAPSE measured with different methods and outcomes (exploratory analysis)

In general, TAPSE measured by M-mode methods and TAAD showed mild to moderate correlations with RVFAC and RVFWS measured by TTE, and with the hemodynamic parameters measured by RHC (Figure 4a).

Among the five different methods, TAAD had the highest association with the combined outcome of death or transplantation in 5 years (C-statistic 0.64, 95% CI

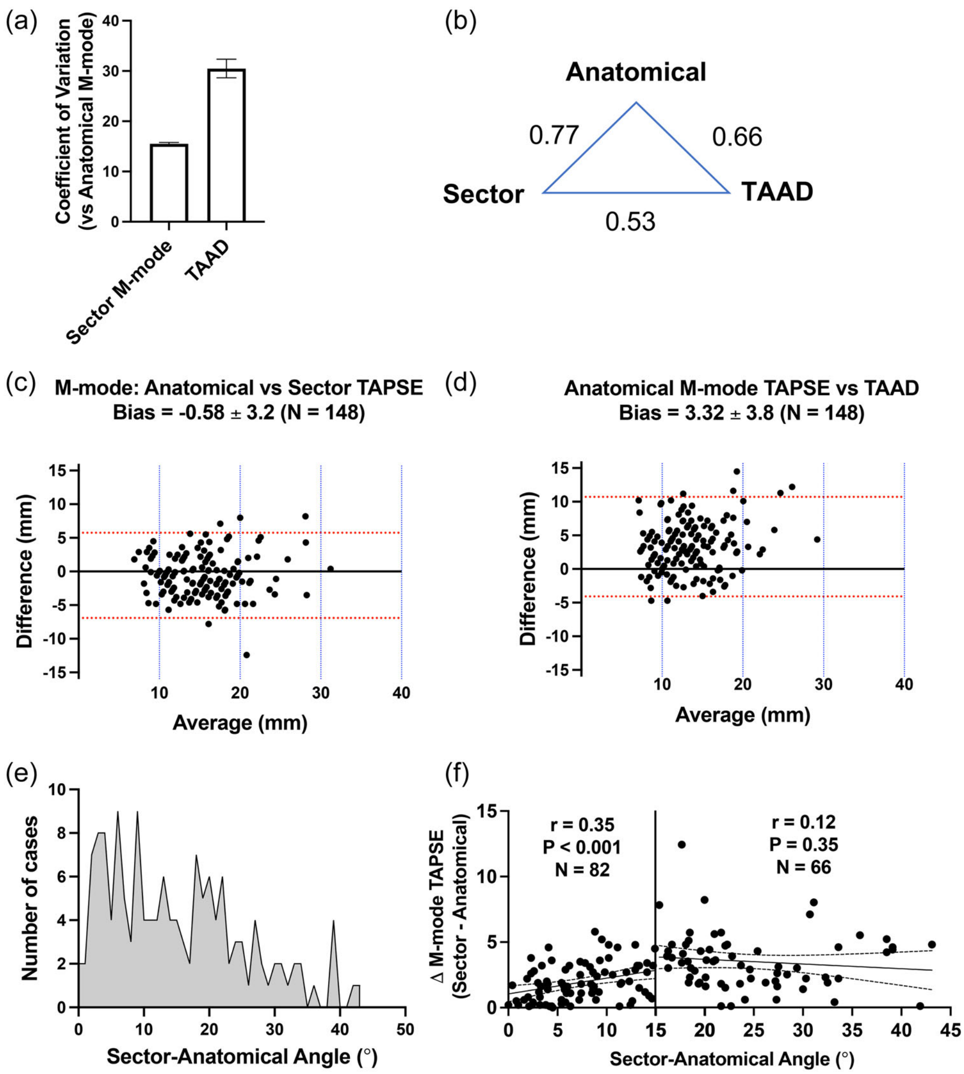

FIGURE 2 TAPSE measured by M-mode methods and TAAD. (a) Coefficient of variation between TAPSE was measured with anatomical M-mode and sector M-mode, or TAAD. Data are shown as mean ± SD. (b) Correlation between TAPSE measured in different methods calculated with Spearman's correlation. Correlation coefficient (r) is overlayed in the diagram. (c) Bland–Altman plot showing the average and difference of TAPSEs measured with M-mode methods (anatomical vs sector). (d) Bland–Altman plot showing the average and difference of anatomical M-mode TAPSE and TAAD. (e) Histogram showing the distribution of sector-anatomical angle measured in the patient cohort of PAH. (f) Simple linear regression model shows the correlation between the sector-anatomical angle and the discrepancy between M-mode TAPSE measured with sector and anatomical methods (ΔTAPSE). Model is separated with a sector-anatomical angle cutoff of 15°. PAH, pulmonary arterial hypertension; TAAD, tricuspid apico-annular displacement; TAPSE, tricuspid annular plane systolic excursion; SD, standard deviation.

0.57–0.71; Figure 4b). Similarly, the forest plot of TAPSE/RVSP ratio calculated with the five different methods also showed that TAAD/RVSP had the highest C-statistics (0.63, 95% CI 0.56–0.71) followed by sector 2D sector TAPSE/RVSP with the C-statistics of 0.61 (95% CI 0.54–0.68, Supporting Information S1: Figure 1). Similarly, in subgroup analyses of patients with sector-anatomical angle below or equal to 15° (Supporting Information S1: Figure 2a) and in patients with the angle above 15° (Supporting Information S1: Figure 2b), TAAD had the numerically highest C-statistics. However, the 95% CI of the C-statistics all overlapped to each other, showing that none of the methods are superior to each other.

Kaplan–Meier curve of anatomical M-mode TAPSE method showed patients with TAPSE above 17 mm had slightly better survival compared to those with 17 mm or less but without statistical significance ($p = 0.23$; Figure 4c), whereas patients with TAAD above 14 mm had significantly better outcome compared to those with 14 mm or less ($p = 0.0008$; Figure 4d). This difference was also found in patients with a sector-anatomical angle

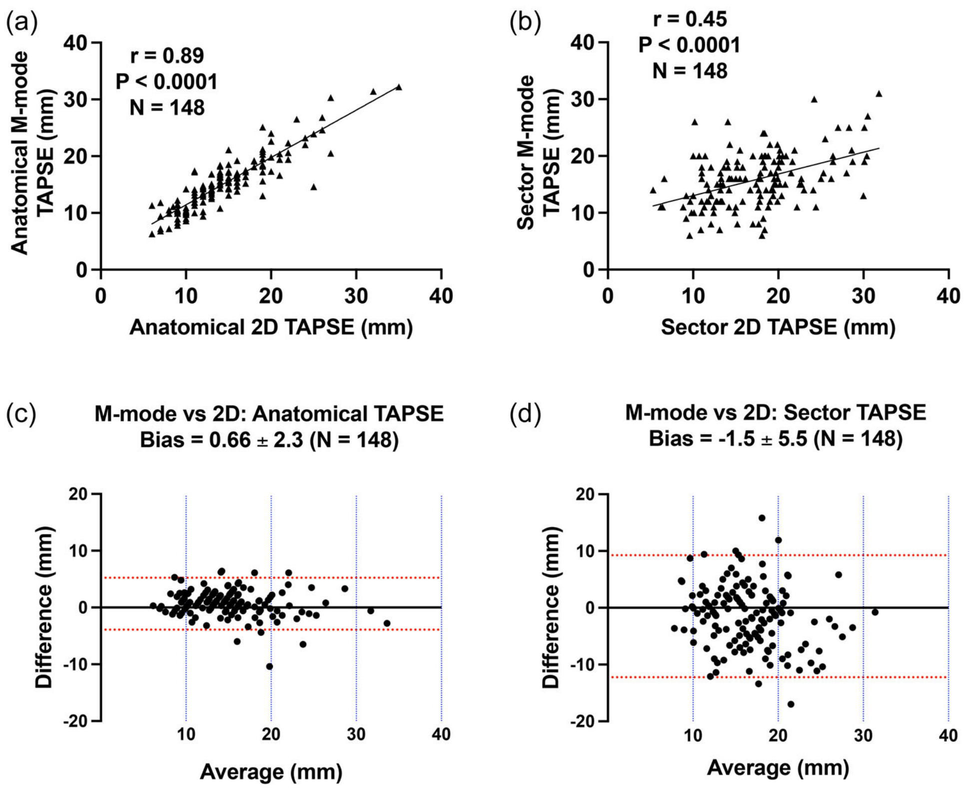

FIGURE 3 TAPSE measured by 2D methods. (a) Simple linear regression model shows the correlation between anatomical M-mode and anatomical 2D TAPSE. (b) Simple linear regression model shows the correlation between sector M-mode and sector 2D TAPSE. (c) Bland-Altman plot showing the average and difference of TAPSEs measured with anatomical methods (M-mode vs 2D). (d) Bland–Altman plot showing the average and difference of TAPSEs measured with sector methods (M-mode vs 2D). TAPSE, tricuspid annular plane systolic excursion.

below or equal to 15° (Supporting Information S1: Figures 2c,e) and in patients with an angle above 15° (Supporting Information S1: Figures 2d,F).

DISCUSSION

Our study had three main findings. First, we demonstrate that the TAPSE measured using anatomical or sector M-mode are not interchangeable; in addition, they also differ from TAAD.

We have also shown that the difference between sector and anatomical M-mode TAPSE is dependent on the sector-anatomical angle. Second, we have demonstrated that in the absence of M-mode, 2D methods especially anatomical M-mode show a strong association; this could be valuable for retrospective analysis or when the quality of the M-mode does not allow clear delineation of annular motion. Third, our exploratory analysis suggests that TAAD, a measure of apico-annular shortening, also carries prognostic information.

TAPSE is widely accepted as an easy and reliable method to measure RV systolic function. Sector M-mode is the most widely used method and is reproducible in the absence of translational motion or respiratory-phasic variations. Compared to other methods it also has the advantage of having better spatial and temporal resolution. It has, however, the disadvantage of not always aligning with the direction of tricuspid annular motion. For this reason, anatomical M-mode was introduce offering flexibility in interrogation angles, however, at the cost of lower resolution. TAAD was first introduced by Speiser et al. as a method to measure RV shortening along the apico-annular axis in cardiac magnetic resonance[12] and has been shown to predict prognosis in patients with PH.[19] This method has the benefit of incorporating the entire RV motion in the calculation, whereas other methods only consider the motion of the tricuspid annulus. This is important as RV contraction involves not only the longitudinal motion of the lateral wall but also the helical motion caused by the cardiac wrap, which is continuous to the LV-free wall.[10] When M-mode measures are not available for TAPSE measures, other investigators have introduced 2D-based methods. Qureshi et al. introduced an alternative method to measure TAPSE using 2D images (sector 2D method),

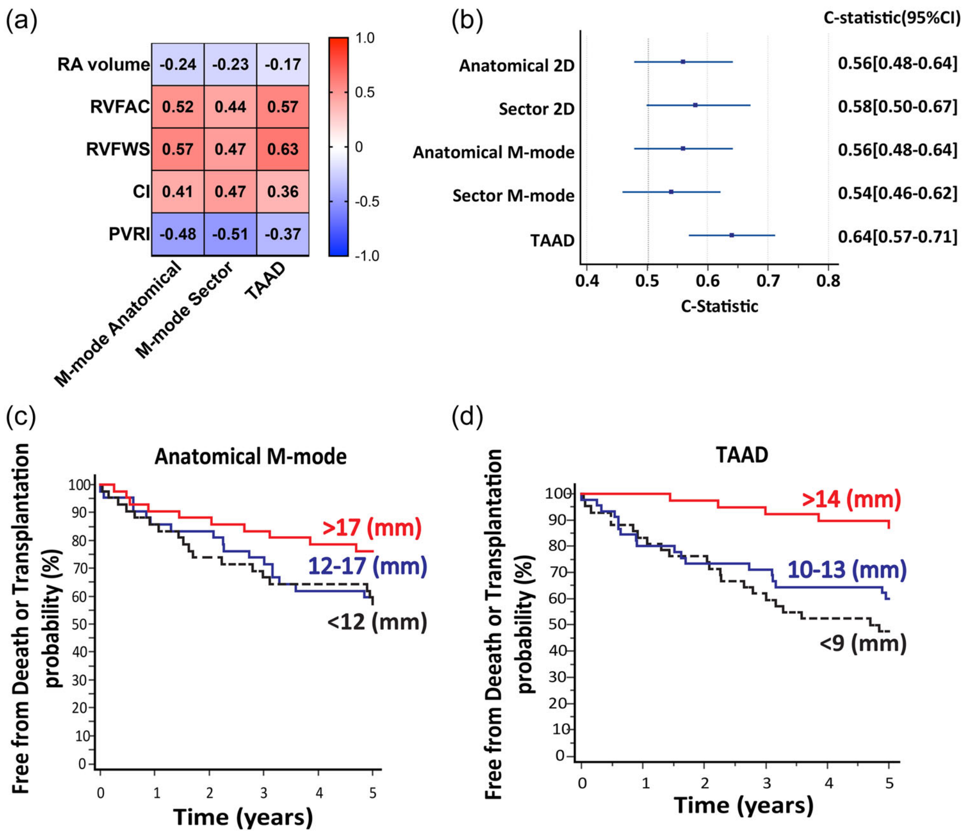

FIGURE 4 Comparison of TAPSE measured with different methods and outcomes. (a) Correlation map was created with Spearman's correlation. Correlation coefficient (*r*) is overlayed in the map. (b) Forest plot comparing the C-statistic of 5 years outcome (death or transplantation) predictive performance of each TAPSE method. (c) Kaplan-Meier curve stratified by tertile groups of anatomical M-mode TAPSE. (d) Kaplan–Meier curve stratified by tertile groups of TAAD.

which enables TAPSE measurements in cases where M-mode has not been acquired as part of the routine study.[20] Although this study was initially performed on a pediatric population, Skinner et al. demonstrated a strong correlation between M-mode TAPSE and 2D TAPSE using transesophageal echocardiography. [13]

Original to our study, we compared TAPSEs measured by M-mode methods (anatomical and sector) and showed that they correlate well when the sector-anatomical angle is small. This suggests the importance of aligning the tricuspid annular motion and the sector-anatomical line when measuring TAPSE in sector methods. Efforts should therefore be made to modify the view to best align the sector line with the axis of motion. However, when this is technically challenging, anatomical 2D method can be a reasonable alternative to measure TAPSE. We measured anatomical 2D TAPSE utilizing image analysis software that allowed us to annotate images with a labeled marker in both in ES and ED (Figure 1c) and showed that anatomical 2D method is the most consistent method with anatomical M-mode TAPSE. The inclusion of annotation systems that are easy to use will be essential for implementing 2D methods. We have also measured TAAD using TTE and demonstrated its feasibility, of which the measurements were on average lower than M-mode and 2D measurements. Interestingly, in our predefined exploratory analysis, TAAD had a stronger signal with outcome when compared to other methods with lower cutoff (14 mm) compared to the current guideline recommendation (17 mm).[2]

Our findings have three implications. First, TAPSE measured by different methods are not interchangeable, and it will likely be important to select the same method for longitudinal comparison. Second, when M-mode TAPSE has not been obtained during routine studies or is technically challenging, 2D-based methods can be used as an alternative. In that case, measuring with anatomical 2D method appears to be reasonable as the measurement correlates better with that of anatomical M-mode method. Lastly, more studies are needed to assess the value of TAAD in echocardiography.

This study has several limitations. First, this study is intended as a methodological study and thus our focus was not on the outcome analysis and had a relatively small sample size. Second, we did not report the image quality of individual patients. Third, due to the limited number of patients that were treatment naïve and the overall cohort size, we were not able to compare the effect of therapy on TAPSE values. However, we performed a sensitivity analysis in patients who had RHC before or after TAPSE and found that TAPSE values did not differ between these two cohorts (Supporting Information S1: Figure 3). Lastly, our analysis included every patient that had RHC and TTE within 2-week time window regardless of their clinical setting (i.e., inpatient or outpatient) or heart failure status (i.e., acute or chronic right heart failure). However, TAPSE values were comparable between patients that had RHC and TTE within 2-day time window and others (Supporting Information S1: Figure 4).

In conclusion, the different methods to measure TAPSE are not interchangeable. Thus longitudinal studies with TAPSE need to be conducted using the same TAPSE method. Further studies are needed to validate the value of TAAD using echocardiography in PAH.

AUTHOR CONTRIBUTIONS

Kenzo Ichimura and Francois Haddad contributed to the study design, conceptualized the study conception, and interpreted the data. Kenzo Ichimura and Bettia E. Celestin acquired and analyzed the data. Kenzo Ichimura, Bettia E. Celestin, Shadi P. Bagherzadeh, and Francois Haddad participated in drafting the manuscript. Roham T. Zamanian, Michael Salerno, and Edda Spiekerkoetter revised the manuscript critically for important intellectual content. All authors approved the final version for publication and take responsibility for appropriate portions of the content.

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CONFLICT OF INTEREST STATEMENT

Dr. Haddad reports research grants from Actelion Pharmaceuticals, a Janssen Company of Johnson & Johnson, focused on computational approaches for the diagnosis and monitoring of pulmonary hypertension. The other authors report no conflicts relevant to this study.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

This study was approved by the Stanford University Institutional Review Board (IRB #14083, #20942) and all patients gave written informed consent.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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