Characteristics and Significance of Tricuspid Valve Prolapse in a Large Multidecade Echocardiographic Study

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Background: Characteristics of tricuspid valve prolapse (TVP) on transthoracic echocardiography are not well defined. As tricuspid valve interventions are increasingly considered, information on the definition and clinical significance of TVP is needed.

Methods: At the authors' institution, between January 26, 2000, and September 20, 2018, 410 patients (0.3%) were determined to have suspected TVP. These transthoracic echocardiograms and those of 97 age- and sex-matched normal control subjects were reviewed. Interrater agreement on TVP by visual inspection was assessed in a blinded subset. Leaflet atrial displacement (AD) > 2 SDs above the mean in normal control subjects was used to identify an empiric definition of TVP Features of patients meeting this definition were evaluated.

Results: Three hundred twelve transthoracic echocardiograms with available and interpretable images (76.1%) were included. Interrater agreement on TVP diagnosis by visual inspection was moderate. Normal values of AD were up to 4 mm in the right ventricular inflow view and 2 mm in all other views. AD > 2 mm in the parasternal short-axis view had the best accuracy against suspected TVP to identify TVP. Those with TVP by this definition more frequently had 3 to 4+ tricuspid regurgitation (22.2% vs 3.1%; $P < .001$), mitral valve prolapse (MVP; 75.0% vs 3.1%; $P < .001$), and more clinically significant MVP (greater prevalence of 3 to 4+ mitral regurgitation). No difference in mortality was observed in those with isolated TVP versus TVP and MVP (log-rank $P = .93$).

Conclusions: In the largest study of TVP to date, interrater agreement on TVP diagnosis by visual inspection was moderate. A cutoff of >2-mm AD in the parasternal short-axis view was optimal to define TVP. Those with TVP by this definition had more significant tricuspid regurgitation, larger right ventricles, and more clinically significant MVP. Overall, these results suggest an increased role for surveillance for TVP and the need for clear diagnostic criteria in updated guidelines. (J Am Soc Echocardiogr 2021;34:30-7.)

Keywords: Tricuspid valve, Prolapse, Mitral valve prolapse

Tricuspid valve prolapse (TVP) leading to systolic prolapse of leaflets across the tricuspid annular plane is a rare finding on transthoracic echocardiography and of uncertain clinical significance. In totality, fewer than 50 cases have been reported in the literature,[1-8] leading to uncertainty about the true prevalence of TVP, associated clinical disorders, and its impact on outcomes. Moreover, as diagnostic criteria for TVP have not yet been established, TVP diagnosis is on the basis of visual inspection of the tricuspid valve, yet agreement among physicians on the diagnosis of TVP using this method remains unclear.

Given the emergence of transcatheter interventions for tricuspid regurgitation (TR) and recent data suggesting the adverse impact of isolated TR on clinical outcomes,[9] there is a growing need to understand the prevalence TVP and associated clinical conditions. As such, we sought to (1) define clinical TVP from a clinical database of 218,943 transthoracic echocardiographic reports at Beth Israel Deaconess Medical Center (BIDMC) and (2) identify associations between TVP and associated clinical conditions and echocardiographic findings, most notably mitral valve prolapse (MVP).

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Abbreviations

4CH = Apical four-chamber

AD = Atrial displacement

BIDMC = Beth Israel Deaconess Medical Center

eTVP = Empiric tricuspid valve prolapse

MR = Mitral regurgitation

MVP = Mitral valve prolapse

PSAX = Parasternal short-axis

RVI = Right ventricular inflow view

sTVP = Suspected tricuspid valve prolapse

TR = Tricuspid regurgitation

TTE = Transthoracic echocardiogram

TVP = Tricuspid valve prolapse

METHODS

Study Population

Structured echocardiographic report data from 218,943 consecutive transthoracic echocardiograms (TTEs) obtained from January 1, 2000, to September 20, 2018, at BIDMC and stored in the ENCOR data set were queried. As part of routine care at BIDMC, echocardiographic data were entered, at the time of clinical interpretation, by National Board of Echocardiography level III certified faculty echocardiographers into reporting software that stores echocardiographic measurements and findings in a large electronic database (the ENCOR database). The ENCOR database is maintained by clinical informatics and is evaluated routinely for accuracy and completeness. All echocardiographic images were acquired using GE E-95, Vivid 7 and 9, Vivid Q, Vivid i, and Vivid S70 (GE Medical Systems, Milwaukee, WI) and Hewlett-Packard Medical Products (Palo Alto, CA) 5000 and 5500 echocardiographs.

TVP is a structured field in the ENCOR data set. All transthoracic echocardiographic reports with suspected TVP (sTVP) were identified and images manually reviewed by two resident physicians (M.K.L., M.J.B.), trained in image interpretation by a board-certified echocardiographer (J.B.S.). The maximal systolic atrial displacement (AD) of each of the tricuspid valve leaflets from the tricuspid annular plane to the belly of the leaflets was measured in three views (apical four-chamber [4CH] view, parasternal short-axis [PSAX] view at the level of the aortic valve, and right ventricular inflow [RVI] view; Figure 1). Leaflets in each view were named according to published convention.[10] Additionally, annular dimensions were measured in mid-systole, and the presence of tricuspid annular disjunction or mid to late systolic TR was recorded. If the tricuspid leaflets did not extend beyond the tricuspid annular plane into the right atrium during systole, AD was recorded using negative values as the maximal distance from the tricuspid annular plane to the belly of the leaflets (Figure 2). Tricuspid leaflet excursion above the tricuspid annular plane was recorded using positive values (Figure 2). Those TTEs not available for review in EchoPAC version 2.0 (GE, Boston, MA) or with insufficient image quality in all three views for accurate measurements were excluded. Additionally, stress echocardiograms, intracardiac echocardiograms, transesophageal echocardiograms, and TTEs with tricuspid valve replacement or demonstrating mitral or tricuspid valve endocarditis were excluded. All measurements were made with a leading edge–to–leading edge convention as per American Society of Echocardiography guidelines.[11] Only an individual's first TTE was used. This study was approved by the institutional review board at BIDMC with a waiver of the requirement to obtain informed consent.

Definition of TVP

To identify AD cutoffs that best distinguished patients with TVP from normal control subjects, a random subset of 100 age- and sex-matched individuals with normal tricuspid valves and no histories of MVP were manually reviewed by two physicians (M.K.L., M.J.B.) and both AD and annular dimensions were measured in all three views. In a random subset of 40 TTEs (20 from patients with sTVP and 20 from control subjects), images were reviewed in a blinded fashion by two reviewers (M.K.L., J.B.S.) to determine agreement on visual assessment of TVP status.

Covariates and Outcomes

Basic demographics (age, sex, blood pressure, heart rate, height, weight, inpatient or outpatient status) and echocardiographic variables were extracted from the TTE demonstrating TVP. All linear measurements were indexed for body surface area according to the Mosteller formula.[12] Echocardiographic variables included left atrial anteroposterior and superoinferior linear dimensions,

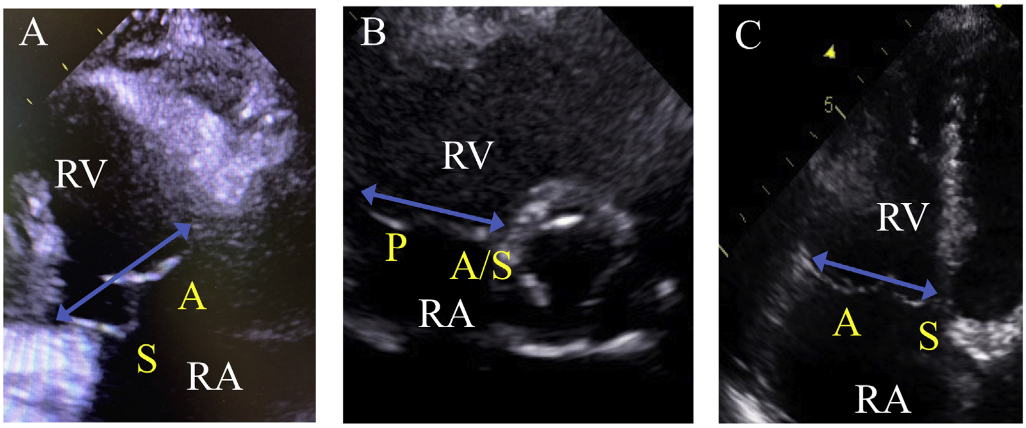

Figure 1 Sample transthoracic echocardiographic images demonstrating location of the tricuspid annular plane in multiple views. Transthoracic echocardiographic views of individuals with TVP demonstrating the location of the tricuspid annular plane *(blue double-headed arrow)* in the RVI view **(A)**, the PSAX view at the level of the aortic valve **(B)**, and the 4CH view **(C)**. *Yellow letters* indicate the respective tricuspid valve leaflets identified. *A*, Anterior; *A/S*, anterior or septal; *P*, posterior; *RA*, right atrium; *RV*, right ventricle; *S*, septal.

HIGHLIGHTS

- TVP is rare on transthoracic echocardiography and of uncertain significance.
- Over 18 years, sTVP was present in 0.3% of individuals.
- Seventy-five percent of those with TVP had associated MVP.
- Leaflet AD > 2 mm in the PSAX view best defined TVP.
- TVP was associated with more TR and clinically significant MVP.

right atrial superoinferior length, left ventricular end-diastolic and end-systolic diameter, interventricular and inferolateral wall thickness, left ventricular ejection fraction (as recorded in the transthoracic echocardiographic report), right ventricular basal diastolic diameter, peak aortic valve velocity by continuous-wave Doppler, transmitral valve peak E-wave and A-wave velocities by pulsed-wave Doppler at the mitral valve tips (and their ratio), E/e′ ratio using an average of lateral and septal e′ velocity measurements, and the estimated peak TR pressure gradient by the modified Bernoulli equation. Mitral regurgitation (MR), TR, and aortic regurgitation severity were semiquantitatively graded (0+, 1+, 2+, 3+, or 4+) per the American Society of Echocardiography guidelines.[13] The presence of MVP, flail or partial flail mitral valve leaflet, or aortic valve prolapse at the time of the TTE demonstrating TVP was determined by query of structured data fields. The primary outcome included all-cause mortality determined from linkage to the Social Security Death Master File.

Statistical Analysis

Among the 40 TTEs with blinded review, κ statistics were used to quantify interreader agreement on TVP status by visual inspection.

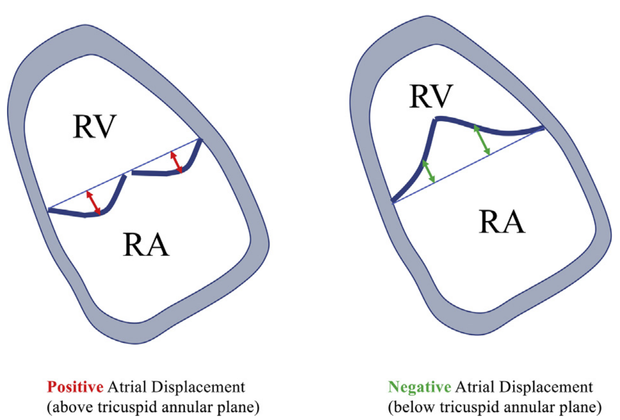

Figure 2 Schematic of the RVI view demonstrating measurement of tricuspid leaflet AD. Schematic demonstrating sample measurements of tricuspid leaflet AD in the RVI view. Displacement of the leaflets beyond the tricuspid annular plane into the right atrium is denoted with positive numbers *(left)* and displacement below the tricuspid annular plane with negative numbers *(right)*. Absence of displacement in either direction is denoted by zero values. Measurements are done from the annular plane to the midpoint of the belly of the leaflets using a leading edge–to–leading edge technique. *RA*, Right atrium; *RV*, right ventricle.

Subsequently, TVP was empirically defined as AD > 2 SDs above the mean value in the control population. For a given view, if the AD differed between the two leaflets, the AD with the highest SD was used to determine the definition of empiric TVP (eTVP). Using this definition, TTEs with sTVP were reclassified, and the extent of reclassification was determined. Agreement between the eTVP and sTVP definitions was determined using sTVP as the criterion standard. The sensitivity, specificity, and positive and negative predictive values for eTVP against sTVP were determined in each view.

Subsequently, demographic and echocardiographic features of those TTEs with eTVP were compared with those without TVP in the overall ENCOR data set. Continuous variables are expressed as mean ± SD or as median (interquartile range [IQR]) and categorical variables as counts and percentages. Characteristics of TTEs with and without TVP were compared using Student's *t*-tests, Wilcoxon Rank Sum tests, or Fisher's exact tests for continuous and categorical variables respectively. Kaplan Meier estimates were used to evaluate time to all-cause mortality for those with isolated TVP versus TVP with concomitant MVP and compared using the log-rank test, censoring at the end of death follow-up (December 31, 2017). All statistical analyses were performed using JMP v14.0 (SAS Institute, Cary, NC) using a two-sided *P*-value < .05 to define statistical significance.

RESULTS

Overall Results and Agreement between Physicians

Of 218,943 TTEs on 118,442 individuals in the ENCOR data set after exclusions, sTVP was identified in 410 individuals (0.3%; Figure 3). Of these, 91 (22.2%) were excluded from manual review because images were unavailable for review in EchoPAC (all but two TTEs were obtained before the start of digital image acquisition and storage in July 2005), and seven (1.7%) were determined to have insufficient image quality. Thus, a total of 312 individuals with subjectively determined TVP were included. Among 100 age- and sex-matched control subjects, images were unavailable for review in three (3.0%), and thus 97 control patients were included.

Agreement on TVP Status by Visual Inspection

Interindividual agreement (i.e., between reviewers 1 and 2) on TVP status by visual inspection was poor (κ = 0.15; 95% CI, −0.15 to 0.45). However, compared with the reference standard (i.e., the sTVP definition), both reviewer 1 (κ = 0.46; 95% CI, 0.18 to 0.74) and reviewer 2 (κ = 0.47; 95% CI, 0.19 to 0.74) had moderate agreement on TVP status by visual inspection.

Definition of TVP

Using 2 SDs above the mean in the control group as the definition for eTVP, eTVP was defined AD > 2 mm in the 4CH or PSAX view or >4 mm in the RVI view (Table 1). Comparing against sTVP as the criterion standard, eTVP ascertained via the PSAX and RVI had the highest specificity and positive predictive value (100.0% for both) but the lowest sensitivity (15.5% and 4.3%, respectively; Table 2). Similarly, eTVP ascertained on the basis of meeting criteria in any view had the highest sensitivity (44.6%) but the lowest specificity (98.4%). The highest overall accuracy was achieved by use of an eTVP definition of >2-mm AD in the PSAX view (99.8%). Using this definition, 276 (88.5%) of those with sTVP would be reclassified as not having TVP.

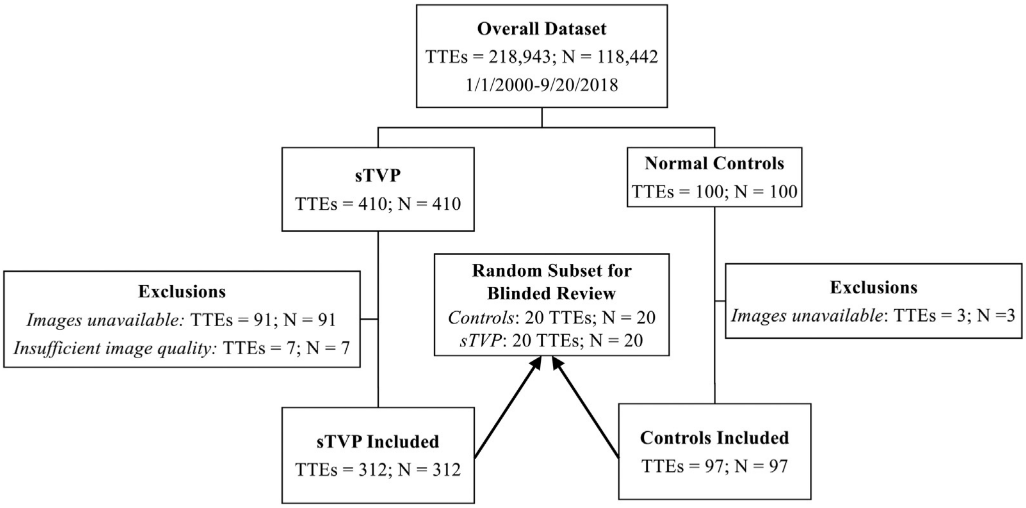

Figure 3 Flow diagram illustrating study inclusions and exclusions.

Table 1 Characteristics of the tricuspid valve, right atrium, and right ventricle in individuals with and without TVP on transthoracic echocardiography

Morphologic parameter	Number of observations	Measurement in individuals with sTVP (*n* = 312)	Measurement in individuals with eTVP (*n* = 36)	Measurement in age- and sex-matched control subjects (*n* = 97)	*P**	*P*†
4CH AD (mm)						
Septal	409	1 ± 1 (0 to 5)	2 ± 1 (0 to 4)	0 ± 1 (−6 to 2)	<.001	<.001
Anterior	409	2 ± 1 (0 to 7)	3 ± 1 (0 to 7)	0 ± 1 (−5 to 3)	<.001	<.001
Annulus	409	29.6 ± 5.1	30.1 ± 4.8	26.9 ± 5.4	<.001	.06
PSAX AD (mm)						
Posterior	307	1 ± 2 (0 to 4)	3 ± 1 (0 to 4)	0 ± 1 (−6 to 2)	<.001	<.001
Anterior/septal	308	1 ± 2 (0 to 5)	3 ± 1 (0 to 5)	−1 ± 1 (−5 to 2)	<.001	<.001
Annulus	308	30.0 ± 4.8	31.8 ± 4.3	28.1 ± 5.3 (18 to 42)	.006	.002
RVI AD (mm)						
Septal	306	1 ± 1 (0 to 6)	2 ± 2 (0 to 6)	0 ± 2 (−6 to 3)	<.001	<.001
Anterior	306	1 ± 1 (0 to 5)	2 ± 1 (0 to 5)	0 ± 2 (−6 to 4)	<.001	<.001
Annulus	310	32.9 ± 5.6 (20 to 48)	30.4 ± 5.1 (20 to 41)	30.0 ± 5.4 (17 to 42)	<.001	.11
Mid- to end-systolic TR	407	25 (8.0)	4 (11.1)	1 (1.0)	.01	.26
Indexed right atrial size, cm/m^2	374	2.9 ± 0.6 (1.7 to 5.5)	2.9 ± 0.5 (2.0 to 4.4)	2.7 ± 0.6 (1.6 to 8.7)	.003	.03
Indexed right ventricular size, cm/m^2	112	2.2 ± 0.5 (1.0 to 3.9)	2.5 ± 0.5 (1.8 to 3.1)	1.8 ± 0.3 (0.8 to 6.1)	.0002	.0008

Annulus, Annular measurement in mid-systole; *anterior*, anterior leaflet of tricuspid valve; *anterior/septal*, either anterior or septal leaflet of the tricuspid valve; *posterior*, posterior leaflet of tricuspid valve; *septal*, septal leaflet of tricuspid valve.
Data are expressed as mean ± SD (range) or as number (percentage). No patients had tricuspid annular disjunction. eTVP was determined as >2-mm AD in the PSAX view.
*Represents the *P* value for the comparison of patients with sTVP and control subjects.
†Represents the *P* value for the comparison of patients with eTVP and control subjects.

Echocardiographic and Clinical Characteristics of Individuals with TVP

Demographic and echocardiographic characteristics of TTEs with and without TVP (according to the eTVP definition in the PSAX view) are presented in Table 3. Patients with TVP were more frequently women ($P = .04$) and more frequently had 3 to 4+ TR (TVP vs no TVP, 22.2% vs 3.1%; $P < .001$). MVP was present in 75.0% of TTEs with TVP versus 3.1% of those without ($P < .001$). TVP was associated with higher rates of 3 to 4+ MR overall (TVP vs no TVP, 13.9% vs 2.7%; $P < .001$). TVP was present in 0.4% of TTEs with MVP versus 0.004% without ($P < .0001$). Aortic valve prolapse was unrelated to TVP status ($P > .99$).

The mean left ventricular ejection fraction was higher in patients with TVP than those without ($P = .045$). Right ventricular dimensions

Table 2 Performance characteristics of view-specific eTVP definitions compared with sTVP as the criterion standard

View	Number (%) of patients with TVP by eTVP definition (*n* = 312)	Number (%) of control subjects with TVP by eTVP definition (*n* = 97)	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	Accuracy, % (95% CI)
Apical 4-chamber	77 (24.7)	1 (1.0)	24.7 (20.0–29.9)	99.0 (94.4–99.9)	6.7 (1.00–33.8)	99.8 (99.8–99.8)	98.8 (97.1–99.6)
PSAX	36 (11.5)	0 (0.0)	15.5 (11.1–20.7)	100.0 (95.1–100.0)	100.0	99.8 (99.7–99.8)	99.8 (98.3–100.0)
RVI	10 (3.2)	0 (0.0)	4.3 (2.1–7.8)	100.0 (95.1–100.0)	100.0	99.7 (99.7–99.7)	99.7 (98.3–100.0)
Any	100 (32.1)	1 (1.0)	44.6 (38.0–51.4)	98.4 (91.2–100.0)	7.6 (1.2–36.5)	99.8 (99.8–99.9)	98.2 (95.9–99.4)

NPV, Negative predictive value; *PPV*, positive predictive value.
The number of patients (those with sTVP) and control subjects determined to have TVP by the empiric definition (eTVP) is listed along with the sensitivity, specificity, PPV, and NPV of each definition against the sTVP definition. Disease prevalence is assumed for calculations to be 0.3% (prevalence of TVP in the present study population).

($P = .0008$) were larger in patients with TVP. Among those TTEs with ≤2+ MR, indexed right ventricular basal diameter continued to be larger in those with TVP (2.5 ± 0.5 vs 1.9 ± 0.5 cm/m^2, $P = .002$). Using the American Society of Echocardiography reference standards for normal right ventricular and right atrial size (>4.1 and >5.3 cm, respectively), 50.0% of patients with eTVP versus 21.6% of those without TVP had dilated right ventricles ($P = .03$), and 25.7% of patients with eTVP versus 31.4% of those without TVP had dilated right atria ($P = .59$).[14] The estimated TR pressure gradient was not different by TVP status ($P = .57$).

Time to All-Cause Mortality

Over a median follow-up period of 8.0 years (IQR, 3.7–12.3 years), there were 70 deaths at a median of 344.5 days (IQR, 96.8–1,177.8 days) after transthoracic echocardiography. The median time to death was not different among those with MVP and TVP (1,026 days; IQR, 51.5–2,014 days), isolated TVP (648.5 days; IQR, 645–652 days), or neither (324 days; IQR, 104.5–1,137.5 days; log-rank $P = .93$).

DISCUSSION

At a single large academic medical center over 18 years, sTVP was identified in only 0.3% of individuals. Visual assessment of TVP demonstrated, at best, moderate agreement between reviewers. An empirically derived threshold value of >2 mm of AD in the PSAX view to define TVP had the overall highest accuracy for TVP diagnosis compared with visual assessment. Using this definition, TVP was present in 0.4% of TTEs with MVP, and 75.0% of TTEs with TVP had associated MVP. TVP was associated with worsened TR severity, right ventricular dilation, and greater degrees of 3 to 4+ MR. Although limited by small numbers, mortality was not different between those with isolated TVP or TVP and MVP. These results in totality suggest that TVP, while uncommon outside of concomitant MVP, is associated with adverse echocardiographic features and the diagnosis should be sought in individuals with MVP.

Prior Literature on TVP

Previous literature on TVP has been limited to small case series, describing a total of 34 cases of isolated TVP.[1,2,4-8,15] Although associations between TVP and comorbid conditions such as coronary artery disease, dilated cardiomyopathy, endocarditis, and others have been previously noted, these findings have not been consistent across studies.[16]

Additionally, multiple case reports have separately described the prevalence of TVP among individuals with MVP.[2,3,6,15,17-20] With a reported TVP prevalence of 5% to 52%, this wide range may in part be related to differences in the views used to assess for TVP (i.e., RVI view alone vs all views of the tricuspid valve).

To our knowledge, the present study represents the largest study of TVP to date. We found that 25% of TVP cases occurred in isolation, with 75% occurring in the context of concomitant MVP. TVP was far less common than in prior studies, occurring in only 0.3% of individuals, though it was more prevalent among individuals with MVP.

Diagnosis of TVP

In the absence of diagnostic guidelines or consensus criteria for TVP, the diagnosis of TVP has largely been made by visual inspection of the tricuspid valvular leaflets and subvalvular apparatus. In the present study, we demonstrate that visual inspection of TVP status has, at best, only moderate interrater agreement. One potential reason for this finding is the observation that up to 2 mm of AD in the 4CH and PSAX views and up to 4 mm of AD in the RVI view can occur in normal individuals. Like the mitral valve, the tricuspid valve has a three-dimensional saddle-shaped structure.[21] The high points of the tricuspid valve annulus are visualized in the RVI view, making AD in this view theoretically most specific for TVP.[21] Congruent with this, a definition of TVP based on ADs in the RVI and PSAX views had the highest specificity (100.0% for both) for identifying TVP by visual inspection. The cutoff with the best overall accuracy was >2 mm of AD in the PSAX view. We suggest that this cutoff be used in the guidelines and future studies to define the presence of TVP. Using this definition, 11.1% of patients with TVP had mid to late systolic TR. Overall, annular measurements in those with TVP were larger than in control subjects, suggesting that like MVP, annular dilation may contribute to the pathophysiology of regurgitation.[22] No patients in the present study had tricuspid annular disjunction. The degree of AD observed was similar across tricuspid leaflets in a given view.

The Relationship of TVP to MVP

A finding consistent across studies of TVP, including the present analysis, is the strong association between MVP and TVP. MVP was present in the vast majority of TTEs with TVP, and TVP was present in 0.4% of TTEs with MVP. Additionally, TVP was associated with

Table 3 Demographic and echocardiographic characteristics of TTEs obtained in individuals with and without TVP

Variable	Number of observations	TVP (*n* = 36)	No TVP (*n* = 218,907)	*P*
Age, y	218,929	63.3 ± 18.1	62.4 ± 18.0	.77
Sex, female	218,868	24 (66.7)	109,774 (50.2)	.04
Inpatient status	218,943	12 (33.3)	102,344 (46.8)	.13
Suboptimal image quality	218,943	5 (13.9)	37,561 (17.2)	.82
Height, cm	209,595	169.2 ± 12.6	168.4 ± 10.7	.73
Weight, kg	211,090	64.8 ± 11.8	80.2 ± 22.2	<.001
Body surface area, m^2	208,940	1.74 ± 0.20	1.92 ± 0.29	<.001
Systolic blood pressure, mm Hg	209,272	120.7 ± 19.4	127.2 ± 31.0	.054
Diastolic blood pressure, mm Hg	20,883	70.9 ± 11.1	72.5 ± 32.6	.40
Heart rate, beats/min	183,093	73.7 ± 18.4	75.2 ± 20.5	.64
Indexed left atrial anteroposterior dimension, cm/m^2	196,294	2.1 ± 0.5	2.1 ± 0.5	.80
Indexed left atrial superoinferior dimension, cm/m^2	183,691	2.8 ± 0.6	2.8 ± 0.5	.60
Indexed right atrial length, cm/m^2	182,438	2.9 ± 0.5	2.7 ± 0.5	.03
Interventricular septal wall thickness, cm	193,480	1.0 ± 0.1	1.1 ± 0.2	<.001
Inferolateral wall thickness, cm	193,239	1.0 ± 0.2	1.1 ± 0.2	.0009
Indexed left ventricular diastolic diameter, cm/m^2	194,776	2.6 ± 0.4	2.5 ± 0.4	.03
Indexed left ventricular systolic diameter, cm/m^2	146,461	1.6 ± 0.3	1.6 ± 0.4	.32
Left ventricular ejection fraction, %	193,305	64.1 ± 10.8	60.3 ± 17.4	.045
Indexed right ventricular basal diastolic diameter, cm/m^2	33,839	2.5 ± 0.5	1.9 ± 0.5	.0008
Peak aortic valve transvalvular velocity, m/sec	165,402	1.3 ± 0.3	1.7 ± 0.7	<.001
Transmitral Doppler peak E-wave velocity, m/sec	183,195	0.9 ± 0.4	0.9 ± 0.3	.71
Transmitral Doppler peak A-wave velocity, m/sec	166,275	0.7 ± 0.2	0.8 ± 0.4	.004
Transmitral Doppler E/A ratio	166,091	1.4 ± 0.7	1.2 ± 0.6	.08
Average E/e′ ratio	112,194	9.7 ± 5.9	10.5 ± 5.3	.50
Estimated tricuspid regurgitant pressure gradient, mm Hg	150,477	30.4 ± 14.2	29.0 ± 11.5	.57
TR grade	176,947			<.001
0+		1 (2.8)	1,992 (0.9)	
Trace/1+		19 (52.8)	156,044 (71.3)	
2+		7 (19.4)	12,011 (5.5)	
3+		6 (16.7)	5,098 (2.3)	
4+		2 (5.6)	1,767 (0.8)	
MR grade	175,410			<.001
0+		0 (0.0)	8,682 (4.0)	
Trace/1+		22 (61.1)	150,512 (68.8)	
2+		2 (5.6)	10,174 (4.6)	
3+		3 (8.3)	4,501 (2.1)	
4+		2 (5.6)	1,512 (0.7)	
Aortic regurgitation grade	119,813			<.001
0+		8 (22.2)	58,400 (26.7)	
Trace/1+		12 (33.3)	57,533 (26.3)	
2+		0 (0.0)	2,897 (1.3)	
3+		0 (0.0)	700 (0.3)	
4+		0 (0.0)	263 (0.1)	
MVP	218,943	27 (75.0)	6,767 (3.1)	<.001
Flail or partial flail mitral valve leaflet	6,794	1 (2.8)	568 (0.3)	.72

All values are means ± standard deviations unless otherwise specified. *m/s*, Meters per second; *no.*, number.

more clinically significant MVP, as evidenced by worsened MR and a numerically higher proportion with flail or partial flail mitral valve leaflets. Thus, TVP may serve as a risk marker for severe myxomatous disease and suggest a more malignant presentation of MVP, and suggests the need for increased awareness of possible TVP in patients with MVP. Consistent with known data regarding MVP,[23] TVP was also significantly more common in women than men.

TVP and Right Ventricular Remodeling

Individuals with TVP also had increased severity of TR and larger indexed right ventricular diameters, despite equivalent TR gradients, which may reflect the greater degree of TR among these patients. As TVP was associated with larger indexed right ventricular diameters even in the setting of ≤2+ MR, this suggests that the larger right ventricular sizes observed are possibly due to volume loading of the right ventricle from primary tricuspid valvular insufficiency rather than TVP's association with worsened MVP and MR causing World Health Organization group II pulmonary hypertension[24] and subsequent right ventricular remodeling. Although limited by small numbers of individuals with adverse outcomes, no significant difference in all-cause mortality was observed between those with isolated TVP and those with TVP with concomitant MVP.

Limitations

Our study had several limitations. Our results are from retrospective review of a single-center echocardiographic database. Although large, it may not generalize to other settings. Furthermore, because of ascertainment bias, estimates of TVP rates may not reflect prevalence in the community or general population. Second, because it was not feasible for the physician performing manual image review to evaluate the entire ENCOR data set, it is possible that the prevalence of TVP is underestimated. Third, because there is no clear consensus definition for TVP, estimates of TVP were made via comparison with normal control subjects without pathologic confirmation, and thus misclassification is possible. Although we used sTVP as the reference standard, we do not mean to imply that it represents a true gold standard; rather it represents an alternative definition for comparison. Fourth, longitudinal changes in echocardiographic variables were not evaluated and should be the topic of future investigation. Fifth, as the prevalence of TVP may differ across laboratories, the performance of the eTVP definition used should be evaluated in an external sample. Sixth, because control patients were not matched on echocardiograph, image quality and thus measurement variability may differ across the study. Last, because transesophageal echocardiograms, intracardiac echocardiograms, and stress echocardiograms were not included, results of this analysis may not generalize to these other settings.

CONCLUSION

In this large, single-center, multidecade study, TVP was overall uncommon. Visual assessment of TVP had, at best, moderate interrater agreement. An empirically derived threshold AD value of >2 mm in the PSAX view to define TVP had the overall highest accuracy compared with visual assessment. TVP was associated with worsened TR, larger right ventricular size, and more clinically significant MVP. In total, these results suggest an increased role for surveillance for TVP and the need for diagnostic criteria in updated guidelines.

REFERENCES

1. Tei C, Shah PM, Cherian G, Trim PA, Wong M, Ormiston JA. Echocardiographic evaluation of normal and prolapsed tricuspid valve leaflets. Am J Cardiol 1983;52:796-800.
2. Brown AK, Anderson V. Two dimensional echocardiography and the tricuspid valve. Leaflet definition and prolapse. Br Heart J 1983;49:495-500.
3. Mardelli TJ, Morganroth J, Chen CC, Naito M, Vergel J. Tricuspid valve prolapse diagnosed by cross-sectional echocardiography. Chest 1981;79:201-5.
4. Sasse L, Froelich CR. Echocardiographic tricuspid prolapse and nonejection systolic click. Chest 1978;73:869-70.
5. Karayannis E, Stefadouros MA, Abdulla AM, Blackwell JC. Use of echocardiography in the diagnosis of prolapsed tricuspid valve. J Med Assoc Ga 1978;67:205-8.
6. Maranhao V, Gooch AS, Yang SS, Sumathisena DR, Goldberg HH. Prolapse of the tricuspid leaflets in the systolic murmur-click syndrome. Cathet Cardiovasc Diagn 1975;1:81-90.
7. Horgan JH, Beachley MC, Robinson FD. Tricuspid valve prolapse diagnosed by echocardiogram. Chest 1975;68:822-4.
8. Chandraratna PN, Lopez JM, Fernandez JJ, Cohen LS. Echocardiographic detection of tricuspid valve prolapse. Circulation 1975;51:823-6.
9. Mutlak D, Khoury E, Lessick J, Kehat I, Agmon Y, Aronson D. Lack of increased cardiovascular risk due to functional tricuspid regurgitation in patients with left-sided heart disease. J Am Soc Echocardiogr 2019;32:1538-46.
10. Anwar AM, Geleijnse ML, Soliman OI, McGhie JS, Frowijn R, Nemes A, et al. Assessment of normal tricuspid valve anatomy in adults by real-time three-dimensional echocardiography. Int J Cardiovasc Imaging 2007;23:717-24.
11. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2015;28:1-39.e14.
12. Mosteller RD. Simplified calculation of body-surface area. N Engl J Med 1987;317:1098.
13. Zoghbi WA, Adams D, Bonow RO, Enriquez-Sarano M, Foster E, Grayburn PA, et al. Recommendations for noninvasive evaluation of native valvular regurgitation: a report from the American Society of Echocardiography developed in collaboration with the Society for Cardiovascular Magnetic Resonance. J Am Soc Echocardiogr 2017;30:303-71.
14. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr 2010;23:685-713.
15. Werner JA, Schiller NB, Prasquier R. Occurrence and significance of echocardiographically demonstrated tricuspid valve prolapse. Am Heart J 1978;96:180-6.
16. Weinreich DJ, Burke JF, Bharati S, Lev M. Isolated prolapse of the tricuspid valve. J Am Coll Cardiol 1985;6:475-81.
17. Schlamowitz RA, Gross S, Keating E, Pitt W, Mazur J. Tricuspid valve prolapse: a common occurrence in the click-murmur syndrome. J Clin Ultrasound 1982;10:435-9.
18. Ogawa S, Hayashi J, Sasaki H, Tani M, Akaishi M, Mitamura H. Evaluation of combined valvular prolapse syndrome by two-dimensional echocardiography. Circulation 1982;65:174-80.
19. Gooch AS, Maranhao V, Scampardonis G, Cha SD, Yang SS. Prolapse of both mitral and tricuspid leaflets in systolic murmur-click syndrome. N Engl J Med 1972;287:1218-22.
20. Pomerance A. Ballooning deformity (mucoid degeneration) of atrioventricular valves. Br Heart J 1969;31:343-51.

21. Ton-Nu TT, Levine RA, Handschumacher MD, Dorer DJ, Yosefy C, Fan D, et al. Geometric determinants of functional tricuspid regurgitation: insights from 3-dimensional echocardiography. Circulation 2006;114:143-9.
22. Perazzolo Marra M, Basso C, De Lazzari M, Rizzo S, Cipriani A, Giorgi B, et al. Circ Cardiovasc Imaging 2016;9:e005030.
23. Avierinos JF, Gersh BJ, Melton LJ III, Bailey KR, Shub C, Nishimura RA, et al. Natural history of asymptomatic mitral valve prolapse in the community. Circulation 2002;106:1355-61.
24. Kolte D, Lakshmanan S, Jankowich MD, Brittain EL, Maron BA, Choudhary G. Mild pulmonary hypertension is associated with increased mortality: a systematic review and meta-analysis. J Am Heart Assoc 2018;7:e009729.