Normal Reference Values and Reproducibility of Tricuspid Annulus Dimensions Using Cardiovascular Magnetic Resonance

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Tricuspid annular (TA) dilation is a key process in functional tricuspid regurgitation, but normal TA dimensions using cardiovascular magnetic resonance have not been established. We measured TA diameters in 66 healthy volunteers, aged 38 ± 11 years, during 3 different phases of the cardiac cycle (end-systole, early diastole, and end-diastole) and in 2 routinely acquired cardiovascular magnetic resonance imaging planes (4-chamber [4C] and right ventricular inflow-outflow [RVIO]). Three readers independently measured each value and 1 reader repeated measurements 1 month apart. The upper limit of normal (ULN) was calculated as 1.96 standard deviations above the mean. We assessed inter- and intraobserver reliability using the intraclass correlation coefficient (ICC) and Bland-Altman analysis. We found the TA diameter largest during early diastole in the 4C view with an ULN of 43 mm (22 mm/m^2). Men had larger absolute TA diameters (36 mm, 95% CI 27 to 44 mm) than women (30 mm, 95% CI 23 to 37 mm) but not after indexing for body surface area (both 18 mm/m^2). In the RVIO view, the largest TA diameter occurred during early diastole with a ULN value of 46 mm (27 mm/m^2). In this view, females had a larger indexed TA than men (21 mm/m^2 vs 17 mm/m^2). Reproducibility of measurements was excellent in all cardiac phases with an inter-rater ICC between 0.90 to 0.96 and an intrarater ICC 0.89 to 0.96. In conclusion, we have provided normative data regarding TA dimensions in routinely acquired 4C and RVIO views, and these values are larger than the current thresholds of annular dilation measured by echocardiography. Gender differences with the TA diameter in the RVIO view may be an important finding with consideration of future tricuspid devices. **(Am J Cardiol 2019;00:1−5)**

Functional tricuspid regurgitation (TR), caused by leaflet tethering and tricuspid annular (TA) dilation, is recognized as an independent risk factor for mortality.[1−3] Full 3D visualization of the TA can be performed using cardiovascular magnetic resonance (CMR) and cardiac computed tomography, but a large amount of acquisition time, radiation, or postprocessing time may be required, and therefore is reserved for patients being evaluated for possible tricuspid valve intervention. Standard routine CMR examinations can visualize the tricuspid apparatus in the 4-chamber (4C) and right ventricular inflow-outflow (RVIO) view. Recognizing annular dilation based on routinely acquired CMR views can help identify patients that may benefit from dedicated imaging and transcatheter interventions. There are currently no established CMR normal reference TA diameter measurements in the 4C and RVIO views. Specific to CMR, timing of cardiac motion is challenging, because postprocessed generated images do not display the surface electrocardiography (ECG), and this may decrease the accuracy and reproducibility of these measurements. Therefore, we sought to define reference values for the tricuspid valve annulus at 3 separate phases in the cardiac cycle and assess the reproducibility of these measurements.

Methods

We recruited healthy volunteers from our local institution who were ≥18 years of age and without known cardiovascular disease or cardiovascular risk factors, such as systemic hypertension, current or previous history of smoking, dyslipidemia, family history of premature coronary disease, or diabetes. We excluded volunteers with body mass index ≥30, pregnancy, those with standard contraindications to CMR, and those with an incidental abnormal CMR finding. We obtained baseline demographics on each volunteer. Body surface area (BSA) was calculated using the Mosteller formula.[4]

We imaged volunteers on 3 commercially available CMR scanners: 1.5T Aera, 1.5T Avanto, and a 3T Skyra (all Siemens Healthcare, Erlangen, Germany). We acquired cine images of the left and right ventricle (RV) using a short axis stack with a slice thickness/gap of 6 mm/4 mm. We used standard imaging parameters to achieve a spatial in-plane resolution of 1.5 mm × 1.5 mm and a temporal resolution of 30 to 40 ms.[5] From the most basal ventricular

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slice, we constructed a 4C view by transecting the largest portion of the RV and the inferoseptal-anterolateral walls of the left ventricle (Figure 1). In a subset of volunteers, we also imaged the RVIO view to visualize the RV inflow, apex, and RV outflow tract (Figure 1).

From the 4C and RVIO view, we measured the TA at end-systolic, early diastolic, and end-diastolic cardiac phases. We defined these phases as follows:

(a) End-systole: the last frame the tricuspid valve was closed before passive right atrial emptying.

(b) Early diastole: the first frame during diastole where the tricuspid valve leaflets are at maximal excursion and parallel to the inflow of the RV.

(c) End-diastole: the frame just prior to the onset of ventricular contraction.

To determine interobserver and intraobserver reproducibility 3 observers (YZ, DD, and MK) independently measured the annulus on all volunteers. To standardize interpretation technique, each observer obtained measurements on 5 initial cases and results were compared among observers. Any adjustments in measurement technique were agreed upon at this time. None of these cases were included in the final study. A month later, one observer (YZ) remeasured the TA diameter on all volunteers in a blinded and randomized fashion. All tracings were conducted using a commercially available CMR analysis package (Heart IT Precession, Durham, North Carolina).

Baseline data are reported as mean ± standard deviation (SD). The measurements of the TA diameters were recorded as mean (95% confidence interval [CI]). Differences between groups were compared using the Wilcoxon rank-sum test for continuous variables and chi-square test for categorical variables. Inter-rater and intrarater reliability was assessed using the intraclass correlation coefficient and represented by intraclass correlation coefficient (95% CI) and F-statistic p values.[6] Upper and lower limits of normal were calculated using mean ± 1.96 SD. Modified Bland-Altman tables were constructed with 95% limits of agreement with the mean being estimated as ±1.96 * (SD of the differences for all raters).[7] All analyses were performed on Stata MP version 14.2 (StataCorp LLC, College Station, Texas).

Results

Our study included 66 normal volunteers (mean age 38 ± 11 years, 38% women), all of whom had the TA imaged on the 4C view, and a subset of 40 volunteers (38% women) with RVIO views. Demographic volunteer data for the entire cohort, as well as stratified by gender, are displayed in Table 1. All volunteers had no significant arrhythmias (e.g., atrial fibrillation, premature atrial contractions, or premature ventricular contractions), during the scan. Between genders there were no significant differences in age, blood pressure, or heart rate. Men were taller, heavier, and had higher BSA values.

TA diameters are shown in Table 2. Overall, the cardiac phase of early diastole was largest for both the 4C and RVIO views. Men, compared with women, had significantly larger absolute 4C values, but had similar indexed values after adjusting for BSA ($p = 0.96$). The absolute TA diameter in the RVIO view was similar between men and women ($p = 0.56$). However, after adjustment for BSA, women had larger indexed RVIO diameters than men (21 mm/m^2 vs 17 mm/m^2, $p < 0.01$).

Both inter-rater and intrarater reproducibility of all parameters was excellent (Table 3). In both the 4C and RVIO views, the early diastolic cardiac phase was slightly more reproducible among the same and different readers. Bland-Altman analysis showed minimal bias with excellent agreement in all cardiac phases in the 4C view, with a maximum mean difference between any 2 readers of −1.31 mm (SD ±1.85 mm; Table 4). In the RVIO view, the end-systolic

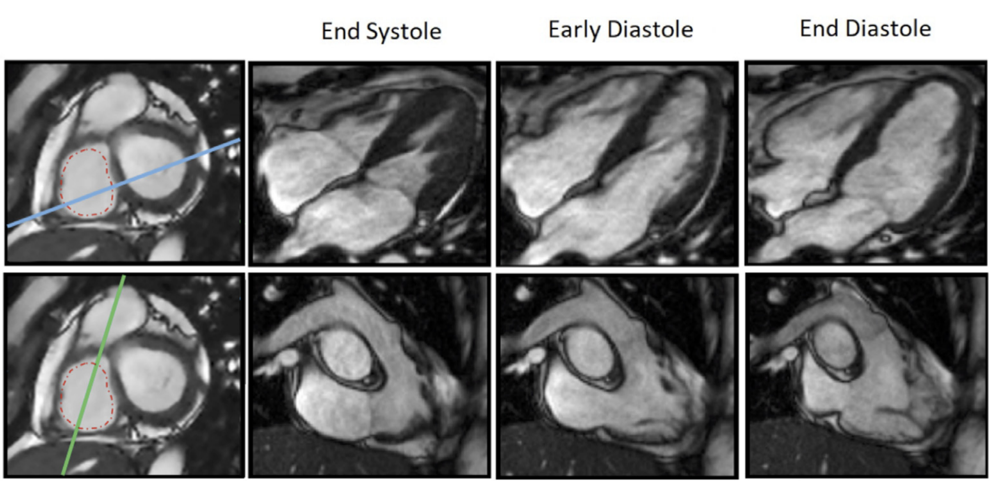

Figure 1. Generation of the 4C (*top*, blue) and RVIO (*bottom*, green) imaging planes. The phases of end-systole, early diastole, and end-diastole are shown. The tricuspid annulus is traced in red. (Color version of figure is available online.)

Table 1
Baseline characteristics of healthy volunteers

Variable	Total (n = 66)	Women (n = 25)	Men (n = 41)	p value
Age (years)	38 (11)	35 (13)	39 (10)	0.22
Height (cm)	171 (10)	163 (7)	176 (8)	<0.001
Weight (kg)	71 (15)	59 (7)	78 (14)	<0.001
BSA (m^2)	1.8 (0.2)	1.6 (0.1)	1.9 (0.2)	<0.001
BMI (kg/m^2)	24.1 (3.4)	22.2 (3.1)	25.2 (3.0)	<0.001
Heart rate (bpm)	73 (12)	71 (12)	73 (13)	0.74
Systolic BP (mm Hg)	122 (12)	121.0 (15)	122 (11)	0.91
Diastolic BP (mm Hg)	77 (12)	72 (15)	79 (12)	0.35

BMI = body mass index; bpm = beats per minute; BSA = body surface area; n = number; SD = standard deviation.
Values are expressed as mean (SD).

and early diastolic phases had similar bias and agreement (mean bias −1.45 mm [SD ±1.71 mm]), but there was less agreement in the end-diastolic phase (Table 4).

Discussion

We reported normal reference TA diameters, both absolute and indexed to BSA, using CMR in 2 routinely acquired cardiac views and in 3 phases of the cardiac cycle. We chose these 3 phases because they were easily identifiable without ECG tracings, well reported in the literature, and do not rely on atrial contraction. Timings free from atrial contraction are important because many patients with significant tricuspid valve disease are in atrial fibrillation. Despite relying on cardiac timing based on leaflet motion for guidance, and not ECG timing, we found excellent reliability in all measurements and cardiac phases, although there was less agreement with the RVIO end-diastolic phase. Early diastole of both the 4C and the RVIO views had the greatest reproducibility. The TA was largest in early diastole, with an upper limit of normal (ULN) of 43 mm (22 mm/m^2) in 4C and 46 mm (27 mm/m^2) in RVIO. Interestingly, after adjusting for BSA, there were gender differences in TA diameter in the RVIO but not for the 4C view.

Currently, a dilated TA is defined as >40 mm or >21 mm/m^2.[8] These parameters were derived from apical 4C echocardiographic views from studies that did not uniformly report the time in the cardiac cycle to conduct these measurments.[9−11] Chopra et al[11] identified that a maximum diastolic TA of >21mm/m^2 as a threshold for tricuspid surgery in those with severe TR and also who underwent aortic or mitral valve surgery. In our normal cohort, however, in the 4CH view, we found 7 of our 66 healthy volunteers (11%) with a TA >40 mm and 5 (8%) with a TA >21 mm/m^2. It is likely that older studies using 2D echocardiography were unable to always obtain the largest TA in the 4C view. The usage of 3D transthoracic echocardiography (TTE) is able to overcome this limitation, with studies reporting an ULN TA diameter of >23 mm/m^2.[12] Additionally, our measurements demonstrated differences in TA diameter depending on the phase of the cardiac cycle, with the largest value in early diastole, similar to the previously reported echocardiographic parameters in the 4C view.[13] Addetia et al[14] also looked at TA throughout the cardiac cycle and concluded that the largest value was at the post-a wave near end-diastole, but it should be noted that early diastole was not measured in that study.

Dilation of the TA is a key mechanism in the development and progression of significant TR.[3] Severe TR secondary to left-sided disease persists in patients with TA dilation who only undergo corrective left-sided surgery.[10,15] In these patients, surgical repair of the tricuspid is safe and can effectively decrease future incidence of severe TR.[10] Therefore, current guidelines recommended intervention in patients with a dilated TA at the time of left-sided heart surgery.[16−18] However, intervention in patients with isolated

Table 2
Normal tricuspid annulus diameter

Tricuspid annulus diameter	Total (n = 66)	Women (n = 25)	Men (n = 41)	p value
4C end systole (mm)	31 (22-40)	27 (21-34)	33 (26-40)	<0.001
4C early diastole (mm)	33 (24-43)	30 (23-37)	36 (27-44)	<0.001
4C end diastole (mm)	29 (21-37)	26 (20-32)	31 (25-37)	<0.001
RVIO end systole (mm)	33 (23-42)	32 (24-41)	33 (22-43)	0.91
RVIO early diastole (mm)	33 (21-46)	34 (21-47)	33 (20-45)	0.56
RVIO end diastole (mm)	29 (18-40)	28 (19-38)	29 (18-41)	0.55
4C end systole index (mm/m^2)	17 (13-21)	17 (13-20)	17 (13-21)	0.51
4C early diastole index (mm/m^2)	18 (15-22)	18 (15-22)	18 (14-23)	0.96
4C end diastole index (mm/m^2)	16 (13-20)	16 (12-20)	16 (13-20)	0.71
RVIO end systole index (mm/m^2)	18 (11-25)	20 (14-25)	17 (11-24)	0.013
RVIO early diastole index (mm/m^2)	18 (9.8-27)	21 (13-29)	17 (9.3-25)	0.01
RVIO end diastole index (mm/m^2)	16 (9.1-23)	17 (11-23)	15 (8.2-22)	0.11

n = number; RVIO = right ventricular inflow outflow view; SD = standard deviation; 4C = 4-chamber view.
Values are expressed as mean (95% confidence interval).

Table 3
Inter-rater and intrarater reliability among 3 raters

	Among all 3 raters		Rater 1 versus rater 2		Rater 1 versus rater 3		Rater 2 versus rater 3		Intrarater	
	ICC (95% CI)	p value	ICC (95% CI)	p value	ICC (95% CI)	p value	ICC (95% CI)	p value	ICC (95% CI)	p value
4C										
End systole	0.92 (0.87-0.95)	<0.001	0.89 (0.75-0.95)	<0.001	0.97 (0.95-0.98)	<0.001	0.94 (0.90-0.96)	<0.001	0.90 (0.63-0.96)	<0.001
Early diastole	0.93 (0.88-0.95)	<0.001	0.94 (0.90-0.96)	<0.001	0.94 (0.90-0.96)	<0.001	0.90 (0.69-0.95)	<0.001	0.92 (0.74-0.96)	<0.001
End diastole	0.90 (0.86-0.93)	<0.001	0.90 (0.78-0.95)	<0.001	0.95 (0.91-0.97)	<0.001	0.90 (0.83-0.94)	<0.001	0.89 (0.82-0.93)	<0.001
RVIO										
End systole	0.95 (0.91-0.97)	<0.001	0.93 (0.86-0.97)	<0.001	0.97 (0.94-0.98)	<0.001	0.96 (0.91-0.98)	<0.001	0.92 (0.57-0.97)	<0.001
Early diastole	0.96 (0.92-0.98)	<0.001	0.94 (0.74-0.98)	<0.001	0.98 (0.96-0.99)	<0.001	0.95 (0.70-0.98)	<0.001	0.96 (0.93-0.98)	<0.001
End diastole	0.90 (0.84-0.94)	<0.001	0.90 (0.81-0.94)	<0.001	0.92 (0.86-0.96)	<0.001	0.88 (0.79-0.94)	<0.001	0.89 (0.81-0.94)	<0.001

CI = confidence interval; ICC = interclass correlation coefficient; RVIO = right ventricular inflow outflow view; 4C = 4-chamber view.

Table 4
Bland-Altman analysis among 3 raters

	Rater 1 versus rater 2 mean difference (mm) (95% CI)	Rater 1 versus rater 3 mean difference (mm) (95% CI)	Rater 2 versus rater 3 mean difference (mm) (95% CI)	Intrarater mean difference (mm) (95% CI)
4C				
End systole	1.2 (−2.6, 5.0)	−1.4 (−4.7, 2.0)	−0.2 (−3.2, 2.9)	−0.2 (−2.5, 2.1)
Early diastole	−0.1 (−3.5, 3.3)	−1.2 (−4.4, 2.1)	−1.3 (−4.9, 2.3)	−0.5 (−3.6, 2.7)
End diastole	−0.9 (−4.2, 2.4)	0.3 (−3.6, 4.2)	−0.6 (−4.0, 2.8)	−0.1 (−2.7, 2.5)
RVIO				
End systole	0.7 (−2.5, 4.0)	−1.4 (−4.2, 1.4)	−0.7 (−3.0, 1.7)	0.0 (−2.5, 2.4)
Early diastole	−1.5 (−4.8, 1.9)	0.0 (−3.6, 3.6)	−1.4 (−4.5, 1.6)	−0.4 (−2.9, 2.1)
End diastole	−0.1 (−5.2, 5.0)	−0.7 (−5.8, 4.4)	−0.8 (−6.2, 4.5)	0.2 (−4.3, 4.7)

CI = confidence interval; ICC = interclass correlation coefficient; RVIO = right ventricular inflow outflow view; 4C = 4-chamber view.

functional TR and TA dilation is less well known. This is partly because isolated severe TR is rarely intervened upon due to its high mortality and perceived limited benefit.[19]

In our study, after adjusting for BSA, there were significant differences in TA diameter between genders, but only in the RVIO view and not the 4C view. The RVIO view is unique to CMR, and usually transects near the long axis of the annulus (Figure 1). It is unclear why the long axis of the TA in females is proportionally larger than males, but this finding was also noted in a separate study utilizing 3D echocardiography where the long axis was identified larger in females after BSA adjustment.[14]

There were certainly some limitations to our study. The number of women and men was not equal in our study, and there were a limited number of elderly healthy volunteers >60 years old. This raises concern of the generalizability to the elderly population. However, elderly volunteers without any cardiovascular risk factors are not common in the general population. Manual creation of the 4C and RVIO imaging planes can create slight variations in the angle between such acquisitions in different volunteers but reflects common practice. Patients with TR can present with atrial fibrillation, which can challenge in image acquisition and may make TA measurements less reliable. Lastly, the TA dilates along the lateral free wall, which can be measured in the 4CH view, but will not be well accounted for in the RVIO view.

In conclusion, this is the first study to report normal reference diameters for the TA using routinely acquired CMR 4C and RVIO views. Such measurements show excellent reproducibility with minimal bias despite lack of ECG guidance for cardiac cycle timing. The TA diameter was largest in the early diastolic cardiac phase with values slightly larger than those reported with current 2D echocardiography. Based on our measurements, upper limits of normal were 43 mm (22 mm/m^2) in the 4C and 46 mm (27 mm/m^2) in the RVIO views. These values are specific to CMR and are larger than reported 2D echocardiographic values. Additionally, after adjusting for BSA, women had increased RVIO diameters compared with men. Our findings may help guide which patients should undergo dedicated imaging for tricuspid annular sizing and tricuspid interventional device selection.

Disclosures

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