

# Right Atrium and Tricuspid Remodeling in Atrial Fibrillation patients with Functional Tricuspid Regurgitation: A-Two Dimensional and Three Dimensional Transthoracic Echocardiography Study

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## Abstract

**Background:** A frequent valvular heart disease(VHD) is tricuspid regurgitation(TR), the most common form of which is 2nd TR. Atrial fibrillation(AF) is a prominent cause of functional tricuspid regurgitation(FTR).

**Aim and objectives:** Assessment of the mechanism of FTR in a patient with non-paroxysmal AF.

**Patients and methods:** This analytic cross-sectional study was performed in the Cardiology department, Al-Azhar University at Al-Husain University Hospital from August 2023 to May 2024. It included 100 consecutive patients diagnosed with AF for more than 1 year, referred for echocardiographic assessment

**Results:** AF is associated with FTR The main mechanism is TA dilatation with increasing TA area, perimeter, and all diameters. Tenting volume has a direct correlation with the degree of TR severity, but tenting height and coaptation distance show no change and are not correlated with FTR in AF patients.

**Conclusion:** There is a strong relationship between AF and the development of significant FTR, with the main mechanism being TA dilatation.

**Keywords:** TR(FTR); AF; Echocardiography; AFTR; Tricuspid annulus

## 1. Introduction

Of the four valves in the heart, the tricuspid valve is the largest one. Its opening area is usually between seven and nine square centimeters.<sup>1</sup>

The most prevalent valve lesion in the right side of the heart, tricuspid regurgitation (TR), causes a lot of problems and even deaths.<sup>2</sup>

The rising death rate in individuals with moderate to severe TR, irrespective of pulmonary hypertension or left ventricular systolic function, has prompted research into the several factors that contribute to TR.<sup>3</sup>

There are two types of TR according to pathology: primary and secondary. When the

pathology of TR is related to the TV apparatus, it is called primary TR; on the other hand, when TR is related to neighboring structures such as RV or RA, it is called secondary(functional ) TR.<sup>4</sup>

Tricuspid annular dilatation, especially along the posterior edge of the valve, can be caused by persistent atrial fibrillation(AF), which can progress to TR.<sup>5</sup>

AF is a big risk factor for the development of AFTR and is present in a large percentage of patients with the condition. The criteria for atrial TR, according to Schlotter et al., include a tricuspid valve(TV) tenting height of 10 mm or less, a midventricular right ventricular diameter of 38 mm or less, and a left ventricular ejection fraction of 50% or more.<sup>6</sup>

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The purpose of this study is to examine the remodeling of the right atrium, right ventricle, and TV annulus using 2D and 3D echocardiography in patients with non-paroxysmal AF in order to determine the cause of functional TR.

## 2. Patients and methods

This prospective observational study was performed in the Cardiology Department, Al-Azhar University at Al-Husain University Hospital from August 2023 to May 2024. It included 100 consecutive patients diagnosed with non-paroxysmal AF referred for echocardiographic assessment

Inclusion criteria:

Functional tricuspid regurgitation in non-paroxysmal AF patients.

Exclusion Criteria:

Poor Echocardiographic window, organic tricuspid valve disease, previous tricuspid valve surgery, congenital or pericardial heart disease, pacemaker/defibrillator wire across the tricuspid valve, patients with known myocardial diseases, and significant pulmonary HTN more than 50mmHg.

Methods:

The following was done for all patients:

Detailed medical history, detailed clinical examination, and a twelve-lead surface electrocardiogram (ECG) and long strip.

RV assessment by 2D-Echocardiography:

Assessment of:

RV diameters, all assessed in apical 4 chamber view at end diastole basal diameter with normal value(25-40)mm, Middle diameter with normal value(19-35)mm and longitudinal diameter with normal value(59-83)mm; RV systolic function, all assessed in apical 4 chamber view, by TAPSE(normal more than 16mm), Tissue Doppler(normal more than 9.5cm/s) & FAC(normal more than 35%); RV volumes assessed in apical 4 chamber view ESV measured at end systole and EDV measured at end diastole.

Assessment of RA by 2D-Echocardiography:

Assessment of RA total function which is calculated through measuring total emptying volumes divided by RA max volume with normal value(58±9ml), RA Max volume which is maximum volume of RA measured at end systole with normal value(41±14ml), and Min volume which is the minimal volume of RA measured at end diastole with normal value(17±7ml), RA area normal less than 18cm<sup>2</sup>, right atrial remodeling in AF patient and relationship between longevity of AF period(AF pattern) and progression of remodeling through assessment of changes occurring in RA volumes and functions.

Assessment of TR severity by 2D-

Echocardiography:

Assessment of: TR severity by color Doppler, CW Doppler, PW Doppler, Through assessment of color jet area, VC the most narrow part of TR jet at TV annulus measured in apical 4Ch view(sever TR if more than 7mm and mild if less than or equal 3mm), PISA measured in apical 4Ch view(TR is sever when PISA radius more than 9mm and TR is mild if less than 6mm), EROA it is the effective regurgitant orifice area measured at apical 4Ch view (TR is sever when EROA more than 40cm<sup>2</sup> and mild if less than 20cm<sup>2</sup>), Regurgitation Volume measured at apical 4Ch view(TR is sever when regurgitation volume more than 60ml and mild if less than 30ml), Reg. Fraction measured at apical 4Ch view(TR is severe when the regurgitant fraction is more than 50%), TR peak velocity measured in apical 4CH view by CW Doppler. Grouping patients according to severity of TR into: Grade-II TR, Grade-III TR, Grade IV TR(severe). And finally, finding a relationship between right atrial remodeling and the severity of TR

Assessment of TV apparatus by 2D and 3D-echocardiography:

Assessment of: TV annulus diameters by 2D echocardiography and 3D echocardiography

TV annulus diameters by 3D echocardiography, including: 4Ch diameter defined as the maximum diameter between septum and RV free wall(mild if less than 3.65cm and moderate to severe if more than 4.15cm). 2Ch diameter is defined as the maximum diameter between the RV anterior and posterior wall(mild if less than 3,25cm and moderate to severe if more than 3,56cm).

Major axis diameter is defined as the longest axis of TA (mild if less than 3,75cm and moderate to severe if more than 4.55cm). Minor axis diameter is defined as the shortest axis of the TA(mild if less than 3.05cm and moderate to severe if more than 3.25cm). An assessment of other TV apparatus parameters by 3D echocardiography TV area defined as the area of the non-planar surface delineated by the 3D contour of TA(mild if less than 9.05 cm<sup>2</sup> and moderate to severe if more than 12.95cm<sup>2</sup>). Tenting height is defined as the maximum distance from the valve surface to the TV plane. Tenting volume is defined as the volume between the leaflets, and TA surface perimeter is defined as the length of the 3D contour representing TA circumference(mild if less than 11,05 and moderate to severe if more than 12.85cm)

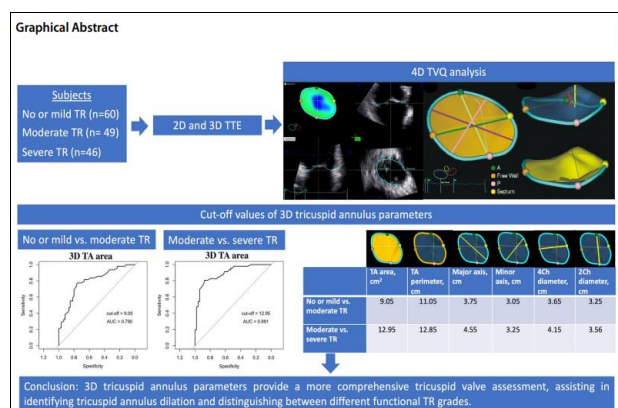


Figure 1. Measure tricuspid valve remodeling indexes.

Ethical considerations:

Signed informed consent from each patient. Ethical approval was obtained from the ethics and research committee.

Statistical analysis:

This study's overarching goal is to use the Statistical Package for the Social Sciences (SPSS) version 25 for data analysis. The qualitative data were presented using percentages and frequencies. The mean±standard deviation (Mean±SD) was used to express continuous quantitative data. Central value of a discrete set of integers, calculated by dividing the sum of values by the number of values; sometimes known as the mean or average. The dispersion of a group of values can be measured by looking at their standard deviation (SD). If the standard deviation is small, then the values are clustered around the set mean, and if it's large, then the values are more dispersed.

P-values less than 0.05 were deemed significant, P-values less than 0.001 were deemed very significant, and P-values greater than 0.05 were deemed inconsequential in terms of probability.

Various tests were conducted:

For data that is normally distributed, a one-way analysis of variance (F) is used when comparing more than two groups. To compare non-parametric categorical data, researchers utilized a chi-square test to examine the remodeling of the right atrium, right ventricle, and TV annulus as assessed by 2D and 3D echocardiography in patients with non-paroxysmal atrial fibrillation.

### 3. Results

The study showed well-balanced gender distribution, comprising 51-males (51%) ensuring a representative sample for gender-related analyses. The mean age of the participants was 60.7 years.

Furthermore, the study population presented with several notable risk factors. Hypertension (HTN) was prevalent among 54% of the

participants. Diabetes Mellitus (DM) was observed in 32% of the patients, as shown in table (1)

Table 1. Description of demographic data in all studied patients.

DEMOGRAPHIC DATA		ALL PATIENTS (N=100)	
GENDER		Males	51 51.0%
AGE	Mean±SD	60.7±7	
	Min-max	48-78	
BMI	Mean±SD	25.7±2.4	
	Min-max	21-31	
HTN		54	54.0%
DM		32	32.0%
SMOKING		33	33.0%

The statistical analysis revealed a highly significant correlation ( $p < 0.001$ ) between the pattern of AF and the severity of TR in the studied patient, this correlation provides valuable insights into the relationship between AF progression and TR deterioration, which has important clinical implications, as shown in table (2).

Table 2. Correlation between AF pattern and TR severity in all studied patients

		AF						X2	P-VALUE
		Persistent (n=29)		Long standing (n=43)		Permanent (n=28)		85.3	<0.001 HS
TR GRADE	II	24	82.8%	5	11.6%	0	0.0%		
	III	5	17.2%	33	76.7%	10	35.7%		
	IV	0	0.0%	5	11.6%	18	64.3%		

X2: Chi-squared analysis. A p-value of less than 0.001 is regarded as very significant.

The echocardiographic assessment of the study population revealed several significant findings regarding the correlation between various cardiac measurements and the severity of TR. These parameters provide valuable insights into the structural and functional changes associated with TR Progression, as shown in table (3).

Table 3. Comparison of all studied groups of TR severity grades (II-III-IV) as regard TV regurgitation parameters in all studied patients.

TV REGURGITATION PARAMETERS		TR SEVERITY			STAT. TEST	P-VALUE
		Grade-II (n=29)	Grade-III (n=48)	Grade-IV (n=23)		
REG.	Mean±SD	26.8±1.3	38.6±2.5	60.3±2.4	1522	<0.001
	Min-Max	24-29	33-47	55-64		HS
VOLUME	Mean±SD	3.6±0.5	6±0.7	8.5±0.5	412	<0.001
	Min-Max	3-4	57	8-9		HS
PISA R	Mean±SD	5.8±0.6	7.9±0.8	10.8±0.7	309	<0.001
	Min-Max	5-7	7-9	10-12		HS
EROA	Mean±SD	0±0.2	0.4±0.02	0.5±0.02	876	<0.001
	Min-Max	0-0.3	0.3-0.4	0.4-0.5		HS
SYSTOLIC ANNULAR DIAMETER	Mean±SD	29.8±1.1	33.5±0.9	36.6±0.7	330	<0.001
	Min-Max	28-32	32-35	36-38		HS
DIASTOLIC ANNULAR DIAMETER	Mean±SD	33.9±0.7	37.2±1.1	41±0.7	393	<0.001
	Min-Max	33-35	35-39	40-42		HS

F: ANNOVA test value. It is deemed very significant when HS:P<0.001. X2: Chi-squared test

The comprehensive echocardiographic assessment of RV dimensions, volumes, and function across different grades of TR severity has yielded several intriguing findings. The analysis revealed a consistent pattern of non-significant differences in various RV parameters among patients with different TR grades -I, III, IV, as shown in table (4).

*Table 4. omparison of all studied groups of TR severity grades(II-III-IV) as regard RV parameters in 2D echo in all studied patients*

RV PARAMETERS IN 2D ECHO		TR SEVERITY			F	P-VALUE
		Grade-II (n=29)	Grade-III (n=48)	Grade-IV (n=23)		
LONGITUDINAL DIAMETER	Mean±SD	69.9±3.6	69.2±3.7	68.4±4.3	0.95	0.4 NS
	Min-Max	62-76	63-78	61-77		
MID DIAMETER	Mean±SD	27.1±3.1	26.9±3.6	26±4.1	0.6	0.55 NS
	Min-Max	21-33	20-34	20-34		
BASAL DIAMETER	Mean±SD	32.6±2.9	32.4±3.4	31.7±3.5	0.48	0.62 NS
	Min-Max	27-38	26-39	26-39		
ESV	Mean±SD	45.6±3.1	45.5±3.6	45.7±5.2	0.04	0.96 NS
	Min-Max	40-52	36-54	37-55		
EDV	Mean±SD	86.1±4.4	86.1±4.9	87±4.2	0.34	0.72 NS
	Min-Max	75-94	75-95	78-94		
TAPSE	Mean±SD	23.3±2.1	22.8±2.5	23±2.7	0.38	0.69 NS
	Min-Max	19-28	18-29	18-27		
S'	Mean±SD	12.7±1.6	12.4±1.6	12.5±1.6	0.26	0.77 NS
	Min-Max	9.5-16	9.5-15	9.5-15		
FAC %	Mean±SD	46.8±3.1	55.2±57.4	47.4±4.5	0.52	0.6 NS
	Min-Max	40-53	39-444	40-57		

F:ANNOVA test value. It is deemed non-significant if NS:P>0.05.

The echocardiographic evaluation of RA function in patients with varying grades of TR severity has yielded significant insights into the impact of TR on atrial mechanics. The analysis revealed several notable findings regarding RA Vmax, RA Vmin, and RA Function%, as shown in table (5)

*Table 5. Comparison of all studied groups of TR severity grades(II-III-IV) as regard RA parameters in 2D echo in all studied patients*

RA PARAMETERS IN 2D ECHO		TR SEVERITY			F	P-VALUE
		Grade-II (n=29)	Grade-III (n=48)	Grade-IV (n=23)		
V. MAX	Mean±SD	66.2±2.4	80±3.8	95±2.2	542	<0.001 HS
	Min-Max	61-72	74-88	90-99		
V. MIN	Mean±SD	35.6±2.2	46.4±2	58.7±3.3	583	<0.001 HS
	Min-Max	30-42	42-50	47-64		
FUNCTION%	Mean±SD	46.3±2.5	41.7±1.7	37.5±1.7	128	<0.001 HS
	Min-Max	41-52	39-45	35-41		

F:ANNOVA test value. It is deemed very significant when HS:P<0.001.

NS:P>0.05 is regarded as not being significant..

The comprehensive three-dimensional(3D) echocardiographic assessment of the TV annulus and leaflets in patients with varying grades of TR

severity has yielded several significant findings, providing valuable insights into the structural changes associated with TR progression, there is a clear relationship between TV annulus area, perimeter, Diameters and progression of TR severity in relation to longevity of AF, as shown in table (6).

*Table 6. Comparison of all studied groups of TR severity grades(II-III-IV) as regard 3D TVQ data in all studied patients.*

3D TVQ DATA		TR SEVERITY			F	P-VALUE
		Grade-II (n=29)	Grade-III (n=48)	Grade-IV (n=23)		
TV ANNULUS	Area	Mean±SD 8.5±0.5 Min-Max 7.8-9.2	Mean±SD 11.3±0.9 Min-Max 9.8-12.6	Mean±SD 14.7±1 Min-Max 12.9-16.2	358	<0.001 HS
	Perimeter	Mean±SD 10.8±0.5 Min-Max 10-11.5	Mean±SD 12.4±0.7 Min-Max 10.9-13.4	Mean±SD 14.9±0.7 Min-Max 13.8-15.9	243	<0.001 HS
	Max Axis	Mean±SD 3.6±0.2 Min-Max 3.4-3.9	Mean±SD 4.4±0.2 Min-Max 4-4.6	Mean±SD 4.8±0.2 Min-Max 4.6-5.2	264	<0.001 HS
	Min Axis	Mean±SD 3±0.1 Min-Max 2.8-3.1	Mean±SD 3.5±0.1 Min-Max 3.2-3.7	Mean±SD 4.2±0.2 Min-Max 3.9-4.5	396	<0.001 HS
	4Ch diameter	Mean±SD 3.5±0.1 Min-Max 3.4-3.7	Mean±SD 3.7±0.2 Min-Max 3.4-4.1	Mean±SD 4.6±0.3 Min-Max 4.2-5	17.7	<0.001 HS
	2Ch diameter	Mean±SD 3±0.2 Min-Max 2.7-3.4	Mean±SD 3.6±0.2 Min-Max 3.3-3.8	Mean±SD 4.1±0.2 Min-Max 3.8-4.5	225	<0.001 HS
LEAFLET	Tent. H	Mean±SD 0.3±0.1 Min-Max 0.1-0.5	Mean±SD 0.3±0.1 Min-Max 0.1-0.5	Mean±SD 0.3±0.1 Min-Max 0.1-0.5	0.41	0.67 NS
	Tent. V	Mean±SD 0.8±0.2 Min-Max 0.6-1.5	Mean±SD 1.3±0.3 Min-Max 0.7-1.8	Mean±SD 2.5±0.4 Min-Max 1.6-2.9	243	<0.001 HS
	COAPT. H	Mean±SD 0.3±0.1 Min-Max 0.1-0.5	Mean±SD 0.3±0.1 Min-Max 0.1-0.5	Mean±SD 0.3±0.1 Min-Max 0.1-0.5	0.41	0.67 NS

F:ANNOVA test value. It is deemed very significant when HS:P<0.001.

It is deemed non-significant if NS:P>0.05. Statistical significance is defined as S:P<0.05.

#### 4. Discussion

The relationship between persistent AF and RA and TA dilatation has been clarified by numerous investigations in the literature.

Sagie et al.,<sup>7</sup> emphasized how RA volume is a key factor in determining TA size. However, the exact process by which AF causes TA dilatation and regurgitation is yet unknown. Many theories have been put up, such as degenerative changes of the TA, RA dilatation and/or dysfunction, right ventricular dysfunction, or simply being referred to as "idiopathic annular dilatation" in relation to "isolated/idiopathic FTR."

Up until recently, researchers paid little attention to the role of RA remodeling in the etiology of TA dilatation and FTR formation. Modern three-dimensional echocardiography reveals the complex pathophysiology of FTR by thoroughly evaluating the tricuspid valve, right atrial septum, and right ventricle.

The RA myocardial wall contains unique muscle features, including the pectinate and crista terminalis, even though it is thinner than the left atrial myocardial wall. Furthermore, the tricuspid valve opening is encircled by the RA vestibule, a smooth muscular rim that anchors the pectinate muscles; the leaflet hinges are penetrated by its thin muscular fibers. The atrial flutter circuit and the TA's "sphincteric-like" contraction are both aided by these muscle fibers.



Whereas the mitral annulus is connected to the myocardium via the fibrous trigones at the base of the anterior mitral leaflet, the TA is characterized by a singular right fibrous trigone that sustains contact with the RA myocardium for the majority of its circumference. Because there is less fibrotic tissue in the TA, it may be easier to dilate it during remodeling of the chambers next to it, unlike in the mitral annulus.<sup>8</sup>

Research by Spinner et al.<sup>9</sup> Using data from 64 individuals with different levels of functional TR, researchers found that the severity of TR is correlated with the annular area and apical displacement of the anterior papillary muscle(PM).<sup>10</sup>

Kwak et al.,<sup>11</sup> in a recent study have shed light on the significance of AFTR as a distinct entity, accounting for approximately 10% of significant tricuspid regurgitation cases. While the prevalence of AF is high among AFTR patients, limited research has explored AF as a potential risk factor for TR progression. Yet, there are some caveats to the current research. For example, a large portion of the patients included in these trials had left-sided valvular disorders or a decreased left ventricular ejection fraction, both of which can lead to substantial secondary TR on their own. This means that we still don't know much about the long-term relationship between AF and AFTR.

We aimed to enroll people in this trial who did not have any preexisting diseases or disorders that might cause TR.

Our results showed that patients with AF were more likely to experience new-onset moderate or higher TR. In addition, we found that long-term AF was the main factor in the advancement of TR in the majority of substantial TR cases; since no other causes were discovered, these data provide strong evidence that AF is an important contributor to the development of significant TR.

As AFTR develops, the right heart's geometric abnormalities and its connection to the TV may play a role. A greater RA-RV end-systolic volume ratio, lower RV end-systolic volume, and substantial RA enlargement were observed in patients with severe AFTR, according to recent research, in comparison to those with ventricular functional TR. Strong correlation between the RA-RV end-systolic volume ratio and the TV annular orientation angle suggests that geometric alterations in the TV might be caused by an imbalance in RA and RV remodeling.

Our data lends credence to this idea by demonstrating that an early indicator of AFTR development is an elevated RA-RV end-systolic area ratio, which in turn increases the likelihood of AFTR progression.<sup>11</sup>

Utsunomia et al.,<sup>12</sup> informed us that in their

cohort study of patients with moderate to severe TR, they used a TR spectrum based on three-dimensional trans-esophageal echocardiography(3D-TEE) to learn more about the frequency and features of tricuspid regurgitation(AF-TR). Among the individuals included in the study, 9.2% had AF-TR. Age(mean 79years), female gender, systemic hypertension, and a distinctive cardiac morphology(enlarged right atrium (RA) more than left atrium(LA)) and reduced systolic pulmonary artery pressure(average 37.0mmHg) were the clinical features linked with AF-TR.

Past research has looked into the link between AF and AF-TR, and the results show that AF causes the RA to widen and the TV annular dilatation to follow. But whether a dilated TV annulus is enough to generate substantial FTR is still up for debate. Several small-scale studies have established an association between chronic AF and FTR, with normal leaflet motion being a notable feature. Girard et al.,<sup>13</sup> Initially, three patients were documented who suffered from severe idiopathic TR and chronic AF. Upon surgical examination, all three patients had dilated annuli and normal TV leaflets.

Additionally, we enhanced our comprehension, with Yamasaki et al.,<sup>14</sup> According to a study that looked at 42 patients with severe FTR and AF, it was shown that older patients with chronic AF, enlarged RA, changed RV function, and dilatation of the TV annulus were more likely to experience FTR, which aligns with our current findings.

Florescu et al.,<sup>15</sup> showed that the TV annulus regions of AFTR patients were greater than those of VFTR patients. The significance of RA volume, tenting height, and tenting area/volume in distinguishing AFTR from VFTR has been highlighted by other research, which has found substantial variations between the two circumstances. Schlotter et al.,<sup>16</sup> Further research in this area found that AFTR patients had smaller RVs, lower TV tenting areas and heights, smaller TV annuli, and larger but smaller RA areas compared to VFTR patients.

The results of this investigation are consistent with those of Florescu et al.,<sup>15</sup> AFTR patients are shown to have reduced RV dimensions(with the exception of basal RV diameter), better RV function, a bigger TV annular diameter, larger RA dimensions, and less leaflet tenting compared to VFTR patients. This provides more support for the initial hypothesis. This innovative categorization method employs readily available echocardiographic information to delineate underlying anatomical, pathophysiological, and clinical distinctions. It might have major effects on patient care and treatment plans if used systematically in the assessment of FTR etiology.<sup>11</sup>

**Strength:** Our study's strength lies in its comprehensive echocardiographic assessments, employing both 2D and 3D techniques, to meticulously evaluate RV and RA parameters in patients with long-standing AF and functional TR. The study's focus on the relationship between AF duration and right atrial remodeling, along with TR severity, provides valuable insights into the pathophysiology of these conditions.

**Limitations:** In a relatively small sample size of 100 patients, the TV annulus was only assessed by 3D Echocardiography without assessment of RA and RV by the same modality; there is some sort of selection bias in the cases, all patients already had significant TR without follow-up for progression of severity.

#### 4. Conclusion

There is a strong relationship between AF and the development of significant FTR, with the main mechanism being TA dilatation.

#### Disclosure

The authors have no financial interest to declare in relation to the content of this article.

#### Authorship

All authors have a substantial contribution to the article

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#### Conflicts of interest

There are no conflicts of interest.

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