

Atrial Remodeling and Atrial Tachyarrhythmias in Arrhythmogenic Right Ventricular Cardiomyopathy

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Less is known about atrial remodeling and atrial tachyarrhythmias (ATa) in arrhythmogenic right ventricular cardiomyopathy (ARVC); this cross-sectional study aimed to determine the prevalence, characterization, and predictors of atrial remodeling and ATa in a large series of patients with ARVC. From February 2004 to September 2014, 294 consecutive patients who met the task force criteria for ARVC were enrolled. The prevalence, characterization, and predictors of atrial dilation and ATa were investigated. Right atrium (RA) dilation was identified in 160 patients (54.4%) and left atrium dilation in 66 patients (22.4%). Both RA and left atrium dilation were found in 44 patients (15.0%). Twenty-five patients (8.5%) had atrial fibrillation (AF), whereas 19 patients (6.5%) had atrial flutter (AFL). Of which, 7 patients (2.4%) had both AF and AFL. Multivariate analysis showed that AFL (odds ratio [OR] 10.309; 95% confidence interval [CI] 2.770 to 38.462; $p < 0.001$), hypertension (OR 9.174; 95% CI 2.364 to 35.714; $p = 0.001$), and RA dilation (OR 6.993; 95% CI 1.623 to 30.303; $p = 0.009$) were associated with increased risk for AF. AF (OR 10.526; 95% CI 2.786 to 40.000; $p = 0.001$) increased the risk of AFL. In conclusion, atrial remodeling and ATa were common in patients with ARVC. © 2016 Elsevier Inc. All rights reserved. (Am J Cardiol 2016;■:■-■)

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an inherited cardiomyopathy characterized predominantly by ventricular arrhythmias, right ventricular dysfunction, and sudden cardiac death.¹⁻³ At present, less is known about atrial remodeling and atrial tachyarrhythmias (ATa) in ARVC. Atrial remodeling and ATa often coexist and interact with each other, which increase the risk of inappropriate implantable cardioverter defibrillator (ICD) shocks, thromboembolism events, and even bradyarrhythmias.⁴⁻⁹ This study aimed to assess the prevalence, characterization, and predictors of atrial remodeling and ATa in a large series of patients with ARVC.

Methods

From February 2004 to September 2014, consecutive patients who had a definite diagnosis of ARVC in our hospital were enrolled. The diagnosis of ARVC was based on the criteria set by the Task Force of the Working Group of Myocardial and Pericardial Disease of the European Society of Cardiology and of the Scientific Council on Cardiomyopathies of the International Society and

Federation of Cardiology¹⁰ and was rechecked according to the 2010 revised Task Force Criteria.¹¹

All patients underwent transthoracic echocardiogram (TTE) and magnetic resonance imaging (MRI). The TTE and MRI parameters of the 4 cardiac chambers were abstracted. The right atrium (RA) dilation was defined as RA diameter ≥ 40 mm in vertical section to atrial septum, and the right ventricle (RV) dilation was defined as RV transverse diameter ≥ 40 mm in 4-chamber view in the end-diastolic. The left atrium (LA) dilation was defined as LA diameter ≥ 36 mm in parasternal long-axis view in the end-diastolic. The TTE and MRI data were evaluated independently by 2 groups of doctors without knowledge of clinical data, and inconsistencies between the TTE and MRI were adjudicated by a third cardiologist.

A careful interview of ATa history including atrial fibrillation (AF) and atrial flutter (AFL) was performed in all patients. In addition, all patients underwent 24 hours Holter and 48 hours telemetry monitoring. Paroxysmal AF was defined as AF that terminated spontaneously or with intervention within 7 days of onset, and persistent AF was defined as continuous AF sustained beyond 7 days.

Statistical analyses were performed using SPSS 19.0 software (SPSS Inc., Chicago, Illinois). Continuous variables were described as mean \pm SD, and comparison between groups were performed with the Student's *t* test or Wilcoxon test. Categorical variables were described as counts and compared by the chi-square analysis. For the multivariate logistic regression analysis, the continuous variables were appropriately transformed where required to render them normally distributed. The following variables included gender, age, presence of hypertension, and diabetes

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Table 1
Clinical characteristics of the study cohort (n = 294)

Age, (years)	37.7 ± 14.8
Male	221 (75.2%)
Right ventricle dilation	200 (68.0%)
Mean left ventricle dimension, (mm)	47.4 ± 6.0
Mean left ventricular ejection fraction, (%)	58.7 ± 11.4
Hypertension	27 (6.6%)
Diabetes mellitus	8 (1.9%)
Task force criteria	
Epsilon wave	50 (17.0%)
Prolonged terminal activation duration	98 (33.3%)
Negative T waves	189 (64.3%)
V ₁ -V ₃ or beyond	143 (48.6%)
V ₁ -V ₄ or beyond with complete right bundle branch block	21 (7.1%)
V ₁ -V ₂	15 (5.1%)
V ₄ -V ₆	8 (2.7%)
Left bundle branch block ventricular tachycardia with superior axis	249 (84.7%)
Premature ventricular contractions > 500/24h	71 (24.1%)
Structural major task force criteria	142 (48.3%)
Structural minor task force criteria	95 (32.3%)
Family history	33 (11.2%)

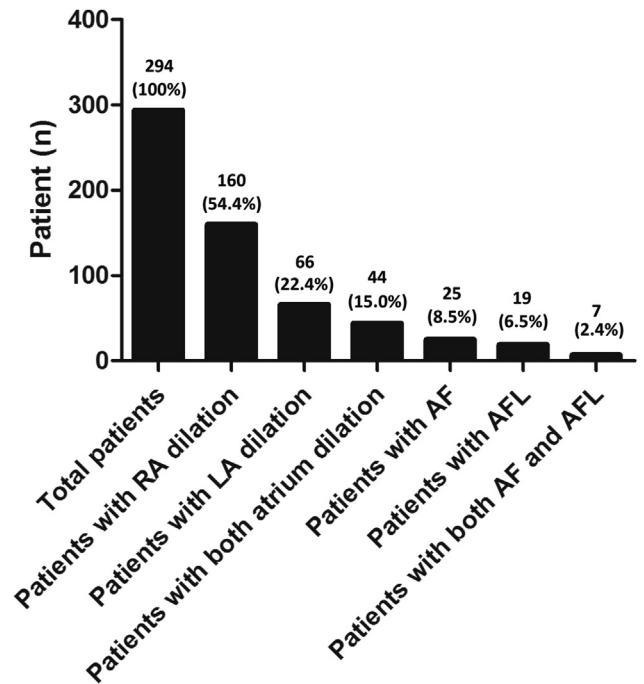


Figure 1. The prevalence of atrial dilation and ATa.

mellitus; parameters of cardiac chambers and left ventricular ejection fraction were analyzed to evaluate in association with the presence of atrial dilation and ATa. All tests were 2 tailed, and a statistical significance was established at a $p < 0.05$.

Results

From February 2004 to September 2014, 312 consecutive patients with ARVC were admitted in our hospital. Of these, 18 patients with contraindication (ICD implanted) to MRI examination were excluded from the study. Therefore, there were 294 patients enrolled. The clinical characteristics were listed in Table 1.

The prevalence of atrial dilation and ATa were shown in Figure 1. In patients with LA dilation, 44 (66.7%) had RA dilation. In patients with RA dilation, 43 (26.7%) had LA dilation. Of the 25 patients with AF, 9 (3.1%) were persistent AF, and the other 16 were paroxysmal AF. The median time of the recorded episodes of ATa to the initial presentation of ARVC was 9 months (1 to 226 months). The AFLs recorded in all the 19 patients were cavotricuspid isthmus dependent based on 12-lead surface electrocardiogram, whereas 4 were confirmed by electrophysiological studies. The maximum ventricular rates noted with AF or AFL were 210 and 172 bpm, respectively. No sustained atrial tachycardia was found.

The comparisons of clinical characteristics in patients with and without atrial dilation were shown in Table 2. Multivariate analysis showed that RV dilation (odds ratio [OR] 7.519; 95% confidence interval [CI] 3.906 to 14.493; $p < 0.001$), LV dysfunction (OR 8.475; 95% CI 2.591 to 27.778; $p < 0.001$), and LV dilation (OR 6.154; 95% CI 1.277 to 29.654; $p = 0.024$) were associated with increased risk for RA dilation. LV dilation (OR 12.987; 95% CI 2.564 to 66.667; $p = 0.024$) increased the risk of LA dilation.

The comparisons of patients with and without ATa were listed in Table 3. RA dilation (OR 6.993; 95% CI 1.623 to 30.303; $p = 0.009$), AFL (OR 10.309; 95% CI 2.770 to 38.462; $p < 0.001$), and hypertension (OR 9.174; 95% CI 2.364 to 35.714; $p = 0.001$) were associated with increased risk for AF. AF (OR 10.526; 95% CI 2.786 to 40.000; $p = 0.001$) increased the risk of AFL.

Discussion

In this study, data from a large series of patients with ARVC revealed an un-ignorable prevalence of atrial remodeling and ATa. These ATa are more common in patients with RA dilation and hypertension, whereas atrial dilation tend to be more common in patients with LV dilation, LV dysfunction, and RV dilation.

Malignant ventricular arrhythmias are generally considered as the cause of sudden death in patients with ARVC. Although several studies of ARVC with ATa have been reported,^{12,13} the issue was often been ignored. However, atrial remodeling and ATa may increase the risk of intracardiac thrombosis, thromboembolism complications, and even sudden deaths. The relative high prevalence of ATa and atrial remodeling found in this study also highlight the value of early screening and management in certain subgroup of patients with ARVC.

The prevalence of ATa also has relevance related to ICD programming and device selection. Potential overlap of ventricular tachycardia and ATa with rapid ventricular response requires careful device diagnostic capabilities and accuracy to minimize risk of inappropriate ICD shocks. Successful management of ATa helps reduce ICD shocks and improve the quality of life.

It was interesting that a relatively high incidence of LA enlargement in a disease that predominately affects the RV.

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