



## Original article

# Patients with drug-refractory atrioventricular nodal reentrant tachycardia: Clinical features, electrophysiological characteristics, and predictors of medication failure



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## ARTICLE INFO

## Article history:

Received 17 November 2013

Received in revised form

23 December 2013

Accepted 13 January 2014

Available online 24 February 2014

## Keywords:

Atrioventricular nodal reentrant tachycardia

Catheter ablation

Slow tachycardia

Antiarrhythmic agents

## ABSTRACT

**Background and purpose:** Drug responses vary markedly from patient to patient in atrioventricular nodal reentrant tachycardia (AVNRT), the most common form of paroxysmal regular supraventricular tachycardia in adults. However, clinical and electrophysiological (EP) characteristics of patients with AVNRT whose tachycardia attacks could not be adequately controlled by antiarrhythmic agents have not been studied in a large patient cohort. We aimed to define the clinical and EP features of patients with drug-refractory AVNRT.

**Methods and results:** A total of 266 consecutive patients with AVNRT undergoing catheter ablation after a period of medical treatment were analyzed: 144 patients with drug-refractory AVNRT (Group 1) and 122 patients with drug-responsive AVNRT (Group 2). Age was significantly higher ( $p = 0.027$ ) and the presence of hypertension ( $p = 0.030$ ), diabetes mellitus ( $p = 0.047$ ), and valvular heart diseases ( $p = 0.008$ ) was more frequent in Group 1 compared to Group 2. Among the EP features, atrial-His jump (81% vs 69%,  $p = 0.028$ ) and atrial vulnerability (26% vs 14%,  $p = 0.018$ ) were significantly higher, echo zone was significantly more long-lasting ( $44 \pm 24$  ms vs  $38 \pm 22$  ms,  $p = 0.018$ ), and tachycardia cycle length (TCL) was significantly longer ( $348 \pm 41$  ms vs  $329 \pm 38$  ms,  $p = 0.000$ ) in Group 1 than in Group 2. Multivariate analysis showed that hypertension ( $p = 0.036$ ), valvular heart disease ( $p = 0.014$ ), atrial vulnerability ( $p = 0.037$ ), TCL ( $p = 0.003$ ), and wide echo zone ( $p = 0.028$ ) were independent predictors for drug-refractory AVNRT. **Conclusion:** In the presence of hypertension, valvular heart disease, atrial vulnerability, long-lasting echo zone, and relatively slow AVNRT, medical treatment is less likely to prevent the tachycardia episodes.

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## Introduction

Atrioventricular nodal reentrant tachycardia (AVNRT) is the most common form of paroxysmal regular supraventricular tachycardia (SVT) in adults, accounting for 60% of the cases [1]. Radiofrequency (RF) catheter ablation has become the first-line treatment approach with high acute success and low complication rates [2–4]. On the other hand, antiarrhythmic therapy still plays a role in the majority of patients in the acute and long-term management of SVT [5]. However, drug responses vary markedly from patient to patient in AVNRT, satisfactory control being

achieved in only 60% of the cases [6–8]. Even the so-called tailored therapy regimens as directed by electrophysiological (EP) studies before initiation of antiarrhythmic treatment can barely reach success rates of 70–80% [9–12]. Thus, drug-refractory AVNRT is a considerable health problem hampering the individual's quality of life [13]. Data are not yet available about the clinical characteristics and EP features of patients with drug-refractory AVNRT. The aim of this study was to compare clinical and EP characteristics as well as catheter ablation results in patients with drug-responsive and drug-refractory AVNRT.

## Methods

## Patients

The subjects of this study consist of 266 consecutive patients treated with RF catheter ablation for symptomatic AVNRT. All

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patients had a history of paroxysmal palpitations ranging from 6 months to 26 years. The frequency of tachycardia attacks documented on electrocardiographic (ECG) or Holter recordings varied from at least once in a month to three to four attacks in a year. Patients who experienced at least one documented episode of AVNRT in the previous 3 months before ablation despite maximum tolerable doses of antiarrhythmic agents were taken as the study group ( $n=144$ ; Group 1). Patients who did not have any palpitations on medications in the previous 6 months but opted to discontinue medication and undergo catheter ablation served as the control group ( $n=122$ ; Group 2). Patients with poor drug compliance or different EP diagnoses other than AVNRT were excluded from the study. The study was approved by the institutional ethical committee and informed written consent was obtained from each patient for the ablation procedure.

All the patients underwent 12-lead surface ECG, X-ray examination, echocardiography, and blood chemistry measurements including thyroid testing and, when clinically indicated, stress test and 24-h Holter ECG recording.

#### *EP study and RF catheter ablation*

EP study and catheter ablation were performed in a single session in all patients in the fasting, unsedated state and after discontinuation of all antiarrhythmic drugs for at least five half-lives. The standard protocol consisted of decremental high right atrial ( $A_1A_1$ ) pacing, usually starting from 600 ms and decreasing in steps of 10 ms until the atrioventricular (AV) node Wenckebach cycle length was reached, and single atrial extrastimulus ( $A_1A_2$ ) testing at three different drive train cycle lengths (600, 500, and 430 ms) to induce tachycardia. During pacing with the first drive train, the  $A_1$ – $A_2$  interval was shortened by 10 ms until the AV node effective refractory period (ERP) had been reached. A jump of the atrial-His bundle (AH) interval was defined as the difference between any consecutive AH intervals equal to or more than 50 ms during programmed or incremental atrial pacing. Programmed electrical stimulation was performed from the right ventricle to investigate the ventriculoatrial (VA) conduction at baseline. All basic EP data were collected with the patients unsedated and before infusion of any pharmacological stimulants except for tachycardia parameters in those patients whose tachycardia could be induced only under pharmacologic stimulation. AVNRT was diagnosed according to the standard criteria [1,14].

Slow pathway ablation was done with the integrated (electrogram-guided anatomic) approach, using 7Fr quadripolar tip-deflectable catheters with 4-mm tip electrodes (Marinr MC, Medtronic Co., Minneapolis, MN, USA). Fifty watts of energy with a temperature limit of 65°C was applied at successful sites for 60–90 s. RF delivery was terminated if junctional rhythm did not appear in the first 15 s and the catheter was moved to the mid- and anterior septum to repeat the procedure until the endpoints were reached. The endpoints of ablation were the demonstration of either a slow pathway block or a slow pathway modification with no more than one single echo beat along with noninducibility of AVNRT.

#### *Follow-up after RF catheter ablation*

All the patients were discharged 2 days postoperatively. After hospital discharge, all patients were scheduled for a visit 4–6 weeks later and every 3 months thereafter in the first year. If palpitations recurred, the patients were asked to obtain an ECG as soon as possible and contact our center.

#### *Statistical analysis*

Continuous variables were expressed as mean  $\pm$  standard deviation. Groups were compared by means of chi-square analysis or Fischer's exact test when needed for discrete variables and with unpaired Student's *t* test for continuous variables.

Logistic regression analysis was used to examine and determine the predictors for drug-refractory AVNRT. The following variables were put into the model: age, gender, duration of symptoms, presence of hypertension, diabetes mellitus, valvular heart disease, coronary artery disease, left ventricular hypertrophy, left ventricular ejection fraction, and EP parameters; AV node Wenckebach cycle length, AV node anterograde ERP, presence of AH jumps, multiple AH jumps, echo zone duration, atrial vulnerability, the frequency of using pharmacologic stimulation to induce AVNRT, type of AVNRT, and tachycardia cycle length (TCL). Variables with  $p < 0.20$  in univariate analyses were included into the multivariate analyses. In multivariate analysis, backward LR elimination was used to compare and build the appropriate model. Likelihood ratio values were considered for the reduction of the model.

Statistical comparisons were performed using the statistical software package SPSS 15.0 (SPSS Inc., Chicago, IL, USA). Calculated *p*-values of less than 0.05 were considered significant.

#### **Results**

The study group (Group 1) included 144 patients (79 women and 65 men; mean age  $43 \pm 15$  years, range 17–84 years) and the control group (Group 2) consisted of 122 patients (64 women and 58 men; mean age  $39 \pm 14$  years, range 20–78 years).

#### *Clinical characteristics*

Clinical characteristics of groups are shown in detail in [Table 1](#). Age was significantly higher ( $p=0.027$ ) and hypertension ( $p=0.030$ ), diabetes mellitus ( $p=0.047$ ), and valvular heart diseases ( $p=0.008$ ) were more frequent in Group 1 as compared to Group 2. There was no difference between the study and control groups regarding the antiarrhythmic therapy regimen ([Table 1](#)).

#### *Electrophysiological characteristics*

The presence of discontinuous AV conduction was more frequent ( $p=0.028$ ) and the echo zone was seen to last slightly but significantly longer ( $44 \pm 24$  ms vs  $38 \pm 22$  ms,  $p=0.018$ ) in Group 1 than in Group 2. The TCL was significantly longer in Group 1 ( $p < 0.001$ ). The lower rate of AVNRT was due to the longer AH intervals ( $p=0.019$ ) in this group. The His-ventricle and VA intervals during tachycardia did not differ between the groups ( $p > 0.05$  for both). The need for pharmacological stimulation to induce tachycardia did not differ between the groups ( $p > 0.05$ ). EP characteristics of patients are shown in detail in [Table 2](#).

Sustained atrial fibrillation (AF) lasting for more than 30 s was induced (atrial vulnerability) in 54 of 266 patients during EP study. Thirty-seven of these cases were in Group 1 (26%) and 17 were in Group 2 (14%) ( $p=0.018$ ). AF was converted spontaneously into sinus rhythm in the first 15 min in 47 patients (87%) and was electrically converted in 7 patients (13%). AF was induced through the degeneration of AVNRT in eight patients (15%); of these, three were in Group 1 and 5 in Group 2, the difference between the groups not being statistically significant ( $p > 0.050$ ). AF was induced during programmed atrial stimulation or burst pacing in the rest of the 46 patients (85%). AF occurring during catheter manipulation was not taken into consideration.

A comparison of the EP variables of the groups with regard to the antiarrhythmic drugs failed to reveal any additional statistically significant difference between the groups. Among patients taking

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