Advances in Medical Sciences 63 (2018) 249–256

Contents lists available at ScienceDirect

Advances in Medical Sciences

journal homepage: www.elsevier.com/locate/advms

Original research article

A simplified approach for evaluating sustained slow pathway conduction for diagnosis and treatment of atrioventricular nodal reentry tachycardia in children and adults

Janusz Sledz[a,b,c], Michal Labus[d], Mariusz Mazij[d], Monika Klank-Szafran[a], Dariusz Karbarz[e], Bartosz Ludwik[d], Jacek Kusa[d], Karol Deutsch[a], Leslaw Szydlowski[f], Adrian Mscisz[g], Jerzy Spikowski[d], Aleksandra Morka[h,*], Tomasz Kameczura[i,g], Aleksandra Swietoniowska-Mscisz[a], Sebastian Stec[a,g,i]

[a] Elmedica, EP-Network, Kielce, Poland
[b] Department of Cardiology, G.V.M. Carint, Ostrowiec Swietokrzyski, Poland
[c] Carint Medica, EP-Network, Cracow, Poland
[d] Department of Cardiology, Regional Specialist Hospital, Centre for Research and Development, Wroclaw, Poland
[e] Department of Cardiology, County Hospital, Radom, Poland
[f] Department of Pediatric Cardiology, Medical University of Silesia, Katowice, Poland
[g] Chair of Electroradiology, Faculty of Medicine, University of Rzeszow, Rzeszow, Poland
[h] Department of Pediatric Cardiosurgery and Cardiosurgical Intensive Care University Children Hospital, Faculty of Health Sciences Jagiellonian University Medical College, Krakow, Poland
[i] Podkarpackie Center for Cardiovascular Intervention, G.V.M. Carint, Sanok, Poland

ARTICLE INFO

Keywords:
Atrioventricular nodal reentry tachycardia
Pacing
Diagnosis
Ablation
Children

ABSTRACT

Purpose: During incremental atrial pacing in patients with atrioventricular nodal reentrant tachycardia, the PR interval often exceeds the RR interval (PR > RR) during stable 1:1 AV conduction. However, the PR/RR ratio has never been evaluated in a large group of patients with pacing from the proximal coronary sinus and after isoproterenol challenge. Our study validates new site of pacing and easier method of identification of PR > RR.
Material and methods: A prospective protocol of incremental atrial pacing from the proximal coronary sinus was carried out in 398 patients (AVNRT-228 and control-170). The maximum stimulus to the Q wave interval (S-Q = PR), SS interval (S-S), and Q-Q (RR) interval were measured at baseline and 10 min after successful slow pathway ablation and after isoproterenol challenge (obligatory).
Results: The mean maximum PR/RR ratios at baseline were 1.17 ± 0.24 and 0.82 ± 0.13 ($p < 0.00001$) in the AVNRT and controls respectively. There were no PR/RR ratios ≥1 at baseline and after isoproterenol challenge in 12.3% of the AVNRT group and in 95.9% of the control group ($p < 0.0001$). PR/RR ratios ≥1 were absent in 98% of AVNRT cases after slow pathway ablation/modification in children and 99% of such cases in adults (P = NS). The diagnostic performance of PR/RR ratio evaluation before and after isoproterenol challenge had the highest diagnostic performance for AVNRT with PR/RR > = 1 (sensitivity: 88%, specificity: 96%, PPV-97%, NPV-85%).
Conclusions: The PR/RR ratio is a simple tool for slow pathway substrate and AVNRT evaluation. Eliminating PR/RR ratios ≥1 may serve as a surrogate endpoint for slow pathway ablation in children and adults with AVNRT.

1. Introduction

Atrioventricular (AV) nodal reentrant tachycardia (AVNRT) is the most common form of paroxysmal regular supraventricular tachycardia in pediatric and adult patients referred for invasive electrophysiological study and catheter ablation (CA) [1–4]. The presence of dual AV nodal physiology (DAVN) is typically reported as a substrate for AVNRT. The classical definition of DAVN is an atrio-His (AH) jump greater than

* Corresponding author at: Department of Pediatric Cardiosurgery and Cardiosurgical Intensive Care University Children Hospital, Wielicka 265 St., 30-663 Krakow, Poland. Tel.: +4812 658 2011 ext.1635; Fax: +4812 658 4446.
E-mail address: pediatric.cardiology@interia.pl (A. Morka).

https://doi.org/10.1016/j.advms.2018.01.001
Received 12 June 2017; Accepted 8 January 2018
Available online 10 February 2018

Table 1
Comparison of previous and simplified approaches for PR/RR ratio measurement.

Authors	Baker et al. [6]	Kannankeri et al. [9]	Blurton et al. [8]	Martinez-Sanchez et al. [7]	Sledz et al. (present study)
AVNRT (n)	30	61	92	85	228
Control (n)	27	0	46	56	170
Pacing site	HRA	HRA	HRA	HRA	PCS
Children < 18 (%)	0	90	100	0	26
DAVN by only A2H2 evaluation (S2, Jump value)	Yes (ND)	YES (≥50 ms)	YES (≥40 ms)	YES (≥50 ms)	NO (S2, S3 or S4 ≥ 50 ms)
PR/RR ratio ≥ 1 accepted only in 1 beat	no, continuous stable for 15 s	no, continuous	no, continuous	no, continuous	yes
Isoproterenol challenge when neccessary for induction	no	yes	yes	yes	yes
Isoproterenol challenge and PR > RR measurement in all cases after ablation	no	no	no	no	yes
Catheters (number)	4	4	3	3	2
General anesthesia (% of patients)	0	0	> 50	0	0
PR > RR in AVNRT(%)	93	93	60	78	88
PR > RR in controls (%)	11	ND	13	12	4
% of standard „jump" in AVNRT	57	52	42	61	49
% of standard „jump" in controls	11	ND	30	18	9

Abbreviations: AVNRT – atrioventricular nodal reentrant tachycardia; HRA – high right atrium; PCS –k proximal coronary sinus; DAVN – dual AV nodal (physiology); A2H2 – atrial potential after premature extrastimulus; S2 – the first premature extrastimulus after train (S1); ND – not declared; S3 – the second premature extrastimulus after S2 and train; S4 – the third premature extrastimulus after S2, S3 and train; PR/RR ratio – PR interval to RR interval ratio: from the atrial stimulus to earliest R wave on ECG during incremental atrial pacing; PR > RR – the PR interval often exceeds the RR interval.

50 ms with a 10-ms decrement in A1A2. However, this condition is only met in approximately half of pediatric patients with AVNRT [4]. Moreover, criteria for DAVN have been reported in up to 44% of patients without AVNRT, especially in the pediatric population [4–9]. In patients with AVNRT, however, DAVN is documented less often than sustained slow pathway conduction (SSPC) during incremental atrial pacing (IAP). In patients with AVNRT and a fast rate of IAP, the PR interval often exceeds the RR interval (PR/RR > 1) during stable 1:1 AV conduction. This phenomenon could be a substrate for the inducibility of AVNRT, and its absence could be a marker of slow pathway ablation or modification [6–9].

SSPC has never been evaluated in such a way in a large, unselected group of patients (more than 100) with AVNRT. Moreover, there has been no prospective study on a simplified approach for evaluating SSPC with pacing from the proximal coronary sinus (PCS) at baseline and when needed after isoproterenol infusion. Previous studies involved only the high right atrium pacing site and IAP with several PR intervals exceeding the RR interval with stable 1:1 AV conduction (Table 1) [4–9].

The aim of our study is to characterize the baseline and post-ablation AV nodal conduction features during IAP from the PCS in unselected pediatric and adult patients with AVNRT. We also compared our findings to a control population of patients without AVNRT. The results show that the simplified approach for SSPC evaluation could be a simple, fast, and accurate technique for AVNRT diagnosis and endpoint of SP ablation or modification.

SP ablation was defined as lack of dual atrioventricular physiology and non-inducibility of AVNRT. SP modification was defined as non-inducibility of AVNRT with residual jump and/or single echo beat.

2. Material and methods

Data were collected from a prospective multicenter registry that covers procedures from six centers. Patients were recruited between 2010 and 2013. The intracardiac signals and measurements shown in Figs. 1 and 2 were obtained from procedures performed in the year 2016. All of the patients investigated had been referred for electrophysiological study and radiofrequency catheter ablation. A prospective protocol of IAP was carried out in 398 patients who were referred for ablation due to documented AVNRT (n = 228, study group) and other non-SP-dependent arrhythmias (control, n = 170).

All patients in the AVNRT group had documented narrow QRS tachycardia prior to EPS. In the control group, 70 patients with accessory pathway had orthodromic tachycardia, 24 patients had atrial flutter (narrow QRS), and 10 patients had atrial tachycardia. Therefore, narrow QRS tachycardia was documented in 104 patients in the control group. The study protocol complies with the Declaration of Helsinki and was approved by 2 local Institutional Review Boards: 1) Bioethics Committee of the Regional Specialist Hospital, Centre for Research and Development in Wroclaw, Poland (approval number KB/2/2010, 2 June 2010); 2) Bioethics Committee of the Swietokrzyska Chamber of Physicians and Dentists in Kielce, Poland (approval number 6/A/2009, 9 February 2009). All patients gave informed consent prior to the procedure. Antiarrhythmic drugs were discontinued for a minimum of 5 half-lives prior to the study.

2.1. Electrophysiological study and ablation

Minimally invasive non-fluoroscopic imaging and catheter ablation were performed with minimum fluoroscopy exposure (4–8 frames/s) or non-fluoroscopic navigation and imaging. A detailed description of the approach is reported in previous studies [10,11]. Shortly, the left anterior oblique view (or biplane left and right anterior oblique view for the MINI CA approach) was used to assess the catheter position and electroanatomical mapping. An EP-tracer (EP Recording System, CardioTek, Maastricht, the Netherlands) was used for all procedures to record the input from all 12 electrocardiography (ECG) leads and intracardiac signals simultaneously. Under fluoroscopic or non-fluoroscopic guidance, a decapolar catheter was placed in the coronary sinus, and one mapping/ablation catheter was positioned using a "dynamic approach" in the His bundle region, PCS, right atrium, and right ventricle. The catheter was either a 4 or 8-mm gold tip catheter (Biotronik), a 4-mm platinum-iridium catheter (St. Jude Medical, St. Paul, Minn., USA), or an 8-mm gold tip catheter (Osypka AG, Germany).

A three-dimensional electroanatomical system (3D-EAM, Ensite Velocity, St. Jude Medical) was used according to the discretion of the treating physician or the availability in the center. Bipolar intracardiac electrograms were filtered between 40 and 500 kHz and recorded at 100 mm/s. All pacing maneuvers from the ventricle or atrium were performed at a minimum of twice the diastolic threshold using a programmable stimulator built into the recording system.

Electrophysiological measurements were obtained in the baseline

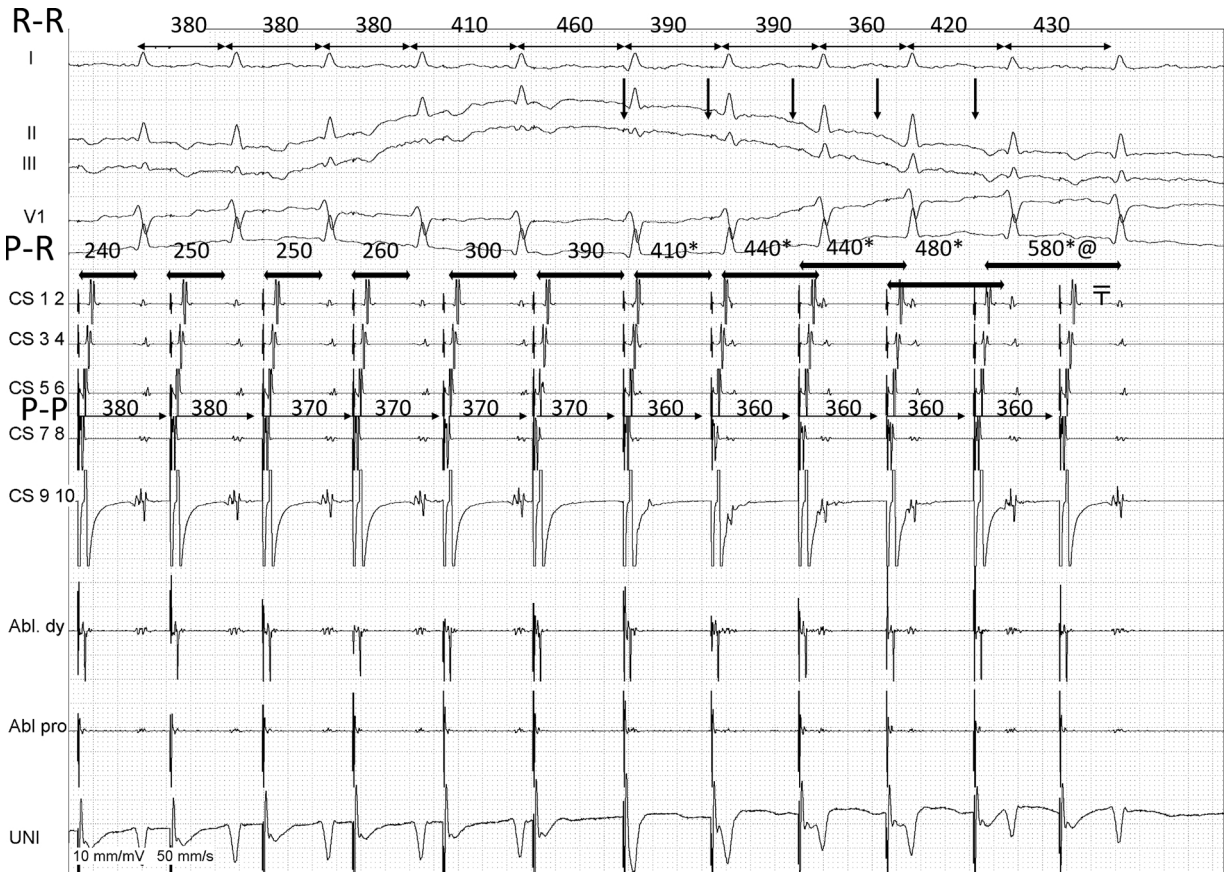

Fig. 1. Electrocardiograph measurements during incremental atrial pacing from PCS in patients with AVNRT (familial form of AVNRT in mother and daughter) prior to ablation of SP. Five standard ECG leads (I, II, III, V1, V6) and five leads from a decapolar catheter were located in coronary sinus (CS) CS 1 2, CS 3 4, CS 5 6, CS 7 8, CS 9 10. In the PCS (CS 9 10), there are three ablation catheter leads: Abl dys (ablation 1–2 distal bipolar), ABL pro (ablation 3–4 proximal bipolar), and UNI (unipolar from ablation 1). Standard PR, RR, and RR interval measurements were done with a paper speed of 50 mm/s. The black arrow represents the pacing spike, which is visible in the front of the QRS complex. PR intervals with a star ("*") represent PR intervals longer than the RR interval. "$\overline{\top}$" represents pacing spikes that are not conducted to the ventricle due to refractoriness of the SP. An PR interval with "@" represents the maximum PR/RR ratio. Note that at least the last 5 PR intervals are longer than the RR intervals. Max PR (PR@) = 580 msec, max RR = 430 msec, max PP = 360 msec. Max PR/max RR = 1.35. Note that during IAP, two sudden prolongations of PR > 50 msec occurred: pacing spikes 6 and 11.

state. When necessary for tachycardia induction isoproterenol were administered and measurements were repeated after administering an ultra-rapid intravenous bolus of isoproterenol via the peripheral route at an initial dose of 0.01–0.03 mg (0.2 mg/mL, 0.5–1 mL of a 1:50000 dilution), which was repeated within 3 min when necessary to increase the sinus rhythm to higher than 30% of the baseline state and at least 100 bpm. The final protocol of arrhythmia induction was performed after intravenous bolus administration of 1 mg of atropine. Radiofrequency energy was delivered in temperature-control mode using an EP-Shuttle Generator (Stockert, Biosense Webster, Cordis, Bar Diamond, Calif., USA) to the target area with a power output of 50–60 W and a temperature of 60 °C.

For slow pathway ablation, short pulses of radiofrequency energy were applied continuously with a maximum 8 continuous junctional beats. All patients achieved at least 15 junctional beats in the AVNRT group. None of the patients in the AVNRT group required left-sided ablation. When junctional beats were not induced during 15 s of radiofrequency application, further application at this site was stopped, and the ablation catheter was repositioned.

2.2. Simplified approach for electrophysiological measurement

IAP involved automatic performed pacing from only the PCS. During IAP maximum values of the PR interval, Wenckebach point, and RR interval were validated. The PR interval was calculated from the pacing spike to the first deflection of the QRS complex (stimulus to Q wave interval = PR interval) with consistent 1:1 AV conduction measurement prior to the Wenckebach point. The PP interval (stimulus to stimulus) prior to AV Wenckebach was measured. The RR interval was calculated between the first deflections of QRS complexes prior to the Wenckebach point. The standard pacing protocols included automated IAP (pre-defined from the pacer configuration) with a decrease of 10 ms every 2 s the atrial or atrioventricular node refractory period.

Programmed atrial and ventricular stimulation with S1S2 was typically performed. Therefore, a standard jump was documented as a PR interval "jump" greater than 50 ms with a 10-ms decrement in S1S2. However, when necessary for the induction or documentation of a PR jump, up to four drive trains including 8 beats (500, 400, 350, 300 msec) and up to three extra stimuli (S2, S3, S4) tests were employed [11,12]. Therefore, a combined jump was documented as a PR interval jump greater than 50 ms with a 10-ms decrement in S1S2, S2S3, or S3S4.

To detect the onset of the QRS, we used the earliest ventricular wave from surface lead II. The AH, HV, VA, and SA intervals were also measured for differential diagnosis during the sinus rhythm and sustained tachycardia by dynamic repositioning of the ablation catheter in the AVN region. Detailed analysis of the reasons for PR/RR < 1 during IAP is reported prospectively. The presence of DAVN before and after ablation was also assessed. After ablation, measurements were repeated 10–15 min after successful ablation and performed after isoproterenol administration in all patients.

For the diagnostic definition of a standard jump, an increase in AH by 50 ms for a 10-ms decrement in A1–A2 coupling interval indicates increase in the PR interval by 50 ms for a 10-ms decrement in S1–S2,

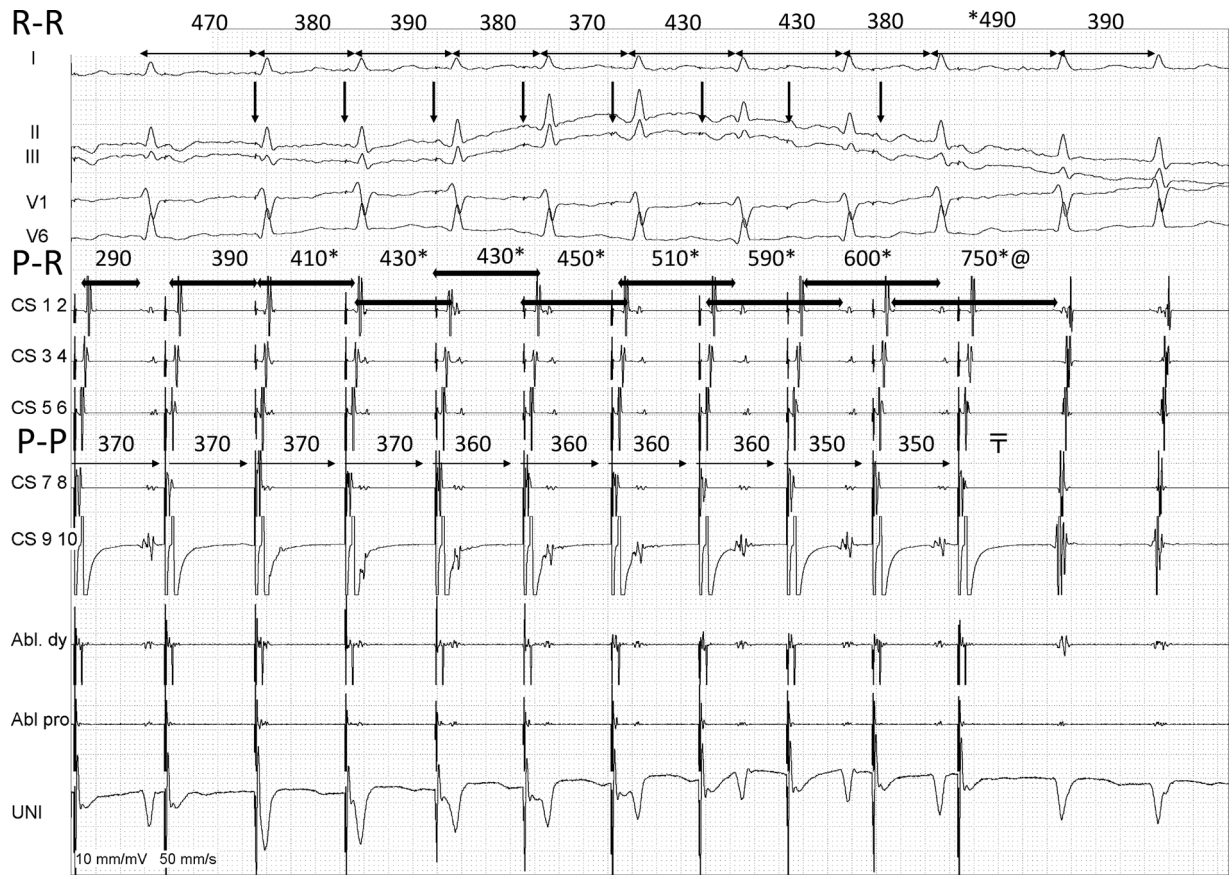

Fig. 2. Electrocardiograph measurements during IAP from PCS in patients with AVNRT prior to ablation of SP. There is induction of typical slow-fast AVNRT with a very long max PR interval after isoproterenol challenge. The external and intracardiac leads and symbols are similar to those shown in Fig. 1. Note that at least 8 PR intervals are longer than RR intervals. There are 8 pacing spikes preceeding the QRS complex. Max PR (PR@) = 750 msec, max RR = 490 msec, max PP = 350. Max PR/max RR = 1.53. The last pacing was not conducted due to induction of slow-fast AVNRT. Note that during IAP, three sudden prolongations of PR > 50 msec occurred: pacing spikes 2, 8, and 10.

while combined jump includes an increase in the PR interval by 50 ms. SSPC was defined as the ability to conduct two impulses from PCS pacing in succession. These definitions were obtained from previous studies. The jump was defined as repeatedly confirmed increments of a minimum of 50 ms in the PR interval in response to a 10-ms decrement after S2 (standard) and after S2S3, or S3S4 (combined). Examples of these measurements are presented in Figs. 1–3. For electrophysiological measurements, the recorded tracings were measured off-line by two investigators (J.Sl. and S.S.).

2.3. Differential diagnosis of supraventricular tachycardia with simplified 2-catheter approach

A detailed description of the simplified two-catheter and MINI CA approach was reported in previous studies, which included DAVN and VA interval evaluation, the atrial activation sequence during supraventricular tachycardia (SVT) and right ventricular overdrive pacing (RVOP), the response to RVOP (PPI-TCL evaluation), and exclusion of other possible mechanisms of SVT [11–13]. Moreover, when the diagnosis was uncertain, additional techniques or 3D mapping were performed to validate the atrial activation pattern. The site of successful radiofrequency energy application was used in combination with the diagnostic techniques to confirm the mechanism of SVT [4].

2.4. Statistical analysis

The results are presented as the mean ± standard deviation (SD). Continuous variables were compared using an unpaired *t*-test. A P value < 0.05 was considered significant. The sensitivity, specificity, positive and negative predictive values, and accuracy were calculated using standard definitions. Data were analyzed using Stata version 10 (Stata Statistical Software, Release 10, College Station, Tex., USA; Stata Corporation LP 2007).

3. Results

3.1. Patient population

The AVNRT group consisted of 228 pediatric and adult patients (age: 39.9 ± 20.7 years; 67% women; children (age < 18): 26%), while the control group consisted of 170 pediatric and adult patients (age: 37.6 ± 22.4 years (p = NS); 43% women (P < 0.05); children: 26% (P = NS)). The control group underwent invasive electrophysiological studies for accessory pathways (n = 117), atrial flutter (n = 24), atrial tachycardia (n = 10), and idiopathic ventricular tachycardia (n = 20). One patient from the control group had idiopathic ventricular tachycardia and orthodromic tachycardia. Ultimately, 226/228 AVNRT patients were successfully ablated (Table 2).

Structural heart disease were defined as any significant heart or valvular diseases associated with limitation of antiarrhythmic treatment (left ventricular hypertrophy, dilated cardiomyopathy, significant valvular heart disease). They were present in 4.6% of the patients in the AVNRT group and 9.4% of the control group (P < 0.05). The mean ejection fraction was above 60% in both groups (P = NS). In the AVNRT group, 99% (226/228) of the cases were successfully ablated, while the rate was 92% (156/170) in the control group. There were 6 cases of redone procedures in the AVNRT group and 12 redone or second procedures (for the second substrate) in the control group. There

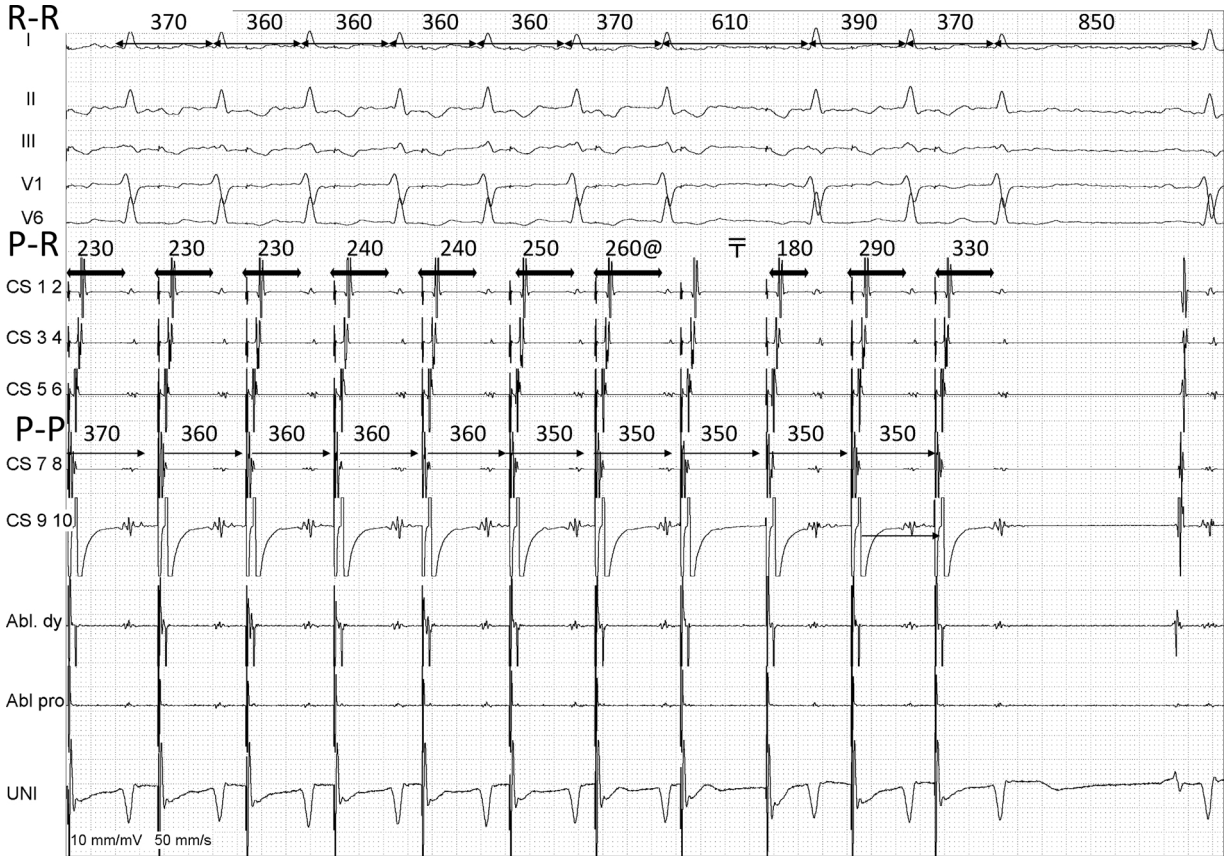

Fig. 3. Electrocardiograph measurements during incremental atrial pacing from PCS in patient with AVNRT after ablation of SP. The external and intracardiac leads and symbols are similar those in Fig. 1. Note that all PR intervals are shorter than RR intervals. Max PR (PR@) = 260 msec, max RR = 350 msec, max PP = 350. Max PR/max RR = 0.74. Eight pacing spike were not conducted due to a lack of continuous conduction via SP. No sudden prolongation of PR > 50 msec with a similar PP max (Wenckebach point) shows improvement of fast pathway conduction after SP ablation. The last pacing was not conducted due to the refractory period of the fast pathway and a lack of continuous SP conduction. Similar PR/RR ratio (below 1) were calculated following the isoproterenol challenge after SP ablation. At baseline and after isoproterenol challenge PR/RR ratio was > 1, but after ablation of SP region PR/RR < 1 were recorded in these cases (a 36-year-old mother and her 14-year-old daughter) during the same-day procedure for the familial form of slow-fast AVNRT.

Table 2
General characteristics.

	AVNRT (n = 228)	Control (n = 170)	P value
Age (year)	39.9 ± 20.7	37.6 ± 22.4	NS
Women (%)	67.0	43.0	$p < 0.05$
Children (%)	26.0	26.0	NS
Structural heart disease (%)	4.6	9.6	$p < 0.05$
Diabetes (%)	10.0	12.9	NS
Hypertension (%)	24.5	24.7	NS
Smoking (%)	10.5	11.7	NS

Abbreviations: AVNRT – atrioventricular nodal reentrant tachycardia; NS – non-significant.

were no severe cardiovascular complications associated with the procedures.

3.2. Sustained slow pathway conduction before and after ablation

Induction of slow-fast AVNRT prior to ablation was documented in 210 cases in the AVNRT group. There were 168 patients with induction of slow-fast AVNRT with a "jump" and 42 patients with slow-fast AVNRT induction without a jump. Induction of fast-slow AVNRT with a jump was documented in only 4 cases (and simultaneously with slow-fast AVNRT in 2 cases). In one patient two types of AVNRT were induced: slow-slow AVNRT and typical slow-fast AVNRT.

Despite the administration of several boluses of isoproterenol and finally 1 mg of atropine, 12 patients showed no induction of AVNRT but showed dual atrioventricular physiology (standard or combined jump). These patients had documented paroxysmal regular narrow QRS tachycardia with typical ECG of AVNRT. In 2 cases, there was no reproducible induction of AVNRT nor a jump, but the baseline PR/RR ratio was > 1. In these 2 cases SSPC was the only indicator and endpoint for ablation.

In the AVNRT and control groups, the mean maximum PR/RR ratios at baseline were 1.17 ± 0.24 (median: 1.19; min-max: 0.50–1.74; 1 st and 3rd quartiles: 1.05 and 1.33) and 0.82 ± 0.13 (median: 0.83; min-max: 0.37–1.2; 1 st and 3rd quartiles: 0.75 and 0.91, $p < 0.00001$), respectively. At baseline, a PR/RR ratio ≥1 (at least one PR interval longer than the RR interval) during IAP from PCS was documented in 76.3% of the patients with AVNRT and in only 2.3% of patients from the control group ($p < 0.0001$). Moreover, isoproterenol challenge increased the incidence of PR/RR ratios ≥1 from 76.3% to 87.7% ($p < 0.01$) in the AVNRT group. In contrast, isoproterenol infusion did not significantly increase the value in the control group (2.3%–4.1%, p = NS).

At baseline, a standard jump after S2 and combined jump after S2, S3, or S4 was documented in 112/228 (49%) and 170/228 (74.5%, $p < 0.05$) AVNRT patients. After isoproterenol infusion, a standard jump and combined jump was documented in 7 more cases and 12 more cases of AVNRT (after S2: 52% (119/228), $P > 0.05$, and after S2, S3 and/or S4: 79.8% (182/228), $P < 0.05$, respectively). The absence of PR/RR ≥ 1 during IAP at baseline and after isoproterenol challenge prior to ablation was found in 12.3% (28/228) of the AVNRT group and 95.9% (163/170) of the control group ($p < 0.0001$). Standard and combined jumps were observed in 8.8% (16/170) and 8.8% (20/170) of

Table 3
Diagnostic performance of various parameters of atrioventricular conduction during PCS pacing in patients with AVNRT and controls.

	AVNRT $n = 228$		Control $n = 170$		Sensitivity	Specificity	PPV	NPV
	+	−	+	−				
Baseline standard „jump"	112	116	15	155	49% (CI: 42–56)	91% (CI:86–95)	88 % (CI: 82–92)	57% (CI:54–60)
Baseline combine „jump"	170	58	20	150	75% (CI:68–80)	88% (CI:82–93)	89% (CI:85–93)	72% (CI:67–76)
Baseline PR/RR ≥ 1	174	54	4	166	76% (CI:70–82)	98% (CI: 94–99)	98% (CI:94–99)	75% (CI: 71–80)
Isoproterenol challenge standard „jump"	119	107	22	148	53% (CI:46–59)	87% (CI:81–92)	84% (CI:78–89)	58% (CI:54–62)
Isoproterenol combine „jump"	182	46	25	145	80% (CI:74–85)	85% (CI:79–90)	88% (CI:83–91)	76% (CI:71–80)
Isoproterenol PR/RR ≥ 1	200	28	7	163	88% (CI:83–92)	96% (CI:92–98)	97% (CI:93–98)	85% (CI:85–89)

Abbreviations: AVNRT – atrioventricular nodal reentrant tachycardia; PPV – positive predictive values; NPV – negative predictive values; CI – confi-dence interval; PR/RR – PR interval to RR interval ratio: from the atrial stimulus to earliest R wave on ECG during incremental atrial pacing.

the control group. After isoproterenol challenge, these numbers increased to 12.9% (22/170) and 14.7% (25/170). Among the 46 AVNRT patients with no combined jump at baseline and after isoproterenol challenge, a standard jump and combined jump were present in 26.1% (12/46) and 36.9% (17/46) after ablation, respectively.

The diagnostic performance of PR/RR ratio evaluation prior or after isoproterenol challenge had the highest diagnostic performance for AVNRT with PR/RR > = 1 (sensitivity: 88%, specificity: 96%, PPV (positive predictive value): 97%, NPV (negative predictive value): 85% (Table 3). The following mechanisms were documented for the absence of PR/RR ≥ 1 during IAP: 1) an effective anterograde refractory period of both pathways and the atrioventricular node during IAP before PR becomes greater than the RR interval (n = 17); 2) a reproductive single retrograde junctional echo beat (n = 6) during IAP and permanent induction of sustained AVNRT during IAP (n = 4); and 3) repetitive atrial fibrillation induction during IAP (n = 1). Permanent reproducible induction of orthodromic atrioventricular reentrant tachycardia (OAVRT) was documented in one case of double tachycardia (coincident with OAVRT and typical slow-fast AVNRT) during IAP, which prevented us from evaluating PR/RR. PR/RR > 1 was observed only after left-sided concealed accessory pathway ablation, but a reproducible jump and induction of typical slow-fast AVNRT were achieved only after isoproterenol infusion.

The mean maximum PR/RR ratio decreased significantly to 0.76 ± 0.14 after slow pathway ablation and to 0.74 ± 0.14 after modification (p = NS between groups, and P < 0.00001 as compared to the maximum value prior to ablation). The absence of a PR/RR ratio ≥1 was documented in 99.6% of cases of AVNRT after slow pathway ablation or modification with and without isoproterenol infusion. In contrast, slow pathway ablation (no jump during programmed atrial stimulation with up to 3 extra stimuli and isoproterenol infusion) was documented less frequently (61% (140/228) cases, p < 0.001 as compared to the absence of PR/RR ≥ 1).

In the subgroup of children (AVNRT: n = 60, age: 14.0 ± 3.0, 58% girls; controls: n = 58, age: 14.3 ± 3.1, P = NS, 39% girls, p = NS, 96% OAVRT), the mean maximum PR/RR ratios prior to ablation were 1.14 ± 0.25 in the AVNRT group vs. 0.80 ± 0.12 in the control group (P < 0.0001). In the AVNRT group, PR/RR ≥ 1 was present in 80.0% before ablation (48/60, in 6 cases after isoproterenol) and in 1.6% (1/60) after ablation. In the control group, there were no cases of PR/RR ratio ≥1.

In symptomatic patients, recurrences of AVNRT were referred for additional procedures (n = 6). During the second procedure, recurrences of PR/RR ≥ 1 were revealed despite the confirmation of its absence during the observation period with IAP and isoproterenol challenge after the first ablation. Among the entire study group, only 2 patients had a reproducible PR/RR ≥ 1 without a jump and AVNRT induction. In these cases, the first and third applications of thermal mapping with junctional beats induced sustained typical AVNRTs. Therefore, PR/RR ratio validation was determined as an end-point for slow pathway ablation in these cases. In our current practice, PR/RR ≥ 1 during IAP from the PCS with or without isoproterenol infusion in patients with documented narrow QRS tachycardia (and no other mechanisms of tachycardia) has become an additional indicator for SP ablation, despite the lack of a typical jump or inducibility of AVNRT during EPS.

4. Discussion

The results showed that PR/RR ≥ 1 during IAP from the PCS is associated with the presence of anterograde SSPC and predicts the inducibility of AVNRT in both children and adults. The use of this simplified approach for validating SSPC may have important implications for fast and easy testing before and after the ablation of AVNRT. PR/RR ratio ≥1 during IAP from PCS may be an additional indication or a pure single end-point for successful slow pathway ablation, even in patients with non-inducible AVNRT, without dual atrioventricular physiology, and after isoproterenol infusion. Moreover, it may predict recurrences of AVNRT, despite non-inducibility of arrhythmia.

We have reported that PR > RR during IAP represents continuous conduction via the slow pathway.

There were not attempts for fast pathway ablation therefore the conclusion on impact of fast pathway ablation on PR/RR can not be provided.

Despite being a common focus of many studies, the diagnosis of AVNRT and the electrophysiological properties of the AVNRT substrate remain challenging and not completely clear. The rate of typical jump after S2 in patients with AVNRT is reported to be 60 to 80% and is less common in younger patients. On the other hand, in some pediatric populations without AVNRT, the incidence of the classic definition of jump after S2 (an increase of 40–50 ms within S2) is reported to be 20–40% [4–9]. Moreover, ECGs recorded in an episode of narrow QRS tachycardia in pediatric patients are unreliable for differential diagnosis, which makes the diagnosis in this group much more challenging [14].

Autonomic tone balance, hormonal imbalance, and sedation may play important roles in the inducibility of AVNRT and the characteristics of slow pathway conduction [3–5]. Sometimes, only thermal mapping of the slow pathway region or atypical maneuvers may induce sustained AVNRT and a reproducible, confirmed diagnosis after additional maneuvers or mapping techniques [11,12,14,15]. In our study, the incidence of standard jumps was about 50%, which increased significantly when S3 and S4 were accepted with aggressive pacing protocols and isoproterenol challenge.

The PR/RR ratio evaluation has been incorporated into the electrophysiological diagnosis of AVNRT and guidelines for ablation [4–9]. In patients with and without jumps, the PR/RR ratio may be used as a simple method to evaluate the effects of radiofrequency energy after applications to the slow pathway. In patients without a typical jump and non-inducibility of AVNRT, the PR/RR ratio may be the only reliable method for determining the presence of the slow pathway. Moreover, some data suggest that non-inducibility of AVNRT after ablation

with a remaining PR/RR ratio ≥1 may be associated with the risk of AVNRT recurrence. From a practical point of view, evaluating the SSPC should have priority when performing an atrial pacing protocol before and after SVT ablation and with the administration of isoproterenol [4–9].

Previous techniques for PR/RR ratio measurements required HRA pacing and several QRS complexes with a continuous occurrence of PR > RR. However, our simplified approach (Table 2) enables easy detection of PR/RR ratios ≥1 using just a single pacing spike in front of the QRS complex during IAP from the PCS. Therefore, in a majority of cases, observations did not even require off-line or review screen measurements, and they were visible to operators when watching IAP continuously on-line on a screen (Fig. 1–3). On contrary, the study of Baker was performed in selected, small group of patients and was done in time-consuming protocol [6]. Our study validate new site of pacing and easier method of identification of PR > RR in a large group of patients.

Several inputs of AVN (especially in children) may share the same electrophysiological properties during incremental atrial pacing as slow pathway. Therefore, evaluation of PR/RR ≥ 1 should be combined with other diagnostic maneuvers.

This technique may be very attractive for the growing number of cryoablation cases and non-inducible cases often reported in pediatric populations [2,16,17]. The catheter tip adheres to the endocardium during cryomapping and cryoablation, which prevents catheter dislodgement. Moreover, junctional rhythms are not common during cryoablation, so the effectiveness of cryoablation cannot be evaluated easily. Cryoablation is associated with definitive prolongation of the procedure and higher rates of recurrence [2,16,17]. Therefore, IAP from the PCS and evaluation of the PR/RR ratio (even after isoproterenol infusion with a stable frozen catheter position) may be used as a direct method for evaluating SSPC during 4–6 min of a single cryoapplication. The time to change the PR/RR ratio during the first minute of cryoablation may indicate an important target for additional cryoapplication, but a prospective evaluation of this approach is needed.

Previous studies used complicated approaches for PR/RR ratio evaluation. Up to 4 catheters were used, only high right atrium pacing was performed, the IAP protocol was time-consuming, and a limited number of controls were evaluated in the selected AVNRT patient groups. Moreover, there has been no standard evaluation of isoproterenol (Table 2). Our approach clearly simplifies the procedure and makes it fast and easily reproducible for a variety patient populations and approaches (children, two-catheter approach, non-fluoroscopic approach) (5–9). Moreover, PR/RR ≥ 1 was also observed before slow pathway ablation but not longer after in all patients with a familial form of AVNRT. Therefore, there may be an association with the genetic substrate for this arrhythmia [18].

4.1. Limitations

One of the limitations of this study is that groups were not matched for several clinical factors that may influence the results. Typically, only narrow QRS tachycardia should be compared, but such cases were represented with the highest numbers, and the results were consistent among subgroups (children and induced SVT). No prospective evaluation of the PR/RR ratio was performed after each application, so successful and unsuccessful application sites cannot be compared.

Recurrences of PR/RR > = 1 during observation period often proceeded recurrences of inducibility of AVNRT and need for additional application. However, those observations were not consistently evaluated and they are insufficient for predicting further recurrences. Recurrences of PR/RR > = 1 were not evaluated invasively in late follow-up in asymptomatic patients.

Moreover, our approach and the PR/RR interval measurement during IAP were not directly compared with HRA pacing and a multicatheter approach. Despite the inducibility of a typical jump or AVNRT at baseline, not all patients were given isoproterenol. Therefore, the direct impact of isoproterenol on the PR/RR ratio in all AVNRT cases prior to ablation was not evaluated. Current pediatric guidelines reported that eliminating SSPC (PR/RR > 1) using radiofrequency ablation or cryoablation when it is initially present also appears to reduce recurrences and is an acceptable endpoint [4,19,20].

5. Conclusions

This study demonstrated the following: (1) a standard jump was present less frequently at baseline and after isoproterenol challenge than PR/RR ratio ≥1 during IAP; (2) isoproterenol infusion significantly increased the incidence of PR/RR ratio ≥1 during IAP; (3) successful catheter ablation was more frequently associated with the elimination of PR/RR ≥ 1 during IAP with and without isoproterenol challenge than elimination of DAVN; and (4) the presence and recurrence of PR/RR ≥ 1 during IAP within the same procedure or further procedures indicate a residual substrate for tachycardia, despite an inability to induce tachycardia. A PR/RR ratio ≥1 during IAP from PCS, even without a jump and AVNRT induction, may serve as an indicator and end-point of ablation in selected patients with documented narrow QRS tachycardia and the exclusion other substrates. Finally, the absence of SSPC with PR < RR within IAP from the PCS in AVNRT patients may have appeared due to the reproduction echo beats, permanent AVNRT inducibility, or the refractory period of atrioventricular node.

Conflict of interest and Financial Statement

Sl. J. author and patent holder of diagnostic and ablation catheter (CATHAIO Mini Max). L.M. project partially supported by Wroclaw Centre of Biotechnology programme The Leading National Research Centre (KNOW) for years 2014–2018. S.S. receives consulting fees from and is a stock holder of Medinice S.A. Poland and Medinice B + R. He also holds patents for a pace-press, cryoapplicator, ablation and diagnostic catheters, and a navigation system. D.K. curently conducting research sponsored by the budget resourceson science in years 2016–2018 as a study project of program “Diamentowy Grant”.

There are no other potential conflicts of interest related to this article.

References

[1] Blomstrom-Lundqvist C, Scheinman MM, Aliot EM, Alpert JS, Calkins H, Camm AJ, et al. ACC/AHA/ESC guidelines for the management of patients with supraventricular arrhythmias—executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients with Supraventricular Arrhythmias). Circulation 2003;108:1871–909.

[2] Brugada J, Blom N, Sarquella-Brugada G, Blomstrom-Lundqvist C, Deanfield J, Janousek J, et al. European Heart Rhythm Association; Association for European Paediatric and Congenital Cardiology. Pharmacological and non-pharmacological therapy for arrhythmias in the pediatric population: EHRA and AEPC-Arrhythmia Working Group joint consensus statement. Europace 2013;15:1337–82. http://dx.doi.org/10.1093/europace/eut082.

[3] Page RL, Joglar JA, Caldwell MA, Calkins H, Conti JB, Deal BJ, et al. ACC/AHA/HRS guideline for the management of adult patients with supraventricular tachycardia: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Heart Rhythm 2015;13:e136–221. 2016.

[4] Philip Saul J, Kanter RJ, Abrams D, Asirvatham S, Bar-Cohen Y, Blaufox AD, et al. PACES/HRS expert consensus statement on the use of catheter ablation in children and patients with congenital heart disease: developed in partnership with the Pediatric and Congenital Electrophysiology Society (PACES) and the Heart Rhythm Society (HRS). Endorsed by the governing bodies of PACES, HRS, the American Academy of Pediatrics (AAP), the American Heart Association (AHA), and the Association for European Pediatric and Congenital Cardiology (AEPC). Heart Rhythm 2016;13(June (6)):e251–89.

[5] Li HG, Klein GJ, Stites HW, Zardini M, Morillo CA, Thakur RK, et al. Elimination of slow pathway conduction: an accurate indicator of clinical success after

radiofrequency atrioventricular node modification. J Am Coll Cardiol 1993;22. 18499:1849.
[6] Baker JH, Plumb VJ, Epstein AE, Kay GN. PR/RR interval ratio during rapid atrial pacing: a simple method for confirming the presence of slow AV nodal pathway conduction. J Cardiovasc Electrophysiol 1996;7. 287ol 19.
[7] Martínez-Sánchez J, García-Alberola A, Sánchez-Muñoz JJ, Cerdán-Sánchez C, Redondo-Bermejo B, Ruipérez-Abizanda JA, et al. Usefulness of incremental atrial pacing for evaluating the effectiveness of the ablation of the slow perinodal pathway. Rev Esp Cardiol 2007;60:32–7.
[8] Blurton DJ, Dubin AM, Chiesa NA, Van Hare GF, Collins KK. Characterizing dual atrioventricular nodal physiology in pediatric patients with atrioventricular nodal reentrant tachycardia. J Cardiovasc Electrophysiol 2006;17:638–44.
[9] Kannankeril PJ, Fish FA. Sustained slow pathway conduction: superior to dual atrioventricular node physiology in young patients with atrioventricular nodal reentry tachycardia? PACE 2006;29:159–63.
[10] Stec S, Sledz J, Mazij M, Ludwik B, Labus M, Spikowski J, et al. Simplified automated right ventricular overdrive pacing for rapid diagnosis of supraventricular tachycardia. Cardiology 2014;129:93–102.
[11] Stec S, Sledz J, Mazij M, Ras M, Ludwik B, Chrabaszcz M, et al. Feasibility of implementation of a simplified, no-X-ray, no-lead apron, two-catheter approach for ablation of supraventricular arrhythmias in children and adults. J Cardiovasc Electrophysiol 2014;25:866–74.
[12] Femen F, Arce M, Arrieta M, Palazzolo J, Trucco E. Long-term results of slow pathway ablation in patients with atrioventricular nodal reentrant tachycardia: simple approach. J Electrocardiol 2012;45:203–8.
[13] Katritsis DG, Josephson ME. Classification of electrophysiological types of atrioventricular nodal re-entrant tachycardia: a reappraisal. Europace 2013;15:1231–40.
[14] Deutsch K, Stec S, Kukla P, Morka A, Jastrzebski M, Baszko A, et al. Validation of standard and new criteria for the differential diagnosis of narrow QRS tachycardia in children and adolescents. Medicine 2015;94(December):e2310.
[15] Yamini Sharif A, Vasheghani Farahani A, Davoodi GR, Kazemisaeid A, Fakhrzadeh H, Ghazanchai F. A new method for induction of atrioventricular nodal reentrant tachycardia in non-inducible cases. Europace 2011;13:1789–92.
[16] Gil-Ortega I, Pedrote-Martinez A, Fontenla-Cerezuela A. Spanish catheter ablation registry collaborators Spanish catheter ablation registry. 14th official report of the Spanish society of cardiology working group on electrophysiology and arrhythmias (2014). Rev Esp Cardiol (Engl Ed) 2015;68:1127–33.
[17] Hanninen M, Yeung-Lai-Wah N, Massel D, Gula LJ, Skanes AC, Yee R, et al. Cryoablation versus RF ablation for AVNRT: A meta-analysis and systematic review. J Cardiovasc Electrophysiol 2013;24:1354–60.
[18] Stec S, Deutsch K, Zienciuk-Krajka A. The world's largest family with familial atrioventricular nodal reentry tachycardia. Kardiol Pol 2015;73(12):1339. http://dx.doi.org/10.5603/KP.2015.0249.
[19] Eckhardt LL, Leal M, Hollis Z, Tanega J, Alberte C. Cryoablation for AVNRT: importance of ablation endpoint criteria. J Cardiovasc Electrophysiol 2012;23:729–34.
[20] Sandilands A, Boreham P, Pitts-Crick J, Cripps T. Impact of cryoablation catheter size on success rates in the treatment of atrioventricular nodal re-entry tachycardia in 160 patients with long-term follow-up. Europace 2008;10:683–6.