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A prospective evaluation of the impact of individual RF applications for slow pathway ablation for AVNRT: markers of acute success

Short running title: Junctional response during AVNRT ablation

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"The data that support the findings of this study are available from the corresponding author upon reasonable request"

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Abstract

Background:

Catheter ablation is highly effective for AVNRT. Generally junctional rhythm(JR) is an accepted requirement for successful ablation however there is a lack of detailed prospective studies to determine the characteristics of JR and the impact on slow pathway conduction.

Methods:

Multicentre prospective observational study evaluating the impact of individual radiofrequency(RF) applications in typical AVNRT(Slow/Fast). Characteristics of JR during ablation were documented and detailed testing was performed after every RF application to determine outcome. Procedural success was defined as ≤1 AV nodal echo.

Results:

Sixty-seven patients were included(mean age 53±18years, 57% female and a history of SVT 2.9±4.7years). RF(50w,60degrees) ablation for AVNRT was applied in 301 locations with JR in 178(59%). Successful slow pathway modification was achieved in 66(99%) patients with slow pathway block in 30(46%). Success was associated with JR in all patients. Success was achieved in 6 patients with RF<10 seconds. There was no significant difference in the CL of JR during RF between effective(587±150ms) vs ineffective (611±193ms,p=0.4) applications. Inadvertent JA block with immediate termination of RF was observed in 19(28%) patients with AVNRT no longer inducible in 14(74%). Freedom from SVT was achieved in 66(99%) patients at a mean follow up of 15±6 months.

Conclusion:

In this prospective study, JR was required during RF for acute success in AVNRT. Cycle length of JR during RF was not predictive of success. Although unintended JA block during faster JR was associated with slow pathway block, this is a precursor to fast pathway block and should not be intentionally targeted.

Keywords: SVT, Ablation, Junctional response, cycle length, duration, success, outcomes

INTRODUCTION:

Atrioventricular nodal re-entrant tachycardia (AVNRT) is the most common cause of supraventricular tachycardia (SVT)[1-6]. Slow pathway ablation is the first line treatment for recurrent symptomatic AVNRT with high long term success[2,3,5,7-15], however heart block requiring pacemaker implant can occur in up to 1%[16-18]

AVNRT is the archetypal re-entrant tachycardia utilizing functionally distinct but anatomically variable inputs within a transitional zone of junctional tissue within the triangle of Koch termed the slow and fast pathways[5,19-23]. Initial ablation strategies targeted the fast pathway with an unacceptable incidence of AV block[24]. In recent times the slow pathway has been established as the target for ablation with junctional rhythm generally required to achieve acute success[7]. Although there is general consensus regarding the need for junctional rhythm during RF, retrospective studies reporting the characteristics of junctional rhythm during RF required for successful slow pathway modification have been inconclusive [25-27].

The purpose of the present study was to prospectively evaluate the effect of each and every radiofrequency (RF) application in the region of the slow pathway to determine if junctional rhythm can predict procedural and long-term success.

METHODS

Study population

This prospective observational study was conducted at The Alfred, The Royal Melbourne, The Melbourne Private and Cabrini Hospitals in Melbourne, Australia between November 2017 and October 2019. Consecutive patients with documented SVT undergoing electrophysiological study (EPS) with a view to ablation were invited to participate. The participants were included in the study if typical AVNRT was inducible and sustained on at least 2 occasions. AVNRT was diagnosed based on established criteria during detailed EPS using atrial and ventricular pacing manoeuvres[23,28-30]. Patients with other forms of SVT or if non-inducible were excluded from the study. The study was approved by institutions ethics review committees. All participants provided written informed consent to be in included in the study.

EP procedure

Antiarrhythmic medications were discontinued approximately 5 half-lives prior to the procedure. An EPS was performed as previously described[31]. In general, the procedure was performed under sedation with ultrasound guided femoral venous access for the deflectable decapolar CS, quadripolar His and the ablation catheters. A retrograde study with single ventricular extra stimulus testing was performed first followed by the antegrade study with a single atrial extra stimulus. A reproducible increase in the last atrial extra stimuli -His (A_1A_2/A_2H_2) interval of 50 milliseconds or greater in response to a decrease in the last A-A coupling interval of 10 milliseconds was defined as dual AV nodal conduction or an AH 'jump'. Next, atrial then

ventricular pacing to Wenckebach AV nodal conduction was performed. At that stage if AVNRT was non inducible then sensed double and/or triple atrial extra stimuli in 10msec increments was completed. Testing continued until AVNRT was sustained. If sustained tachycardia could not be induced, intravenous isoproterenol (1, 2 or 4mcg/minute) was administered and the pacing manoeuvres repeated. AVNRT was diagnosed using established criteria[29,32,33]

Ablation was performed in sinus rhythm. A non-irrigated 4mm deflectable solid tip ablation catheter was used with a long vascular sheath to facilitate stability. The region of slow pathway was identified using a combination of anatomic and electrogram characteristics under fluoroscopic guidance[7,31,34-36] with 3 dimensional mapping when available (Figure 1). The target sites typically had a multi component atrial electrogram with an AV ratio of < 0.5. Ablation was performed with a maximum power of 50W and temperature limit set to 60 degrees Celsius. Ablation generally commenced at the posterior septal tricuspid annulus (TA) immediately adjacent to the inferior margin of the ostium of the coronary sinus in the region of the triangle of Koch. Subsequent RF applications progressed superiorly if initial ablation attempts did not result in junctional acceleration. JR was defined as a QRS complex identical to that of the sinus beat without evidence of atrioventricular (AV) conduction. RF was discontinued after 30 seconds if no junctional rhythm occurred. RF was also discontinued immediately if any degree of AV or (Junctional beat-atrial) JA block occurred or in the presence of rapid junctional rhythm (<350ms). Every ablation was included in the analysis if there were any JR during ablation or a lesion duration of ≥5 seconds regardless of the presence of JR. After each RF application, the EP manoeuvres responsible for inducing AVNRT were repeated. Further testing was repeated on isoproterenol if AVNRT was non inducible. Acute procedural

success was defined by (1) complete loss of slow pathway conduction or (2) by the presence of no more than a single AV nodal echo beat (slow pathway modification). Isoproterenol was administered after every ablation if it had been required for arrhythmia induction prior to ablation or persistent AV nodal echo beats were present after ablation. Following successful RF application, EP testing was repeated on isoproterenol in all patients throughout a mandatory 20-minute waiting period. If there was recurrence of inducible tachycardia or more than one echo beat during the waiting period, additional ablation was performed as per the protocol.

For each RF application: ablation duration, cycle length of JR, the presence of AV and VA conduction during JR and any change in AV conduction following ablation were recorded.

Antiarrhythmic therapy was not recommenced after the ablation procedure. Patients were followed up prospectively for a minimum of 6 months. Recurrence was defined as documented AVNRT lasting >30seconds occurring at any time after the ablation procedure. Clinical symptoms of palpitations were investigated with a Holter monitor in addition to serial ECG's and provision of an Alivecor monitor.

Statistical analysis

For normally distributed continuous parametric variables Student's t-test was used and expressed as mean ± standard deviation (SD). Kruskal-Wallis test was used when normal distribution was not present. Fisher exact test or the $\chi 2$ test was used for categorical variables and expressed as number and percentage. Paired Student's *t*-test was used to compare means from baseline to follow-up. A p-value of <0.05 was considered statistically significant. Continuous variables of baseline demographics are

expressed as mean ± SD. Results are expressed as mean ± SD. Categorical variables were expressed as number and proportion. Analysis was performed using SPSS version 24 (IBM SPSS statistics, IBM corporation, Armonk, New York).

RESULTS

One-hundred and fifty-three patients underwent EPS for clinically suspected or documented SVT. Eighty-six patients were excluded due to: protocol non-adherence in 32 (20.9%), atrial tachycardia or orthodromic reciprocating tachycardia in 30 (19.6%) and non-inducibility in 24 (15.7%). A total of 67 patients with a mean age of 53.3 ± 17.6 years, 57% women with an average body mass index (BMI) of 26.7 ± 6.3 kg/m^2 were included in the study. Paroxysmal SVT was present for 2.9 ± 4.7 years requiring 2.3 ± 2.2 emergency department presentations prior to catheter ablation.

Electrophysiological characteristics

At EPS, the average presenting sinus rhythm cycle length was 857 ± 207 milliseconds (ms) with a baseline A-H interval of 86.6 ± 20.4ms and a H-V interval of 42.7 ± 7.4ms. At baseline, retrograde VA conduction was present at a pacing cycle length of 600ms in 60 (89.6%) patients. The remaining 7 (10.4%) demonstrated VA conduction with use of isoproterenol. Overall, 10 (14.9%) patients required isoproterenol for AVNRT induction. Antegrade refractory period testing demonstrated an AH 'jump' of >50ms in 42 (62.7%) patients with a median 'jump' of 90ms (range 50-175ms). Among the 42 patients with a typical 'AH jump', slow pathway effective refractory period (ERP) was identifiable in 33 (78.5%) of patients with a mean of 284.8 ± 50.3ms and fast pathway ERP of 353.6 ± 70.6ms. AV nodal Wenckebach was at 373 ± 75ms. AVNRT was inducible in all patients with a combination of atrial pacing manoeuvres including single atrial extras, sensed atrial doubles and triple extra stimuli. The mean AVNRT cycle length was 370 ± 64ms with a septal VA timing of

25.7 ± 23.2ms.

Catheter Ablation characteristics

A total of 301 RF applications were delivered (mean 4.5 ± 4.5 lesions per patient) with an average RF duration of 28.2 ± 18.8 seconds per lesion. Junctional rhythm was observed during 178 (59.1%) RF applications. Effective RF application resulting in slow pathway modification or elimination occurred after 66 (37%) RF applications with JR in all. Slow pathway modification was not achieved by any RF application which did not result in JR (Table 1). One (1.5%) patient with readily inducible AVNRT had 2 echo beats after 15 RF applications for a total of 7.95 minutes RF. No further RF was applied as AVNRT was no longer sustained and the catheter position was in close proximity to the compact AV node.

Effective RF applications were significantly longer in duration (38.5 ± 25.6 vs ineffective: 26.9 ± 18.4seconds, p = 0.002, Table 1, Figure 2) and ranged from 5 to 60 seconds. Successful slow pathway ablation was achieved in 6 patients with RF applications less than 10 seconds. The fastest (406 ± 152ms vs 438 ± 179ms, p=0.2), median (587 ± 150ms vs 611 ± 193ms p=0.4) cycle length of the junctional rhythm and proportion of junctional rhythm (43.2 ± 28.4% vs 36.3 ± 23.7% p=0.1, Figure 2) observed during RF application was not significantly different between effective and ineffective lesions. Complete loss of slow pathway conduction after catheter ablation occurred in 30 (45.5%) patients. The median cycle length of JR was significantly faster during RF applications that resulted in complete loss of slow pathway (546 ± 128ms) compared with slow PW modification and those that did not affect slow pathway conduction (613 ± 185ms, p=0.02).

Cycle length of the junctional rhythm observed during RF application was compared between effective and ineffective lesion for individual patient. First RF application

with junctional response was effective in 28 (42%) patients with a median cycle length of 604 ± 180ms. Among the 38 (57.6%) patients who had >1 RF, 2.7 ± 2.6 ineffective lesions with junctional response was performed prior to the successful lesion.

Transient AV block occurred in 1 (1.5%) which resolved within 60 seconds of cessation of RFA. There were no cases of persistent AV block or of any patients with a >10msec increment in the AH interval. JA block was observed during faster JR in 19 (28%) patients during RF application. RF application was terminated immediately if JA block was seen with no prolongation of the AH interval in the next conducted beat (Figure 3). Fourteen of 19(73.7%) RF applications associated with JA block were successful with AVNRT no longer inducible including complete loss of slow pathway conduction in 10 (52.6%). See Table 1.

Following successful RF application, difference in AV nodal Wenckebach threshold was not statistically significant (373 ± 75ms pre to 365 ± 99ms post RF (p=0.8). Fast pathway ERP shortened from 347 ± 64 to 319 ± 84ms, p = 0.003.

The average procedure duration was 78.0 ± 35.5 minutes with an average fluoroscopy time of 8.4 ± 5.6minutes. There were no acute complications. At a median follow up of 1.4 ± 0.7 years, 66 (98.5%) had no further documented SVT. One (1.5%) patient presented with an early recurrence after an initial procedure which had achieved the acute endpoint after an RF time of 45 seconds with a cycle length of junctional rhythm during RF as short as 350ms. A second procedure demonstrated inducible AVNRT with RF resulting in adequate modification of slow pathway conduction with no further recurrence.

We performed a logistic regression on the 178 (59%) lesions with junctional response during ablation. Procedural endpoint of non-inducibility with or without single echo beat was used as the binary outcome with the following predictors included in the model: (1) Median cycle length of junctional rhythm (ms), (2) Radiofrequency (RF) duration, (3) Proportional of junctional rhythm during ablation and (4) presence of JA block during ablation. RF duration (p=0.0002, odds ratio 1.03) and JA block (p=0.0009, odds ratio 7.0) were predictive of successful procedural endpoint.

DISCUSSION:

Typical AVNRT is the most common cause for SVT and slow pathway ablation provides long term cure in > 95% of patients. To date there is a paucity of prospective studies evaluating the acute impact of catheter ablation in the region of the slow pathway on inducibility of AVNRT. Prior retrospective studies exploring the characteristics of JR have reported variable outcomes on slow pathway conduction[26,37,38]. In the present study we prospectively evaluated the impact of each individual radiofrequency application on slow pathway conduction. The main findings were:

1. Junctional rhythm was required during RFA for successful slow pathway ablation in all;
2. The median cycle length of junctional rhythm was similar during effective and ineffective RF applications (587 ± 150 vs 611 ± 193 p = 0.4);
3. *Unintended* Junctional atrial (JA) block during faster junctional rhythm was associated with a high likelihood of successful slow pathway modification and;

4. RF applications as short as 5-10 seconds can result in successful modification of the slow pathway.

Slow pathway ablation

Catheter ablation for AVNRT targets discrete slow pathway potentials at the mid to posterior septum adjacent to the tricuspid annulus[7,29]. The established procedural endpoint is slow pathway block or modification with a single AV nodal echo beat[39]. To date there have been few prospective studies evaluating the characteristics of RF applications required to achieve slow pathway modification or block. Retrospective studies have not identified a clear relationship between the characteristics of JR and success although have been limited by a smaller sample size than the present study and an absence of rigorous testing after each ablation [25-27] reported no relationship between the cycle length of JR and outcome. Hence the current approach is a variable duration of RF determined by the electrophysiologist generally aiming for junctional rhythm without causing AV block and periodic subjective testing to determine if acute success has been obtained. The duration of RF required is highly variable as demonstrated in the present study where RF applications as short as 5-10 seconds resulting in junctional rhythm were successful in some patients. Junctional rhythm during RF in the region of the slow pathway has long been accepted as a requirement for successful ablation for AVNRT[7,13,26,40]. The mechanism responsible for junctional automaticity during RF application is direct heating of the nodal – type cells within the transitional zone which accelerates phase 4 depolarisation and shortens the action potential duration[41]. The fast and slow pathways are anatomically and functionally distinct. The Slow pathway runs as the posterior / inferior extension from the AV node to the bundle of HIS with the fast pathway more superior/anterior. Functional

differences in the direction of impulse propagation have been demonstrated in animal models[42].

The presence of JA block during faster junctional rhythm was associated with slow pathway block or modification in 74% in the present study. As per the study protocol the occurrence of JA block during RF led to the immediate termination of RF delivery and prompt repeat testing for AVNRT. Observation of JA block during ablation should be considered as a precursor to fast pathway block. JA block was NOT targeted by the operators but an unintended occurrence during faster junctional rhythm.

Long term success of slow pathway ablation

Feldman et al reported high long-term success with slow pathway ablation in 1419 patients with AVNRT[31]. Independent predictors of AVNRT recurrence were age < 20 years and female gender. No significant difference in the incidence of late recurrence was observed in presence or absence of residual slow pathway conduction, use of isoproterenol testing or general anaesthesia[31]. Katritis et al reported non inducibility despite isoproterenol challenge as the most reliable predictor of clinical success in a retrospective analysis of 1007 patients who underwent RFA for AVNRT[8]. The presence of junctional rhythm during ablation was highly sensitive but not specific for procedural success nor was the presence of residual slow pathway conduction. Jentzer et al reported the individual response to RFA [26] in 52 patients with AVNRT. RF was delivered for 20-40seconds prior to testing and terminated if JA block occurred. In keeping with the present study, procedural success was associated with a longer duration of junctional beats and total number of junctional beats but not the cycle

length of JR. EP testing was only performed if RF was delivered for ≥ 20 seconds and included some cases retrospectively.

STUDY LIMITATIONS:

This was a prospective observational study and is subject to the inherent limitations of the study design. A larger sample size may have identified smaller differences in the characteristics of effective vs ineffective RF applications.

CONCLUSION:

In this prospective study evaluating the impact of each RF application for slow pathway ablation for AVNRT junctional rhythm was required in all for acute success. Cycle length of JR during RF was not predictive of success. Although unintended JA block during faster JR was associated with slow pathway block, this is a precursor to fast pathway block and should not be intentionally targeted.

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Figures

Figure 1: Fluoroscopic and 3-D images of catheter position at start of AVNRT ablation in RAO and LAO projections. RAO = Right Anterior Oblique, LAO = Left Anterior Oblique, RAA = Right Atrial Appendage, ABL = Ablation catheter, CS = Coronary sinus catheter, HIS = His catheter, SVC = Superior Vena Cava and IVC = Inferior Vena Cava. Images A & B: relative catheter orientation and position in the RAO 30-degree projection on fluoroscopy and 3-D mapping. C&D: relative catheter orientation and position in the LAO 30-degree projection respectively. C: relative catheter orientation and position on fluoroscopy and 3-D mapping respectively.

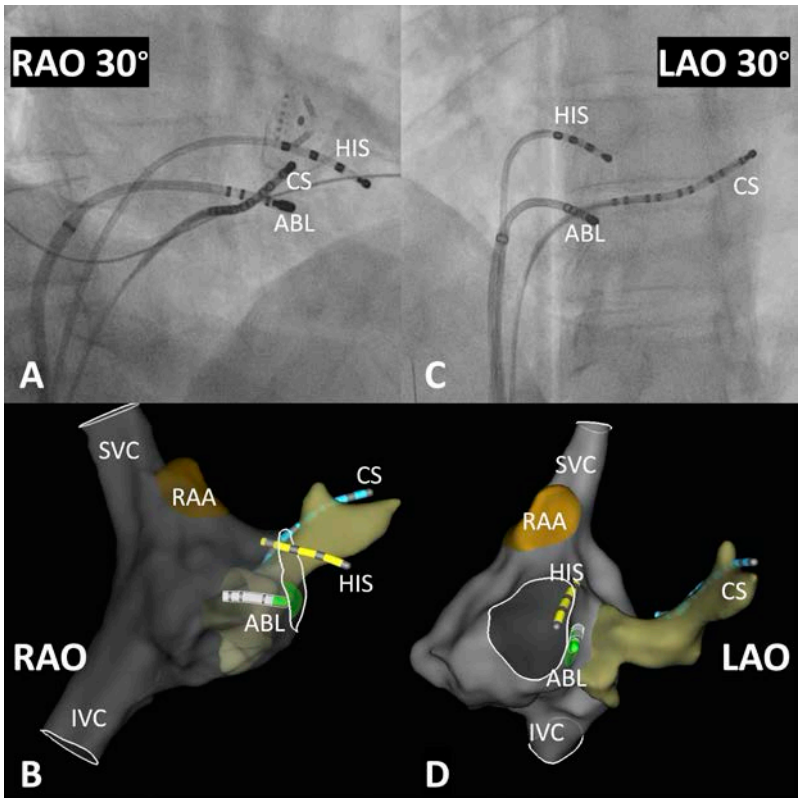

Figure 2: Association between effective RF applications and periprocedural findings. Panel A illustrates difference in cycle length between effective and ineffective RF application with junctional response. Panel B illustrates the outcome of lesions with junctional response based on lesion characteristics. RFA = Radiofrequency application; JR = Junctional response; JA = Junctional beat – atrial.

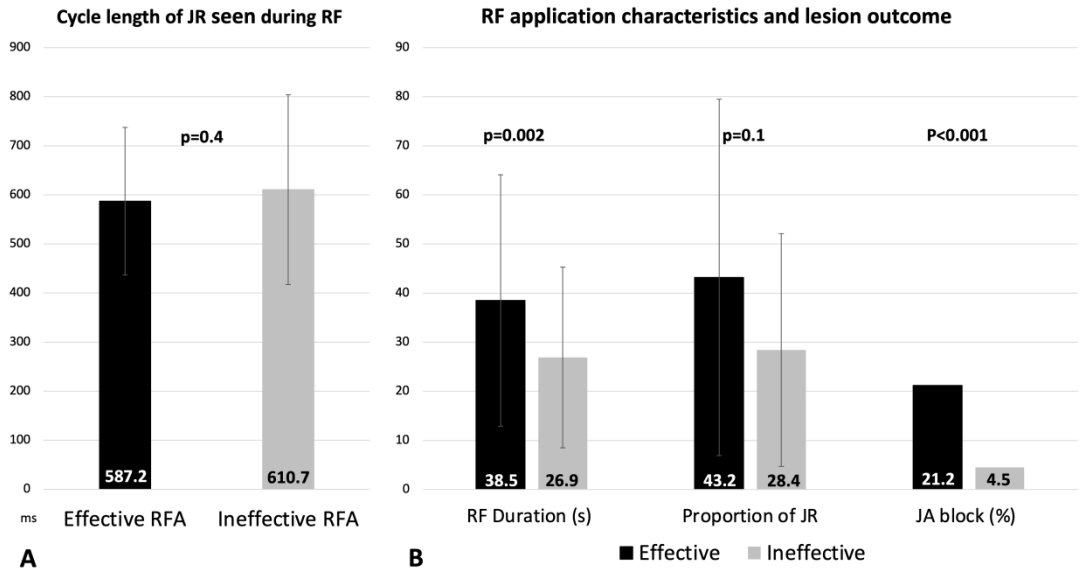

Figure 3: JA block during junctional rhythm with immediate cessation of RFA. * = Junctional beat, = JA block. JA = Junctional atrial, RF = Radiofrequency application.

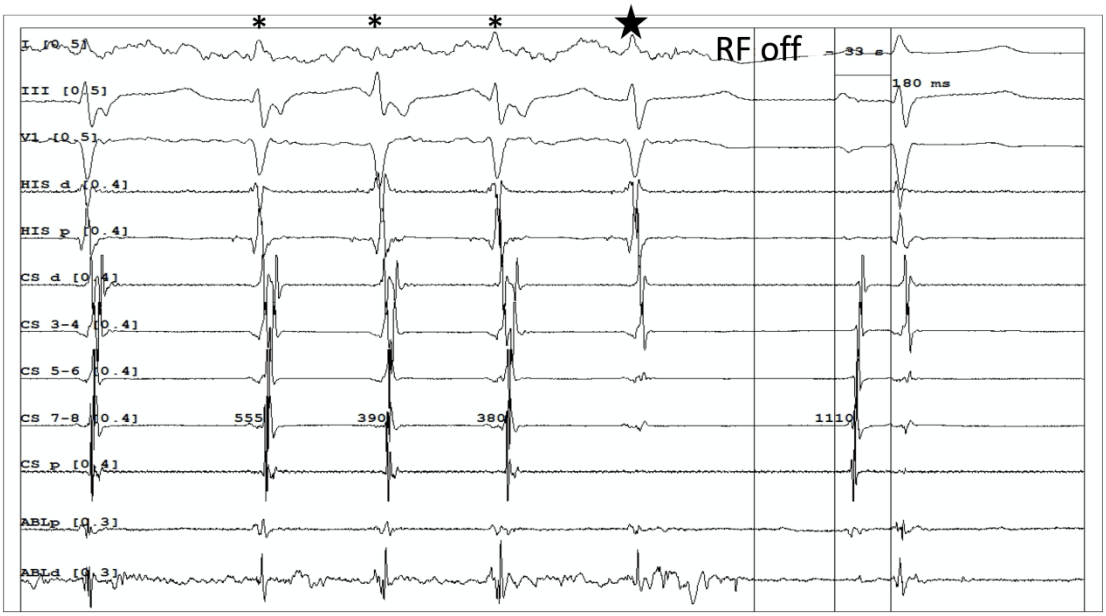

Table 1: Comparison of lesion characteristics between successful and unsuccessful RF applications lesions with junctional response during ablation

Junctional Response and procedural success	**Effective application**	**Ineffective applications**	**p Value**
Total number of RF applications	66 (37.1)	112 (62.9)	NA
Mean RF duration per application	38.5 ± 25.6	26.9 ± 18.4	0.002
Number of junctional beats	26.0 ± 26.7	13.4 ± 16.1	0.001
Proportion of Junctional rhythm, %	43.2 ± 28.4	36.3 ± 23.7	0.1
Median Junctional cycle length, ms	587.2 ± 150.3	610.7 ± 193.3	0.4
Fastest junctional cycle length, ms	405.7 ± 151.6	438.4 ± 178.7	0.2
Unintended VA block during RF	14 (21.2)	5 (4.5)	<0.001

Values are n (%) and mean ± SD, unless indicated otherwise. RF = Radiofrequency, ms = milliseconds, VA block = Ventriculoatrial block.