Cryoablation for Atrioventricular Nodal Reentrant Tachycardia in Young Patients: Predictors of Recurrence

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Background: *Recurrence rates of atrioventricular nodal reentry tachycardia (AVNRT) after cryoablation continue to remain high despite excellent initial success rates. Our objective was to evaluate the clinical outcomes of cryoablation for AVNRT with the 4-mm and 6-mm tip cryoablation catheters in a young population and to elicit predictors of arrhythmia recurrence.*

Methods: *We retrospectively reviewed all patients who underwent cryoablation for AVNRT at the UCSF/Stanford Pediatric Arrhythmia Center from January 2004 to February 2007.*

Results: *One hundred fifty-four patients (age 13.7 years (3.2–24.4)) underwent cryoablation for AVNRT of which 144 patients had inducible AVNRT (123 sustained and 21 nonsustained) and 10 had presumed AVNRT. Initial success was achieved in 95% (146/154), with no difference between the 4-mm (93%) and 6-mm (98%) cryoablation catheter tips (P = 0.15). There was no permanent atrioventricular (AV) block. Transient third-degree AV block occurred in nine patients (6%), with no difference between the 4-mm (4%) and 6-mm (9%) tip (P = 0.13). AVNRT recurrence was documented in 14% in a median time of 2.5 months (0.25–20). Recurrences were lower with the 6-mm (9%) versus the 4-mm (18%) tip, but this did not reach statistical significance (P = 0.16). With univariate analysis, a longer fluoroscopy time was the only significant factor associated with recurrence. Multivariate analysis failed to identify any significant predictor of AVNRT recurrence.*

Conclusion: *Outcomes of cryoablation for AVNRT continue to be good without the complication of AV block. We could not identify any specific parameter associated with AVNRT recurrence. Further improvements in cryoablation technique will be necessary to reduce recurrences. (PACE 2008; 31:1152–1159)*

atrioventricular node, catheter ablation, reentry, cryoablation, recurrence, pediatric

Introduction

Cryoablation has been demonstrated to be a viable and safer alternative to radiofrequency ablation for the treatment of atrioventricular nodal reentrant tachycardia (AVNRT), with preliminary studies reporting initial success rates of 83–95% and no reported permanent atrioventricular (AV) block.[1–4] However, the recurrence rates of 7–20% are consistently higher than recurrence rates after radiofrequency (RF) catheter ablation (3–5%).[5] Proposed explanations for these higher recurrence rates include operator learning curve, a relatively smaller lesion size for cryoablation, and the need for lengthier cryoablation lesions or "bonus" cryoapplications.[6,7] Most of the published studies on cryoablation of AVNRT have reported outcomes for the 4-mm tip cryoablation catheter. In response to the higher recurrence rates, many centers have empirically transitioned to the 6-mm tip cryoablation catheter. The theoretical advantage of the 6-mm tip is that it generates a lesion size more approximating those of standard RF catheters, but with the safety of cryoablation.[8] Two recent studies in adults supported this concept, with an improved recurrence-free survival for the 6-mm tip catheter, but an overall recurrence rate of 12% and 13%, respectively, still significantly higher than RF ablation.[9,10] In addition, proxy endpoints of cryoablation for AVNRT continue to be sought, particularly in patients where AVNRT is difficult to induce in the electrophysiology laboratory.[11] For example, it has been suggested that achieving complete slow pathway block is necessary to prevent recurrences in patients undergoing cryoablation.[12,13]

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The purposes of this study were to evaluate clinical outcomes of cryoablation of AVNRT with the 4-mm and the 6-mm tip cryoablation catheters and to investigate predictors of AVNRT recurrence in a young population treated at a large pediatric arrhythmia center.

Methods

Patient Population

We retrospectively reviewed consecutive patients with AVNRT who underwent cryothermal catheter ablation (cryoablation) of the slow AV nodal pathway at the Pediatric Arrhythmia Center at the University of California, San Francisco, and Stanford University from January 2004 through February 2007. Approval for medical chart review was obtained from the Committee for Human Research at both institutions. This study includes patients previously reported in our initial studies of cryoablation, but is expanded significantly.[8,11] This study was conducted over a longer time period. It also includes all patients with cryoablation for AVNRT, with no exclusion for structural heart disease, additional arrhythmias, prior ablations, or specific age criteria. From January 2004 to November 2005, all cryoablations were performed using a 4-mm tip cryoablation catheter. After November 2005, the 6-mm tip cryoablation catheter was the primary catheter of choice. However, the 4-mm tip continued to be utilized in smaller patients at the discretion of the attending electrophysiologist. There was no specific size or weight parameter. During the entire study period, all ablation procedures were performed with standard fluoroscopic guidance and without 3D mapping.

Anesthesia

General anesthesia or intravenous sedation was utilized for the electrophysiology and ablation procedure at the discretion of the attending physician. For intravenous sedation, the patient was given intermittent boluses of pentobarbital, fentanyl, and midazolam.

Electrophysiology Study and Definitions

Written informed consent was obtained prior to the procedure. All patients underwent a standard electrophysiology study, with recording of parameters, as previously described.[11] The electrophysiologic data analyzed in this study represent the baseline (off isoproterenol) antegrade conduction study, from both pre- and post-ablation.

Dual AV nodal physiology was defined as a ≥50-ms increase in A2H2 in response to a 10-ms decrease during A1A2 stimulation. The *finding of PR ≥ RR* measured during atrial overdrive pacing with 1:1 AV conduction and just prior to AV block or prior to induction of AVNRT was recorded. The need for isoproterenol for AVNRT induction was documented. AVNRT was defined as typical or atypical based on standard definitions.[14] *Sustained AVNRT* included patients who had inducible AVNRT for > 3 beats. *Nonsustained AVNRT* included patients who had AVNRT lasting 1–3 beats. The tachycardia cycle length and VA measurement were recorded. *Presumed AVNRT* was reported in patients with no inducible tachycardia in the laboratory, but with a clinical history suggestive of AVNRT, evidence of dual AV nodal physiology or the finding of PR ≥ RR, and prior documented regular narrow complex tachycardia without identifiable P waves.

After documentation of the tachycardia mechanism, cryomapping (with the 4-mm tip cryoablation catheter) and cryoablation (both 4-mm and 6-mm tips) were carried out as previously described.[11] Our typical approach was to place an initial series of cryoablation lesions in the posterior to midseptum region of the triangle of Koch, each lesion placed in an adjacent but slightly different location. AV nodal conduction was monitored during the cryomapping or cryoablation applications. Repeat atrial stimulation testing was conducted at the conclusion of these first series of lesions. We generally performed atrial stimulation testing after four lesions had been placed. There was no difference in this approach between the 4-mm and the 6-mm tip catheters. If AVNRT remained inducible, then more lesions would be placed higher on the septum. During the period of this study, our technique did not include "freeze-thaw-freeze" cycles. Because of our general approach of not identifying a single lesion as the successful site, we could not specifically identify "bonus" lesions. The duration of each cryoablation lesion was recorded. We report the number of all cryoablation lesions as well as all lesions with a duration of ≥240 seconds. The latter were considered permanent lesions.[6] The total application time reflects the sum of all cryoablation lesions, regardless of the time of each individual lesion.

Approximately 30 minutes after the final cryoablation lesion, atrial extrastimulus testing was repeated to document the change in electrophysiologic parameters and demonstrate the lack of AVNRT inducibility.[15] The use of isoproterenol during postablation testing was recorded.

Outcome Measurements

Initial success after cryoablation was defined as an inability to induce AVNRT (with or without isoproterenol). The continued presence of AV nodal echo beats postcryoablation was recorded. One or two AV nodal echo beats were an acceptable

endpoint if there was easily inducible sustained AVNRT prior to the ablation. In patients with nonsustained or presumed AVNRT preablation, success was defined as change in electrophysiologic parameters (AV block cycle length, loss of PR ≥ RR, elimination of dual AV nodal physiology) and absence of echo beats, or AVNRT. *Initial procedural failure* was defined as persistent inducibility of AVNRT after cryoablation. In these patients, the attending electrophysiologist chose to cross over to RF ablation for additional lesions during the same ablation procedure. Patients were placed in an *indeterminate* category if no atrial stimulus testing was conducted following the final cryoablation lesions.

AVNRT recurrence following an initially successful cryoablation was defined as a documented occurrence of a narrow complex tachycardia on a 12-lead electrocardiogram, 24-hour ambulatory monitor, event monitor, or cardiac rhythm strip. Time to recurrence was reported as time from procedure to documented tachycardia. If a patient was without symptoms following a successful ablation, they were generally discharged from follow-up at 1 year.

Other reported outcome measures included fluoroscopy time, study duration, electrophysiologic parameters, and procedural complications. Study duration was the time the patient entered the electrophysiology laboratory and had a baseline surface electrocardiogram recorded to the conclusion of pacing. Electrophysiologic parameters of interest were dual AV nodal physiology, PR ≥ RR, and the presence of AV nodal echo beats. The primary complication of concern was AV block. If AV block occurred, then the association with mechanical contact from the catheter, cryoablation energy, the type of AV block (first, second, or third degree), the duration, and any therapies administered were recorded.

Statistical Analysis

Descriptive data are presented with mean ± SD or median (range). Comparisons between groups were completed with the Student's *t*-test, Fisher's exact test, or Mann-Whitney ranks sum test. Following univariate analysis, multivariate analysis was performed using logistic regression for selected variables. A statistical software package (JMP, SAS Institute, Cary, NC, USA) was utilized for statistical analysis.

Results

Patient Population

A total of 154 patients underwent cryoablation for AVNRT during the study period (Table I). Most patients had a normal heart structure,

Table I.

Comparison of Cryoablation Procedures for AVNRT with the 4-mm Versus 6-mm Cryoablation Catheter Tips

	Total Population	4-mm Tip	6-mm Tip	P Value
N	154	98	56	
Age (years)	13.7 (3.2–24.4)	13.5 (3.2–24.4)	15.9 (7.4–22.3)	0.002
Weight (kg)	53.7 ± 19.3	50.1 ± 20	59.7 ± 17	0.004
Congenital heart disease	10 (6%)	8 (8%)	2 (4%)	0.16
General anesthesia	116 (75%)	69 (70%)	47 (84%)	0.06
Fluoroscopy time (minutes)	16 (4–57)	17 (4–57)	15 (4–38)	0.14
Procedural time (minutes)	120 (60–310)	138 (70–310)	120 (60–160)	< 0.001
No. of cryoablation lesions ≥ 240 Seconds				
Median (range)	4 (0–11)*	4 (0–11)*	4 (0–11)*	0.02
Mean ± standard deviation	4.1 ± 2.1	3.9 ± 2.1	4.6 ± 2.1	0.05
No. of cryoablation lesions of all duration				
Median (range)	4 (0–13)*	4 (0–12)*	5 (1–13)	0.04
Mean ± standard deviation	4.9 ± 2.5	4.6 ± 2.4	5.4 ± 2.6	0.04
Total duration of all cryoablation lesions (sec)	1,031 ± 510	987 ± 497	1,109 ± 528	0.16
Initial success	146 (95%)	91 (93%)	55 (98%)	0.15
Follow-up time (months)				
Median (range)	12 (6–31)	12 (6–31)	12 (6–12)	< 0.001
Mean ± standard deviation	11.7 ± 3.2	12.7 ± 3.4	10.1 ± 2.5	< 0.001
AVNRT recurrence	21/146 (14%)	16/91 (18%)	5/55 (9%)	0.16

*Data encompass all patients with intent to treat, including patients with cryoablation lesions lasting < 240 seconds. AVNRT = atrioventricular nodal reentrant tachycardia.

with AVNRT as the only arrhythmia substrate. A total of 10 patients (6.5%) had congenital heart disease, consisting of atrial septal defects (three), aortic valve abnormalities (three), Ebstein's anomaly (one), patent ductus arteriosus (one), unbalanced AV canal defect (one), L-transposition of the great arteries (one). Nineteen patients had additional arrhythmias either documented previously or identified during this electrophysiology study. The additional arrhythmias included Wolff-Parkinson-White syndrome (seven), concealed accessory pathway (one), ectopic atrial tachycardia (six), atrial fibrillation (four), and junctional ectopic tachycardia (one). Ten patients underwent previous electrophysiology studies, five of whom had successful RF ablations for an accessory pathway. Two patients had prior RF ablations for AVNRT at other institutions. Three patients had prior studies but no ablation was performed secondary to small patient size at the initial electrophysiology study. One patient had had a prior pacemaker placed for cardioinhibitory syncope. Two of our patients had RF ablation of an accessory pathway during the same procedure as the cryoablation for AVNRT.

During the electrophysiology study and ablation, sustained AVNRT was identified in 123 (79%) patients and nonsustained in 21 (14%). Ten (7%) had presumed AVNRT. Of the 144 patients with identified AVNRT, these tachycardias were typical in 128 (89%) and atypical in 14 (10%). Two patients had typical and atypical AVNRT.

The 4-mm tip cryoablation catheter was utilized in 98 (64%) patients and the 6-mm tip in 56 (36%) patients. Patients undergoing cryoablation with the 4-mm tip catheter were younger ($P = 0.002$) and smaller ($P = 0.004$) than those with the 6-mm tip catheter (Table I).

Initial Outcomes

Initial success of cryoablation for AVNRT was documented in 146/154 (95%) (Fig. 1). In comparing the 4-mm cryoablation catheter tip to the 6-mm tip, there was no difference in initial success rates (93% vs 98%, respectively, $P = 0.15$). Patients undergoing cryoablation with the 4-mm tip cryoablation catheter had a significantly longer procedural time but had fewer cryoablations lasting ≥240 seconds compared to patients with the 6-mm tip. Interestingly, both populations had the same median number of four lesions, but distributions that were different enough to result in a statistically significant difference when evaluated by the Mann-Whitney ranks sum test. Furthermore, the mean number of cryoablations for each population was significantly different (the mean number of lesions lasting ≥240 seconds for the population treated with the 4-mm tip was 3.9; for the 6-mm tip it was 4.6 lesions) (Table I).

Six patients had procedural failures for cryoablation secondary to the following: one patient developed transient third-degree AV block with mechanical contact from a 4-mm tip cryoablation catheter and no lesions were delivered (reported in a previous series)[8] and five (four with the 4-mm tip, one with the 6-mm tip) patients had persistent AVNRT and crossed over to RF. Two patients (both 4-mm tip) were listed as indeterminate. After the initial series of cryoablation lesions, these two patients continued to have inducible

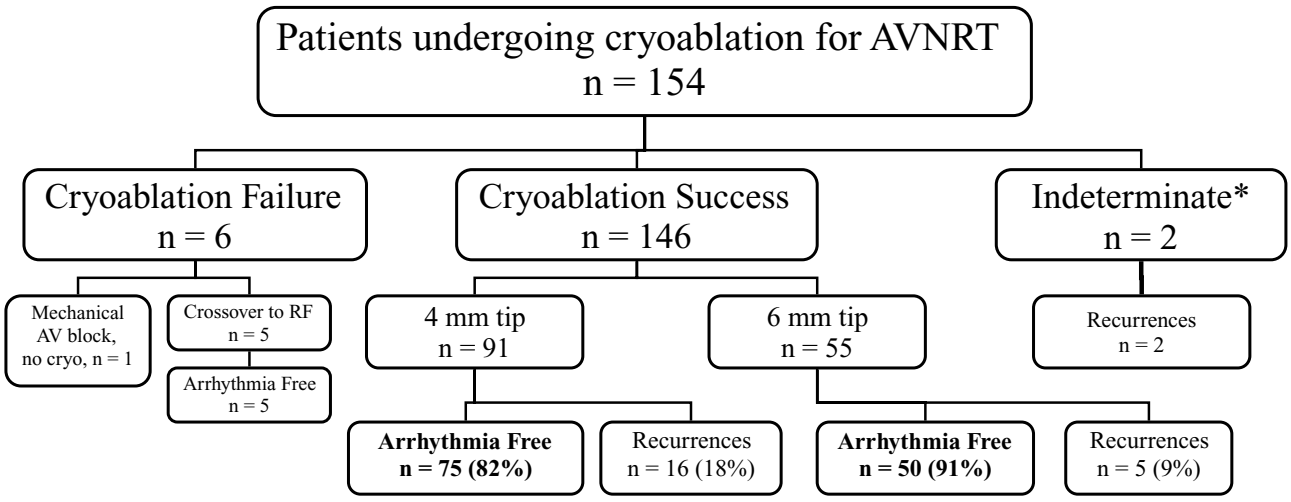

Figure 1. *Outcomes of patients presenting for cryoablation of atrioventricular nodal reentrant tachycardia (AVNRT). *Procedures concluded without retesting after developing transient atrioventricular block during cryoablation, both with the 4-mm tip cryoablation catheter.*

AVNRT. Several additional cryoablation lesions were then placed. On the final cryoablation lesion, transient first (one patient) or second- (one patient) degree AV block occurred and the procedure was concluded without repeat atrial extrastimulus testing.

For patients with successful procedures, AV nodal echo beats continued to be present in 34/139 (24%) patients. A vast majority of these patients (32/34) had single echo beats, and two patients had two AV nodal echo beats. Dual AV nodal physiology was present in 68/134 (51%) preablation and this was reduced to 32/119 (27%) postcryoablation ($P < 0.001$). The finding of PR $\geq$ RR was documented in 71/125 (57%) preablation and this was reduced to 8/110 (7%) postablation ($P < 0.001$). There was no difference between the 4-mm and 6-mm tip with regards to these parameters.

Procedural Complications

Transient third-degree AV block developed in 9/154 (6%) patients. The AV block occurred with catheter contact (five) or during cryoablation (four). The AV block was generally only a few beats and recovered with moving the catheter away from the AV nodal area or on rewarming of the cryoablation catheter. One patient developed third-degree heart block 39 seconds after the onset of cryoablation with a 6-mm tip, at which point cryoablation was terminated. After recovery of atrioventricular conduction without any intervention, no further lesions were placed, and on further extrastimulus testing, no evidence of AVNRT remained. This patient has not recurred. Another patient required temporary pacing for 10 minutes after mechanical contact prior to the delivery of any lesions, and then went on to have a successful ablation.

Midterm Outcomes

Follow-up was available for all 146 patients at a median duration of 12 months (6–31). The overall AVNRT recurrence rate for patients after an initially successful cryoablation was 21/146 (14%). The recurrence rate for the 4-mm tip cryoablation catheter (18%) was higher than for the 6-mm tip (9%), but did not reach statistical significance ($P = 0.16$). The median time to recurrence was 2.5 months (range 0.25–20 months). Patients who underwent cryoablation with the 4-mm tip cryoablation catheter had a longer duration of follow-up compared to the 6-mm tip (Table I and Fig. 2).

Of the 19 patients with additional arrhythmias, only one had a recurrence. This patient had atrial fibrillation/flutter during the initial procedure. His arrhythmia recurrence was identified as AVNRT during a follow-up electrophysiology study.

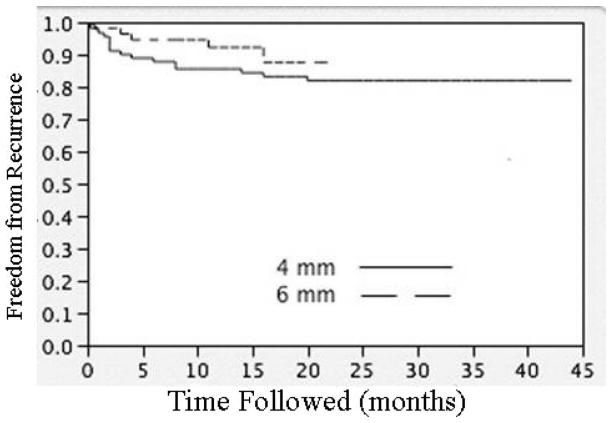

Figure 2. *Kaplan-Meier freedom from arrhythmia recurrence following an initially successful cryoablation for atrioventricular nodal reentrant tachycardia (AVNRT). Patients are grouped based on cryoablation catheter tip size. Log-rank P = 0.2729.*

Predictors of AVNRT Recurrence

With univariate analysis, a longer fluoroscopy time was the only significant factor associated with AVNRT recurrence (Table II). The presence of AV nodal echo beats after an ablation was not associated with a recurrence. Furthermore, neither of the two patients with two AV nodal echo beats had a recurrence. The presence of dual AV node physiology postablation trended toward a significant association with a recurrence ($P = 0.08$). However, only 51% (68/134) of our population had dual AV nodal physiology preablation.

Multivariate analysis using logistic regression failed to identify any significant predictor of AVNRT recurrence. This multivariate analysis was performed with a number of different models incorporating age, weight, additional arrhythmias, congenital heart disease, fluoroscopy time, procedural time, PR $\geq$ RR (before and after ablation), dual AV node physiology (before and after ablation), cryoablation catheter tip size, number and duration of cryoablation lesions, presence of AV block, and follow-up time.

Discussion

This study of 154 patients is one of the largest series to date presenting outcomes for cryoablation of AVNRT in young patients, including patients with congenital heart disease. The results confirm prior reports of excellent initial success with cryoablation (95%) with no permanent AV block. However, the recurrence rate (14%) continues to be higher than those reported for RF (3–5%).[5] The only predictor of arrhythmia recurrence identified was a longer fluoroscopy time. Our data

Table II.

Comparison of Patients with and without AVNRT Recurrence Following an Initially Successful Cryoablation

	No Recurrence	Recurrence	P Value
N	125/146 (86%)	21/146 (14%)	
Age (years)	14.4 (3.2–24.4)	15.3 (7.4–17.2)	0.73
Weight (kg)	53.5 ± 19	58.2 ± 22	0.31
Male	58 (46%)	10 (48%)	0.92
Congenital heart disease	7 (6%)	2 (10%)	0.49
Additional arrhythmias	16 (13%)	1 (5%)	0.29
Fluoroscopy time (minutes)	16 (4–57)	19 (6–53)	0.03
Procedural time (minutes)	120 (60–310)	140 (90–218)	0.09
Isuprel necessary to induce AVNRT	76/116 (66%)	9/19 (47%)	0.13
Cryoablation catheter tip size			0.16
4 mm	75 (60%)	16 (76%)	
6 mm	50 (40%)	5 (24%)	
Cryoablation lesions ≥ 240 seconds (no.)	4 (0–11)	4.5 (1–8)	0.19
Cryoablation lesions of all duration (no.)	4 (0–13)	4 (1–9)	0.16
Total duration of all cryoablation lesions (seconds)	987 ± 509	1,133 ± 496	0.23
Transient third-degree AV block	6/125 (5%)	3/21 (14%)	0.09
Inducible AVNRT (preablation)			0.80
Sustained (> 3 beats)	98 (78.4%)	17 (81%)	
Nonsustained (< 3 beats)	19 (15.2%)	2 (9.5%)	
Presumed	8 (6.4%)	2 (9.5%)	
AV block cycle length (ms)			
Preablation	363.0 ± 85	346.7 ± 82	0.42
Postablation	339.2 ± 69	331.5 ± 72.8	0.65
PR ≥ RR			
Preablation	58/108 (54%)	13/17 (76%)	0.08
Postablation	7/96 (7.3%)	1/14 (7.1%)	0.70
Dual AV nodal physiology			
Preablation	58/113 (51%)	10/21 (48%)	0.76
Postablation	25/102 (25%)	7/17 (41%)	0.08
AV nodal echo beats (postablation)	28/118 (24%)	6/21 (29%)	0.53
Follow-up time (months)	12 (12–31)	12 (12–20)	0.26

AV = atrioventricular; AVNRT = atrioventricular nodal reentrant tachycardia.

do not convincingly show a specific advantage of the larger 6-mm tip cryoablation catheter over the 4-mm tip for this arrhythmia substrate.

Predictors of Recurrence

Four studies in adult patients have attempted to identify predictors of AVNRT recurrence following successful cryoablation. Two studies identified the 4-mm tip cryoablation catheter as having higher recurrence rates than the 6-mm tip cryoablation catheter.[5,9] The 4-mm versus 6-mm tip cryoablation outcomes will be discussed below. One study identified AVNRT recurrence as being associated with the continued presence of AV nodal echo beats postablation and with fewer number of cryoablation lesions (1.5 cryoablation lesions vs 3.0 cryoablation lesions).[7] In our study, the number of cryoablation lesions did not predict recurrences. Notably, our overall number of cryoablation lesions per procedure was 4–5 in both groups, which is more than was used in that prior study.

Another study identified AVNRT recurrences as being associated with younger age and the presence of valvular heart disease, but not with the procedural endpoint of slow pathway ablation or AV nodal echo beats.[12] Our patient population is different from this prior study. Our patients are significantly younger and some have congenital heart disease. The AV node not only has size differences, but is also thought to develop and change with patient age.[16,17] For our population, patient age was not a predictor of recurrence. The presence of congenital heart disease was also not a

predictor; however, the number of patients with congenital heart disease in our study was modest, at only 10 patients. In our patient population, the only predictor of AVNRT recurrence after a successful cryoablation was a longer fluoroscopy time. Fluoroscopy time could be a marker for a more technically challenging procedure. However, other measures to assess procedural complexity, such as number of cryoablation lesions and actual procedural time, were not correlated with recurrence. Further study will be warranted in order to make more definitive conclusions.

Over the years, many authors have attempted to evaluate if procedural endpoints such as persistent dual AV nodal physiology or the presence of AV nodal echo beats would modulate arrhythmia recurrences with RF or cryoablation.[7] With cryoablation, it would be important to identify surrogate outcome measures, especially for the patients with difficult-to-induce tachycardia or with presumed AVNRT. In our patient population, the presence of echo beats or PR $\geq$ RR after ablation were not significant predictors of recurrence. The presence of dual AV node physiology did trend toward significance and could potentially be of use in patients who have this finding preablation. Unfortunately, as only half of our population actually manifested dual AV node physiology prior to any ablations, the postablation presence of dual AV node physiology becomes a difficult endpoint to apply broadly. Patients with presumed AVNRT and empiric slow pathway modification with cryoablation were equally as likely to have a recurrence as the patients with sustained or nonsustained tachycardia. Clearly, new and better markers of successful ablation are needed.

Cryoablation Catheter Tip Size: 4 mm Versus 6 mm

Cryoablation lesions in the myocardium have been shown to be more discrete and smaller in overall dimensions when compared to RF lesions.[18] This is often cited as a strength of cryoenergy since it could potentially minimize complications, particularly permanent damage to the AV node.[19] Unfortunately, outcome studies have shown a consistently higher recurrence rate for cryoablation compared to RF ablation for AVNRT, as well as other arrhythmia substrates.[7] To address this discrepancy, many centers have empirically transitioned from the standard 4-mm tip cryoablation catheter to the 6-mm tip cryoablation catheter in an effort to more closely approximate the broader and deeper lesion of the RF catheter. Three recent studies in adult patients reported that the 6-mm tip cryoablation catheter was positively associated with arrhythmia-free survival.[5,9,10] Other authors did not find any differences in outcomes between the 4-mm and 6-mm tip cryoablation catheters.[7,12]

In our population, we found that the initial success rates for AVNRT were similar with both the 4-mm and the 6-mm tip cryoablation catheters and that recurrence rates were different, although not at a statistically significant level. We found several other differences between the 4-mm and the 6-mm tip cryoablation catheter groups. Patients with the 4-mm tip were younger and smaller, reflecting operator bias to use the 6-mm tip cryoablation catheter primarily, but continue to reserve the 4-mm tip cryoablation catheters for younger patients. There was no difference in the total cryoablation duration time. However, patients treated with the 6-mm tip had a greater number of discrete cryoablation lesions. As the 6-mm tip patients were generally later in our experience, with a growing awareness of the recurrence rate, we were more likely to deliver additional lesions. Patients in the 6-mm tip group also had a shorter procedural duration, likely reflecting improved operator experience with the technology.

There are a few explanations for the recurrence rate in the 4-mm tip group being higher than the 6-mm tip group, but not reaching statistical significance. The 6-mm tip may have a lower recurrence rate but our study population was not of significant size to have the statistical power to detect such a difference. At an alpha of 0.05 and a power of 0.80, to detect a difference at these recurrence rates we would need a population size of nearly 200 patients. In the recent study by Rivard et al., the study population was 289 adult patients who underwent cryoablation for AVNRT. The AVNRT recurrence rates in our study population were very similar to those reported by that center.[9] After cryoablation with the 4-mm tip, our recurrence rate was 18% compared to 16% in their adult population. Similarly, our recurrence rate for the 6-mm tip was 9% compared to 8% in their 6-mm group. With these similar recurrence rates, they were able to demonstrate a statistically significant difference in recurrence rates ($P = 0.0252$), most likely due to their larger patient population. Thus, it is highly probable that our study failed to find a difference in groups because of statistical power.

Alternatively, we may be underestimating the recurrence rate for the 6-mm tip cryoablation catheter because of a shorter duration of follow-up. Our initial report of cryoablation for AVNRT with the 4-mm tip cryoablation catheter had a recurrence rate of 8%.[8] After a longer duration of follow-up, several more patients went on to have documented arrhythmia recurrence. According to our Kaplan-Meier analysis, however, there was no correlation between tip size and time to

recurrence, implying that duration of follow-up did not contribute significantly to the different recurrence rates. Other differences between our initial published study and this is that this study included a larger number of patients and patients that were previously excluded such as those with congenital heart disease, those with other arrhythmia substrates, and those with presumed AVNRT.

With regard to safety, we found that the risk of transient AV block remains quite low (6%) and that there was no difference in AV block rate between the catheter tip sizes. We, like other authors, have had no permanent AV block with cryoablation. For those patients with transient AV block, the time course to recovery of AV nodal conduction was generally short, with the vast majority recovering with removal of the catheter or within two-three beats of catheter tip warming.

Study Limitations

Our study was retrospective. The primary limitation is that there was no specific protocol for choice of cryoablation catheter tip size or for determining cryoablation failure and transitioning to RF. There was also no defined number of cryoablation lesions placed prior to retesting for AVNRT inducibility. The longer follow-up in patients with the 4-mm tip cryoablation catheter versus the 6-mm tip also poses a challenge in data interpretation. However, a majority of recurrences were documented in < 3 months, and there were no differences between the recurrence and nonrecurrence population with regards to length of follow-up.

Clinical Significance and Future Directions

Our study shows the safety and efficacy of cryoablation for the treatment of AVNRT in a young population. We were unable to identify any significant predictors of arrhythmia recurrence that could be altered to improve long-term outcomes in these patients. The overall AVNRT recurrence rate continues to be higher than the recurrence rate reported for RF ablation of the same arrhythmia substrate. Because of the improved safety profile of cryoablation, however, the continued use of cryoablation as a first-line therapy may be warranted. Our study underscores the need for identifying further measures that can be used to gauge procedural success in addition to the standard outcome of inability to induce tachycardia at the conclusion of the procedure.

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