Pediatr Cardiol (2012) 33:1147–1153
DOI 10.1007/s00246-012-0273-0

ORIGINAL ARTICLE

Cryoablation Therapy for Atrioventricular Nodal Reentrant Tachycardia in Children: A Multicenter Experience of Efficacy

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Received: 10 October 2011 / Accepted: 27 February 2012 / Published online: 20 March 2012

Abstract Atrioventricular nodal reentrant tachycardia (AVNRT), a common tachycardia in children, is routinely treated by catheter ablation using radiofrequency or cryothermal energy. Acute success rates of 95–97 % are reported for cryoablation, similar to those achieved with radiofrequency ablation (RFA). However, early studies reported higher recurrence rates after cryoablation for treatment of AVNRT than those reported for RFA. This study evaluated the success and recurrence rates for cryoablation in a current cohort of pediatric patients across several institutions. Patients 21 years old or younger with AVNRT who underwent cryoablation at five participating centers between 2004 and 2009 were retrospectively reviewed. Patient demographics and procedural data were extracted from patient records and analyzed. A total of 434 patients with AVNRT who underwent cryoablation were identified. Cryoablation was used as the exclusive ablation method for 379 patients. For 97 % (368/379) of these patients, cryoablation was acutely successful. A higher acute success rate was found with the 6-mm-tip catheter (99 %) than with the 4-mm-tip catheter (91 %) ($p < 0.01$). Recurrence was experienced by 7.3 % of the patients. Recurrence was more likely for those treated with the 4-mm-tip catheter (6/42, 14 %) than for those who had the larger catheters (12/204, 6 %) No patient experienced permanent heart block. Success and recurrence rates for this cohort of patients were similar to those reported for RFA used to treat AVNRT in pediatric patients. The findings show a higher success rate and a lower recurrence rate after cryoablation with a 6-mm-tip catheter than after use of the 4-mm-tip catheter, with an associated excellent safety profile.

Keywords Atrioventricular nodal reentrant tachycardia · Cryoablation · Radiofrequency ablation

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Atrioventricular nodal reentrant tachycardia (AVNRT) is a common tachycardia in children [21]. The acute success rate for the treatment of AVNRT is 95–97 % when cryoablation is used [5, 6, 9, 10, 12, 23]. This rate is comparable with that reported for radiofrequency ablation (RFA) [6, 24].

In contrast to RFA, the catheter tip adheres to the myocardium during cryoablation, preventing migration of the catheter tip and possible damage to surrounding tissue (most importantly the atrioventricular node). Cryoablation is not associated with junctional ectopy, which allows monitoring of fast-pathway conduction [29]. It has a low propensity for thrombus formation [15] and is painless [4, 9].

Probably the most important advantage of cryoablation over RFA for the pediatric population is a decreased incidence

of inadvertent permanent atrioventricular (AV) block during slow-pathway ablation [15, 19, 29]. To date, no case of permanent AV block complicating cryoablation in the treatment of AVNRT has been reported. Heart block continues to be reported for 1–3 % of the patients treated with RFA [13, 31]. Although rare, heart block has significant implications in an otherwise healthy child undergoing ablation of AVNRT, a non-life threatening arrhythmia, because it necessitates a lifetime of ventricular pacing.

It is suggested that the added safety associated with cryoablation comes at the cost of lower acute success rates and higher arrhythmia recurrence rates. The reported recurrence rates after cryoablation range from 5 to 14 % in various studies investigating children [5, 6, 12, 24] and adults [3, 9, 28]. This is higher than the 4–5 % rate reported for RFA in adult trials [9, 28]. With increased collective experience, a more common use of larger-tip cryoablation catheters, and more aggressive lesion applications, we hypothesized that the recurrence rates for AVNRT after cryoablation in children may approach those of patients treated with RFA. This decrease in the frequency of tachycardia recurrence after cryoablation has been demonstrated in adult patients with AVNRT [26, 28]. We therefore reviewed all cases of AVNRT in children treated with cryoablation at five pediatric cardiac centers in the United States over a recent 5-year period to determine acute success and recurrence rates and to evaluate predictors of recurrence.

Methods

We reviewed data from all patients with AVNRT 21 years old or younger at the time of cryoablation who presented for catheter ablation at five participating centers between 1 January 2004 and 31 December 2008. The study was approved by the institutional review boards of each institution. The participating centers were Children's Healthcare of Atlanta, Emory University, Atlanta, Georgia; C.S. Mott Children's Hospital, University of Michigan, Ann Arbor; Children's Hospital, University of Iowa, Iowa City; Primary Children's Medical Center, University of Utah, Salt Lake City; Children's Heart Center, Las Vegas, Nevada.

Electrophysiology study records were reviewed to determine success or failure of the procedure, procedural complications, catheter size, and number of total lesions applied. All lesions treated 240 s or longer were designated as full lesions, whereas those terminated within the first minute were regarded as "freeze mapping" lesions. The first successful lesion, determined by the operator, was defined as a full lesion that terminated the AVNRT, eliminated inducibility of the AVNRT, or eliminated slow-pathway conduction.

Acute success was defined as either elimination of inducible tachycardia or slow-pathway conduction before the patient left the electrophysiology laboratory. A recurrence of AVNRT was defined by any of the following: suggestive clinical history; narrow complex tachycardia documented on electrocardiogram, Holter monitoring, event recorder, or repeat electrophysiology study.

Statistical analysis was performed using Stata 11.0 software. Descriptive data are presented as means ± standard deviations and percentages. Comparisons between groups (4- vs. 6- vs. 8-mm-tip and recurrence vs. no recurrence) were completed using Student's t test or analysis of variance (ANOVA) for continuous variables and Fisher's exact test for categorical variables. After univariate analysis, multivariable analysis was performed using a logistic regression model with selected variables. A p value less than 0.05 was considered statistically significant.

Results

The study population consisted of 434 children with AVNRT. The outcomes of the ablation procedures are summarized in Fig. 1. For 55 patients, both cryoablation and RFA were used. For 33 of these 55 patients, cryoablation was successful after RFA failure, or the operator switched to cryoablation due to a perceived increased risk with the use of RFA. All 55 cases were excluded from analysis of success or recurrence rates.

During the follow up period, 246 of the 368 patients who underwent successful cryoablation had adequate follow-up assessment and were included in the analysis for arrhythmia recurrence. To be included, the patients needed to have documentation of a return visit to one of the clinics belonging to the included study centers. Because the five centers are referral centers for a large geographic area, many of the patients had clinical follow-up assessment at outlying sites and therefore were not included in the follow-up data set. Of the 246 individuals with available follow-up data after an initially successful cryoablation procedure, 18 had a recurrence of arrhythmia, giving a recurrence rate of 7.3 % over an average follow-up period of 24 months (Table 1). None of the patients in the study population experienced permanent first-, second-, or third-degree AV block.

The ablation procedure characteristics of the study group are illustrated in Table 2. Cryoablation used as the exclusive ablation method was acutely successful for 97 % (368/379) of the patients. The 4-mm-tip catheter was used for only 18 % (70/379) of the study population and rarely during the latter part of the study because all the participating centers had changed from primarily using a 4-mm-tip catheter to using the 6-mm-tip catheter, and occasionally the 8-mm-tip catheter. The 8-mm-tip catheter also was used sparingly during the study period, although a bit more frequently

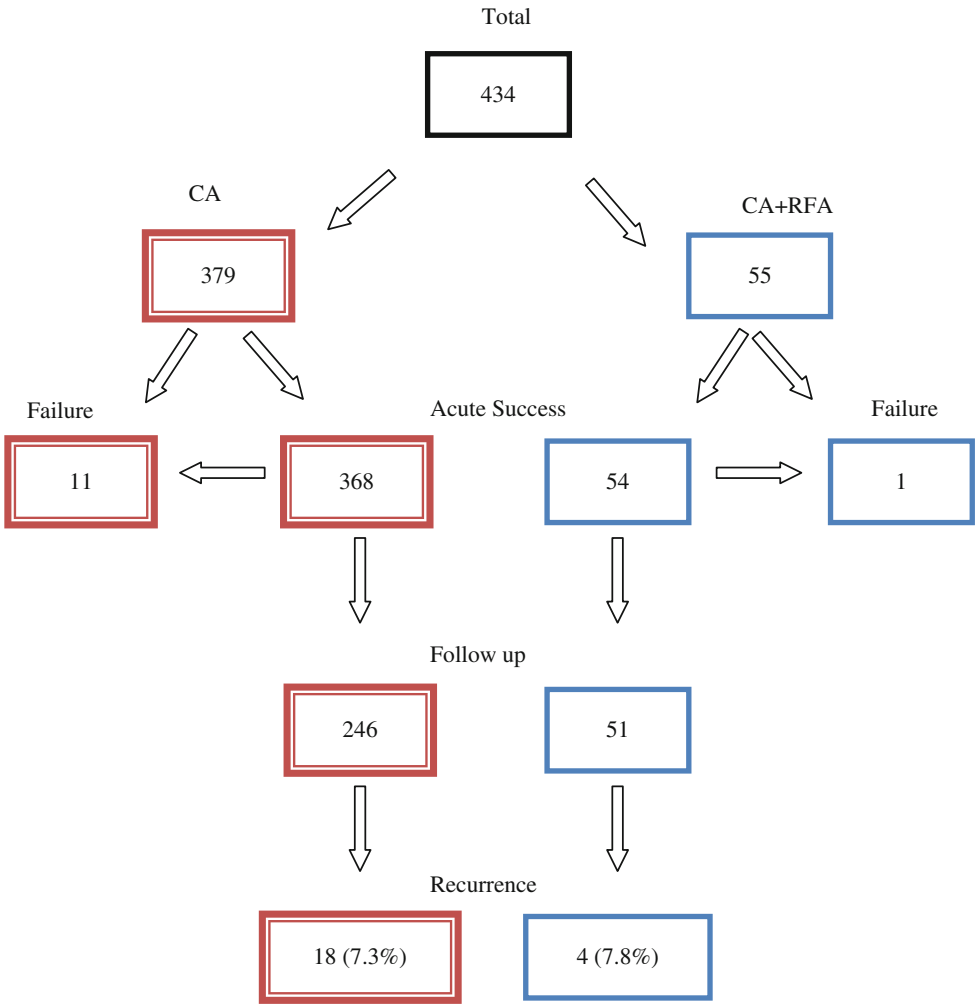

Fig. 1 Study population profile. *CA* cryoablation, *RFA* radiofrequency ablation

Table 1 Baseline characteristics of the study population ($n = 434$)

Characteristic	Mean ± 2 SD	Range
Age (years)	13.1 ± 0.3	2–21
Weight (kg)	55 ± 2.2	14.7–133.2
Body surface area (m^2)	1.5 ± 0.1	0.63–2.26
Males	41.3 %	
Follow up (months)	24 ± 2.3	1–64
Recurrence: *n* (%)	18/246 (7.3)	

SD standard deviation

Table 2 Cryoablation characteristics of the study population

Characteristic	*n* (%)	Range
Cryoablation only used	379	
Acute success after cryoablation	368 (97)	
Cryomapping lesions (mean ± 2 SD)	7 ± 0.9	0–76
Full lesions >240 s (mean ± 2 SD)	6 ± 0.5	0–30
Post first success lesions (mean ± 2 SD)	4 ± 0.6	0–17
Total lesions	13 ± 1	0–98
Catheter tip size (mm)		
4	70 (19)	
6	243 (64)	
8	66 (17)	

SD standard deviation

toward the latter portion of the study. Nonetheless, when the patients treated with cryoablation alone were segregated into three groups based on catheter tip size (4, 6, or 8 mm), a significantly higher acute success rate was found with the 6-mm catheter tip (99 %) and 8-mm-tip (97 %) than with the 4-mm-tip (91 %) (Table 3) ($p < 0.01$).

The demographic and cryoablation features of the patients with and without AVNRT recurrence (18 recurrence cases; 228 no recurrence cases) who underwent cryoablation only are displayed in Table 4. The overall recurrence rate was 7.3 %. Recurrences were less frequent after ablation with a larger-tip catheter (12/204, 6 %) than after ablation with the 4-mm-tip catheter (6/42, 14 %; $p = 0.017$). Of the 12 recurrences after cryoablation with a larger-tip catheter, a 6-mm-tip was used in eight cases

Table 3 Comparison of patients who had cryoablation using 4-mm-tip catheter vs. 6- or 8-mm-tip catheter

Characteristic	Catheter tip size			
	4 mm ($n = 70$)	6 or 8 mm ($n = 309$)		p value
Age (mean years ± 2 SD)	12 ± 1.1	13.3 ± 0.4		0.03
Weight (mean kg ± 2 SD)	55.3 ± 7.2	54.9 ± 2.4		0.91
Body surface area (m^2)	1.5 ± 0.2	1.5 ± 0.1		0.53
Males (%)	35	45		0.46
Follow-up (mean months ± 2 SD)	43 ± 5	17 ± 2		<0.01
	4 mm ($n = 70$)	6 mm ($n = 243$)	8 mm ($n = 66$)	
Acute success: n (%)	64/70 (91)	240/243 (99)	64/66 (97)	0.007
Recurrence: n (%)	6/42 (14)	8/178 (4.5)	4/26 (15.4)	0.018
Cryomapping lesions: mean (SD)	8.5 (10.8)	7.2 (7.1)	7.5 (12.0)	0.60
Full lesions >240 s: mean (SD)	5.7 (4.4)	6 (5.3)	5.6 (5.4)	0.82
Total lesions: mean (SD)	14.2 (13.3)	13 (9.0)	13.1 (14.2)	0.74

SD standard deviation

Table 4 Comparison of patients with and without recurrence of trioventricular nodal reentrant tachycardia (AVNRT) after cryoablation

Characteristic	Recurrence ($n = 18$)	No recurrence ($n = 228$)	p value
Age (mean years ± 2 SD)	12.9 ± 1.8	13.2 ± 0.4	0.77
Weight (mean kg ± 2 SD)	53.7 ± 8.8	54.8 ± 2.6	0.80
Body surface area (m^2)	1.4 ± 0.5	1.5 ± 0.1	0.46
Males (%)	75	40	0.30
Follow up (mean months ± 2 SD)	25 ± 8	21 ± 3	0.42
Cryomapping lesions (mean ± 2 SD)	11.2 ± 7	6.7 ± 1	0.18
Full lesions >240 s (mean ± 2 SD)	6.8 ± 2.2	6.7 ± 0.8	0.95
Total lesions (mean ± 2 SD)	18.4 ± 7.6	13.2 ± 2.3	0.17
Catheter tip size (mm)			
4	6	36	0.02
6	8	170	0.02
8	4	22	0.02

SD standard deviation

(8/178, 4.5 %), whereas an 8-mm-tip was used in four cases (4/26, 15 %). For four patients, a combination of 6- and 8-mm-tip catheters was used, and one of these patients had a recurrence.

To determine predictors for AVNRT recurrence, we performed logistic regression analysis using multiple variables. The results are summarized in Table 5. Using a catheter tip of 6 mm for cryoablation reduced the risk of recurrence by nearly 60 % (odds ratio 0.41; $p = 0.002$).

Table 5 Multivariable model of risk factors for recurrence after acute success of cryoablation

Variable	OR	95 % CI	p value
Age (years)	1.0	0.87–1.2	0.93
Cryomapping lesions	1.1	0.95–1.2	0.31
Total lesions	1.0	0.92–1.1	0.89
Catheter tip 6 mm	0.41	0.23–0.73	0.002
Catheter tip 8 mm	1.0	0.7–1.6	0.72

OR odds ratio, *CI* confidence interval

Similarly, only a larger catheter tip was significantly predictive of acute success after cryoablation (odds ratio 3.0; $p = 0.007$).

Discussion

The largest study comparing the outcomes between RFA and cryoablation in adults with AVNRT has been published recently [9]. To date, our study is the largest report of cryoablation used to treat AVNRT in the pediatric population. The authors of the adult study [9] report that the acute success rates with both methods are similar. Similarly, we found that cryoablation is highly effective for the treatment of AVNRT in children, with an acute success rate equivalent to that reported for RFA in the current era (97 % in our study). Although we did not analyze our data on a year-to-year basis, our study period involved a time span with a trend toward the use of 6- or 8-mm-tip catheters [5, 16, 25, 26], application of "bonus" lesions [11], a freeze-thaw-freeze technique, and evaluation of sustained

slow-pathway conduction suppression [8, 26] as the end point denoting better efficacy.

This study adds to the growing experience with the safety of cryoablation used for children. There were no cases of permanent AV block or any other serious complications such as cardiac perforation after cryoablation in the study population despite the smaller size of the children, the use of larger-tip catheters, and the application of several "insurance lesions" in most cases.

A novel finding of this study was the distinct advantage offered by a larger-tip catheter (6 mm) compared with the 4-mm-tip catheter in pediatric patients, with better success and lower recurrence rates. This observation has been made in the adult population [3, 7, 25], but pediatric experience has been limited to date [5].

Deisenhofer et al. [9] reported comparable acute success rates between cryoablation and RFA in their prospective trial using only the 6-mm-tip catheter and a bonus freeze at the successful site. An interesting observation in their study was the high number of device functionality failures in the cryoablation group ($n = 18$) compared with the RFA group ($n = 2$). Whether this had any impact on the success and procedure duration was not explained.

Our arrhythmia recurrence rate of 7.3 % after cryoablation over an average follow-up period of 2 years is lower than that reported in previous smaller studies and only marginally higher that those reported for RFA in adults [5, 6, 9, 11, 20, 23, 24]. Deisenhofer et al. [9] prospectively showed a lower recurrence rate with the 6-mm-tip cryoablation catheter than in their pilot study [32] a few years ago using the 4-mm-tip. Speculations as to the mechanisms for higher recurrence rates after cryoablation include a comparatively smaller lesion and absence of a large colliquation necrosis [30]. Our lower recurrence rate of 7.3 % compared with the 9.4 % observed in the landmark trial group of Deisenhofer et al. [9] may be partly related to a more aggressive approach among the investigators, which included the application of more lesions. In particular, the centers included in this study all delivered several "bonus" lesions surrounding the successful ablation site rather than a single "bonus" lesion. In fact, four of the five participating centers routinely used the EnSite NavX system (Endocardial Solutions, St. Jude Medical, Inc., St. Paul, MN, USA) for all cases and delivered one to five extra lesions guided by the successful mapped location.

In our study, the results with the 8-mm-tip catheter were worse than those achieved with the 6-mm-tip catheter in terms of arrhythmia recurrence. The reason for this difference is unclear. Use of the 8-mm-tip catheter may involve a learning curve. Because of the larger catheter size, operators may have limited the energy delivered (number of lesions) to the region of the slow-pathway and may have avoided a more anterior catheter position, thereby limiting efficacy and possibly increasing instances of recurrences. The selection of patients for use of the 8-mm-tip catheter also may have influenced the recurrence rate by limiting its use for more difficult cases. However, the number of patients analyzed who underwent ablation with the 8-mm-tip was too small for any significant conclusions to be drawn.

The risk of AV block, concerns for proarryhythmia, the possibility of lesion enlargement [18, 27], and thromboembolic events with RFA [1, 2, 15] make cryoablation a potentially safer option for treating AVNRT in children. These concerns are particularly important with the pediatric population because AVNRT is a condition that is relatively benign, whereas the consequences of inadvertent heart block at a young age are life changing.

Although transient adverse effects on AV conduction may be observed, we had no patients noted to have any permanent first-, second-, or third-degree heart blocks as a complication of the procedure. Such transient blocks have been reported, and we certainly observed that impingement on the conduction system was possible during cryoablation despite no evidence of such an effect during cryomapping. This may be explained by a larger cooling zone created during cryoablation relative to cryomapping which may impinge on the electrophysiological properties of adjacent structures [14]. Recently, cryothermal lesion expansion in immature infant swine myocardium has been demonstrated [17]. This serves as a cautionary note and calls for careful follow-up assessment, at least in the intermediate term, to ensure that no problems with AV conduction evolve.

Due to the retrospective nature of our study, which included five American pediatric centers, a uniform methodology was not available to enable analysis of its impact on success or recurrence rates. Also, different modes of mapping are used at these centers.

The choice between RFA and cryoablation was determined by the operator based on many factors including experience and equipment availability. In most of the centers included in this report, cryoablation is the default choice for catheter ablation of pediatric patients with AVNRT. These biases could not be excluded from our retrospective study.

This study also was limited by restricted data set variables available for analysis. Anecdotally, we noted a larger number of lesions during certain difficult cases that had recurrence. Enhanced safety with cryoablation may have influenced persisting endeavors from the operator in such cases. Full follow-up data were available for only 246 of 368 patients, which may have introduced bias into the results. It is likely, however, that those patients who had an arrhythmic recurrence would have been more likely to return for medical attention than those without recurrences. Therefore, the recurrence rate may be even lower than described in this report.

A further possible limitation of this retrospective study was that the 4-mm-tip catheter was used more frequently in the early portion of the study period. The possibility exists that the additional operator experience later in the study contributed to improved outcomes. A similar trend of improvement in efficiency with RFA was noted early after its introduction [22]. Our study results suggest that with more procedural experience, the efficacy and recurrence rates for cryoablation may mirror those of RFA.

Conclusion

In this largest review of cryoablation use with pediatric patients to treat AVNRT to date, the success and recurrence rates are similar to those for RFA use. A lower recurrence rate for AVNRT after cryoablation using a 6-mm-tip catheter was demonstrated as well as an associated excellent safety profile. This experience suggests that the 6-mm-tip catheter can be used safely and effectively in children.

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