Europace (2009) **11**, 630–634
doi:10.1093/europace/eup045

'Time to effect' during cryomapping: a parameter related to the long-term success of accessory pathways cryoablation in children

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Received 21 October 2008; accepted after revision 31 January 2009; online publish-ahead-of-print 5 March 2009

Aims Cryoablation is an effective treatment for children with an accessory pathway (AP). Nevertheless, AP may recur after a successful procedure. The aim of this study was to identify the factors predictive of AP recurrence.

Methods and results Thirty patients (mean age 12.6 ± 2.9 years) with acutely successful cryoablation of supraventricular tachycardia caused by a right-sided AP were studied. In 20 patients, a lengthier cryoablation and a single 'bonus' cryoapplication to consolidate a permanent lesion were delivered. During the follow-up (mean duration 20 months, range 4–25), no permanent cryo-related complications occurred. Accessory pathway recurrence was observed in six patients (20%) overall, specifically in 30% of patients who did not undergo a bonus cryoapplication and in 15% of the others. The likelihood of AP recurrence was correlated with the 'time to effect' (TTE), i.e. the time interval between the onset of cryomapping at −30°C and the disappearance of AP conduction. The mean TTE in the patients without AP recurrence was 8.2 ± 8.4 s, in contrast with 16.7 ± 9.8 s in the others ($P = 0.04$). The receiver-operating characteristic (ROC) curve of TTE values demonstrates that if the pathway does not lose its conduction capacity until 10 s after reaching −30°C, the probability of arrhythmia recurrence is higher (area under curve = 0.767, sensitivity 83.3%, and specificity 66.7%).

Conclusion The long-term success of cryoablation of right-sided AP is closely correlated to the TTE during cryomapping.

Keywords Supraventricular tachycardia • Accessory pathway • Children • Cryoablation

Introduction

Cryoablation is a very safe and effective technique for the definitive treatment of reciprocating supraventricular tachycardia (SVT) in children, particularly those where the re-entry circuit is very close to the atrio-ventricular (AV) junction.[1–6] The benefit of this system over radiofrequency ablation is its ability to find the most suitable site for the ablation through a transient, reversible loss of electrical function in the area of interest frozen to −30°C (cryomapping). Moreover, the stability of the catheter tip, which adheres to the myocardium, enables arrhythmia inducibility through programmed atrial stimulation to be assessed without dislodging the catheter. A permanent lesion is created only subsequently, with further temperature lowering (cryoablation). Both the benefits and any unwanted effects can thus be assessed in the cryomapping stage and, if necessary, cryoenergy application can be stopped before any permanent damage is caused.

So far, cryoablation has shown better results in the definitive treatment of AV nodal re-entry tachycardia than of accessory pathways (APs).[1–5] The last 3 years have also demonstrated an increased acute success rate with the introduction of new cryoablation protocols.[7] Nevertheless, the high acute success rate is complicated by a significant number of recurrences and improvements in long-term cryoablation success rates are thus required.

This retrospective study was conducted in order to identify those factors able to predict long-term success after an acutely successful cryoablation of a right-sided AP.

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Methods

Patient population

Since January 2003, 31 paediatric patients with SVT caused by an AP have undergone cryoablation in our Institution.

Patients were selected for cryotherapy: (i) in the case of a manifest AP and ECG characteristics of the delta wave predictive of an ablation site close to the AV junction or (ii) in the case of a concealed AP when electrophysiological mapping during the ablation procedure identified the optimal ablation site very close to the AV junction.

Cryoablation was ineffective in only one patient, who had a concealed anterior-septal AP. The other 30 patients (96.8%), 16 males and 14 females (mean age 12.6 $\pm$ 2.9 years, range 5–17), in whom cryoablation was acutely successful were therefore enrolled for this study.

Among these patients, 29 had a manifest AP and 1 a concealed AP. The AP site was anterior-septal in 15 patients, right lateral in 3, posterior-septal in 3, para-Hisian in 2, and mid-septal in the remaining 7. In one of these, two other APs were present: one right anterior and the other right lateral. Only three patients had previously been unsuccessfully treated with radiofrequency in other Institutions.

Cryoablation system

The cryoablation system consists of a central console (Cryo Console, CryoCath Technologies Inc., Kirkland, Canada) and a steerable 7 FR catheter (Freezor®, CryoCath Technologies Inc.) with a 4 mm tip electrode using N_2O as refrigerant fluid. The cryoablation system has already been described.[8]

Cryomapping

Cryomapping was performed in all cases as described in detail in previous studies.[3,7] In brief, the tip temperature was progressively reduced to -30°C for a maximum of 60 s and the cryomapping was considered positive when loss of ventricular preexcitation or interruption of SVT was observed.

The 'time to effect' (TTE), i.e. the time interval between the onset of cryomapping at -30°C and the disappearance of AP conduction, was calculated for every successful cryomapping that preceded the definitive successful cryoablation. Time to effect was considered as 0 when AP conduction disappeared before or immediately on reaching the temperature of -30°C.

Cryoablation

The ablation procedure for these SVTs was performed as already detailed elsewhere.[3,7] A brief description follows: *manifest ventricular preexcitation*—the site of earliest ventricular activation was identified during sinus rhythm. Cryomapping was then performed and, if there was a sudden loss of ventricular preexcitation, a full cryoapplication was delivered to create a permanent irreversible lesion; *concealed APs*—the tricuspid annulus area was mapped during AV re-entrant tachycardia and the site of earliest retrograde atrial activation was identified. Cryomapping was performed at this site and, if a sudden interruption of SVT in retrograde conduction was observed, it was followed by permanent lesion formation.

In 10 patients, cryoapplications were delivered to create a permanent lesion at -75°C for a minimum of 4 min up to a maximum of 8 min. During cryoablation, surface ECG and endocavitary signals were continuously monitored. If conduction recurrence or arrhythmia induction was apparent, the catheter was repositioned at an adjacent site and cryomapping was repeated. In the last 20 patients, our modified ablation protocol, described in detail elsewhere,[7] was used. In brief, cryoapplication was always $>$6 min and, if successful, a single 'bonus' cryoapplication (-75°C for a minimum of 6 min) was delivered to consolidate the lesion.

A post-ablation electrophysiological study at baseline and during isoproterenol infusion was performed immediately and after 30 min in all cases in order to demonstrate complete and persistent interruption of conduction over the AP and/or the non-inducibility of SVT. In all cases, there was a total waiting time of 45 min after the successful cryoablation in order to check any subtle changes in the ECG potentially predictive of preexcitation recurrence.

Post-ablation assessment

An echocardiogram was performed 24 h post-procedure in all patients. In addition, patients had a physical examination and ECG prior to discharge. Arrhythmia recurrence was documented by ECG and patient diary records. In detail, patients were checked 1, 3, and 6 months after cryoablation by a clinical evaluation and standard ECG, then after 1 year and every year thereafter by Holter monitoring and exercise stress testing.

Statistical analyses

SPSS (version 12.0) and MedCalc statistical softwares were used for all descriptive and inferential statistical analyses. A Mann–Whitney test was used for group comparisons of procedure characteristics. The significance level was set at $P = 0.05$.

The receiver-operating characteristic (ROC) curve[9] was calculated using every single TTE value, i.e. the time interval from onset of cryomapping to loss of AP conduction, with the goal of finding a cut-off time for more probable recurrence of SVT.

Results

A total of 188 cryomaps were attempted with an average of 6 cryomaps (range 3–16) per patient. In all patients (except one) with manifest ventricular preexcitation, loss of preexcitation was sudden during successful cryomapping. In the patient with gradual loss of preexcitation, it took $\sim$15 s for the total disappearance. A total of 82 cryoablations were attempted with an average of 2.5 $\pm$ 1 (range 2–6) per patient. The mean cryoablation temperature was $-76 \pm 4^{\circ}$C (range -68 to -80°C) with a mean duration of 422 $\pm$ 53 s for the first successful irreversible lesions. During the waiting period after successful cryoablation, no subtle ECG changes that might be predictive of recurrence of AP conduction were noted in any patient. There were no permanent cryo-related complications or adverse outcomes.

During a mean follow-up of 20 months (range 4–25 months), a recurrence of AP conduction was observed in 6 of 30 (20%) acutely successful procedures, specifically in 3 of 10 (30%) patients treated by the standard protocol and 3 of 20 (15%) of the others (P = NS). All these patients had a manifest AP, which was anterior-septal in four patients, mid-septal in one, and posterior-septal in the other. Accessory pathway recurrence was seen within the first 24 h in five patients and after 1 month of follow-up in one. The latter was the patient with a gradual loss of preexcitation during cryomapping, who had a mid-septal AP.

Age, sex, weight, AP site, average cryoablation temperature, and the mean duration of first successful cryoablation were not significantly different between patients who did and those who did not experience arrhythmia recurrence during follow-up. The

Table 1 Descriptive statistics and *P*-value of individual, electrophysiological, and ablation characteristics, and TTE during cryomapping of patients with and without AP recurrence during the follow-up

Parameters	Pts without AP recurrence (*n* = 24, 26 AP)	Pts with AP recurrence (*n* = 6)	*P*-value
AP site	11 RAS, 6 MS, 3 RL, 2 RPS, 2 PH, 1 concealed RAS, 1 concealed RL	4 RAS, 1 MS, 1 RPS	NS
Age (years): mean ± SD (range)	12.8 ± 2.8 (7.6–17)	11.8 ± 3.5 (5.1–14.2)	NS
Weight (kg): mean ± SD (range)	53.4 ± 12.2 (28.5–70)	43.8 ± 13.2 (26–55)	NS
Sex	13 M, 11 F	3 M, 3 F	NS
Cryoablation temp (°C): mean ± SD	−76.3 ± 4.7	−75 ± 3.5	NS
Duration of 1st successful cryoablation (s): mean ± SD (range)	423 ± 54 (300–480)	395 ± 82 (270–480)	NS
Standard/modified protocol (*n*)	7/17	3/3	NS
TTE (s): mean ± SD (range)	8.2 ± 8.4 (0–24)	16.7 ± 9.8 (0–26)	0.04

AP, accessory pathway; MS, mid-septal; *n*, number; NS, not significant; PH, para-Hisian; Pts, patients; RAS, right anterior-septal; RL, right lateral; RPS, right posterior-septal; SD, standard deviation; TTE, time to effect.

probability of SVT recurrence was statistically related to the TTE only (for details, see *Table 1*).

Moreover, the ROC curve of TTE values demonstrated that if the AP does not lose its conduction capacity until 10 s after reaching −30°C, the probability of arrhythmia recurrence is higher [area under curve = 0.767; sensitivity (83.3%), and specificity (66.7%), see *Figure 1* and *Table 2*]. Accessory pathway recurrence was observed in 1 patient (who received a bonus cryoapplication) out of 17 (5.9%) when AP conduction disappeared within 10 s of reaching −30°C and in 5 patients (3 who did not receive a bonus cryoapplication and 2 who did) out of 13 (38.5%) when the TTE was longer than 10 s.

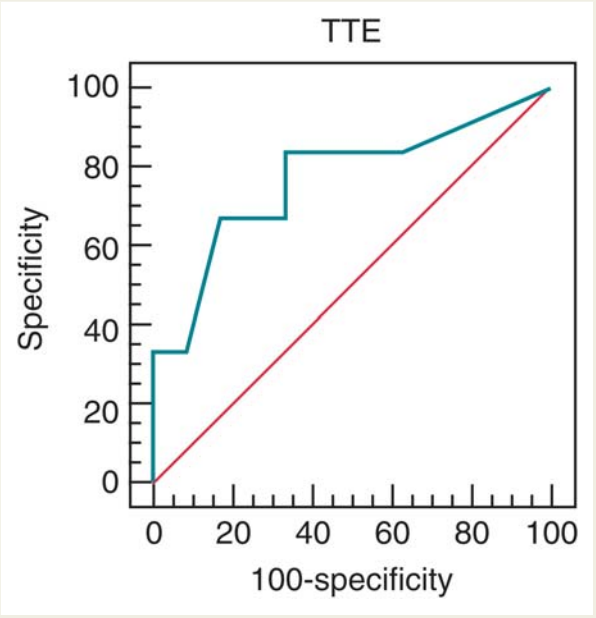

Figure 1 Receiver-operating characteristic curve: profile was obtained by plotting sensitivity and 1-specificity values of each 'time to effect' to predict the probability of long-term accessory pathway conduction recurrence.

Discussion

The first study of transcutaneous transcatheter cryoablation in the treatment of paediatric SVT was conducted by Gaita *et al.*[6] in 2004. Four patients with a mean age of 15 ± 4 years with permanent junctional reciprocating tachycardia refractory to antiarrhythmic drugs were subjected to cryoablation, with 100% acute success rate and 75% long-term success rate.

To date, the literature has reported acute success rates ranging from 55% to 100% and long-term failures during follow-up ranging from 0% to 52%. Cryo-related complication rate or adverse outcomes range from 0% to 4% and a permanent AV block has never been reported.[1–5,7,10–13]

In our already published experience,[7] the use of a modified protocol consisting of lengthier cryoablation and the supply of a bonus cryoapplication to consolidate the acutely successful irreversible lesion[7] increased both the acute (100%) and long-term success rate (80%), without any further complications in the ablation of AP very close to the AV junction.

In this study, the acute and long-term success rate of paediatric cryoablation is comparable to that reported by the Paediatric Radiofrequency Ablation Registry for radiofrequency ablation.[14,15]

Recently, Theuns *et al.* recently reported that the temperature time constant—which is reflected in the time interval between the onset of ice mapping and the steady-state mapping temperature of −30°C and is therefore an indication of electrode contact with the endocardium—was significantly shorter during successful ice mapping than unsuccessful ice mapping. Furthermore, the response time to a mapping temperature of −30°C, calculated as the interval between the onset of ice mapping and the onset of steady-state mapping temperature, was significantly longer in unsuccessful ice mapping attempts. However, Theuns' study, in contrast with our own, was conducted mostly in adult patients (only three patients were <18 and >15) and investigated whether the time course of temperature during ice mapping of the

Table 2 Sensitivity and specificity of each TTE value for probability of arrhythmia recurrence after acute successful cryoablation

Recurrence (%)	20	
Area under the ROC curve	0.767	
TTE (s)	Sensitivity (%)	Specificity (%)
=0	100	0
>0	83.33	37.5
>2	83.33	41.67
>5	83.33	50
>7	83.33	54.17
>10[a]	83.33	66.67
>11	66.67	66.67
>13	66.67	70.83
>16	66.67	75
>17	66.67	83.33
>18	50	87.5
>20	33.33	91.67
>23	33.33	95.83
>24	33.33	100
>25	16.67	100
>26	0	100

[a]Cut-off time for higher probability of arrhythmia recurrence.

AP would predict a successful outcome. Furthermore, this study addressed the acute success rate only, with no attention to long-term success. Even so, the data obtained in that very small patient population (12 patients) demonstrated that the time interval between the onset of ice mapping and the disappearance of AP conduction was significantly shorter in acutely successfully ablated AP than in unsuccessfully ablated AP.[16]

In a more recent study, Kaltman *et al.*[17] evaluated the time and temperature profile for successful cryoablation for right-sided AP. They decided, without the use of cryomapping, to continue cryoablation at -80°C for 240 s if AP was successfully interrupted within an empirical cut-off time of 25 s. In this way, they were able to demonstrate that critical TTE (time interval from cryoadherence to loss of AP conduction) during cryoablation was significantly shorter for permanently successful cryolesions, compared with transiently successful lesions (6.3 ± 4.1 vs. 11.2 ± 2.2 s, $P < 0.001$). The success rate was 96% and during a mid-term follow-up (7.6 ± 3.8 months), the recurrence rate was 4%.

In contrast to these studies, our study was conducted in order to identify which factors are able to predict the long-term success of an acutely successful cryoablation of a right-sided AP in children, and the time interval from cryoadherence to loss of AP conduction was only evaluated during cryomapping (TTE). In this respect, our data showed that AP recurrence, over an almost 2-year mean follow-up, showed no correlation with patients' age or sex, the cryoablation time, or the site of the AP, but was correlated with a longer TTE only. The gradual loss of AP conduction was also predictive for an unsuccessful ablation in the long-term, in accordance with the data reported by other authors,[18] but this was seen in one patient only and is clearly not statistically significant.

The ROC[9] curve of TTE values demonstrated that if the pathway loses its conduction capacity during freezing and in any case within 10 s of reaching -30°C, the probability of arrhythmia recurrence seems to be extremely low. In fact, recurrence of AP conduction was observed in 20% of cases overall but in only 5.9% of cases where TTE during cryomapping was <10 s. This is probably a result of the extreme vicinity of the cryoablation catheter tip to the AP in the selected ablation site, as suggested by Gaita *et al.*[13]

Anatomical features such as the AP's thickness and the depth of penetration into the myocardium may explain the long-term failure of an acutely successful cryoablation with a long TTE during cryomapping. In these cases, the use of a larger cryocatheter tip might be more effective. In fact, the only patient who experienced SVT recurrence in the group with a short TTE during the acutely successful procedure was successfully retreated with a 6 mm tip catheter in the same site, and on that occasion too, the TTE was very short (7 s).

In conclusion, in our opinion, cryoablation should be considered an effective treatment for SVT caused by right-sided AP in school-age children, especially if the AP is located in the para-Hisian, anterior-septal, or mid-septal region. In this respect, the long-term efficacy of cryotherapy is closely correlated with the sudden block of AP conduction within 10 s of reaching -30°C during cryomapping.

Conflict of interest: none declared.

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