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Impact of cryoablation catheter size on success rates in the treatment of atrioventricular nodal re-entry tachycardia in 160 patients with long-term follow-up

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Aims To determine the efficacy and safety of cryoablation for the treatment of atrioventricular nodal re-entry tachycardia (AVNRT).
Methods and results We analysed the procedural characteristics, acute success, and recurrence rates of 160 consecutive patients treated with cryoablation for the AVNRT and followed up for 18 months. Mean procedural time was 119.1 $\pm$ 3.7 min, with an average of 4.6 $\pm$ 0.2 Cryo lesions and an acute procedural success rate of 93%. Recurrence rates were 19 (11.9%) cases and were significantly higher in the 4 mm cryocatheter-treated group (12/59, 16.9%), compared with the 6 mm cryocatheter-treated group (9/101, 6.9%, $P = 0.01$). Recurrence rates were greater where slow pathway block was not achieved 8/12 (66.7%), compared with complete slow pathway block 11/129 (8.5%, $P < 0.0001$). Recurrence was significantly more likely if atrial echo beats were still present after cryoablation, 12/130 (9.2%) patients with no recurrence vs. 7/19 (36.8%) patients with recurrence ($P < 0.0001$).
Conclusion Cryoablation is a safe and efficacious treatment for AVNRT. Complete slow pathway block is associated with long-term success, together with the use of the larger 6 mm cryocatheter. There is always a risk of heart block with radiofrequency ablation, although this experience confirms previous findings that the risk with Cryo is zero.

Introduction

For several years, radiofrequency (RF) ablation has been the treatment of choice for patients with atrioventricular node re-entry tachycardia (AVNRT) especially, when medical therapy has either failed in the short-term or is not preferred in the long-term.[1] Despite being safe and highly efficacious with low recurrence rate, RF ablation can cause pain, thrombo-embolic events, cardiac perforation but more importantly inadvertent irreversible atrioventricular (AV) block necessitating implantation of a permanent pacemaker.[2] For many young patients with Supraventricular tachycardia, this risk, even if estimated at 1–2%, significantly hinders the uptake of this form of treatment. Catheter cryoablation is not associated with these adverse effects and particularly reduces the risk of permanent pacemaker.[3–5] By utilizing the technique of cryomapping, an intermediate temperature is used to create a reversible lesion at preferred slow pathway sites before the development of a permanent lesion, thereby avoiding permanent loss of electrical activity. However, compared with RF ablation, the short- and long-term success of cryoablation has been reported to be lower.[6] In this study, we assess the effectiveness of cryoablation as an effective ablative treatment of AVNRT in a large group of patients with long-term follow-up and determine predictive factors for success.

Methods

A total of 160 consecutive patients undergoing cryoablation for AVNRT from July 2003 to April 2006 were followed up for 18 months. Anti-arrythmic drugs were stopped at least 5 days before the procedure. A standard 4-wire electrophysiology study was performed to diagnose AVNRT, confirmed by the presence of dual AV nodal physiology. Tachycardia was initiated during programmed atrial extrastimulation with or without the administration of isoprenaline. Atrioventricular nodal re-entry tachycardia was confirmed by earliest retrograde activation during tachycardia at the His catheter with failure to reset atrial activation with His synchronous ventricular paced beats. The procedure was deemed success if a

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complete slow pathway block was achieved or in the presence of single atrial echo beats with no inducible tachycardia with isoprenaline, where the tachycardia was initially easily inducible.

Cryoablation was performed with either 4 or 6 mm tip catheters (Freezor™ and Freezor Xtra™, respectively; Cryocath Technologies, Montreal, Canada). Potential slow pathway sites were mapped initially at a temperature of -30°C for up to 60 s and then ablation performed at -80°C for 2 min if no prolongation of AH interval was seen. Programmed atrial stimulation was then performed to determine the slow pathway block, echo beats, or induction of AVNRT. Cryoablation was then continued at -80°C for 4 min if the slow pathway block or echo beats were evident. This was undertaken with fluoroscopy screening at regular intervals during the freeze time to ensure the stability of the catheter position. Further sites were mapped if slow pathway block was not achieved or if tachycardia was induced. Cryolesions were repeated until either complete slow pathway block or single atrial echo beats only were initiated together with non-inducibility of AVNRT with pacing and isoprenaline. Radiofrequency was then used to complete slow pathway ablation if cryoablation failed and time permitted.

All patients were followed up for a minimum of 18 months, using a postal questionnaire for cryoablation patients at 3, 12, and 18 months enquiring about the recurrence of symptoms with or without outpatient clinical review together with telephone follow-up if required. All patients with recurrence had cardiac monitoring to confirm the presence of AVNRT and were offered a repeat procedure.

Results are expressed as the mean $\pm$ SEM except age (mean $\pm$ SD). Continuous data were compared using Student's *t*-test or Mann–Whitney *U*-test. All other categorical data were analysed using the χ^2 test. Statistical analysis was performed using SPSS for windows version 14.0. *P*-values less than 0.05 were considered significant.

Results

All the 160 patients undergoing ablation for AVNRT had normal structural heart except one patient who had dilated moderately impaired left ventricular systolic function. These patients treated with cryoablation resulted in an acute procedural success rate of 149 (93%), with five patients requiring additional RF ablation (three because of cryocath console failure) to achieve success and there were six failures (tachycardia still inducible). Of the 19 patients with recurrence following cryoablation, 7 underwent successful repeat cryoablation (included in the group), 5 underwent successful RF ablation, with other patients controlled on medication or deciding about repeat procedure. Complications included 1 femoral haematoma, 2 vasovagal episodes, and 13 episodes of transient AV block (initially third degree of no longer than 30 s proceeding to second degree then first degree) of <2 min total duration after re-warming, but no patient required a permanent pacemaker either in the early or late post-procedural phase.

Table 1 Characteristics of cryoablation group

	Cryoablation ($n = 160$)
Age	44.2 ± 15.0
Sex (M/F)	42/118
Proc time (min)	119.1 ± 3.7
Screening (min)	17.0 ± 1.0
Fluoro dose (cGy^2)	28.9 ± 2.6
Number of lesions	4.6 ± 0.2
Acute success	149 (93.1%)
Slow pathway block	129
Echo beats	19 (11.9%)
Non-inducibility	1 (0.63%)
Recurrence[a]	19 (11.9%)
Pacemaker	0

[a]Does not include acute failures (cryoablation six with five converted to RF).

Proc time, procedure time from local to skin until catheter withdrawal.

In order to determine procedural factors that could affect outcome, we compared patients with and without recurrence. In the cryoablation group, patients were evenly aged and sex matched (*Table 2*). There were no significant differences in procedure time, freeze time, or number of lesions. Despite increased screening times for patients who suffered recurrence compared with those having no recurrence [16.9 (1.5) vs. 22.6 (2.8) min $P = 0.03$], there was no difference in fluoroscopy dose [26.4 (2.2) vs. 41.5 (9.1) cGy^2, $P = 0.243$]. Recurrence was significantly more likely to occur without complete slow pathway block, 8/19 (42% recurrence group) vs. 12/130 (9.2% non-recurrence group) ($P < 0.0001$). Similarly, the presence of echo beats following cryoablation was significantly more greater in the recurrence group when compared with the non-recurrence group [7/19 (36.8%) vs. 12/130 (9.2%), $P < 0.0001$].

Further, we analysed the cryoablation data according to catheter tip size (*Table 3*). For both the 4 and 6 mm catheter, groups were well matched for age and gender. All other variables were not significantly different: procedure time, fluoroscopy dose and time, the number of lesions together with freeze time, and incidence of slow pathway block/echo beats and non-inducibility. However, there was a significant increase in recurrence rates in the 4 mm catheter tip group when compared with the 6 mm catheter tip group (12/59, 16.9% and 7/101, 7%, respectively, $P = 0.01$).

Discussion

Our data confirm that cryoablation is a safe and suitable alternative treatment for AVNRT. Our data are also in keeping with the majority of published literature on cryoablation for AVNRT with high acute success of 93% with 11.9% recurrence rate when compared with other studies ranging from 85 to 99% for acute success together with ~10–38% recurrence rate.[1,5–11] The strength of our results is suggested by the larger sample size of 160 patients, compared with the other above studies with the longest follow-up period of 18 months. Where two previous studies have directly compared RF and cryoablation for AVNRT, our Cryo results are similar confirming the marginally lower acute success rate (98 and 97% for RF, 97 and 84.6% for Cryo) but higher recurrence rate for cryoablation vs. RF ablation (19.8 and 8% vs. 5.6 and 1%).[6,7] Nevertheless, the safety profile means that cryoablation is still our preferred treatment of choice for this tachycardia.

Increased safety is one of the major benefits and differences between Cryo and RF ablation with regard to pacemaker implantation for inadvertent complete heart block, further strengthening our choice of cryoablation. There were no cases of prolonged AV block with cryoablation. Published data suggest a risk of 1–2% for inadvertent complete heart block with RF or marginally higher in our unpublished

Table 2 Comparison of cryoablation patients with and without recurrence of tachycardia

	No recurrence[a,b] ($n = 130$)	Recurrence[a,b] ($n = 19$)	*P*-value
Age	44.0 ± 14.7	45.2 ± 17.0	0.8
Sex (M/F)	30/100	12-Jul	0.194
Procedure time (min)	115.4 ± 3.6	135.7 ± 11.6	0.126
Screening (min)	16.9 ± 1.5	22.6 ± 2.8	0.03
Freeze time (s)	1193 ± 47	1566 ± 232	0.334
Fluoro dose (cGy^2)	26.4 ± 2.2	41.5 ± 9.1	0.243
Number of lesions	4.4 ± 0.2	5.8 ± 0.9	0.378
Slow pathway block	118 (90.8%)	11 (57.9%)	<0.000
Echo beats	12 (9.2%)	7 (36.8%)	<0.0001
Non-inducibility	0	1 (5.3%)	0.013

[a]Does not include five patients converted to RF.
[b]Does not include acute failures (cryoablation six patients).

Table 3 Comparison of cryoablation patients by catheter size

	Cryotip 4 mm ($n = 59$)	Cryotip 6 mm ($n = 101$)	*P*-value
Age	43.5 ± 11.4	44.6 ± 16.8	0.5
Sex (M/F)	Sep-50	33/68	0.1
Procedure time (min)	127.54 ± 7.4	113.2 ± 3.5	0.342
Screening (min)	19.5 ± 3.0	16.8 ± 1.2	0.597
Fluoro dose (cGy^2)	28.1 ± 4.1	29.2 ± 3.0	0.843
Number of lesions	4.7 ± 0.4	4.6 ± 0.2	0.697
Freeze time (s)	1251 ± 106	1252 ± 61.2	0.55
Slow pathway block	45 (76.7%)	84 (83.2%)	0.12
Echo beats	8 (13.6%)	11 (10.9%)	0.6
Non-inducibility	1 (1.7%)	0	0.19
Procedure outcome[a]	54 (91.5%)	95 (94.1%)	0.12
Failures	4 (6.8%)	2 (2%)	0.58
Recurrence[b]	12 (16.9%)	7 (6.9%)	0.01
Convert to RF	1 (1.7%)	4 (4.0%)	0.42

[a]Does not include patients converted to RF.
[b]Does not include acute failures (cryoablation six patients).

observations of 3.5%. This may be due to the following factors. The cryocatheter enables increased stability as the tip of the catheter adheres to the endocardium when the lesion develops, compared with the RF catheter that moves with the heartbeat and respiratory movements.[12] The predominant rhythm change during RF energy applications includes accelerated junctional rhythm during which the presence of ventriculoatrial block can be a harbinger of AV block such that even if energy is halted promptly, inadvertent block can still occur. This compares with cryoablation where the rhythm can be easily monitored with atrial pacing during junctional rhythm which is not a precursor to the AV block. Also, the development of AV block is more likely to be permanent with RF energy but is completely reversible on re-warming with cryoablation. Therefore, utilizing cryoablation appears to eliminate the risk of permanent pacemaker due to the inadvertent AV block. The rate of the AV block varies between centres; although small, nevertheless, can have a devastating effect when it occurs. As a result, the curative effects of ablation can be opened to a larger group of patients, with results equally good to those achieved with RF.

Cryoablation catheter tip size was the most interesting predictive factor for long-term recurrence. Our data showed that recurrence was more likely when using the smaller 4 mm Cryotip catheter when compared with the 6 mm catheter. This strengthens the results of De Sisti *et al.*,[11] as we compared significantly more patients in each group (59 vs. 101, compared with their 8 vs. 61). It has been suggested that the size and number of lesions may be predictive of recurrence.[12] Although the number of lesions and total freeze time were similar between the two catheters, it is likely that the 6 mm tip produces a larger lesion that is deeper and, therefore, more effective. This has been confirmed in recent animal studies, in which 4 and 8 mm cryocatheters delivered cryoablation to porcine ventricular myocardium in a saline bath. Lesion sizes and tissue temperatures were related to electrode size and also to electrode orientation and contact pressure. Electrode temperature was a poor predictor of lesion size, whereas time to cryoablation electrode rewarming was a better predictor.[13,14] The success of a larger lesion size may be suggested in our results by the higher, but not significant, elimination of slow pathway conduction in the 6 mm group together with the

presence of more atrial echoes in the 4 mm group that again does not reach statistical significance. This may require further investigation to provide an insight into the mechanism of relative failure of the 4 mm cryocatheter to include other variables utilized in the animal studies.

The importance of attaining complete slow pathway block is suggested by the significantly lower recurrence rates where complete slow pathway block was achieved. Loss of slow pathway conduction, therefore, seems to predict long-term outcome compared with either sustained single atrial echo beats or non-inducible tachycardia similar to that seen by Gupta *et al*.[7] We also confirmed higher recurrence rates in patients with persistent atrial echo beats after cryoablation, which is a new finding and different from that which occurs with RF ablation. This may be due to differences in lesion characteristics where RF lesions develop further after RF energy is delivered, with fibrosis and vascular damage, hence the risk of delayed AV block, while Cryo lesions contract with time.[12,15] During cryoablation, therefore, the abolition of any residual slow pathway would be the most important to achieve long-term success.

This study has its limitations though. Patients treated with the 4 and 6 mm cryocatheter were not randomized to treatment, even though both groups were evenly age- and sex-matched with a potential for time lag and bias. Although the 4 mm cryocatheter was introduced first, we therefore cannot exclude a learning curve effect that could have contributed to this difference. However, each of the operators has $>$10 years of experience for ablation for AVNRT with many RF cases performed before the Cryo study period commenced. Also, the technique used in identifying potential slow pathway ablation sites did not differ for both forms of ablation.

In conclusion, our single centre results are the largest series of patients undergoing cryoablation with long-term follow-up. We therefore suggest that cryoablation is a safe and efficacious alternative to RF ablation for the treatment of AVNRT. These results also suggest the importance of achieving slow pathway block to improve success together with the larger 6 mm cryocatheter. The failure to cause inadvertent complete AV block in our patients compared with published data for RF energy suggests that cryoablation is a safer alternative that has formed our choice for ablation for AVNRT.

Conflict of interest: none declared.

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