ORIGINAL ARTICLE

Transcatheter ablation of atrioventricular junctional re-entrant tachycardia in children and adolescents in Hong Kong: comparison of cryothermal with radiofrequency energy

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Objective To compare the outcome of cryothermal and radiofrequency energy transcatheter ablation of atrioventricular junctional re-entrant tachycardia in children and adolescents.

Design Case series with internal comparison.

Setting Two hospitals in Hong Kong.

Patients Consecutive transcatheter ablation procedures for atrioventricular junctional re-entrant tachycardia in children and adolescents in our unit from August 2000 to September 2008 were retrospectively reviewed. Radiofrequency ablation was performed from August 2000 to June 2005, and cryoablation from July 2005 to September 2008.

Main outcome measures Demographic data, outcome and procedural details.

Results Thirty-eight procedures were reviewed. The radiofrequency ablation group (n=20) and cryoablation group (n=18) had similar demographic characteristics, except that there were more patients with congenital heart disease in the latter group (P=0.03). Acute procedural success rate was 100% in both groups. One patient from the radiofrequency ablation group had recurrence of atrioventricular junctional re-entrant tachycardia. The frequency of post-ablation persistent heart block was higher in the radiofrequency ablation than cryoablation group (10% vs 0%, P=0.17), but this difference was not statistically significant. A shorter fluoroscopy time was noted in the cryoablation group (31 ± 13 vs 38 ± 18 minutes; P=0.03).

Conclusions Transcatheter cryoablation for atrioventricular junctional re-entrant tachycardia in children and adolescents is as effective as radiofrequency ablation over the medium term. It has an excellent safety profile in terms of avoiding heart block.

New knowledge added by this study

- Transcatheter cryoablation for atrioventricular junctional re-entrant tachycardia in children and adolescents is as effective as radiofrequency ablation.
- The major advantage of cryoablation is the avoidance of inadvertent complete heart block.

Implications for clinical practice or policy

- In children and adolescents, cryoablation should be the choice if transcatheter ablation for atrioventricular junctional re-entrant tachycardia is being considered.

Key words
Catheter ablation, radiofrequency; Cryosurgery; Tachycardia, atrioventricular nodal reentry

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Introduction

Supraventricular tachycardia (SVT) is one of the most common cardiac arrhythmias in children and young adults. Although considered benign, frequent symptomatic SVT imposes significant adversity on quality of life. Transcatheter radiofrequency (RF) ablation was introduced in late 1980s as a definitive treatment for SVTs in adult patients. With growing experience, RF ablation has also become the standard treatment for symptomatic SVT in children.[1] Radiofrequency ablation has excellent efficacy, with acute success rates ranging from 95 to 100%.[1-3] However, when RF energy is applied close to the atrioventricular node (AVN) to ablate atrioventricular junctional re-entrant tachycardia (AVJRT) and septal pathways, the AVN may be inadvertently damaged. Published reports indicated a 1.2 to

導管消融術治療香港小童及青少年的房室交界區折返性心動過速：冷凍消融術與射頻消融術的比較

目的 比較以冷凍消融術和射頻消融術治療小童及青少年的房室交界區折返性心動過速病。

設計 病例系列的內部比較。

安排 香港的兩所醫院。

患者 2000年8月至2008年9月期間，所有因進行導管消融術而入院的房室交界區折返性心動過速病的小童及青少年患者。在2000年8月至2005年6月期間進行的是射頻消融術；而在2005年7月至2008年9月期間進行的是冷凍消融術。

主要結果測量 人口學數據、治療結果及手術資料。

結果 研究期間共進行了38次消融術，射頻消融術20例，冷凍消融術18例。冷凍消融術組別有較多患者有先天性心臟病（P=0.03）；除此以外，兩組都有類似的人口特徵。兩組均有100%的手術成功率。射頻消融術組別的其中一名患者有復發。比較兩組的結果，射頻消融術組別於術後發生持續性房室傳導阻滯的頻率較高（10%比0%），但差異未達顯著性（P=0.17）。冷凍消融術組別則有較短的透視時間（31 ± 13比38 ± 18分鐘；P=0.03）。

結論 導管冷凍消融術治療小童及青少年的房室交界區折返性心動過速的中期結果可媲美射頻消融術。在防止房室傳導阻滯方面，導管冷凍消融術相當安全。

2.6% risk of heart block.[3,4] In order to reduce the risk of heart block, transcatheter ablation using a safer alternative energy was desirable. In this context, application of cryothermal energy can be titrated to a temperature that results in only reversible interruption of cellular function. With this technique, ablation at critical sites that result in inadvertent heart block can therefore be avoided.[5-7]

In 2004, the first case series of successful transcatheter cryoablation of accessory pathways was reported in paediatric patients.[8] Subsequent reports have also demonstrated satisfactory efficacy for the treatment of paediatric AVJRT.[5,7] In our centre at Grantham Hospital, we have performed transcatheter RF ablation for paediatric SVT since 1994. Moreover, ours is the only centre in Hong Kong providing electrophysiological study (EPS) and transcatheter ablation for paediatric patients. The overall risk of transient and permanent AVN damage is 7.6%. Since August 2005, we started using cryothermal energy for transcatheter ablation of AVJRT. The purpose of this study therefore was to compare the outcomes of cryothermal and RF energy used for transcatheter ablation of AVJRT.

Methods

Study population

Retrospectively, we reviewed consecutive transcatheter ablation procedures for AVJRT in our centre from August 2000 to September 2008. Patients were considered for transcatheter ablation if the tachycardia was symptomatic and not satisfactorily controlled by oral anti-arrhythmic medications, or long-term drug treatment was not accepted by the patient. Patients were divided into two groups. The first group consisted of RF ablation procedures performed from August 2000 to June 2005 before cryoablation was available. The second group consisted of cryoablation procedures, which were all performed from July 2005 to September 2008.

Description of procedure

Written informed consent was obtained prior to the procedure. All anti-arrhythmic medications were discontinued for at least 72 hours before the procedure. All procedures were performed in the fasting state. Sedation was given to patients prior to and during the procedure. Most patients received intravenous midazolam or ketamine. A standard EPS was performed before the ablation procedure to confirm the diagnosis. Four electrode catheters were used and positioned at the high right atrium, His bundle area, coronary sinus, and right ventricle (Fig). A 12-lead electrocardiogram (ECG) was recorded together with intracardiac electrograms. Standard atrial and ventricular extra-stimulus testing was

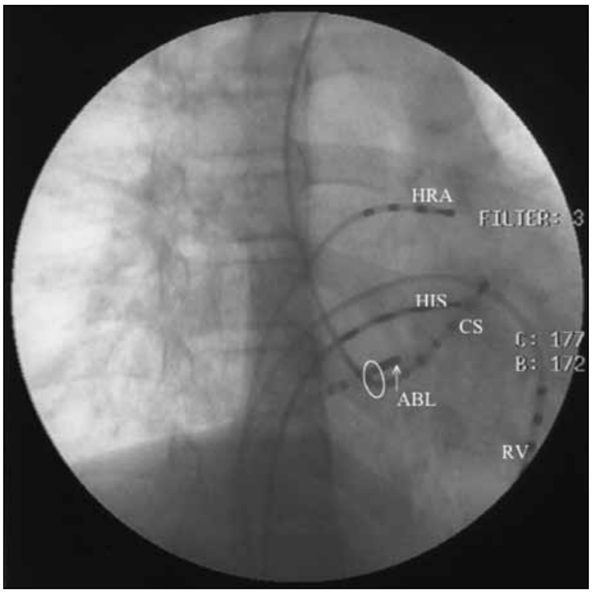

FIG. Right anterior oblique view depicting standard positions of electrodes for electrophysiological study and the initial position of the ablation catheter
The white oval depicts the ostium of the coronary sinus. ABL denotes ablation catheter, CS coronary sinus electrode, HIS bundle of His electrode, HRA high right atrium electrode, and RV right ventricular electrode

performed. Isoproterenol infusion was given if AVJRT was not induced during the extra-stimulus testing.

Cryoablation system, cryomapping, and cryoablation

A 7-French steerable cryoablation catheter (Freezor Xtra; CryoCath Technologies Inc., Kirkland, Canada) with a 6-mm tip electrode was used for cryomapping and cryoablation. The catheter consisted of four electrodes and two concentric lumens for delivery and removal of refrigerant fluid, nitrous oxide, which was supplied by a central console (CryoCath Technologies Inc., Kirkland, Canada). After confirmation of the diagnosis and determination of a reproducible protocol for AVJRT induction, the cryoablation catheter was inserted via the right or left femoral vein. Cryomapping was performed using an electrogram and an anatomic-guided approach, targeting the slow pathway of the AVJRT. The cryoablation catheter tip was initially positioned at the tricuspid-coronary sinus isthmus, just posterior or next to the ostium of the coronary sinus (Fig). Cryomapping was performed by lowering the catheter tip temperature to -30°C for a maximum of 55 seconds, during which the efficacy of cryoapplication was tested by programmed atrial stimulation to induce AVJRT, or elimination of the slow AVN pathway. During cryomapping, the AH interval was monitored to observe impairment of AVN conduction. If cryomapping was positive (ie AVJRT non-inducible), the mapping could proceed to cryoablation by lowering the catheter tip temperature to -75°C for 4 minutes. One to two 'insurance' lesions were created in close proximity to the successful cryolesion. During cryoablation, programmed atrial stimulation was continued to monitor the ablation effect and AVN conduction. If cryomapping was negative, it was stopped and the catheter tip was repositioned to a more anterior site for repeated cryomapping.

Radiofrequency system and ablation

For RF ablation of AVJRT, a 7-French steerable ablation catheter with 4-mm tip electrode (Marinr; Medtronic, Minneapolis, US) was inserted via the right or left femoral vein. The catheter was used to target the slow pathway using an electrogram and an anatomical approach similar to that for the cryoablation procedure. The RF energy was delivered at a power limited to a maximum of 30 W, and temperature limited to 60°C. If accelerated junctional rhythm indicative of a successful lesion was observed within 15 seconds, the ablation was continued for up to 60 seconds. If no effect was obtained in 15 seconds, RF ablation was terminated and the catheter was repositioned to a more anterior site and the ablation procedure was repeated. Similar to cryoablation, 'insurance' lesions were created in close proximity to successful RF ablation sites.

Post-procedural monitoring and follow-up

All patients were observed for 30 minutes after the last ablation. An EPS was performed at the end of the observation period to document the AVN conduction physiology. Induction of the AVJRT was undertaken both with and without isoproterenol infusion. The ablation was regarded as successful if AVJRT was non-inducible, or no more than a single atrial echo beat was noted during atrial stimulation in the presence of a slow pathway conduction.

An ECG was performed prior to discharge from the hospital to evaluate the PR interval. The patients were followed up in the out-patient unit at 1, 3, 6, and 12 months post-ablation, and yearly thereafter. During follow-up, patients were questioned on symptoms of recurrent SVT. An ECG was also performed to assess the PR interval. Recurrence of SVT was to be documented by a 12-lead ECG, event recorder, or 24-hour Holter-type monitoring.

Data collection

Demographic and clinical data including age at the time of cryoablation or RF ablation, gender, body weight, associated cardiac lesions, anti-arrhythmic agent use prior to the procedure, and indication for transcatheter ablation were recorded. The follow-up duration was also recorded.

The acute procedural success rate for AVJRT ablation, recurrence rate, and the time to first recurrence (defined as the interval from ablation to the episode of documented recurrence) were all recorded. Other outcome measures, including total procedural time, fluoroscopy time, and complications such as AVN conduction abnormality, were also recorded.

Statistical analyses

Descriptive data were presented in the form of mean ± standard deviation (SD). Student's *t* test was used to compare means of different groups. Categorical variables were analysed by Chi squared or Fisher's exact tests. A cut-off P value of 0.05 was taken as statistically significant. Statistical analyses were performed with the Statistical Package for the Social Sciences (Windows version 15.0; SPSS Inc, Chicago [IL], US).

Results

Demographics

During the study period, 37 patients underwent a total of 38 transcatheter ablation procedures for

AVJRT. The mean age of the patients was 14 (SD, 4) years. There were 13 males and 24 females, all of whom presented with palpitations. One patient also had dizziness during attacks of SVT. None had any syncope or any life-threatening event. Of the 38 procedures, 20 belonged to the RF ablation group and 18 belonged to the cryoablation group. One patient received two procedures. She developed recurrence of SVT 6 months after initial successful RF ablation, and 2.5 years later underwent successful cryoablation.

Both groups had similar demographic and baseline clinical characteristics (Table 1), except that all four of the patients with congenital heart disease were in the cryoablation group. Regarding the patients with congenital heart disease, two had perimembranous ventricular septal defects, one of whom had had prior surgery, and the other two had pulmonary atresia with intact ventricular septa, both of whom had had prior right ventricular outflow tract reconstructions. The RF ablation group, being a historical group, had been followed up for significantly longer time than the cryoablation group (P=0.04).

TABLE 1. Demographic data

Demographics	No. (%) of patients or mean ± standard deviation		P value
	Cryoablation (n=18)	Radiofrequency ablation (n=20)	
Age (years)	16 ± 3	13 ± 3	0.07
Body weight (kg)	48 ± 7	42 ± 18	0.07
Sex (M/F)	9/9	4/16	0.06
Anti-arrhythmic drug	10 (56%)	11 (55%)	0.61
Congenital heart disease*	4 (22%)	0	0.03
Follow-up duration (years)	2.2 ± 1.0	5.8 ± 1.4	0.04

* Two had ventricular septal defects, and two had pulmonary atresia with intact ventricular septa; all, except one with a ventricular septal defect, had received corrective surgery

TABLE 2. Comparison of outcomes and procedural details

Outcome/procedural details	No. (%) of patients or mean ± standard deviation		P value
	Cryoablation (n=18)	Radiofrequency ablation (n=20)	
Initial success	18 (100%)	20 (100%)	-
Recurrence	0	1 (5%)	0.53
Complications	0	3 (15%)	0.23
Persistent impaired AVN* conduction	0	2 (10%)†	0.17
Procedural time (mins)	172 ± 48	187 ± 59	0.41
Fluoroscopy time (mins)	31 ± 13	38 ± 18	0.03

* AVN denotes atrioventricular node

† Two patients in the radiofrequency ablation group had persistent prolonged PR interval

Acute success rate and procedural characteristics

Relevant data about the RF ablation and cryoablation groups are shown in Table 2. All 38 procedures were successful, and there was no significant difference between them with respect to total procedural time. However, the fluoroscopy time was significantly shorter in the cryoablation group (31 ± 13 vs 38 ± 18 minutes; P=0.03).

Complications

There were three procedural complications, all in the RF group and all entailed AVN conduction abnormalities. Two of these patients had persistent prolonged PR intervals (240 and 320 ms; upper normal reference limit, 200 ms). Both of these patients were asymptomatic at follow-up. One patient developed transient complete heart block during RF ablation, which resolved within 5 minutes of terminating RF energy delivery. Two patients in the cryoablation group developed transient second-degree heart block during cryomapping, which resolved soon after termination of cryomapping. These were not considered to be complications. There was no persistent AVN conduction abnormality after cryoablation. Although persistent AVN conduction abnormality was more common in the RF ablation, the difference was not statistically significant. No other complication was documented in either group.

Medium-term result

None of the patients were lost to follow-up. The mean follow-up duration was 5.8 (SD, 1.4) years for the RF ablation group and 2.2 (SD, 1.0) years for the cryoablation group. Recurrence of arrhythmia occurred in one patient 6 months after initial successful RF ablation; 2.5 years later that patient underwent successful cryoablation.

Discussion

Ablation for AVJRT by RF has been performed by modifying the relevant slow re-entry pathway. Although the efficacy of RF ablation was excellent, inadvertent heart block has been a particular concern. According to previous reports of RF ablation in children, the risk of heart block ranges from 1.2 to 2.6%.[3,4] To reduce the risk of heart block, cryotherapy has been proposed as an alternative to RF energy.

During cryoablation, transient application of a subzero temperature of around -30°C to myocardial cells results in reversible loss of electrical function. As soon as the energy application is terminated, the myocardial tissue rapidly rewarms by convective heat exchange with circulating blood and adjacent tissue vascular supply, which restores its electrical activity. This underlies the concept of cryomapping, which

TABLE 3. Paediatric case series reporting transcatheter cryoablation for atrioventricular junctional re-entrant tachycardia[2,5-7,12-18]

Study (reference no.)	No. of patients	Success rate (%)	Incidence of transient atrioventricular block (%)	Long-term complications	Mean or range of follow-up duration (months)	Recurrence (%)
Kirsh et al, 2005 (6)	30	83	0	0	3	8
Miyazaki et al, 2005 (7)	22	95.5	32	0	8.2	4.8
Kriebel et al, 2005 (12)	13	84.6	23	0	8.9	0
Drago et al, 2005 (5)	14	93	7.1	0	1-22	23
Drago et al, 2006 (15)	19	100	0	0	6-30	0
Papez et al, 2006 (17)	53	94	22.6	0	8.1	12
Collins et al, 2006 (2)	55	98	0	0	5	8
Avari et al, 2008 (13)	37	97.4	24	1/37 (2.6% with 1°HB*)	9.6	2
Chanani et al, 2008 (14)	154	95	6	0	12	14.4
Silver et al, 2010 (18)	76	91	6.5	0	11.6	2.8
LaPage et al, 2010 (16)	61	100	17	1/61 (1.6% with 1°HB)	18	6.5

* 1°HB denotes first-degree heart block

allows determination of the efficacy of the cryothermal energy application and its potential undesirable effect on AVN conduction. By performing cryomapping, sites liable to be associated with impairment of AVN conduction can be identified, and definitive ablation of such targets can be avoided.[5-7] Furthermore, during cryoablation, the catheter tip adheres to the endocardium and prevents accidental catheter tip movement towards the AVN.[9] Lesions created by cryoablation are therefore also more discrete and smaller in size than those due to RF ablation,[10,11] and as a result the risk of damaging AVN is reduced.

In our series, AVN conduction abnormalities were more frequent in the RF ablation group, although the difference was not statistically significant. By resorting to cryomapping, impaired atrioventricular conduction was detected in two patients and delivery of cryothermal energy was immediately stopped. Owing to the reversible nature of cryomapping lesions, the second-degree heart block in these patients resolved forthwith, none of whom had persistent conduction problems. In the RF ablation group, however, two of three patients with evidence of AVN conduction impairment during the procedure had persistent first-degree heart block. By contrast, the safety profile of cryoablation has been demonstrated since the earliest studies in adults and children.[5,7,9,12] In each of these reports, despite occurrence of transient AVN conduction problems during the procedures, none of them reported persistent heart block. To date, out of a total of more than 500 cryoablation procedures (including our series) reported for AVJRT in young patients,[2,5-7,12-18] there were only two instances of persistent first-degree heart block.[13,16] Although the cryoablation data only represent a small percentage of all the AVJRT ablation experience, it appears to be safe. In the future, more data from multicentre trials or international registries may provide further evidence to support the safety profile of cryoablation for AVJRT.

The initial experience with cryoablation in treating paediatric AVJRT showed a variable success (83-95%) and high recurrence rates of up to 23%.[5-7,14] These outcomes were inferior to those following RF ablation, but over the years the acute success rate has improved (Table 3[2,5-7,12-18]). Other than the learning curve effect, a number of factors contributed to the improved success rate, these included use of catheters with larger tips and different ablation strategies.

Some of the early studies that used 4-mm tip cryoablation catheters achieved success rates of less than 85%.[6] Larger-sized tips created bigger lesions and provided better targeting of the arrhythmia substrate. This was observed in a paediatric study comparing 6-mm and 4-mm tip catheters, which showed that larger tips achieved a 98% versus 93% success rate and a 9% versus 18% recurrence rate.[14] The effect of using 6-mm tip catheter in adults also demonstrated less recurrence of AVJRT (6.9% vs 16.9%).[19] In a recently published multicentre trial of paediatric cases, an 8-mm tip catheter was used with an acute success rate of 91% and recurrence rate of 2.8% over a mean follow-up of 12 (SD, 3) months.[18]

Modification of the cryoablation strategy entailed increasing the duration of energy delivery and creation of bonus or 'insurance' lesions. In a paediatric study of cryoablation for SVTs—including AVJRT—this strategy achieved an acute success rate of 100%, and recurrence rate of 10% at the 12-month follow-up.[15] Delivery of 'insurance' lesions has also contributed to the high success rates in other paediatric series.[13,15,17] In our centre, we have used the 6-mm tip cryoablation catheter in all the procedures, together with the delivery of bonus lesions around the initial successful cryoablation. Thus, our 100% acute success rate with cryoablation was similar to that in other recent studies on paediatric AVJRT.[2,13-17]

In our series there was no recurrence of AVJRT after cryoablation after a mean follow-up duration of 2.2 years. The medium-term recurrence rates were similar in the cryoablation and RF ablation groups. This has also been reported by Avari et al[13] and Collins et al[2] who compared the results of cryoablation with RF ablation for paediatric AVJRT.

In our experience, cryoablation entailed a significantly shorter fluoroscopy time than RF ablation (mean ± SD: 31 ± 13 mins vs 38 ± 18 mins; P=0.03). Similar observations have been reported by Avari et al[13] and in a study on adults.[20] In most centres, continuous fluoroscopic monitoring of the catheter position during ablation is a standard practice. For cryoablation, with the catheter tip adhering to the endocardium during energy application, the likelihood of catheter tip dislodgement is reduced, and therefore continuous fluoroscopy is not required. By reducing radiation exposure to the patient, the potential increase in lifetime risk of malignancy may be decreased, which is another possible advantage of cryoablation over RF ablation.

Putting all the evidence together, cryoablation has a similar acute success rate, but a higher recurrence rate compared to RF ablation. It offers a better safety profile and a potential of less radiation exposure, and is therefore a reasonable alternative to RF ablation in young patients.

Study limitations

Since the RF ablation group consisted of historical controls, their follow-up was significantly longer than that for the cryoablation group. A comparably longer follow-up of the cryoablation group would inevitably have increased the chance of detecting recurrence and complications. From reported paediatric series, the median time to recurrence of AVJRT after cryoablation ranged from 2.5 months to 1 year,[5,14,16] with very occasional cases of late recurrence ensuing up to 2 years post-ablation.[16] We therefore believe our mean follow-up period of 2.2 (SD, 1) years would have picked up most if not all recurrences. The small number of patients recruited in each arm of our study also limited its power to detect differences in recurrence and complication rates between the two groups.

Conclusions

Transcatheter cryoablation for AVJRT in children and adolescents is highly effective and comparable to RF ablation over the medium term. From our preliminary experience, the safety profile of cryoablation was excellent. Persistent atrioventricular block after cryoablation was not observed. Cryoablation also has the potential advantage over RF ablation of minimising radiation exposure during transcatheter ablation.

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