Cryotheral Ablation of the Slow Pathway for the Elimination of Atrioventricular Nodal Reentrant Tachycardia

Allan C. Skanes, MD; Marc Dubuc, MD; George J. Klein, MD; Bernard Thibault, MD; Andrew D. Krahn, MD; Raymond Yee, MD; Denis Roy, MD; Peter Guerra, MD; Mario Talajic, MD

Methods and Results—Eighteen patients with typical AVNRT underwent cryoablation. Reversible loss of slow pathway (SP) conduction during cryothermy (ice mapping) was demonstrated in 11 of 12 patients. Because of time constraints, only 2 sites were ice mapped in 1 patient. Seventeen of 18 patients had successful cryoablation of the SP. One patient had successful ice mapping of the SP, but inability to cool beyond −38°C prevented successful cryoablation. A single radiofrequency lesion at this site eliminated SP conduction. No patient has had recurrent AVNRT over 4.9±1.7 months of follow-up. During cryoablation, accelerated junctional tachycardia was not seen and was therefore not available to guide lesion delivery. Adherence of the catheter tip during cryothermy (cryoadherence) allowed atrial pacing to test for SP conduction. Cryoablation in the anterior septum produced inadvertent transient PR prolongation consistent with loss of fast pathway conduction in 1 patient and transient (6.5 seconds) 2:1 AV block in another. On rewarming, the PR interval returned to normal, and the AV nodal effective refractory period was unchanged in both. Accelerated junctional tachycardia was seen on rewarming in both but not during cryoablation.

Conclusions—Cryothermal ablation of the SP was achieved in patients with this novel technique. Successful ice mapping of both the SP and fast pathway was demonstrated. The ability to test the functionality of specific ablation sites before production of a permanent lesion may eliminate inadvertent AV block. (Circulation. 2000;102:2856-2860.)

Key Words: catheter ablation ■ atrioventricular node ■ tachycardia ■ arrhythmia ■ mapping

Radiofrequency ablation of the slow pathway has become first-line therapy for the elimination of AV nodal reentrant tachycardia (AVNRT). Slow pathway ablation is guided by a combination of fluoroscopic landmarks, electrogram morphology, and the induction of accelerated junctional tachycardia (AJT) during the application of radiofrequency energy. Although the success rate of slow pathway (SP) ablation is as high as 97%; transient (2%) or complete heart block requiring permanent pacing occurs in 1.3% to 2.0%. The incidence has been reported to be higher in subgroups with abnormal AV nodal anatomy, especially if there is posterior displacement of the fast pathway (FP) or compact AV node. Unlike radiofrequency ablation, cryothermal ablation creates a lesion that is initially reversible and may obviate this complication. We report our experience using a novel catheter-based cryothermal technology for cryoablation of the SP and the elimination of AVNRT.

Methods

Patients with documented supraventricular tachycardia or a history compatible with paroxysmal supraventricular tachycardia were evaluated in the electrophysiology laboratory in the sedated, postabsorptive state. All drugs had been discontinued for a duration of 5 half-lives. A standard electrophysiology study was performed. Briefly, quadripolar catheters were inserted via the femoral vein and advanced to the high right atrium, right ventricular apex, and His bundle position. A decapolar recording catheter was positioned into the coronary sinus via the left subclavian vein in 9 patients. In the remaining 9 patients, no coronary sinus catheter was inserted. Incremental atrial and ventricular pacing and extrastimulus testing from the high right atrium and right ventricular apex were performed. If sustained tachycardia could not be induced, isoproterenol was infused at a dose of 0.5 to 2 μg/min to facilitate tachycardia. All patients had inducible sustained AVNRT on the basis of standard diagnostic criteria. After the diagnostic study, the His catheter was removed and replaced with a 9F Freezor cryocatheter (Cryocath Technologies Inc).

All patients had signed informed consent before the baseline electrophysiology study. The cryoablation system has been described elsewhere. The catheter is a 9F steerable catheter with a 4-mm-tip electrode with AZ-20 (Genetron) as the refrigerant fluid. The catheter has a hollow tip into which refrigerant is delivered under pressure through an inner lumen from a control console. Within the tip, a phase change occurs (liquid to gas), and the resultant gas is removed under vacuum. The liquid-to-gas phase change results in
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One of the distinct advantages of cryothermal technology is the ability to reversibly demonstrate loss of function of tissue with cooling (ice mapping), thereby demonstrating the functionality of prospective ablation sites without inducing permanent injury. Furthermore, once the catheter tip temperature is reduced below 0°C, progressive ice formation at the catheter tip causes adherence to the adjacent tissue (cryoadherence). Cryoadherence facilitated the demonstration of ice mapping with 2 methods in this study. First, the presence of a reproducible AH jump at baseline, defined as a lengthening of AH interval ≥50 ms with 10-ms decrement in A1,A2 interval, allowed ice mapping during atrial extrastimuli by cooling candidate sites to −28°C (n=7, see below). After catheter adherence, atrial extrastimulus testing was performed to assess the presence of SP conduction (Figure 1). Second, progressive AH lengthening, followed by termination of AVNRT over the SP (AH block) during cooling to −28°C (Figure 2), indicated that the catheter was appropriately positioned before a permanent lesion was created (n=5, see below). After termination of tachycardia but before rewarming, limited atrial extrastimuli were then delivered to demonstrate ongoing block over the SP, thus eliminating the possibility of inadvertent catheter-induced termination. Cryoadherence, defined as adherence of the catheter tip to adjacent tissue during delivery of cryotherapy, prevented dislodgment of the catheter tip during termination of AVNRT (Figure 3) and during atrial extrastimulus testing. Successful ice mapping was discontinued within 45 to 60 seconds of achieving maximum negative temperature to reduce the likelihood of nonreversible effects on the SP. This limited the ability to perform extensive atrial extrastimulus testing during ice mapping. After demonstration of SP conduction block with cooling, cryotherapy was terminated, and the tissue was allowed to passively rewarmed. Reversibility of ice mapping was demonstrated by the

Figure 1. Ice mapping during atrial extrastimulus testing. Recorded surface ECG leads and intracardiac recording sites are as indicated. A and B, Baseline AV nodal conduction properties at baseline cycle length of 600 ms with extrastimuli delivered at 330 and 320 ms, respectively. In B, "jump" to SP is seen with initiation of AVNRT. C and D, Atrial extrastimulus testing during cryomapping. C demonstrates preserved conduction over the FP; D demonstrates block over SP during cryomapping. RVA indicates right ventricular apex; HRA, high right atrium; HBE, His bundle electrogram; CSp, proximal coronary sinus; Csd, distal coronary sinus; and ABL, ablation.

cooling of the tip to temperatures as low as −60°C. Temperature is recorded by a thermocouple at the tip. The catheter has 3 more proximal ring electrodes with 2-mm spacing for recording and pacing purposes.

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In cases in which patients had both dual AV nodal physiology with a clear jump (see above) and easily and reproducibly inducible AVNRT at baseline, ice mapping was performed with extrastimulus testing or during AVNRT at the discretion of the investigator.

Ice mapping was initially performed to a tip temperature of −28°C. Absence of reversible loss of function was followed in some patients by attempts at lower temperatures. Surgical experience has demonstrated that reversible suppression of electrophysiologic function occurred at 0°C. This was performed with a handheld probe at an open procedure in the absence of the warming effect of a blood pool. In the presence of the blood pool, which acts as a heat source, the tip temperature must be cooled below 0°C to achieve this temperature in adjacent tissue. It is also known from the cryosurgical literature that a steep temperature gradient exists in tissues cooled by the cryothermy source. Experimental data from animal studies cryoablation of the AV node with the current catheter-based system demonstrated that a tip temperature of −30°C allowed reproducible ice mapping of the AV node. Presumably, a tip temperature of −28°C or colder was required to cool a reasonably sized

Figure 2. Ice mapping during AVNRT. Cryoablation catheter has been positioned anatomically in SP region (not shown). Abrupt termination of AVNRT over SP is seen 3.5 seconds after initiation of ice mapping at −28°C. On rewarming, AVNRT was easily reinducible. Abbreviations as in Figure 1.

Figure 3. Termination of AVNRT during delivery of cryotherapy. Recorded surface ECG leads and intracardiac recording sites are as indicated. Noise in distal ablation signal (Abl-d) is induced by ice formation (-55°C for 19 seconds) over distal ablation electrode. Baseline cycle length of tachycardia was 450 ms. Alternation of tachycardia cycle length is seen before termination of AVNRT over SP. Abbreviations as in Figure 1.
3-dimensional mass of adjacent tissue to ≤0°C, at which temperature reversible loss of function could be demonstrated.

**Ablation**

At sites of successful ice mapping, permanent lesions were produced by the delivery of 2 consecutive 5-minute lesions separated by a rewarming phase. A rewarming phase was used to ensure tissue destruction and reasonable lesion size. In a manner similar to ice mapping, lesions were delivered during AVNRT, atrial pacing, or atrial extrastimuli after adherence to confirm loss of SP conduction (cryoconfirmation). SP conduction and AVNRT inducibility was retested during the cryoablation.

**Surveillance for AV Block**

If AH block occurred with the atrial extrastimulus that had previously conducted over the SP, a permanent lesion was produced. During production of a permanent lesion, integrity of FP conduction or compact AV node was monitored by (1) atrial extrastimulus testing throughout lesion production and (2) the PR interval during sinus rhythm between atrial extrastimulus testing. Immediate rewarming occurred if PR prolongation or AH block occurred during the atrial drive train, suggesting an FP effect.

**Results**

Eighteen patients (age, 44.1±13.9 years; 5 men) with documented typical AVNRT induced in the electrophysiology laboratory underwent SP cryothermal ablation with a new 9F catheter. At baseline, dual AV nodal physiology was seen in 10 of 18 patients, and typical sustained AVNRT was inducible in 7. The remaining 11 patients required isoproterenol infusion for induction of typical AVNRT.

**Ice Mapping**

Ice mapping was performed in 12 patients during atrial extrastimulus testing (n=7) or AVNRT (n=5). Seven had successful demonstration of ice mapping of the SP at a tip temperature of −28°C. In 4 patients, loss of SP conduction could not be demonstrated at −28°C but could be demonstrated at colder tip temperatures (range, −37°C to −52°C). In 1 patient, ice mapping was performed at 2 sites before cryoablation was begun because of time constraints. In this patient, cryomapping at neither site caused loss of SP conduction. Overall, in 11 of 12 patients, the SP was successfully cryomapped by cooling potential sites during atrial extrastimulus testing or AVNRT. Resumption of SP conduction was seen on rewarming in all cases.

**Cryoablation**

The mean number of cryoablation lesions per patient was 8.2±8.8 (range, 1 to 32) to a mean maximum negative temperature of −50.9±7.8°C. No AJT was induced at successful ablation sites during or immediately after cryoablation. Acute success, defined as inability to reinitiate AVNRT, was achieved in 17 of 18 patients. Thirteen of 18 had no evidence of SP conduction at the end of the study. Three patients had evidence of a nonclinical SP suggested by a persistent jump to an AH interval that was seen before ablation but caused neither echoes nor AVNRT with or without isoproterenol. One patient had persistence of 2 AV nodal echo beats. No sustained AVNRT could be induced despite easily inducible AVNRT at baseline. Isoproterenol infusion did not facilitate sustained tachycardia. This patient had 20 cryoablation lesions delivered at sites throughout the SP and FP regions. No recurrences have occurred in any patient over a mean of 4.9±1.7 months (range, 1 to 6 months) of follow-up.

The single failed procedure occurred because of an inability to achieve deep cryotherapy in the region of the SP. AVNRT was repeatedly terminated over the SP by cryotherapy but not at sites where temperatures colder than −38°C could be achieved. Sites of deep cryotherapy (colder than −50°C) had no effect on AVNRT. Cryotherapy at 1 site resulted in termination of AVNRT over the SP but subsequently resulted in progressive PR prolongation, necessitating termination of cryotherapy (see below). After normalization of the PR interval, AVNRT remained inducible. Radiofrequency energy delivered at a single sight of successful "ice mapping" resulted in AJT during radiofrequency delivery and eliminated SP conduction. Hence, the SP could be successfully ice mapped, but insufficient cooling prevented successful ablation.

Reversible FP block occurred inadvertently during ice mapping in 1 patient as manifested by slow prolongation of the PR interval, resulting in conduction over the SP. Inadver- tent transient AV block (6.5 seconds) occurred during ice mapping in 1 patient while cryotherapy was delivered as high as the mid septum (2:00 to 2:30). This manifested as prolongation of the PR interval followed by transient 2:1 AV block. Reversibility was documented as a return to baseline PR interval and no change in AVN effective refractory period on rewarming in both cases (Figure 4). AJT was seen on rewarming on both occasions at sites where FP or AV nodal cryomapping occurred (Figure 5).

**Discussion**

This is the first report of successful cryoablation of the SP in humans with a catheter-based cryothermal technology. This is a remarkable achievement, considering the warming effects
of the blood pool in the region of the SP where the full cardiac output and coronary sinus flow combine to act as a heat source to continuously warm the catheter tip. We have previously demonstrated the sensitivity of cryoablation to blood pool warming while delivering epicardial linear cryoablation lesions.10 It is quite possible that the catheter itself acts to insulate the underlying tissue from the full warming effect of the blood, allowing successful cryothermal ablation.

The study also validates the concept of ice mapping using this catheter-based technique. The use of cryothermal cooling of tissue to demonstrate reversible loss of function, and thereby map arrhythmogenic substrates, has been well described in the surgical literature. Ice mapping with an ablation catheter allows demonstration of functionality of tissues before the formation of a permanent destructive lesion. As such, one should not expect permanent inadvertent AV block using such a technique, even in cases with posteriorly displaced anatomy.

Several unique features of this technique are worthy of discussion. First, the formation of ice at the catheter tip causes adherence of the catheter to adjacent tissue (cryoadherence). Cryoadherence allows one to ice map or ablate during AVNRT and atrial extrastimulus testing without dislodgment of the catheter. This is obviously advantageous, because the functional effects of any prospective lesion can be tested before the formation of permanent tissue destruction. This is in contradistinction to radiofrequency ablation, in which the effects of the ablation on SP or FP function must be tested after the production of a permanent lesion. As such, cryoablation may have potential advantages when lesions are required adjacent to sensitive structures like the compact AV node. It should also result in less tissue destruction at ineffective sites.

AJT was not induced at sites where the SP was successfully ablated. As such, AJT was not available to guide the delivery of lesions as it is for radiofrequency ablation. The presence of AJT during ablation is a sensitive marker for successful sites of SP ablation.11–13 Recent evidence suggests that AJT during radiofrequency ablation results from direct heating of cells that possess automaticity at or near the compact AV node.14 In these experiments, AJT terminated with cooling of the adjacent tissue to normal temperature. Those experimental results are consistent with clinical experience described for ablation of the SP region. In the present study, AJT was not seen during cryothermy delivery in the region of the SP or adjacent to the compact AV node. AJT was seen on rewarming of tissue, however, when temporary loss of FP or the compact AV nodal function occurred. A similar finding in dogs undergoing complete AV nodal ablation (M. Dubuc, personal communication, 2000) corroborates this phenomenon. The mechanism by which this occurs remains unclear. This may represent a nonspecific response of the AV node to transient “injury.” Alternatively, rewarming may allow release of intracellular potassium or other substances that induce transient enhancement of automaticity in adjacent AV nodal cells.

Third, as noted above, this study demonstrates the efficacy of ice mapping of the SP. It is important to note that reversible ice mapping of the FP and regions very near the AV node was also demonstrated. A similar phenomenon was also seen during cryoablation, in which reversible loss of the FP or compact AV nodal conduction was seen during the ablation itself. Cryoablation was interrupted with no lasting effect on the AV node. As such, cryothermal ablation may be safer than radiofrequency ablation, because reversible FP cryomapping can be performed with no clinically relevant sequelae. Confirmation of this hypothesis is currently being evaluated in a multicenter trial.

Study Limitations
Ice mapping was performed at a tip temperature of ~28°C. This likely resulted in a surface tissue temperature that was
cooler than 0°C and may therefore have resulted in a thin superficial lesion after ice mapping. This is especially true for patients who had ice mapping at temperatures colder than −28°C. In the study of ice mapping of the AV node, 1 animal was demonstrated to have a very superficial lesion after ice mapping of the AV node.9 However, this occurred after an inadvertent reduction in tip temperature to −50°C. Nonetheless, we cannot exclude the possibility of a superficial lesion produced by ice mapping.

By nature of the technology, cryoablation requires greater ablation times, resulting in longer procedure times. Each cryoablation lesion requires two 5-minute applications. Engineering advances in the field may shorten the cryoablation duration. Although the total duration of cryothermy delivery should be offset by more precision with ice mapping, cryoablation is unlikely to be faster than radiofrequency ablation using existing technology. The number of lesions per patient varied considerably, and in some cases, a large number of cryoablation attempts were required. Results are likely to improve as this technology evolves and experience increases. Nonetheless, this technique is very effective, approaching that for radiofrequency ablation. Furthermore, the ability to test the functionality of prospective sites before permanent destruction of the tissue should essentially prevent the occurrences of inadvertent AV block with this technology.

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