Transvenous Catheter Cryoablation of the Atrioventricular Node and Visual Assessment of Freezing of Cardiac Tissue Using Intracardiac Echocardiography

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SUMMARY

We investigated the use of a catheter-based cryoablation system on atrioventricular (AV) junction ablation in dogs. In five dogs, the cryoablation catheter was introduced to the AV junction area in order to create transient high degree or complete AV block. Cryo-freezing energy was applied by lowering the temperature to -75°C for five minutes as a single cycle. This cycle was repeated until significant impairment of the AV conduction appeared. Transient high degree and complete AV block was obtained in all five dogs without any adverse effects. The iceball formation was identified by intracardiac echocardiography. Ablation of the AV junction is effective with several freeze-thaw cycles using a transvenous catheter cryoablation system. (Jpn Heart J 2004; 45: 513-520)

Key words: Catheter ablation, Cryofreezing, Catheter ablation, Intracardiac echocardiography

CATHETER ablation is a very effective and well-recognized treatment for cardiac arrhythmias.1-3) Radiofrequency (RF) current is the usual source of energy for catheter ablation in clinical practice. The effects of RF application at a specific site cannot be predicted before the actual current delivery. As a result, RF applications frequently create several unsuccessful lesions before a successful site is identified. Prior surgical studies have demonstrated that the sites responsible for arrhythmias can be identified by cryofreezing with a hand-held cryo-probe.4,5) Cryofreezing can be used to evaluate potential targets before definitive ablation.
The aim of the present study was twofold: (1) to assess the ability of catheter cryoablation to permanently abolish conduction of the AV junction with prior ice mapping of the target site and (2) to evaluate lesion growth at the target tissue using intracardiac echocardiography.

**METHODS**

The animal experiments were approved by the Institutional Ethical Committee following the guidelines of the Animal Care Council. 

**Cryoablation system:** A brand new steerable 7 Fr catheter with a 4-mm tip electrode (Freezor, CryoCath Technologies Inc., Montreal, Canada) using hydro-nitrogen as a refrigerant fluid was used. Temperature was recorded from the distal tip using a thermocouple. Four electrodes were installed at the distal portion of the catheter and used for pacing and recording. The console delivers the refrigerant fluid into the inner delivery lumen toward the distal electrode. The transformation from liquid to gas taking place at the catheter tip translates into rapid and extreme low temperatures as low as -75°C. The gas is taken away from the catheter tip through the vacuum return lumen with high negative pressure into the console.6) 

**Animal preparation:** Five beagle dogs weighing 12.4 ± 1.7 kg were studied. After intravenous pentobarbital sodium (20 mg/kg), each dog was intubated and ventilated with a Harvard respirator. Surface ECG leads I, II, and III were recorded continuously. Two 9 Fr introducers were inserted into the femoral vein. Under fluoroscopic guidance, a cryoablation catheter was advanced to the AV junction area and positioned to record His-bundle electrograms. Intracardiac electrograms were amplified and filtered (30-500 Hz bandpass filters) and recorded on an optical disk.

The intracardiac echocardiographic system was comprised of a 12.5-MHz rotating ultrasound transducer mounted on the tip of a 6.2 Fr catheter (Boston Scientific Corp., Watertown, MA, USA) and a dedicated imaging console (HP Sonos Intravascular, Andover, MA). Intracardiac echocardiography was performed in all five dogs undergoing cryoablation of the AV junction. The ultrasound catheter was introduced through the femoral vein and manipulated to obtain optimal images of the cryoablation catheter tip. Echocardiographic monitoring was continuously performed before, during, and for at least 3 minutes after every cryoapplication.

**Ice-mapping of the AV junction:** In five dogs, the cryoablation catheter was advanced to the AV junction area, and cryoapplication with progressive lowering of the temperature to a maximum of -50°C was done for five minutes. As soon as high degree AV block or significant lengthening of the PR interval was obtained,
cryoapplication was terminated. When no significant effects were observed, the cryoablation was relocated and the cryoapplication repeated. This procedure was repeated until we could find the optimal site in terms of AV junction modification.

**Cryoablation of the AV junction:** In five dogs, cryoablation was performed to obtain complete AV block. The sites where cryoapplication was performed were exactly the same as those of RF ablation. Cryoapplication was continued at the lowest temperature of -75°C after induction of high degree AV block. If no such high degree AV block occurred, cryoablation was discontinued and the catheter was repositioned. Cryoapplication was repeated until high degree AV block was obtained. After finding the optimal site, freezing was maintained at the lowest attainable temperature for five minutes as a single cycle. This cycle was repeated until persistent complete AV block was created. Success was defined as the persistence of complete AV block at the time of sacrifice. Animals were sacrificed after careful observation of atrioventricular conduction for two hours.

**RESULTS**

The cryocatheters were handled in a manner similar to standard RF ablation catheters. Endocardial contact was ensured in a standard fashion for catheter ablation.

**Ice-mapping of the AV junction:** Gradual prolongation of the PR interval with one to one AV conduction occurred followed by the development of high degree AV block. Subsequently, complete AV block was observed during the freezing for five minutes. After termination of the cryoapplication, the AV conduction resumed in a retrograde fashion. In other words, the AV conduction was complete AV block and then high degree AV block, following which significant PR prolongation with one to one AV conduction appeared. This phenomenon can be regarded as the transient impairment of AV conduction, so-called "ice-mapping".

![Figure 1](image-url)  
*Figure 1.* This figure shows low speed recording of tip temperature. The tip temperature was lowered to -75°C in < 20 seconds. After the cessation of cryofreezing, the tip temperature returned to body temperature progressively over the next 20 seconds.
of the cryoablation method. The time course of the catheter tip temperature change is shown in Figure 1. Approximately 30 seconds was necessary before the target temperature was achieved. After cessation of the cryoapplication, catheter temperature returned to body temperature within approximately 20 seconds. AV conduction recovered within a few minutes after the termination of cryoapplication.

**Cryoablation of the AV junction:** Table I shows the results of cryoapplication with respect to the AV junction. Electrical noise appeared on the intracardiac recording from the tip electrode during the cryoapplication. The first finding was a significant prolongation of the PR interval, followed by high degree AV block, and subsequently complete AV block produced in a gradual manner (Figure 2). After the beginning cycles of cryoapplication, the AV conduction resumed in a retrograde fashion. In other words, just after the cryoapplication the AV conduction was complete AV block, then high degree AV block, followed by PR interval prolongation before finally resuming to the state prior to freezing. A total of 3.4 ± 0.9 cryoapplications were conducted in five dogs. Complete AV block was rapidly achieved in all five dogs and AV conduction resumed in one dog. Repeat cryoapplication was performed in this dog, resulting in complete AV block. All five dogs remained in complete AV block after cryoablation with several cycles of cryoapplication. There were no significant differences with regard to the sites between the successful and unsuccessful cryoablation.

**Intracardiac echocardiography (ICE):** During cryoapplication, iceball formation was identified by intracardiac echocardiography as a hyperechoic zone bordered laterally by a hyperechoic rim and with posterior acoustic shadowing (Figure 3). Iceball formation was only slightly detected by ICE, and the physiological movement of the cardiac tissues of interest was lost after cryoapplication. There was no evidence of microcavitation (gas) during the cryoapplications. With ICE, identification of the extent of the lesion by cryoablation was difficult. Residual lesions were not discernible with ultrasound examination after the completion of the freezing cycles.

<table>
<thead>
<tr>
<th>Dog</th>
<th>Attained Temperature</th>
<th>Application No</th>
<th>Acute success</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-72°C</td>
<td>4</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>-68°C</td>
<td>3</td>
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<td>4</td>
<td>-69°C</td>
<td>4</td>
<td>+</td>
</tr>
<tr>
<td>5</td>
<td>-73°C</td>
<td>3</td>
<td>+</td>
</tr>
</tbody>
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Figure 2. Intracardiac and surface ECG of the dog in which we reversibly blocked AV conduction. (A) Before cryoapplication, (B) After 3 minutes of cryoablation at the first cycle of cryoapplication, the PR interval was significantly prolonged and electrical noise appeared on the intracardiac recording with loss of electrogram due to iceball formation on the catheter tip, (C) During the third cycle of cryoablation, complete AV conduction block was provoked.
DISCUSSION

Transvenous catheter cryoablation has already been reported,\textsuperscript{7,8} however, no electrodes were installed at the tip of the ablation catheter. Previously, hand-held cryoprobe ablation during open heart surgery has been performed, and it was demonstrated that the lesions created by cryoapplication were demarcated and homogeneous.\textsuperscript{9,10} In addition, the lesion volume by cryoablation was reported to be similar to lesions created by RF energy.\textsuperscript{11,12}

The present study has demonstrated that reversible ice-mapping is feasible using a percutaneous cryoablation catheter system. The change in AV conduction was very gradual, and repeated cryoapplication was required to abolish the AV conduction completely and permanently. This characteristic of cryoapplication is very useful for avoiding unnecessary lesion creation which is inevitable in the case of RF energy. Dubuc, \textit{et al} demonstrated that a minimum temperature of approximately -34$^\circ$C was necessary to obtain reversible effects on AV nodal conduction.\textsuperscript{13} In contrast, Rodriguez, \textit{et al} showed that a catheter tip temperature of -20$^\circ$C was sufficient to transiently influence AV conduction using an 8.5 Fr size cryoablation catheter.\textsuperscript{14}
Cryolesions produced in the perfused beating heart approach a maximal possible lesion size after 4 to 6 minutes of cryothermic exposure. We adopted a cryoapplication duration of 5 minutes based on this study. Multiple cycles of cryoapplication were required to produce a sufficient volume of necrotized tissue. A previous report demonstrated that repeat freezings resulted in rather large intracellular ice crystals. In the present study, at least three freeze-thaw cycles were necessary to obtain permanent complete AV block. Ablation of the AV junction with a cryocatheter can be achieved with a high success rate (5/5), which is comparable to RF catheter ablation. We did not investigate histological changes regarding the cryolesions, however, Dubuc, et al demonstrated that multiple freeze-thaw cycles were associated with more complete tissue necrosis.

With intracardiac echocardiography, we demonstrated that there was no microcavitation (gas formation) during cryoablation and no detectable residual lesion after cryoapplication, which is in contrast to other energy sources such as RF or microwaves. This finding may be associated with a reduced likelihood of thrombus formation at the endocardial cryolesion sites. In addition, echocardiography provides additional monitoring information, thereby reducing fluoroscopic exposure time.

Rodriguez, et al demonstrated that a cryoablation system exerted significant effects on the targeted tissue with high blood flow (eg, pulmonary veins, tricuspid annulus) using a different system. The present study also demonstrated that successful ablation of the AV junction was feasible, even at sites where the full cardiac output acts as a heat source to continuously warm the catheter tip, similar to the report in which AV nodal slow pathway cryoablation was successfully performed at the postero-inferior portion of Koch's triangle where cardiac output and coronary sinus flow combine to warm the cryocatheter tip which may have a significant warming effect. In conclusion, ablation of the AV junction is possible using a transvenous catheter cryoablation system. Ice-mapping makes identification of the targeted sites possible. Further investigations are necessary to evaluate this technology in larger and deeper arrhythmogenic substrates.

REFERENCES


