Experimental Study on the Effectiveness and Safety of Radiofrequency Catheter Ablation With the Cooled Ablation System

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Experimental in vitro and in vivo studies were performed to assess the effectiveness and safety of the cooled-tip catheter and the Cooled Ablation System, which enables the creation of deeper and wider burn lesions in the myocardial tissue using radiofrequency current. This system was confirmed to consistently create large burns by cooling the catheter tip with circulating water within the catheter, even under unfavorable conditions. On the other hand, unfavorable effects, as a result of over burning, such as explosive vaporization within the tissue (the ‘pop’ phenomenon), tissue carbonization, coronary artery injury and lung injury were identified. ‘Pop’ was difficult to predict, but it is important to know how it can be avoided. No ‘Pop’ was seen without first observing an impedance decrease, thus it was considered safe to decrease the radiofrequency current if the impedance began to decrease. This system will be very effective for ablation of refractory arrhythmias, such as ventricular tachycardia or atrial flutter, but it is recommended that only experienced electrophysiologists use this system to avoid serious complications. (Circ J 2003; 67: 154–158)

Key Words: Cooling effect; Canine; Complication; Energy output; Temperature

C onventional radiofrequency catheter ablation (RF-CA) systems have not been able to make deep and wide burn lesions, even with high energy delivery, because the increased temperature between the catheter tip and the endocardium becomes a limiting factor! This study aimed to clarify the effectiveness and safety of the newly developed Cooled Ablation System (Cardiac Pathways Co, USA), which uses a catheter tip cooling system that prevents excessive temperature rises.3

Methods

The Cooled Ablation System

The components of this system are a catheter (the CHILLI Cooled Ablation Catheter), radiofrequency (RF) current generator (CABL-IT) and water cooling pump system (Fig 1). The catheter tip can be cooled without infusing the cooling water into the bloodstream because it has specially designed afferent and efferent water pathways.

Experiment 1 (In Vitro Experiment With Porcine Myocardium)

This experimental study used a hand-made acrylic box (24×11×9 cm (L×W×D)), connected to a pump oxygenator similar to that used in cardiac surgery. Saline maintained at a temperature of 35–37°C was supplied and circulated through the box, keeping the wall depth at 6 cm. The grounding plate of the RF-CA system was placed at the bottom of the box. A porcine heart was placed on the grounding plate and completely soaked in the saline. Two
different protocols for circulating the saline in the box were used: (i) the saline was circulated with a pulsating flow and the delivery was set at 3.0L/min, and (ii) the saline was not circulated, keeping the fluid in the box motionless. The catheter was held at a point 15 cm from the tip and the side of the tip electrode was pressed against the endocardium with a force of 10 g. The cooling water used for the catheter tip was maintained at room temperature, and its flow was set at 0.6 ml/s when tip cooling was performed. The RF generator was set to automatically terminate when the temperature of the catheter tip reached 90ºC. The experiments were performed under 4 different conditions: (1) no saline circulation in the box and no catheter tip cooling, (2) circulation of the saline in the box without catheter tip cooling, (3) no saline circulation in the box, but catheter tip cooling and (4) circulation of the saline in the box with catheter tip cooling. Under each of these 4 conditions, repeated ablation applications were performed at various RF generator outputs, from 15 to 60 W, to observe the depth of the burn lesions, the occurrence of the ‘pop’ phenomenon (ie, intra-tissue explosive vaporization) and so on. The energy applications were continued for up to 60 s or until the RF generator automatically terminated.

**Experiment 2 (In Vivo Experiment With Anesthetized Dogs)**

Beagle dogs were anesthetized with pentobarbital and intubated. RF-CA using the Cooled Ablation System was carried out in the right and left ventricles, the atrioventricular node, right atrium and/or coronary sinus using 20, 25, 30, 35, 40 or 50 W of output. The actual energy output, catheter tip temperature, impedance, occurrence of ‘pop’ or other complications were recorded during the current delivery. In addition, the characteristics of the burn lesion and other complications were noted after removal of the heart once the dog was killed with an overdose of pentobarbital. The protocol used for the RF-CA system (ie, catheter cooling water temperature, current delivery duration and settings for automatic termination etc) was the same as in Experiment 1.

**Results**

**Experiment 1: In Vitro Experiment (Fig 2)**

There were 4 different conditions under which this experiment was performed and the results for ‘no catheter tip cooling’ are shown in Fig 2A and those from the use of a ‘cooled catheter tip’ are shown in Fig 2B. There are 2 lines in both Figs, indicating the 2 different protocols for saline circulation in the experimental apparatus (ie, pulsatory flow or no flow). Without catheter tip cooling (Fig 2A), it was difficult to consistently make a deep burn lesion with a power of 25 W or more when the saline in the box was not

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**Fig 2. In vitro experiment: myocardial ablation depth. (A) Results without catheter tip cooling, and (B) with catheter tip cooling. (closed square) Results without circulation of saline through the bath (= Circ (N)), (open circles and triangles) Results with circulation (= Circ (Y)). ‘T’, incidence of temperature rise during the ablation; ‘P’, ‘pop’ phenomenon. Note that catheter tip cooling improved the consistency of creating a deeper lesion, although the incidence of the ‘pop’ phenomenon increased. (*) Statistical significance with Student’s t-test between the corresponding pairs.**

**Fig 3. In vitro experiment: myocardial ablation lesion in a section of the myocardium. (A) Lesion with outputs of 50 W (Left) and 40 W (Right) while the catheter was cooled, and the saline circulated through the bath. The ‘pop’ phenomenon was observed with a 40 W ablation, and a crater-like dimple was created. The center of the lesion with a 50 W ablation was carbonized. (B) Deep tear (12 mm) that occurred with the ‘pop’ phenomenon exceeded the depth of the burn (8 mm) There was no circulation of saline through the bath, but the catheter tip was cooled. A 40 W ablation was performed. The divisions on the ruler indicate 1 mm.**
circulated, because the RF generator automatically terminated whenever there was a high catheter tip temperature (ie, temperature rise). When the saline in the box was circulated, lesions made with a power of 30 W or more were shallow. On the other hand, with catheter tip cooling (Fig 2B), automatic termination of the RF generator because of a temperature rise did not occur under any conditions. Up to 30 W, the burn lesions were consistently deep and stable, and the procedure was unaffected by circulation, or not, of the saline in the box. When the power exceeded 40 W, ‘pop’ sometimes occurred, and a tendency for the lesion depth to decrease was seen when the saline was not circulating.

Representative lesions are shown in Fig 3. When the saline was circulating in the box and there was catheter tip cooling, ‘pop’, which occurred at 40 s with an energy of 40 W, created a crater in the tissue at the center of the burn lesion, and a 50 W delivery carbonized the lesion (Fig 3A). When the saline was not circulating in the box during catheter tip cooling (40 W), ‘pop’ occurred at 49 s and the explosive energy tore the myocardial tissue to a depth beyond that of the burn lesion (burn depth= 8 mm, tear depth = 12 mm) (Fig 3B).

Experiment 2: In Vivo Experiment

Tables 1 and 2 show the results of the in vivo experiment. There were 10 episodes of ‘pop’ events and 8 of temperature rise in a total of 49 ablation applications. The shortest time at which ‘pop’ occurred was 24 s, the longest was 56 s and the average time was 34.2±13.0 s. The shortest time at which a temperature rise was observed was 8 s, the longest was at 55 s and the average was 26.6±16.6 s.

A transmural burn lesion was sometimes obtained (Fig 4A), and such lesions were visible from the epicardial side. Occlusion of a coronary artery because of a burn lesion was noted when the beating heart was observed from the epicardial side (Fig 4B). There was burning of lung tissue (Fig 4C), identified by a color change, caused by the heat conducted from the burnt cardiac muscle that was in contact with the lung.

Examples of the electrical and thermal data during energy delivery are shown in Fig 5. The temperature rose when the output increased, but the decrease in the impedance was slightly delayed and followed the change in the other data. For a short period after the data stabilized at 56 s after energy delivery was started, ‘pop’ occurred. Impedance data obtained during the 40 W ablation application and recordings from the right atrium and intracoronary sinus are shown in Fig 6: ‘pop’ occurred at 33 s and 25 s, respectively. Both of these episodes occurred after the impedance data exhibited a degree of decrease. A temperature rise at

Table 1 Ablation Sites and Complications (In Vivo Experiment): Number of Ablation Trials and Their Outcome

<table>
<thead>
<tr>
<th>Output (W)</th>
<th>RV</th>
<th>LV</th>
<th>AVN</th>
<th>RA</th>
<th>CS</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>25</td>
<td>2</td>
<td>1 (P1)</td>
<td>1</td>
<td>1</td>
<td>1 (P1)</td>
</tr>
<tr>
<td>30</td>
<td>5 (P2)</td>
<td>5</td>
<td>3 (T1)</td>
<td>4 (P1)(T2)</td>
<td>4 (T3)</td>
</tr>
<tr>
<td>35</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1 (P1)</td>
</tr>
<tr>
<td>40</td>
<td>4 (P1)</td>
<td>3</td>
<td>1</td>
<td>1 (P1)</td>
<td>1 (P1)(T1)</td>
</tr>
<tr>
<td>50</td>
<td>1 (P1)</td>
<td>3 (P1)(T1)</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

RV, right ventricle; LV, left ventricle; AVN, atrio ventricular node; RA, right atrium; CS, coronary sinus; P, pop; T, temperature rise.

Table 2 In Vivo Experiment: Detailed Summary of Pop and Temperature Rise

<table>
<thead>
<tr>
<th>Output (W)</th>
<th>RV</th>
<th>Temperature rise</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>25 W/48 s</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>30 W/56 s</td>
<td></td>
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<tr>
<td>30</td>
<td>40 W/24 s</td>
<td>50 W/13 s</td>
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<tr>
<td>35</td>
<td>50 W/20 s</td>
<td></td>
</tr>
<tr>
<td>40</td>
<td>25 W/30 s</td>
<td>30 W/13 s</td>
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<tr>
<td>45</td>
<td>30 W/22 s</td>
<td>30 W/14 s</td>
</tr>
<tr>
<td>50</td>
<td>30 W/28 s</td>
<td>30 W/25 s</td>
</tr>
<tr>
<td>60</td>
<td>40 W/47 s</td>
<td>30 W/25 s</td>
</tr>
</tbody>
</table>

RV, right ventricle; LV, left ventricle; AVN, atrio ventricular node; RA, right atrium; CS, coronary sinus; P, pop; T, temperature rise.

Fig4. In vivo experiment: myocardial ablation lesion. (A, upper panel) Transmural burn in the ventricular wall. (B, middle panel) Epicardium while the heart was beating shows the transmural lesion (arrows) blocking the coronary artery flow, resulting in ST segment elevation on the ECG. (C, lower panel) Color change of the lung (to the left of the photo), which was burnt while the atrial wall was ablated. The divisions on the ruler indicate 1 mm.
Discussion

Development of a RF-CA system that can create a deeper burn has been eagerly anticipated because ventricular tachycardia and atrial flutter are known to be sometimes refractory to conventional RF-CA technique, which cannot make the depth of the burn lesion sufficiently deep in such cases. Important determining factors of the size and depth of the burn lesion created by RF-CA are (1) the size of the electrode (surface area), (2) the frequency of the current, (3) the extent of contact of the electrode to the myocardium, (4) the impedance matching between the RF-CA system, myocardium and body, (5) the energy output of the RF-CA system, (6) the blood flow in the tissue of the ablated myocardium, (7) the cooling of the catheter tip by the surrounding blood in the cardiac chamber, and so on.1

Of these factors, the cooling effect has recently attracted great attention as a key factor in creating deeper and larger burns. Nakagawa et al developed an irrigation catheter system that could create large burns without causing unfavorable or abnormal rises in the catheter tip temperature or impedance, even with extremely high-energy deliveries, by infusing cold saline from holes in the distal ablation electrode.2 Their system was successful in creating large burns, but some investigators worried about over-hydrating the patients, because the system used an open-circuit type cooling system that infused a certain amount of fluid. In contrast, although the Cooled Ablation System uses the same concept to cool the ablation electrode, there is no need to worry about fluid overload, because the system has a closed-circuit cooling system. Moreover, the closed-circuit system has a definite advantage, because no matter what the orientation of the catheter tip to the endocardium, the cooling ability will be consistent and stable.

In the present in vivo study, there was no occurrence of 'pop' or a rise in temperature or impedance with an output of 20 W (Table 1), but for larger outputs, the greater power tended to cause a more abnormal ablation phenomenon. However, it was impossible to find a consistent relationship between the data of the characteristics of the impedance change and the occurrence of the 'Pop' phenomenon, even though the impedance was considered to reflect the burning of the myocardium. For example, in most of cases, 'pop' did not occur even if the impedance definitely decreased and there was a very large energy delivery for some seconds. However, in other cases, 'pop' suddenly occurred during a continuous impedance decrease after a definite decrease had been seen. Such inconsistency in the data and the relationship to the occurrence of 'pop' made it very difficult to determine specific and definite predictors for the 'pop' phenomenon. The circumstances were the same for the temperature data, thus a predictor was not found. Ikeda et al4 also reported similar experimental data with the catheter being cooled with a 0.6 ml/min flow of the cooling water, and they found no impedance rises with a 20 W energy delivery, but it was impossible to predict the danger with a higher energy delivery.

As mentioned earlier, avoidance of 'pop' is critical for system safety. Detailed analysis of our data revealed that every 'pop' incident occurred when the impedance decreased by some degree (Figs 5, 6). 'Pop' did not occur when the impedance was unchanged, which may be useful information. However in some cases, 'pop' occurred before the impedance decrease had reached a plateau phase, thus
making it impossible to quantitatively determine what degree of decrease constitutes a danger signal.

In considering a safe, practical method of performing RF-CA with this system, it is helpful to inspect the burn lesion, which, as shown in Fig. 4, can easily extend to the epicardium. The power of the system to create large lesions would sometimes be very useful and necessary, but the danger is evident from our findings of unintentional burning of the lung or occlusion of the coronary arteries. We strongly advise caution when making a transmural burn lesion. In addition, there is a valuable and informative clinical case of an autopsy of a patient who died from a non-cardiogenic cause on the 21st day after RF-CA using this system. The lesion was huge and 7 mm deep, and was accompanied by thrombogenic necrosis. The photo of the lesion is frightening to see, and makes the fear of over-burning by physicians even greater, which we anticipate with the present clinical use of this system will occur on many occasions. The ability to create a large burn requires additional precautions against arrhythmia induction with autonomic nerve stimulation or delayed thrombosis, even in the follow up period.

Taking our present findings into consideration, we recommend the following guidelines for safe RF-CA using the Cooled Ablation System. (1) Choose the patients carefully. (2) Mapping is extremely important. Try to eliminate the arrhythmia focus with the first energy delivery. Avoid mapping by test ablation. If the focus is not eliminated, it is very difficult to estimate the cause of the failure (mapping failure or under-burn). In such a situation, the physician may hesitate to terminate the delivery, resulting in an unfavorable over-burn. (3) Begin with a 20–30 W output, and increase the power gradually. Pay attention to the impedance data, and once the impedance begins to decrease, consider it a sign of successful myocardial burning and stop increasing the power; maintain or slightly decrease the power. Once it is believed that the arrhythmia has been successfully eliminated, stop the energy delivery. If it is difficult to make that decision, stop the energy delivery when the impedance decrease reaches a plateau. (4) Check the safety of the procedure with coronary angiography, echocardiography, laboratory tests for creatine kinase (CK) and CK-MB etc and other evaluations.

Finally, in order to satisfy these conditions, the use of this Cooled Ablation System should be limited to those who are well trained and very experienced specialists in electrophysiology.

Conclusion

The Cooled Ablation System has a great ability to burn the myocardium with stability and consistency, but its safe application is the full responsibility of the physician and depends on the level of skill. The system can be used for difficult cases that are refractory to other medical treatments or even to other ablation system models. However, even for experienced physicians, it may become very tempting to use a high-energy output and long energy delivery time in order to achieve a successful ablation. Thus, the system can cause serious complications. The high skill level and depth of self-knowledge of only very experienced electrophysiologists is the prime key to safe therapy when using this system for arrhythmias that are refractory to most existing treatment methods.

References