Randomized Study Comparing Radiofrequency Ablation With Cryoablation for the Treatment of Atrial Flutter With Emphasis on Pain Perception

Carl Timmermans, MD; Gregory M. Ayers, MD; Harry J.G.M. Crijns, MD; Luz-Maria Rodriguez, MD

**Background**—Radiofrequency ablation (RF) of atrial flutter (AFL) has a high procedural efficacy, a low recurrence rate, and reports of procedure-related pain. The aim of the present study was to compare RF with cryoablation (cryo) for the treatment of AFL, with emphasis on pain perception during application of energy.

**Methods and Results**—Fourteen patients (55±11 years, 11 males) with AFL were randomized to receive ablation of the cavotricuspid isthmus (CTI) by either RF or cryo. Cryothermia was delivered with the CryoCor Cryoablation System (10F, 6-mm tip), and radiofrequency energy was delivered with the use of an 8-mm–tip catheter. Pain was evaluated according to a visual analogue scale (VAS; 0 to 100). All patients in the cryo group were successfully ablated with a mean of 18 applications (9 sites), and RF was successful in 6 of 7 patients (not significant) with 13 applications (not significant). The mean temperature was 82°C and 55°C for cryo and RF, respectively. One patient in the cryo group perceived pain, versus all 7 patients in the RF group (P<0.05). The proportion of painful applications averaged 75.3% in the RF group and 2.0% in the cryo group (P<0.05), whereas the corresponding VAS for pain was 38.3±25.3 and 0.3±0.86, respectively (P<0.05). At 6-month follow-up, there were no recurrences of atrial flutter.

**Conclusion**—Cryo, as compared with RF, produces significantly less pain during application. Although in the present study there was no significant difference in efficacy, larger studies will be needed to definitively compare efficacy.

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**Key Words:** atrial flutter • catheter ablation • arrhythmia

**Type I atrial flutter (AFL)** has been successfully treated with transvenous radiofrequency ablation (RF) delivered to the cavotricuspid isthmus (CTI) with a high clinical success rate (85% to 100%). Unlike other supraventricular arrhythmias treated with RF, there are occasional recurrences of AFL after acutely successful procedures (5% to 10%). Although not systematically studied, it is recognized clinically that patients often report discomfort during RF.

Recent advances in cryogenics technology have allowed for the development of catheter systems that can deliver cryoablation (cryo) energy from the tip of a transvenous catheter. The aim of the present study was to systematically compare RF with cryo for the treatment of AFL, with emphasis on pain perception during application of energy.

**Methods**

**Study Patients**

Fourteen consecutive patients with ECG-documented type I AFL were studied. On enrollment, patients were randomized to either cryo or RF. The hospital ethics committee approved the study, and patients gave informed consent. All patients were followed up for 6 months after the ablation.

**Electrophysiological Study and Ablation Procedure**

Patients were studied in the fasting state without sedation. Antiarrhythmic drugs were not discontinued before the procedure. As has been previously described, ablation was performed using a sequential application technique. RF was performed with the use of an 8-mm–tip catheter (Biosense-Webster, Inc). The generator was set for 90-second delivery with a preset temperature of 70°C and a power limit of 55 W.

Cryo was delivered with the CryoCor Cryoablation System (CryoCor, Inc), which consists of a console and a 10F, 6-mm–tip catheter. Cryothermia was delivered twice at each catheter tip site for 4 minutes, allowing recovery of the temperature to approximately body temperature between each application.

Pain was evaluated according to a Visual Analogue Scale (VAS) ranging from 0 to 100, with 0 correlating with the statement “no pain at all” and 100 with “the worst possible pain.” The VAS score was determined at the end of each application. Electrogram were observed from the ablation catheter just before the delivery of energy. The amplitude of the atrial and ventricular
component were then compared for the evaluation of pain versus catheter tip location.

**Statistical Analysis**

Results are expressed as mean±SD. Fisher exact test was used for comparing the proportions of patients with pain in the two groups. The within-patient proportion of painful applications and the mean pain amplitude were calculated for each patient in each group and compared by using a Wilcoxon rank-sum test. The effect of the treatment applied (RF or cryo) across applications was assessed with the general linear mixed model, which accounts for repeated measurements within patients and within catheter tip sites. All results were considered to be significant at *P*<0.05.

**Results**

**Patient Characteristics**

The patient characteristics are shown in Table 1. There were no significant differences with regard to these variables for the two groups.

**Radiofrequency Ablation**

Ninety-four applications were delivered to the 7 patients undergoing RF (mean, 13±11; range, 4 to 35). The mean temperature was 55±4 (range, 50 to 62)°C with a mean power of 46±8 (range, 33 to 55) W. After RF, bidirectional isthmus conduction block was present in 6 of 7 patients (86%). In the one patient in whom RF failed, 35 applications were delivered with only a prolongation in conduction indicating incomplete block. Procedure and fluoroscopy time for the RF was 2.6±1.5 (range, 1 to 5) hours and 44±39 (range, 9 to 120) minutes, respectively. There were no acute procedural complications. At 6-month follow-up, none of the 6 successfully ablated patients had recurrence.

**Cryoablation**

The seven patients had 125 applications delivered (mean, 18±4; range, 14 to 22; not significant versus RF) at a mean of 9±2 (range, 7 to 11) sites. The cryo parameters were: a mean nadir temperature of −84±5 (range, −73 to −92)°C and a mean temperature of −82±5 (range, −69 to −89)°C. In all patients, bidirectional isthmus block was obtained (100%, not significant versus RF). The procedure time was 4.1±1.4 (range, 2.5 to 6.5) hours, slightly but not significantly longer than in RF patients (*P*=0.077). With regard to fluoroscopy time, there was no difference as compared with RF (60±48; range, 12 to 152 minutes). There were no procedural complications. At 6-month follow-up, there were no recurrences of AFL.

**Pain Perception**

All RF patients perceived one or more of the applications as painful (VAS >0) versus only one patient (3 applications) in the cryo group (*P*=0.0047). The pain characteristics (proportion of painful applications and mean VAS) for each RF patient are shown in Table 2. For the one patient who perceived pain in the cryo group, 3 of 22 (13.6%) applications were painful with a mean VAS of 2.27±6.12. The overall mean pain proportion in the cryo group was 1.95±5.15%, and the overall group mean VAS was 0.32±0.86. This compares with 75.3±24.4% and a mean VAS of 38.3±25.3 for the RF group. When comparing the proportion of painful applications in the two groups, the result was highly significant (*P*<0.005). When comparing the mean VAS score across the two groups, accounting for repeated values among patients, a significant group effect was observed (*P*<0.0001), confirming the result that there was a difference in proportion of painful applications and mean VAS scores. When including

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**TABLE 1. Patient Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>RF Group</th>
<th>Cryo Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Men/women, n</td>
<td>5/2</td>
<td>6/1</td>
</tr>
<tr>
<td>Age, y</td>
<td>55±10 (39–70)</td>
<td>55±12 (34–69)</td>
</tr>
<tr>
<td>Patients with structural heart disease, n</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Corrected valvular heart disease</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Corrected atrial septal defect type 2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Restrictive cardiomyopathy</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>None</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Left ventricular ejection fraction, %</td>
<td>54±18 (20–70)</td>
<td>61±5 (55–67)</td>
</tr>
<tr>
<td>Left atrial size, mm</td>
<td>45±6 (36–55)</td>
<td>47±8 (39–62)</td>
</tr>
<tr>
<td>Patients with paroxysmal/chronic AFL, n</td>
<td>3/4</td>
<td>4/3</td>
</tr>
<tr>
<td>Cycle length AFL, ms</td>
<td>276±76 (200–400)</td>
<td>255±40 (200–320)</td>
</tr>
</tbody>
</table>

Values are given as n or as mean±SD (range).

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**TABLE 2. Within-Patient Pain Characteristics in the RF Group**

<table>
<thead>
<tr>
<th>Patient</th>
<th>No. of Applications</th>
<th>Proportion of Painful Applications, %</th>
<th>VAS for Pain, mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9</td>
<td>55.6</td>
<td>32.8±34.2</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>100</td>
<td>73.8±16.5</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>100</td>
<td>71.7±7.53</td>
</tr>
<tr>
<td>4</td>
<td>13</td>
<td>69.2</td>
<td>33.8±29.6</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>100</td>
<td>32.0±14.8</td>
</tr>
<tr>
<td>6</td>
<td>22</td>
<td>59.1</td>
<td>14.1±21.7</td>
</tr>
<tr>
<td>7</td>
<td>35</td>
<td>42.9</td>
<td>9.97±15.6</td>
</tr>
<tr>
<td>All</td>
<td>94</td>
<td>75.3±24.4</td>
<td>38.3±25.3</td>
</tr>
</tbody>
</table>
the catheter tip site in the model but restricting the analysis only to RF patients, the analysis further revealed that VAS scores for applications in the atrioventricular groove (9.7±19.0) were significantly lower than for applications delivered in the atrium/atrium-inferior vena cava transition (28.6±29.8, P=0.011) but not less than the scores for applications given in the ventricle (25.0±27.8, P=0.086) (Table 3).

Discussion

The main finding of the present study is that cryo of the CTI, as compared with RF, results in nearly no application-related pain or discomfort. In this small population, both acute and chronic efficacy of cryo was not significantly different from that of RF. The efficacy seen in this study is higher than initially reported for other cryo systems when used to treat either AFL or other supraventricular tachycardias. Further studies are needed to definitively compare efficacy.

The tendency toward longer procedure times associated with cryo is the result of longer, repeated applications at each catheter site (4 minutes versus 90 seconds and double cryoapplications). The similar number of applications required and the total fluoroscopy time substantiate the trend’s being due to application time and number. The method of application of cryoablation (twice, a 4-minute application on the same site) was based on previous cryo experiences in animals and in cardiac surgery. Further studies are needed to define the duration of individual cryoapplications and to evaluate the need for repeated cryoablation delivery, as they may impact significantly procedure duration and efficacy.

The present study is the first systematic evaluation in the nonsedated patient of pain associated with RF of the CTI. Although prior studies have reported that RF may induce patient discomfort, resulting in either the need for more sedation or analgesia, the present study quantifies ablation-induced pain. We clearly show that cryo produces nearly no pain, whereas RF produces pain in all patients. Ablation without pain is also of clinical importance when ablating in sites such as the coronary sinus and the atria, despite the use of conscious sedation. The mechanism of the pain associated with RF remains unclear. We hypothesized that RF applied to thin structures, such as the right atrial wall or inferior vena cava, might be more likely to cause pain because of their proximity to the pericardium and therefore results in pericardial irritation. However, the results of the present study are not in agreement with this hypothesis. It is also possible that certain ablation sites directly stimulate cardiac sensory nerves, perceived by the patient as visceral pain.

Conclusion

The present study shows that cryo is much less painful than RF for ablation of the cavotricuspid isthmus. Because of this advantage, cryo should be considered for cavotricuspid isthmus ablation and for ablations known to cause discomfort or pain with RF delivery. Although in this study there was no significant difference in efficacy, larger studies will be needed to definitively compare efficacy.

References

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