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Catheter-Based Cryoablation Permanently Cures Patients With Common Atrial Flutter

Randy Manusama, MD; Carl Timmermans, MD; Froylan Limon, MD; Suzanne Philippens, RN; Harry J.G.M. Crijns, MD; Luz-Maria Rodriguez, MD

Background—Cryoablation (cryo) has a high success rate in the short-term treatment of atrial flutter (AFL), but evidence of long-term efficacy is lacking. The present study reports the long-term effect of cryo of the cavotricuspid isthmus (CTI) in patients with common AFL.

Methods and Results—Thirty-five consecutive patients (28 men; mean age, 53 years) underwent cryo of the CTI. In 34 patients, the AFL had a counterclockwise rotation (cycle length, 242±47 ms). Eleven patients had structural heart disease. Cryo was performed with a 10F catheter with a 6-mm-tip electrode (CryoCor). Applications (3 to 5 minutes each) were delivered by use of a point-by-point technique to create the ablation line. The acute end point of the procedure was creation of bidirectional isthmus conduction block and noninducibility of AFL. A median of 14 applications (range, 4 to 30) at 10 sites (range, 4 to 19) was given along the CTI with a mean temperature of −80.0±5.0°C. Mean fluoroscopy and procedure times were 40±26 minutes and 3.2±1.3 hours, respectively. Of the 35 patients, 34 were acutely successfully ablated (97%). After a mean follow-up of 17.6±6.2 months (range, 9.6 to 26.1 months), 31 patients (89%) did not have recurrence of AFL. Three of the 4 patients with recurrence had a second successful procedure. One patient had transient ST elevation in the inferior leads during cryoapplication.

Conclusions—Cryo produces permanent bidirectional isthmus conduction block of the CTI. Short- and long-term success rates are comparable to those for radiofrequency ablation. (Circulation. 2004;109:1636-1639.)

Key Words: ablation ■ atrial flutter ■ catheter ablation

Currently, radiofrequency ablation is considered first-line therapy for the treatment of atrial flutter (AFL) because of its high success rate and significant improvement in quality of life compared with conventional medical therapy. Advances in cryotechnology have allowed the development of transvenous cryoablation (cryo) catheter systems that can create transmural lesions in regions with high blood flow. Recently, it was shown that the short-term success rate and safety obtained with cryo for AFL are comparable to those for radiofrequency ablation. Importantly, when the cavotricuspid isthmus (CTI) is ablated, patients feel no pain during cryo in contrast to radiofrequency ablation. To evaluate the safety and efficacy of cryo, long-term follow-up is important. This was the purpose of the present study.

Methods

Patients

Between June 2001 and May 2002, 35 consecutive patients (28 men; mean age, 53±11 years; range, 30 to 73 years) were included. All gave written informed consent for the procedure, and the local hospital ethics committee approved the study. Twenty-eight patients (80%) also had a history of atrial fibrillation. In 11 of these patients (31%), atrial fibrillation organized into AFL during treatment with a class IC antiarrhythmic drug (n=9) or amiodarone (n=2). Of the 35 patients, 11 (31%) had structural heart disease, which was hypertensive (n=7), congestive (n=1), or congenital (n=3). Congenital heart disease consisted of 2 atrial septal defects, 1 of which was surgically corrected, and a ventricular septal defect, which had closed spontaneously by the time of study. One patient was suffering from persistent atrial fibrillation and developed a tachycardia-induced cardiomyopathy. A His-bundle ablation was performed after a pacemaker implantation in this patient. Left ventricular ejection fraction and left atrial size were measured before the procedure with 2D echocardiography. Mean left ventricular ejection fraction and mean left atrial size were 60.1±7.94% (range, 33% to 69%) and 4.7±0.7 cm (range, 3.8 to 6.2 cm), respectively. Three patients had previously failed a radiofrequency ablation procedure. Demographic characteristics of all patients are shown in Table 1.

Follow-Up

Patients living in the region of Maastricht (most patients) were followed up at our outpatient clinic at 1 month and every 3 months thereafter. For patients outside this region, follow-up was obtained by the referring cardiologist. In case of documentation of AFL, the patient was again referred to our hospital for further evaluation and reablation. In patients with antiarrhythmic drug–induced AFL, antiarrhythmic drugs were continued after the ablation procedure. A 24-hour Holter monitor was given immediately after the procedure until hospital discharge and thereafter if symptoms suggested an arrhythmia recurrence. Patients were instructed to contact our center...
if they had any symptoms (eg, palpitations, chest discomfort) that could indicate a recurrence.

Ablation Procedure
All ablation procedures were performed by use of a protocol similar to that used in our center for radiofrequency ablation. Three multipolar catheters were advanced into the right atrium through insertion in the right femoral vein. One 20-pole electrode catheter (2-mm interelectrode spacing, Halow catheter, Biosense Webster) was positioned around the tricuspid annulus for sequential activation mapping. A quadrupolar catheter and a decapolar catheter were placed at the His bundle and in the coronary sinus, respectively. Cryo was performed with the CryoCor Cardiac Cryoablation System, described previously. A steerable 10F bipolar catheter with a 6-mm tip was used, combined with a long venous sheath (St Jude Medical, SL2; 12F, Daig Co) for mapping and ablation of the CTI.

Entrainment to confirm the isthmus dependence of the AFL circuit was performed in patients with AFL only and in patients with AFL and a few episodes of atrial fibrillation. In patients with AFL and frequent atrial fibrillation episodes, entrainment was not performed to avoid induction of atrial fibrillation.

Both catheter tip temperature and system pressure were monitored throughout the procedure to ensure consistent catheter tip energy delivery. Linear lesions were created by use of a point-by-point technique with gradual pullback of the cryocatheter in a VA fashion. The first application was delivered at the ventricular insertion of the isthmus, and applications were continued for 3 to 5 minutes. In patients in whom ablation of the posterior isthmus proved insufficient to suppress AFL, an attempt was made to ablate the septal isthmus. After documentation of bidirectional isthmus conduction block, the atrial pacing (from the proximal coronary sinus) protocol was performed without and with isoproterenol infusion (up to 3 atrial extrastimuli at 3 pacing cycle lengths and incremental block, the atrial pacing protocol was performed without and with isoproterenol infusion (up to 3 atrial extrastimuli at 3 pacing cycle lengths and incremental block, the atrial pacing protocol was performed without and with isoproterenol infusion (up to 3 atrial extrastimuli at 3 pacing cycle lengths and incremental block, the atrial pacing protocol was performed without and with isoproterenol infusion (up to 3 atrial extrastimuli at 3 pacing cycle lengths and incremental block, the atrial pacing protocol was performed without and with isoproterenol infusion (up to 3 atrial extrastimuli at 3 pacing cycle lengths and incremental block, the atrial pacing protocol was performed without and with isoproterenol infusion (up to 3 atrial extrastimuli at 3 pacing cycle lengths and incremental block, the atrial pacing protocol was performed without and with isoproterenol infusion (up to 3 atrial extrastimuli at 3 pacing cycle lengths and incremental block, the atrial pacing protocol was performed without and with isoproterenol infusion (up to 3 atrial extrastimuli at 3 pacing cycle lengths and incremental block, the atrial pacing protocol was performed without and with isoproterenol infusion (up to 3 atrial extrastimuli at 3 pacing cycle lengths and incremental block, the atrial pacing protocol was performed without and with isoproterenol infusion (up to 3 atrial extrastimuli at 3 pacing cycle lengths and incremental block, the atrial pacing protocol was performed without and with isoproterenol infusion (up to 3 atrial extrastimuli at 3 pacing cycle lengths and incremental block, the atrial pacing protocol was performed without and with isoproterenol infusion (up to 3 atrial extrastimuli at 3 pacing cycle lengths and incremental block, the atrial pacing protocol was performed without and with isoproterenol infusion (up to 3 atrial extrastimuli at 3 pacing cycle lengths and incremental block, the atrial pacing protocol was performed without and with isoproterenol infusion (up to 3 atrial extrastimuli at 3 pacing cycle lengths and incremental block, the atrial pacing protocol was performed with the CryoCor Cardiac Cryoablation System, described previously. A steerable 10F bipolar catheter with a 6-mm tip was used, combined with a long venous sheath (St Jude Medical, SL2; 12F, Daig Co) for mapping and ablation of the CTI. Further cryoapplications were delivered.

To determine the presence or absence of a potential learning curve associated with cryoablation, patients were subdivided into 2 nearly equal groups: the first 17 patients treated over the initial 10 months and 18 patients treated thereafter. Fluoroscopy time, number of applications, number of ablation sites, and total procedure time were compared for both patient groups.

Statistical Analysis
Values of procedural results are expressed in mean±SD. Mann-Whitney nonparametric test was used to signify a learning curve by comparing the first half of the study population with the last one. All values were considered significant at P<0.05.

Results
In 34 patients (97%), short-term procedural success was achieved (Table 2). In the remaining patient, unidirectional isthmus block and noninducibility of AFL were demonstrated. This patient had an atrial septal defect with restrictive cardiomyopathy.

All patients had a documented common AFL: 34 counterclockwise and 1 clockwise rotation of the AFL circuit. The median number of freezes needed to obtain the procedure end points was 14 (range, 4 to 30), with a median number of 10 sites (range, 4 to 19). The average temperature was −80.0±5.0°C (range, −57°C to −90°C), and the mean nadir temperature was −82.0±4.6°C (range, −64°C to −92°C). Conversion of atrial fibrillation was undertaken in 5 patients. Sinus rhythm was obtained by internal cardioversion (n=2), intravenous administration of flecainide (n=2), or flecainide followed by external cardioversion (n=1). Mean fluoroscopy and procedure times were 40±26 minutes (range, 12 to 152 minutes) and 3.2±1.3 hours (range, 1 to 6.5 hours), respectively. Two patients (6%) needed additional septal ablation to obtain complete isthmus conduction block. Comparing the first group of patients treated (17 patients) with the second group (18 patients) showed no significant differences in terms of number of applications, number of ablation sites, and fluoroscopy time (P>0.05). However, the procedure time was significant longer for the first group (P<0.001) (Figure). Furthermore, there was a correlation (R=0.60, P<0.05) between the duration of the procedure and the duration of fluoroscopy time.

Complications
One patient had anginal complaints with ST-segment elevation in the inferior leads during 1 cryoapplication in the area

<table>
<thead>
<tr>
<th>TABLE 1. Patient Characteristics</th>
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<tbody>
<tr>
<td>Patients, n</td>
</tr>
<tr>
<td>Age, y</td>
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<tr>
<td>Sex, male/female, n</td>
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<tr>
<td>Structural heart disease, n</td>
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<tr>
<td>Hypertensive</td>
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<td>Dilated</td>
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<td>Congenital</td>
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<td>Mean left ventricular ejection fraction, %</td>
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<td>Mean left atrial size, cm</td>
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<tr>
<td>Concomitant atrial fibrillation</td>
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<td>Patients with implanted pacemaker, n</td>
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<tr>
<td>Patients with previous RF attempts, n</td>
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<tr>
<td>IC AFL, n</td>
</tr>
<tr>
<td>Class III AAD (amiodarone/sotalol/both), n</td>
</tr>
<tr>
<td>Other (metoprolol/disopyramide/digitals), n</td>
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RF indicates radiofrequency ablation; IC AFL, organization of atrial fibrillation to AFL during treatment with class IC antiarrhythmic drugs; and AAD, antiarrhythmic drug.

<table>
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<th>TABLE 2. Electrophysiological Characteristics</th>
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<tr>
<td>AFL: CCW/CW, n</td>
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<tr>
<td>AAD AFL, n</td>
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<tr>
<td>Cycle length, ms</td>
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<tr>
<td>Cardioversion, n</td>
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<tr>
<td>Flecainide</td>
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<tr>
<td>External</td>
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<tr>
<td>Internal</td>
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<tr>
<td>Freezes, n</td>
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<tr>
<td>Sites (median), n</td>
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<tr>
<td>Temperature, °C</td>
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<tr>
<td>Fluoroscopy time, min</td>
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<tr>
<td>Procedure time, h</td>
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<tr>
<td>Acute success, n (%)</td>
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<tr>
<td>Recurrent AFL (total), n (%)</td>
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<td>AF after ablation, n (%)</td>
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<tr>
<td>New, n</td>
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<tr>
<td>Recurrent, n</td>
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<td>IC AFL, n</td>
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CCW indicates counterclockwise; CW, clockwise. Other abbreviations as in Table 1.
of the septal isthmus. The patient fully recovered after the application was stopped and nitroglycerine was administered. Subsequent coronary angiography revealed wall irregularities in the right coronary artery, without significant stenosis. No patients had in-hospital recurrences of AFL. No thromboembolic complications occurred. There were no major adverse events after the ablation procedure and throughout the follow-up period.

**Follow-Up**

After a mean follow-up of 17.0 ± 6.2 months (range, 9.6 to 26.1 months), 31 patients (89%) had no recurrence of AFL. Four patients had a recurrence of AFL after 5, 7, 9, and 14 months, respectively, and 3 patients underwent a second ablation. One had had a failed radiofrequency ablation procedure in the past. After 11, 6, and 5 months, respectively, these patients did not show recurrences of AFL. The remaining patient is awaiting a second cryoablation procedure.

Of the 28 patients with atrial fibrillation before the procedure, 15 patients (54%) continued to have atrial fibrillation episodes after cryoablation of the CTI. In 2 of these patients, the clinical course was complicated by amiodarone-induced hyperthyroidism. No new onset of atrial fibrillation has been reported. Chronic complications were not observed.

**Discussion**

The present study provides evidence, for the first time, of the long-term safety and efficacy of cryo for the treatment of isthmus-dependent AFL. Efficacy, both short and long term, was comparable to that of radiofrequency ablation. Notably, cryo causes no or minimal perception of pain, which is of value during application in the inferior vena cava region when ablation of the posterior isthmus is attempted. This is in contrast to radiofrequency ablation, which can be very painful in this region.

In our study, the long-term results were comparable to those obtained after radiofrequency ablation reporting up to 15% of AFL recurrences after assessment of acute bidirectional isthmus conduction block. Resumption of AFL occurred mostly in the first months after radiofrequency ablation. In our study, 11% of the study population showed recurrence of AFL despite initial demonstration of bidirectional isthmus conduction block. One patient reported a recurrence of AFL after 14 months. In this patient, previous radiofrequency ablation procedures with an 8-mm catheter and a Thermocool catheter were also unsuccessful.

Antiarrhythmic drugs were not withdrawn before the procedure, which could have compromised reliable interpretation of definite bidirectional isthmus conduction block. Class I and III agents are known to depress conduction velocity of myocardial tissue. Temporary block or a critical conduction delay along the CTI at the time of ablation could facilitate reentry when drug concentration is altered and slow conduction is regained. We previously studied the effect of isoproterenol in the evaluation of bidirectional isthmus conduction block in patients treated with radiofrequency ablation. Despite continuation of antiarrhythmic drugs, isoproterenol was able to identify residual isthmus conduction with a subsequent low AFL recurrence rate.

Finally, the number of sites needed to obtain bidirectional isthmus conduction block with cryo is comparable to the number required during radiofrequency procedures with an 8-mm catheter tip and the point-by-point technique. Recurrences of AFL in those studies were comparable to those of the present study using cryo, suggesting a similar lesion size.

**Procedural Considerations**

When the fluoroscopy and the procedure times were compared using cryoablation versus radiofrequency ablation, no differences were observed in fluoroscopy time. If radiofrequency ablation is used with bidirectional isthmus conduction block as an end point, fluoroscopy times vary between 36 and 46 minutes, which are similar to our results using cryo.

In contrast to the fluoroscopy time, the total procedure time was long. This may be explained by the nature of this technology (cryo requires longer ablation times) and by a learning curve in the use of this new technology. This learning curve was demonstrated by a significant decrease in procedure time between the first and the second halves of the study population. In addition, a good relationship was observed between fluoroscopy and procedure time. Thus, increasing experience with the current technique and optimization of the number of applications required to obtain chronic bidirectional isthmus conduction block may shorten the fluoroscopy and procedure times.

**Complications**

One patient showed temporary ST elevation in the inferior leads, which presumably was caused by coronary spasm, considering the angiographic absence of a significant stenosis. Although intramural hemorrhages in the right coronary

![Procedure time of study population](http://circ.ahajournals.org/Downloaded from http://circ.ahajournals.org/ by guest on March 6, 2014)
artery adjacent to the site of lesion and intraluminal narrowing have been described during radiofrequency ablation,18–20 the clinical impact of this finding with regard to cryotechnology remains unclear. This patient had complaints only during the procedure and remained asymptomatic thereafter.

Study Limitations
As in most of the studies reporting on the long-term outcome after ablation of AFL, a late control electrophysiological study to confirm permanent bidirectional CTI block was not done. As in our study, follow-up was based mainly on symptom recurrence.

It was beyond the scope and design of this study to evaluate in detail recurrences of atrial fibrillation after the ablation procedure. Although improvement in atrial fibrillation recurrences has been reported after treatment with radiofrequency ablation, especially in IC AFL,14 the effect of cryo can be evaluated only if the frequency and severity of atrial fibrillation recurrences are carefully monitored. Every attempt was made to evaluate a recurrence of AFL. Most of the analysis was dependent on the patient’s ability to recognize the arrhythmia, which in some cases was difficult because of concomitant atrial fibrillation or lack of symptoms.

Conclusions
Cryo produces permanent bidirectional isthmus conduction block of the CTI. Short-term and long-term success rates are comparable to those for radiofrequency ablation. The safety and long-term results obtained in this study, together with the low perception of pain3 in the CTI, might reinforce the clinical use of cryothermia for the treatment of other arrhythmias, especially those originating in regions like the coronary sinus and atria.

References