Electromyographic Monitoring for Prevention of Phrenic Nerve Palsy in Second-Generation Cryoballoon Procedures

Frédéric Franceschi, MD, PhD*; Linda Koutbi, MD*; Edouard Gitenay, MD; Jérôme Hourdain, MD; Baptiste Maille, MD; Lory Trévisan, MD; Jean-Claude Deharo, MD

Background—Electromyography-guided phrenic nerve (PN) monitoring using a catheter positioned in a hepatic vein can aid in preventing phrenic nerve palsy (PNP) during cryoballoon ablation for atrial fibrillation. We wanted to evaluate the feasibility and efficacy of PN monitoring during procedures using second-generation cryoballoons.

Methods and Results—This study included 140 patients (43 women) in whom pulmonary vein isolation was performed using a second-generation cryoballoon. Electromyography-guided PN monitoring was performed by pacing the right PN at 60 per minute and recording diaphragmatic compound motor action potential (CMAP) via a quadripolar catheter positioned in a hepatic vein. If a 30% decrease in CMAP amplitude was observed, cryoapplication was discontinued with forced deflation to avoid a PNP. Monitoring was unfeasible in 8 of 140 patients (5.7%), PNP occurred in 1. Stable CMAP amplitudes were achieved before ablation in 132 of 140 patients (94.3%). In 18 of 132 patients (13.6%), a 30% decrease in CMAP amplitude occurred and cryoablation was discontinued. Each time, recovery of CMAP amplitude took <60 s. In 9 of 18 cases, a second cryoapplication in the same pulmonary vein was safely performed. We observed no PNP or complication related to electromyography-guided PN monitoring.

Conclusions—Electromyography-guided PN monitoring using a catheter positioned in a hepatic vein seems feasible and effective to prevent PNP during cryoballoon ablation using second-generation cryoballoons. (Circ Arrhythm Electrophysiol. 2015;8:303-307. DOI: 10.1161/CIRCEP.115.002734.)

Key Words: atrial fibrillation ■ cardiac arrhythmias ■ catheter ablation ■ phrenic nerve

The most frequent complication of cryoballoon pulmonary veins isolation (PVI) is right phrenic nerve palsy (PNP).1-4 In a previous report,5 we described a novel preventive technique involving real-time diaphragmatic electromyography using a recording catheter positioned in a subdiaphragmatic hepatic vein. If a 30% decrease in compound motor action potential (CMAP) amplitude was observed, cryoapplication was immediately discontinued with forced deflation to avoid PNP. Since that time, a second-generation cryoballon (CB2)6 has been developed, resulting in a larger and more uniform freezing area.

Our first aim was to ascertain the feasibility and efficacy of electromyography-guided phrenic nerve monitoring (PNM) using a quadripolar catheter positioned in a hepatic vein for prevention of PNP during CB2 procedures. The second goal was to evaluate the safety of repeating cryoapplication in the same pulmonary vein (PV) after discontinuation of a first cryoapplication because of threatened right PNP.

Materials and Methods

Study Design

A total of 140 consecutive patients were included at our center. The indication for CB2 PVI was symptomatic paroxysmal or persistent (<6 months) atrial fibrillation that failed to respond to at least 1 antiarrhythmic drug. Written informed consents were obtained from all the participants. The ethic committee of the University Hospital Timone approved this consent procedure and this study.

Periprocedural Management

All patients underwent transesophageal echocardiography, transthoracic echocardiography, and computed tomographic scan. Patients with left atrial thrombus, severe uncontrolled heart failure, and left atrial dimensions ≥50 mm were not included in the study.

The day after the procedure, transthoracic echocardiography and chest radiograph were performed to rule out pericardial effusion and PNP. In patients receiving vitamin K antagonists, procedures were performed with an international normalized ratio between 2 and 2.5. In patients receiving dabigatran or rivaroxaban, oral anticoagulation was interrupted 48 hours before the procedure and resumed the day after, with a low-molecular weight heparin bridge.

Cryoballoon Ablation Procedure

All procedures were performed under conscious sedation. Briefly, a quadripolar catheter Josephson curve (St. Jude Medical, Minnetonka, MN) was positioned on the His bundle and a deflectable quadripolar catheter (Xtrem catheter; Sorin Group) was placed in the coronary sinus by the femoral route. These 2 catheters were used as landmarks for transeptal puncture to allow placement of a steerable 15 Fr sheath...
WHAT IS KNOWN

- Right phrenic nerve palsy remains a common complication of cryoballoon ablation.
- To prevent this complication, right phrenic nerve monitoring with electromyography using a catheter in a hepatic vein was described with first-generation cryoballoons.

WHAT THE STUDY ADDS

- This approach works with second-generation cryoballoons.
- After discontinuation of a first application for altered diaphragmatic electromyography, a second cryoapplication in the same pulmonary vein, again terminated when diaphragmatic electromyography was altered, achieved pulmonary vein isolation without phrenic nerve palsy.

(Flexcath; Medtronic) in the left atrium. After transeptal puncture, an intravenous unfractionated heparin bolus (100 IU/kg) was administered. Before introducing the balloon catheter in the sheath, a 20-mm diameter Achieve catheter (Achieve mapping catheter; Medtronic) was inserted in the lumen of the cryoballoon. Then a 23- or 28-mm CB2 (Arctic Front Advance; Medtronic CryoCath LP) was advanced through the sheath into the left atrium using the Achieve catheter as a guide. Balloon diameter was selected in function of left atrium and PV size measured on preprocedural computed tomographic scans. Before ablation, the Achieve catheter was positioned in the venous ostium to record baseline electric activity and PV occlusion was tested using contrast agent after wedging the cryoballoon in the ostium. When the operator deemed that occlusion was sufficient, cryoapplication was started. The duration of each cryoapplication was 180 s. A second 3-minute cryoapplication was systematically performed except if real-time PV isolation was observed before the end of the first minute. After each cryoapplication, PV isolation was assessed with the Achieve catheter. After a waiting period of 20 minutes after the last cryoapplication, PV isolation was re-evaluated to detect early recovery of left atrium–PV conduction.

Phrenic Nerve Monitoring
PNM was performed during right PV cryoapplications. The deflectable quadripolar catheter was moved into the superior vena cava to pace of the right PN at 60 per minute (10 V; 2.9 ms). To ensure stable pacing, the distal part of the catheter was placed in the right subclavian vein (Figure 1). The quadripolar catheter was moved to a hepatic vein and connected to the computerized electrophysiology workstation (Prucka CardioLab, General Electric). Bipolar electromyography signals were recorded between the electrodes proximal and distal. Signals were amplified and band-pass filtered between 5 and 150 Hz. The abdomen was continuously palpated during cryoapplications.

If phrenic CMAP amplitude remained stable, cryoapplication was performed for the full 180 s. A second application was performed if deemed necessary. If a 30% decrease in CMAP amplitude was observed, cryoapplication was discontinued using the forced deflation. In that case, fluoroscopy was performed to assess diaphragm motion. If cryoapplication duration was <120 s or if real-time assessment indicated that PVI occurred after the first minute of cryoablation, a second application was performed in the targeted vein after recovery of CMAP amplitude to the baseline.

Interpretation of CMAP Amplitude Variations
PN pacing instability was defined by CMAP amplitude variations >20% from one beat to another. On the opposite, PN threatening was defined by a progressive CMAP amplitude decrease pattern (30% decrease cutoff reached in >10 s). CMAP amplitude monitoring was performed online on the electrophysiology workstation beat per beat, by a trained physician.

Study End Points
The primary study end point was feasibility and efficacy of PNM with CMAP amplitude using a catheter in a hepatic vein. The secondary end point was to evaluate the safety of a second cryoapplication in the same right PV after discontinuation because of threatened right PNP.

Statistical Analysis
Data are presented as mean±SD for continuous variables and as counts (%) for categorical variables. The authors had full access to and take full responsibility for the integrity of data. All authors have read and agreed to the article as written.

Results

Patients and Procedures
Acute PVI was achieved in all patients (Table 1). Three acute complications occurred: 2 groin hematoma and 1 transient ischemic attack.

Feasibility of PNM During CB2 Ablation
In 8 patients (5.7%), electromyography-guided PNM was unfeasible. Steady baseline phrenic CMAP amplitude could not be obtained because of pacing catheter instability at the superior vena cava. Conventional monitoring with abdominal palpation while pacing right PN was performed. In 1 of 8 patients, palpation detected a decrease in contraction strength and ablation was stopped with forced deflation. Nevertheless, PNP occurred and persisted the next day. Follow-up examination 2 months later demonstrated complete regression of PNP. In the remaining 132 patients (94.3%) electromyography-guided PNM was feasible.

Efficacy and Safety of PNM During CB2 Ablation
In 114 patients (86.4%), CMAP amplitude remained stable for each cryoapplication. Next-day chest radiograph showed no right PNP.
In 18 patients (13.6%), a 30% decrease in CMAP amplitude occurred and cryoablation was discontinued with forced deflation (Table 2). At this time, abdominal palpation detected no decrease in diaphragmatic contraction strength. The mean duration of cryoapplication was 121.4±32.5 s. The minimum temperature achieved was −45.9±5.6°C. Baseline CMAP amplitude returned within 60 s. In all cases, PVI had been achieved by the time of forced deflation. No adverse event related to PNM was observed. Fluoroscopic evaluation at the end of the procedure demonstrated normal diaphragmatic movement. Next-day chest radiograph showed no sign of right PNP.

A total of 435 right-sided cryoballoon applications were performed in 132 patients with electromyography-guided PNM. Among these 435 cryoballoon applications, threatened right PN was observed in 27 (6.2%).

### Safety of Second Cryoapplication After Discontinuation With Forced Deflation

A second cryoapplication was performed in 9 patients (Table 2). No particular measure was taken to modify cryoballoon position compared with the first cryoapplication. A >30% decrease in CMAP amplitude was again observed in all the patients. The duration of the second cryoapplication was 10.6±18.7 s longer than the first. Return of baseline CMAP amplitude was observed within <60 s (Figure 2). Fluoroscopic evaluation at the end of the procedure demonstrated normal diaphragmatic movement. Next-day chest radiograph showed no sign of right PNP.

### Discussion

The 3 most significant findings were as follows: first, diaphragmatic electromyography monitoring using a catheter positioned in a hepatic vein seemed feasible and effective in CB2 procedures. Second, >30% decrease in CMAP amplitude signaling imminent PNP was detected in 18 of 132 patients (13.6%). Third, discontinuation by forced deflation does not rule out repeating cryoablation in the same PV, if necessary. Repeated cryoablation was safe in 9 cases.

### Table 1. Baseline Patient and Procedure Characteristics

<table>
<thead>
<tr>
<th>Patients</th>
<th>140</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>60.3±10</td>
</tr>
<tr>
<td>Women</td>
<td>43 (30.7)</td>
</tr>
<tr>
<td>LA diameter, mm</td>
<td>41.2±3.6</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>60.7±4.8</td>
</tr>
<tr>
<td>Idiopathic AF</td>
<td>65 (46.4)</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>50 (37.5)</td>
</tr>
<tr>
<td>Mild structural heart disease</td>
<td>25 (17.9)</td>
</tr>
<tr>
<td>Paroxysmal AF</td>
<td>111 (79.3)</td>
</tr>
<tr>
<td>Recently developed persistent AF</td>
<td>29 (20.7)</td>
</tr>
<tr>
<td>VKA/Dabigatran or rivaroxaban</td>
<td>66 (47.1)/74 (52.9)</td>
</tr>
<tr>
<td>RSPV diameter, mm</td>
<td>20.4±3.1</td>
</tr>
<tr>
<td>RIPV diameter, mm</td>
<td>19.8±3.3</td>
</tr>
<tr>
<td>Procedure time, min</td>
<td>112.6±24.8</td>
</tr>
<tr>
<td>Fluoroscopy time, min</td>
<td>19.8±7.1</td>
</tr>
<tr>
<td>CB applications per procedure</td>
<td>6.4±2.4</td>
</tr>
<tr>
<td>CB size, 23 mm</td>
<td>14 (10)</td>
</tr>
<tr>
<td>CB size, 28 mm</td>
<td>126 (90)</td>
</tr>
</tbody>
</table>

Values are n, n (%), mean±SD. AF indicates atrial fibrillation; CB, cryoballoon; LA, left atrium; LVEF, left ventricular ejection fraction; VKA, vitamin K antagonist; RSPV, right superior pulmonary vein; and RIPV, right inferior pulmonary vein.

In 18 patients (13.6%), a 30% decrease in CMAP amplitude occurred and cryoablation was discontinued with forced deflation (Table 2). At this time, abdominal palpation detected no decrease in diaphragmatic contraction strength. The mean duration of cryoapplication was 121.4±32.5 s. The minimum temperature achieved was −45.9±5.6°C. Baseline CMAP amplitude

### Table 2. Characteristics of Patients in Whom Cryoapplication was Discontinued Because of Threatened Right Phrenic Nerve Palsy

<table>
<thead>
<tr>
<th>Patient</th>
<th>Vein</th>
<th>CB Size, mm</th>
<th>First Application Duration, s</th>
<th>Minimum Temperature, °C</th>
<th>Online Isolation—Timing, s</th>
<th>Second Application Duration, s</th>
<th>Minimum Temperature, °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>RSPV</td>
<td>28</td>
<td>132</td>
<td>−42</td>
<td>Yes—38</td>
<td>No</td>
<td>−48</td>
</tr>
<tr>
<td>2</td>
<td>RIPV</td>
<td>23</td>
<td>97</td>
<td>−49</td>
<td>No</td>
<td>110</td>
<td>−40</td>
</tr>
<tr>
<td>3</td>
<td>RSPV</td>
<td>28</td>
<td>122</td>
<td>−56</td>
<td>Yes—47</td>
<td>No</td>
<td>−40</td>
</tr>
<tr>
<td>4</td>
<td>RSPV</td>
<td>28</td>
<td>76</td>
<td>−38</td>
<td>No</td>
<td>80</td>
<td>−40</td>
</tr>
<tr>
<td>5</td>
<td>RSPV</td>
<td>28</td>
<td>72</td>
<td>−45</td>
<td>Yes</td>
<td>25</td>
<td>−45</td>
</tr>
<tr>
<td>6</td>
<td>RIPV</td>
<td>23</td>
<td>145</td>
<td>−54</td>
<td>No</td>
<td>No</td>
<td>−44</td>
</tr>
<tr>
<td>7</td>
<td>RSPV</td>
<td>28</td>
<td>152</td>
<td>−49</td>
<td>Yes</td>
<td>33</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>RIPV</td>
<td>28</td>
<td>85</td>
<td>−40</td>
<td>No</td>
<td>100</td>
<td>−43</td>
</tr>
<tr>
<td>9</td>
<td>RSPV</td>
<td>28</td>
<td>168</td>
<td>−55</td>
<td>Yes</td>
<td>102</td>
<td>172</td>
</tr>
<tr>
<td>10</td>
<td>RIPV</td>
<td>28</td>
<td>169</td>
<td>−43</td>
<td>Yes</td>
<td>44</td>
<td>No</td>
</tr>
<tr>
<td>11</td>
<td>RSPV</td>
<td>28</td>
<td>109</td>
<td>−42</td>
<td>Yes</td>
<td>27</td>
<td>105</td>
</tr>
<tr>
<td>12</td>
<td>RIPV</td>
<td>28</td>
<td>144</td>
<td>−45</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>13</td>
<td>RIPV</td>
<td>28</td>
<td>97</td>
<td>−40</td>
<td>Yes</td>
<td>37</td>
<td>102</td>
</tr>
<tr>
<td>14</td>
<td>RSPV</td>
<td>28</td>
<td>157</td>
<td>−51</td>
<td>Yes</td>
<td>48</td>
<td>No</td>
</tr>
<tr>
<td>15</td>
<td>RSPV</td>
<td>28</td>
<td>124</td>
<td>−48</td>
<td>Yes</td>
<td>15</td>
<td>No</td>
</tr>
<tr>
<td>16</td>
<td>RIPV</td>
<td>28</td>
<td>105</td>
<td>−43</td>
<td>Yes</td>
<td>53</td>
<td>No</td>
</tr>
<tr>
<td>17</td>
<td>RSPV</td>
<td>28</td>
<td>88</td>
<td>−39</td>
<td>No</td>
<td>95</td>
<td>−44</td>
</tr>
</tbody>
</table>

CB indicates cryoballoon; RIPV, right inferior pulmonary vein; and RSPV, right superior pulmonary vein.
The concept of electromyography monitoring was developed in a preclinical study. A 30% decrease in CMAP amplitude predicted imminent PNP with a comfortable margin. The first clinical application was described in a case report. More recently, we published a 57-patient series with the electromyography-guided PNM using a catheter placed in a hepatic vein during ablation with CB1. The main advantage of hepatic vein placement is stable CMAP amplitude, despite respiratory movements. No PNP occurred but the cut-off value was reached in 6 patients requiring discontinuation of right superior pulmonary vein cryoapplication with forced deflation. Failure to achieve stable phrenic nerve pacing was observed in 12% of cases.

Lakhani et al reported a 109-case series involving surface recording of CMAP amplitude during cryoablation for atrial fibrillation using CB1. The monitoring was straightforward and allowed reliable prediction of PNP.

Mondésert et al described an observational study of diaphragmatic electromyography monitoring with surface electrodes during cryoballoon ablation in 200 consecutive patients. Diaphragmatic motion decreased in 30 patients, preceded by a 30% reduction of CMAP amplitude in all the patients. Three persistent PNP occurred. The main problem with surface electrodes recordings is 30% CMAP amplitude variation with respiratory movements, that is, the exact threshold for discontinuation of cryoapplication to prevent PNP.

The present series confirms that electromyography-guided PNM is an effective technique for procedures using CB2. The 30% cut-off value for CMAP amplitude was still pertinent.

In 9 cases, a second cryoapplication was safely performed after forced deflation to prevent PNP. No previous report has described a second cryoapplication in the same PV. Because electromyography-guided PNM is an objective method allowing early detection, we reasoned that it would be safe to attempt a second cryoapplication to achieve a reasonable ablation duration and durable PVI.

A systematic review of procedures using CB1 reported that the incidence of persistent and permanent PNP was 6.38% and 0.37%, respectively. In studies using CB2, the PNP rate has ranged from 3.5% to 27.5% and the vast majority of cases regressed completely. The rate of threatened PNP in our previous series using CB1 was identical to the 1 observed in this series with CB2: 12% versus 13.6%, respectively. This similarity occurred despite more frequent use of 28-mm CB2 (90% versus 32%).

The main limitations of this study are the limited patient population and the absence of blinding and randomization. Moreover, modest additional fluoroscopy time is necessarily associated with catheter positioning in the hepatic vein. Extra cost and additional femoral access will be required in the electrophysiology laboratory using only 1 diagnostic catheter as usual setup for cryoballoon procedures.

Conclusions

This study indicates that phrenic CMAP amplitude recording using a catheter positioned in a subdiaphragmatic hepatic vein is usually feasible during CB2 procedures. Electromyography-guided PNM seems effective in preventing of PNP. Finally, it seemed safe to perform a second cryoapplication in the same PV after discontinuation of a first because of a 30% decrease of the CMAP amplitude of the diaphragm before the occurrence of a PNP.

Disclosures

None.

References


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