Novel Electromyographic Monitoring Technique for Prevention of Right Phrenic Nerve Palsy During Cryoballoon Ablation

Frédéric Franceschi, MD, PhD; Linda Koutbi, MD; Julien Mancini, MD, PhD; Shahram Attarian, MD, PhD; Sébastien Prevôt, MD; Jean-Claude Deharo, MD

Background—Right phrenic nerve palsy (PNP) is the most frequent complication of cryoballoon ablation. Diaphragmatic electromyography can predict PNP with a comfortable safety margin. Our goal was to evaluate the feasibility, efficacy, and safety of electromography-guided PN monitoring using a novel hepatic vein approach for prevention of PNP.

Methods and Results—This study includes 57 patients (47 males) indicated for cryoballoon ablation for treatment of atrial fibrillation. During right superior pulmonary vein ablation, the PN was paced at 60 beats per minute and diaphragmatic compound motor action potential (CMAP) amplitude was recorded via a quadripolar catheter positioned in a subdiaphragmatic hepatic vein. If a 30% drop in CMAP amplitude was observed, ablation was discontinued with forced deflation. Reliable recording of CMAP before ablation was feasible in 50 of 57 patients (88%). In 7 patients (12%), stable PN pacing could not be achieved. In 44 of 50 patients, CMAP amplitude remained constant during cryoapplication. The mean value of CMAP amplitude was 639.7±240.5 µV; mean variation was 13±4.3%. In 6 of 50 patients (12%) including 5 treated with a 23-mm cryoballoon and 1 with a 28-mm cryoballoon, the 30% reduction cutoff was reached and cryoablation was discontinued. Recovery of CMAP amplitude after discontinuing cryoablation took <60 seconds in all cases. No PNP or complication related to PN monitoring occurred.

Conclusions—Recording of diaphragmatic CMAP using a catheter positioned in a subdiaphragmatic hepatic vein seems feasible during cryoballoon ablation. Electromography-guided PN monitoring seems safe and potentially helpful for prevention of PNP. (Circ Arrhythm Electrophysiol. 2013;6:1109-1114.)

Key Words: atrial fibrillation • catheter ablation • phrenic nerve

Clinical Perspective on p 1114

Our group has been investigating a more objective technique using diaphragmatic electromyography (EMG) to monitor PN function. A preliminary study in dogs showed that diaphragmatic compound motor action potential (CMAP) could be recorded during PN pacing and that a 30% reduction in CMAP amplitude was predictive of impending hemidiaphragmatic paralysis with a wide safety margin. Based on these findings, we hypothesized that PN palsy (PNP) could be prevented by discontinuing cryoablation when a 30% reduction in CMAP was observed. In our animal study, diaphragmatic CMAP recording was performed using an esophageal catheter, thus requiring complete apnea during cryoapplication to obtain stable CMAP amplitude. Because 4 minutes apnea is an unacceptable option in clinical practice, an alternative approach using surface abdominal electrodes was tried but proved to have 3 major drawbacks. First, a major pacing artifact limited recording to a small terminal segment of the CMAP. Second, CMAP amplitude showed variations of 30% with respiratory movements, that is, the exact value of the cutoff for discontinuing cryoablation observed in the animal study. Third, placement of electrodes for effective recording was challenging, particularly in obese patients.

The purpose of this report is to describe a novel approach using a multipolar catheter positioned in a subdiaphragmatic hepatic vein to record phrenic CMAP amplitude as a basis for EMG-guided PN monitoring. The 2-fold aim of this clinical study was to assess the feasibility of the new approach and...
evaluate the safety and efficacy of the technique for prevention of right PNP during cryoballoon procedures.

Materials and Methods

Study Design

From June 2011 to August 2012, a total of 57 consecutive patients indicated for cryoballoon PV isolation at our center were included after providing informed consent. The selection criteria for cryoballoon PV isolation were symptomatic paroxysmal or persistent (<6 months) AF that was refractory to ≥1 antiarrhythmic drug. The day before cryoballoon ablation, all patients underwent 2-dimensional transthoracic echocardiography to rule out thrombi in the left atrial appendage as well as transthoracic examination with determination of left atrial dimensions and assessment of left ventricular and valvular function. Preprocedural evaluation also included computed tomographic scan to map left atrial anatomy. Patients with left atrial thrombus, severe uncontrolled heart failure, and left atrial dimensions ≥50 mm were not included in the study.

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 hexapolar catheter (Xtrem catheter, Sorin Group) was positioned in the coronary sinus via femoral access. These 2 catheters were used as landmarks for transseptal puncture to allow placement of a steerable 15 Fr sheath (Flexcath, Medtronic) in the left atrium. After transseptal 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 cryoballoon (Arctic Front, Medtronic CryoCath LP) was advanced through the sheath into the left atrium using the Achieve catheter as a guidewire. Choice of balloon diameter was based on left atrium and PV dimensions measured on preprocedural computed tomographic scans. Before ablation, the Achieve catheter was positioned in the venous ostium to record baseline electric activity. Then, the cryoballoon was wedged in the ostium and occlusion was tested with contrast agent. When the operator considered that PV occlusion was sufficient, cryoapplication was started. The duration of each cryoapplication was 240 seconds. After each cryoapplication, PV isolation was assessed with the Achieve catheter. If necessary, PV isolation was completed with an irrigated radiofrequency catheter. After a waiting period of 20 minutes after the last cryoapplication, PV isolation was reevaluated to detect early recovery of left atrium–PV conduction.

PN Monitoring

PN monitoring was performed during right superior PV (RSPV) cryoapplication. The deflectable hexapolar catheter was moved to the superior vena cava (SVC) to pace the right PN (10 V; 2.9 milliseconds at 60/min). Particular attention was paid to ensure stable pacing. Pacing was performed with the distal pair of electrodes. The quadripolar catheter (4 mm electrodes spaced 10 mm apart) was moved to a right-sided subdiaphragmatic hepatic vein and connected to the central computerized electrophysiology workstation (Prucka CardioLab, General Electric). Bipolar EMG signals were recorded between the electrodes proximal and distal to the quadripolar catheter so as to create the maximal interelectrode space. Using this technique, EMG recording covered a large part of the right hemidiaphragm. Signals were amplified and band-pass filtered between 5 and 150 Hz. During each RSPV cryoapplication, EMG signals were continuously recorded on a hard disk and stored on an optical drive. During right PN pacing before cryoapplication, the position of the quadripolar catheter in the hepatic vein was optimized to obtain the highest diaphragmatic CMAP signal amplitude (if possible >300 µV). The abdomen was continuously palpated during cryoapplication. If phrenic CMAP amplitude remained stable, that is, varied ≤30% in relation to baseline phrenic CMAP amplitude, the duration of cryoapplication was 240 seconds with the possibility of performing a second cryoapplication at the operator’s discretion. If the 30% reduction cutoff considered as predictive of PNP was reached, RSPV cryoapplication was discontinued using the forced deflation emergency maneuver. In this case, fluoroscopy was performed to assess diaphragm motion with forced respiratory movement.

In the postprocedural analysis, phrenic CMAP amplitudes were measured from the start of each RSPV cryoapplication. Each measurement involved averaging of 4 consecutive phrenic CMAP amplitude values. If cryoapplication was discontinued because of a 30% drop in phrenic CMAP, phrenic CMAP recording was continued for 60 seconds thereafter.

Postprocedural Management

All patients were discharged the day after ablation. Two-dimensional transthoracic echocardiography and chest x-ray were performed in all cases to rule out postprocedural pericardial effusion and PNP. Low-molecular-weight heparin was started the same day after ablation. Oral anticoagulation was started the day after the procedure. Patients were dismissed on both oral anticoagulation and low-molecular-weight heparin. When the target international normalized ratio of 2 to 3 was reached, low-molecular-weight heparin was discontinued and oral anticoagulation was administered alone for 3 months after the procedure. Antiarrhythmic therapy was administered for 3 months after the procedure and then discontinued if AF did not recur.

Follow-Up

In patients in whom cryoapplication was discontinued because of a ≥30% reduction in CMAP amplitude, clinical examination and 24-hour Holter monitoring were performed at 3, 6, and 9 months after ablation. Documented episodes of AF lasting ≥30 seconds were considered as recurrences. No blanking period was considered.

Study End Points

The main study end point was to assess the feasibility and safety of PN monitoring based on CMAP amplitude measured using a multipolar catheter in a subdiaphragmatic hepatic vein during cryoballoon procedure. The secondary end point was to evaluate the efficacy of this monitoring technique for prevention of PNP.

Statistical Analysis

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

Results

Patients and Procedures

Patient and procedure characteristics are summarized in the Table. Acute PV isolation was obtained in all patients. In 3 patients, a radiofrequency catheter was used to complete PV isolation. Three acute complications occurred, that is, groin hematoma in 2 cases and pericardial effusion not requiring pericardiocentesis in 1. The mean size of the RSPV was 21±4×17±3 mm.

Baseline Phrenic CMAP Recording With Catheter in Hepatic Vein

In 7 patients (12%), steady baseline phrenic CMAP amplitude could not be obtained because the pacing catheter could not be positioned properly at the PN level in the SVC. As a result, large variations in CMAP amplitude occurred and EMG-guided PN monitoring was impossible. In the remaining 50 patients (88%), a steady baseline diaphragmatic CMAP was obtained (mean, 639.7±240.5 µV).
CMAP amplitude remained stable after the catheter was placed in a hepatic vein. When positioning was too proximal, respiratory movement caused strong amplitude variations (Figure 1). In that case, the catheter was moved to a more distal position. The phrenic CMAP signal appeared as a sharp stable potential with a minimal pacing artifact (Figure 2).

### Cryoballoon Ablation With EMG-Guided PN Monitoring

**Patients With <30% Reduction in CMAP Amplitude**

In 44 of the 50 patients (88%) in whom EMG-guided PN monitoring was performed, the variation in CMAP amplitude was <30% reduction throughout the 240-second RSPV cryoapplication (Figure 3). In this group, the mean value of maximal CMAP amplitude variation recorded during cryoapplication was 13±4.3% (extremes, +5.5±3.4% and −7.5±3.4%). In all patients, abdominal palpation demonstrated stable diaphragmatic contraction. Next-day chest x-ray showed no right PNP.

**Patients With ≥30% Reduction in CMAP Amplitude**

In 6 patients (12%), variation in CMAP amplitude reached the 30% threshold during the RSPV cryoapplication (Figures 4 and 5). Cryoballoon size was 23 mm in 5 patients and 28 mm in 1. Subjective assessment by palpation did not detect any change in contraction strength in any of these patients. The reduction threshold was reached at 72, 81, 88, 105, 136, and 140 seconds (mean, 104±28 seconds). On recognizing the 30% reduction in CMAP amplitude, the operator discontinued cryoapplication by performing the forced deflation emergency maneuver. In all cases, CMAP amplitude continued to decrease moderately for several seconds after forced deflation and then progressively returned to baseline within 60 seconds. In all cases, RSPV isolation was achieved despite truncated cryoapplication. The mean reduction of CMAP amplitude at the time of forced deflation was 33±4% as compared with baseline. Diaphragmatic movement based on fluoroscopic evaluation after cryoapplication and at the end of the procedure was normal. Next-day chest x-ray showed no right PNP.

**Safety**

No adverse event related to PN monitoring was observed during or after the procedure. Positioning of the catheter in the hepatic vein was painless. The forced deflation emergency maneuver caused no untoward effect.

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**Table. Baseline Patient and Procedure Characteristics**

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<table>
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<tbody>
<tr>
<td>Patients included</td>
<td>57</td>
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<tr>
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<td>59±9</td>
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<tr>
<td>Male sex, n</td>
<td>47</td>
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<tr>
<td>Hypertension/ICM/DCM, %</td>
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<td>LA diameter, mm</td>
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<td>Paroxysmal/persistent, %</td>
<td>86/14</td>
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<tr>
<td>Fluoroscopy time, min</td>
<td>30±12</td>
</tr>
<tr>
<td>Cryoballoon applications, n</td>
<td>9±2</td>
</tr>
<tr>
<td>Cryoballoon 23/28/23–28 mm</td>
<td>63/32/5</td>
</tr>
</tbody>
</table>

DCM indicates dilated cardiomyopathy; ICM, ischemic cardiomyopathy; and LA, left atrium.
Follow-Up

The mean follow-up in the 6 patients in whom cryoapplication was discontinued was 198±92 days. Two patients had documented AF recurrences. One patient did not undergo a redo procedure. In the other patient, redo was performed 7 months after the first procedure. Redo consisted of radiofrequency isolation of the common trunk of left-sided PV. The right-sided veins were not reconnected. In this patient, during the first cryoballoon procedure, only 1 RSPV application was performed, discontinued by forced deflation at 136 seconds. The patient is currently free from AF with a follow-up of 3 months after redo. The remaining 4 patients in whom cryoapplication was discontinued were recurrence free at the time of the last follow-up examination.

Discussion

Cryoballoon catheter ablation is effective for PV isolation. The most frequent complication is right PNP.1 This clinical study describes a novel EMG-guided PN monitoring technique to prevent this complication. The 4 most important findings are as follows. First, diaphragmatic EMG using a catheter positioned in a hepatic vein provides stable reliable CMAP amplitude recording during cryoballoon ablation in most patients. Second, using this technique, no case of PNP occurred in a series of 50 cryoballoon procedures (2/3 with the 23-mm cryoballoon) including 6 in which RSPV cryoapplication was discontinued using the forced deflation maneuver because of a >30% drop in CMAP amplitude. Third, no complication occurred in relation to monitoring. Fourth, the main technical problem was failure to achieve stable PN pacing in 12% of cases.

Advantages of Hepatic Vein for Diaphragmatic EMG Recording

None of the 3 approaches proposed for diaphragmatic EMG recording, that is, surface electrodes, esophageal electrodes, and direct needle,6 are suitable for monitoring during cryoballoon catheter ablation. Because of its invasive nature, direct needle recording is unsuitable for electrophysiology (EP) procedures. Recording with esophageal electrodes is a noninvasive option, but the amplitude of recorded values can vary 2- to 3-fold in function of the distance between the electrodes and the diaphragmatic muscle that fluctuates with respiratory movement. Stable baseline recording values can be obtained with esophageal electrodes by inducing apnea as in our preclinical trial3 in dogs, but this is unacceptable in clinical use. The third approach, that is, electrodes placed on the surface of the abdomen has 3 major drawbacks. The first is that surface electrodes are subject to ≈30% CMAP amplitude variation with respiratory movements, that is, the exact threshold for discontinuation of cryoapplication to prevent PNP. The second is that effective placement of surface electrodes can be a challenge, especially in obese patients. The third is that, in our experience, use of surface electrodes was associated with a large pacing artifact that masked all but a small terminal segment of the phrenic CMAP. The most likely causes for this artifact are the short distance from the pacing catheter in the SVC to the surface electrodes and PN pacing at high amplitude and duration.

The approach to CMAP recording described in this article is totally new and different. It presents several advantages. First, electrode location close to the diaphragm allows recording of high CMAP amplitude values. Second, the distance between the muscle and electrode does not vary during respiration because the liver moves with the diaphragm.

Figure 4. Mean amplitude values of the phrenic compound motor action potential (CMAP) in patients with ≥30% reduction in CMAP amplitude. Curve centered on the time of forced deflation (T0) showing 60 s before and after discontinuation of cryoapplication. Note the stability of CMAP amplitude at the beginning of the curve. After discontinuation of cryoapplication, CMAP increases progressively back to the baseline value in <60 s.

Figure 5. Example of phrenic compound motor action potential (CMAP) amplitude in a patient with threatened right phrenic nerve during right superior pulmonary vein (RSPV) cryoballoon ablation. When cryoballoon ablation in the RSPV is started, baseline CMAP amplitude is 472 µV (T0). Amplitude displayed minimal variations during the first 60 s but then showed a progressive decrease to 340 µV at 72 s (28% decrease from baseline value). At that point, the cryoapplication was discontinued with forced deflation. After deflation, CMAP amplitude gradually returned to the baseline value within ≈40 s.
distance is stable, the CMAP amplitude variation observed during recording was low. This feature is essential because reduction of CMAP amplitude is the key to predicting and preventing PNP based on EMG-guided PN monitoring. A third advantage of the novel method proposed here is that despite its invasive character, setup using a simple venous femoral access and a quadrupolar catheter remains easy in the EP laboratory. Another practical aspect of the technique is that recorded CMAPs can be displayed directly on the central computerized electrophysiology workstation. A fourth advantage is that, unlike surface recording, the pacing artifact is minimal so that CMAP is completely visible.

Diaphragmatic EMG Recording During Cryoballoon Ablation

In our preclinical study,3 we identified a 30% reduction in CMAP amplitude as the cutoff value for predicting hemidiaphragmatic paralysis with a comfortable safety margin. Based on this finding, it was hypothesized that PNP could be prevented by discontinuing cryoapplication as soon as a 30% reduction was observed.

In a subsequent report, we described the first clinical application of this prevention technique. Diaphragmatic CMAP was monitored using surface electrodes during cryoballoon ablation of the RSPV in a 51-year-old man.4 Cryoablation was discontinued with forced deflation maneuver when the decrease in CMAP amplitude reached 20% reduction while the diaphragmatic excursion remained intact. A transient drop in hemidiaphragmatic motion ensued but full recovery was observed within 1 minute.

The present study is the first to describe EMG-guided PN monitoring using an electrode placed in a hepatic vein during cryoballoon ablation. The findings support the hypothesis that PNP can be avoided by EMG-guided PN monitoring, despite the use of 23-mm cryoballoon in more than two thirds of cases.

Although CMAP recording for right PN monitoring in our study was performed only during RSPV cryoballoon application, we recommend PN monitoring for both right PVs because PNP is possible even during right inferior pulmonary vein cryoballoon application.

Forced Deflation Emergency Maneuver

In this study, forced deflation was performed in case of 30% reduction in CMAP amplitude. Our aim was to accelerate rewarming by allowing immediate return of convective blood flow that has been shown to limit the extent of cryolesions.7,8 Indeed, balloon inflation during cryoapplication results in complete occlusion of the vein and stops blood flow. Normally, when cryoapplication is stopped, deflation does not occur until balloon temperature rises to +20°C. This can take a long time if balloon temperature is low. Our reasoning was that, by avoiding this delay, forced deflation would limit cold-induced injury and enable faster PN recovery. Although the safety of this method has not been demonstrated in a large patient cohort, it is noteworthy that no complications were observed in small clinical series and animal studies.9,10

Whether combining CMAP monitoring and forced deflation is necessary to avoid PNP is unclear and will require dedicated study.

Efficacy of PV Isolation

Patients in whom the procedure was interrupted because of the threat of right PN received a single cryoapplication in the RSPV. Mean treatment time in these patients was only 104±28 seconds, but that was sufficient to obtain acute PV isolation. In the patient who underwent redo 7 months later, the RSPV was still isolated. Nevertheless, a larger cohort will be needed to compare long-term procedural success rates in patients undergoing truncated procedures and those receiving full treatment.

Instability of Right PN Pacing

Stable PN pacing could not be achieved in a few patients. Indeed, positioning of the pacing catheter can be challenging because the PN is a narrow structure at the posterior face of the SVC that is a large-sized vessel.11 CMAP amplitude depends on the total number of muscular fibers recruited.8 When PN capture is unstable, CMAP amplitude varies greatly from one beat to another. Stable CMAP amplitude is an indispensable condition for EMG-guided PN monitoring. It would be useful to design a dedicated catheter for PN pacing via the SVC.

Limitations

The main limitations of this study are the small size of the patient population and the absence of blinding and randomization. Larger studies will be needed to confirm the findings reported here. Long-term follow-up will be necessary to assess the efficacy in terms of AF recurrence rate after procedures using the EMG-guided approach. Because this study has been performed using the Arctic Front version of the cryoballoon, another study is needed to determine whether CMAP monitoring remains effective using the new cryoballoon version Arctic Front Advance.

Conclusion

Phrenic CMAP amplitude recording using a catheter positioned in a subdiaphragmatic hepatic vein seems feasible during cryoballoon procedures in most patients. It seems to be a safe and reliable method to obtain stable phrenic CMAP amplitude measurements in the EP laboratory. EMG-guided PN monitoring with forced deflation of cryoballoon ablation on a 30% reduction in the diaphragmatic CMAP amplitude could be helpful in preventing the hemidiaphragmatic paralysis without compromising the success of acute PV isolation.

Disclosures

Dr Franceschi is a consultant for Medtronic CryoCath LP. The other authors report no conflicts.

References

The main complication of cryoballoon procedures is paralysis attributable to injury of the right phrenic nerve. Although paralysis usually regresses within a few months, it can be permanent. The incidence of this complication is around 7%. Up to now, no effective prevention technique has been proposed. Our group has been working on a prevention technique based on real-time electromyographic monitoring of the right diaphragm. The aim is to detect objective early evidence of impending phrenic nerve injury during cryoballoon procedures. An initial feasibility animal study demonstrated that a change in the compound motor action potential of the diaphragm was consistently observed 30 seconds before paralysis. Based on this finding, we developed a novel monitoring technique for use in human patients. It consists of placing an electrophysiology diagnostic catheter at the level of the hepatic vein. This technique eliminates amplitude variations during compound motor action potential recording because the liver and diaphragm move in unison, and thus the distance between the muscle and electrode does not vary. The present study shows the feasibility of this monitoring technique in a clinical setting. By discontinuing the cryoballoon application as soon as any change in diaphragmatic compound motor action potential was detected, no paralysis was observed in this series. This technique is simple and can be easily implemented without special equipment in all electrophysiology laboratories. Further development is needed to automate real-time signal processing and optimize the method used to stimulate the right phrenic nerve.
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