Corticosteroid use during pulmonary vein isolation is associated with a higher prevalence of dormant pulmonary vein conduction

Jason G. Andrade, MD,[*†] Paul Khairy, MD, PhD,[*] Stanley Nattel, MD,[*] Agustin Vanella, MD,[*] Léna Rivard, MD,[*] Peter G. Guerra, MD,[*] Marc Dubuc, MD, FHRS,[*] Katia Dyrda, MD,[*] Bernard Thibault, MD, FHRS,[*] Mario Talajic, MD, FHRS,[*] Blandine Mondesert, MD,[*] Denis Roy, MD, FHRS,[*] Laurent Macle, MD[*]

From the [*]Electrophysiology Service at the Montreal Heart Institute and Department of Medicine, Université de Montréal, Montreal, Canada, and [†]Department of Medicine, The University of British Columbia, Vancouver, Canada.

BACKGROUND Atrial fibrillation (AF) recurrence after pulmonary vein isolation (PVI) is associated with PV to left atrium reconduction.

OBJECTIVE The purpose of this study was to prospectively determine if the use of intraprocedural corticosteroids to limit the extent of tissue edema and/or inflammation alters the prevalence of spontaneous and adenosine-induced acute PV reconnection after PVI.

METHODS Prior to wide circumferential PVI, 45 patients received a single intravenous (IV) bolus of hydrocortisone 250 mg immediately after transseptal access (steroid group). Another 45 consecutive patients underwent standard PVI without IV hydrocortisone (nonsteroid group). After PVI, all patients underwent adenosine testing to unmask dormant conduction. Patients were followed at 3, 6, and 12 months.

RESULTS Dormant conduction was unmasked in a significantly higher proportion of PVs in the steroid group compared with the nonsteroid group (32.8% of PVs [60/183] vs 21.1% of PVs [37/175], $P = .03$). On multivariate generalized estimating equation analysis, steroid use remained independently associated with dormant PV conduction ($P = .03$). There was no difference in the segmental distribution of reconnection between the 2 groups. The 1-year freedom from recurrent AF did not differ between groups ($P = .37$). Radiofrequency time was significantly longer in the steroid group (58 ± 21 minutes vs 48 ± 18 minutes, $P < .01$), whereas procedure duration and fluoroscopy time were comparable ($P = .55$ and $P = .44$, respectively).

CONCLUSION A single bolus of hydrocortisone 250 mg IV prior to PVI results in greater radiofrequency requirements for PVI and a higher prevalence of dormant PV conduction unmasked by adenosine. The utility of these approaches requires evaluation in a long-term prospective randomized study.

KEYWORDS Atrial fibrillation; Ablation; Pulmonary vein; Inflammation; Steroids; Hydrocortisone

ABBREVIATIONS **AF** = atrial fibrillation; **AFL** = atrial flutter; **AT** = atrial tachycardia; **GEE** = generalized estimating equation; **INR** = international normalized ratio; **IQR** = interquartile range; **IV** = intravenous; **LA** = left atrium; **PV** = pulmonary vein; **PVI** = pulmonary vein isolation; **RF** = radiofrequency; **RFCA** = radiofrequency catheter ablation

(Heart Rhythm 2013;10:1569–1575)

Introduction

Radiofrequency catheter ablation (RFCA) is an effective treatment option for patients with medically refractory symptomatic paroxysmal or persistent atrial fibrillation (AF).[1] However, despite initial procedural success, up to 20% to 40% of patients will require a second intervention for arrhythmia recurrence, which most often is due to recovery of conduction between pulmonary veins (PVs) and the left atrium (LA).[2–7] The use of adenosine during pulmonary vein isolation (PVI) procedures has been postulated to reduce PV reconnection and AF recurrence by distinguishing permanent PV–LA block from dormant conduction (ie, viable but latently nonconducting tissue).[8–14]

Address reprint requests and correspondence: Dr. Jason Andrade, Electrophysiology Service, Montreal Heart Institute, 5000 Belanger St. E., Montreal, QC, Canada, H1T 1C8. E-mail address: Jason.guy.andrade@umontreal.ca.

Recently, the use of postablation corticosteroids has shown promise in decreasing the incidence of early AF recurrences after catheter ablation through an abatement of the proinflammatory process triggered by RFCA.[15] We postulated that the same benefit might be achieved by a single intravenous (IV) steroid dose preablation, which might be simpler and safer than the previously described method. The purpose of our study was to determine if the use of intraprocedural corticosteroids to limit the extent of tissue edema and/or inflammation alters the prevalence of spontaneous and adenosine-induced acute PV reconnection after PVI.

Methods

Study population

Ninety patients with symptomatic paroxysmal AF refractory to antiarrhythmic drugs referred for catheter ablation were prospectively enrolled in this cohort study. In 45 consecutive

1547-5271/$-see front matter http://dx.doi.org/10.1016/j.hrthm.2013.07.037

patients, an IV bolus of 250 mg of hydrocortisone was administered immediately after transseptal access (steroid group). Another 45 consecutive patients underwent standard PVI without IV hydrocortisone (nonsteroid group). The study protocol was approved by our institutional review committee. Written informed consent was obtained from each participant.

All patients underwent preprocedural transthoracic echocardiographic and/or cardiac magnetic resonance imaging. Effective anticoagulation with oral vitamin K antagonists (international normalized ratio [INR] 2–3) or dabigatran for at least 1 month or the exclusion of an LA thrombus by transesophageal echocardiography was required prior to ablation. Antiarrhythmic drugs were discontinued before the procedure, allowing a washout period of 5 half-lives (except for amiodarone).

PVI procedure

All patients underwent catheter ablation with an irrigated-tip radiofrequency (RF) ablation catheter using standard techniques. Specifically, via central venous access a multipolar catheter was placed in the coronary sinus to guide electroanatomic mapping and facilitate LA pacing. LA access was obtained via dual transseptal puncture or patent foramen ovale. After transseptal access, IV heparin was administered as a bolus with continuous infusion to maintain an activated clotting time >300 seconds. Through 1 transseptal access, a variable decapolar circular mapping catheter (Lasso, Biosense Webster, Diamond Bar, CA) was advanced into the LA for mapping and confirmation of PVI. Via the second transseptal access, an irrigated 3.5-mm tip mapping and ablation catheter (ThermoCool, Biosense Webster; or Safire BLU, St. Jude Medical, Minneapolis, MN) was advanced into the LA via a long sheath. All procedures were guided by a 3-dimensional electroanatomic mapping system (EnSite NavX, St. Jude Medical; or CARTO, Biosense Webster). Prior to ablation, the circular mapping catheter was placed sequentially within each of the 4 PV antra to record baseline electrical activity (PV potentials). The ostia and antra of the PVs were defined through a combination of examination of the 3-dimensional electroanatomic shell, pulmonary venography, tactile catheter feedback, catheter impedance changes, and signal mapping as the catheter was withdrawn from inside the vein.

Using a standard wide circumferential antral isolation approach, ipsilateral PVs were targeted in pairs with RF lesions placed a minimum of 1 cm outside the PV ostia. Ablation was allowed within 1 cm of the ostium of the left superior PV owing to the narrow ridge of tissue between its anterior aspect and the LA appendage. Radiofrequency energy was delivered at a target temperature of 43°C, power of 30–35 W, and irrigation flow rate of 17–30 mL/min. On the posterior wall, RF power was reduced to 20–25 W with a flow of 17 mL/min. PVI was considered complete when spontaneous associated PV potentials were no longer recorded by the circular mapping catheter (entrance block), and PV to LA dissociation was noted either spontaneously or with PV pacing (exit block). No induction testing (using burst pacing or isoproterenol infusion), prophylactic linear ablation lesions, or ablation of complex fractionated atrial electrograms was performed.

Dormant conduction

Following confirmation of isolation of all PVs, a minimum 20-minute observation period was undertaken to evaluate spontaneous PV reconduction. In the event of spontaneous reconnection, reisolation was performed prior to adenosine testing. Once persistent isolation was confirmed, provocative testing with ≥ 12 mg IV adenosine was performed to evaluate the prevalence of dormant conduction. Adenosine dosing was titrated to achieve at least 1 blocked P wave or a sinus pause ≥ 3 seconds (Figure 1). Sites of dormant conduction, as defined by the transient or sustained reappearance of PV activity on an appropriately positioned circular mapping catheter for ≥ 1 beat, were noted on the electroanatomic map with the PVs divided into 8 segments: superior, anterosuperior, anterior, anteroinferior, inferior, posteroinferior, posterior, and posterosuperior. In cases of dormant conduction, additional ablation at sites of PV reconnection was performed (until dormant conduction could no longer be elicited) at the discretion of the operator.

Follow-up

All patients were discharged home within 2 days of the procedure. Postprocedure, patients continued anticoagulation with warfarin (to maintain INR 2–3) or dabigatran for a minimum of 2 months. Antiarrhythmic medications (sotalol, propafenone, or flecainide) were allowed for a maximum of 3 months postablation, after which they were discontinued. Patients were followed with routine transtelephonic monitoring, and clinical assessment, 12-lead ECG, and 24-hour Holter at 3, 6, and 12 months postablation. The primary outcome was time to first recurrence of symptomatic electrocardiographically documented AF or atrial flutter (AFL), or atrial tachycardia (AT) between days 91 and 365. Qualifying arrhythmia recurrences were required to last ≥ 30 seconds and be documented by 12-lead ECG, surface ECG rhythm strips, 24-hour Holter, or transtelephonic monitoring recordings. A blanking period of 3 months after the initial ablation was used such that recurrences during this time were not counted. No patient was lost to follow-up, and all patients underwent the required outpatient visits and monitoring.

Statistical analysis

Continuous variables are expressed as mean $\pm$ SD or as median, interquartile range (IQR) for nonparametric data and were compared Student *t* tests or Wilcoxon rank sum tests for continuous variables. Categorical variables are expressed as frequency and percentage and were compared by χ^2 or Fisher exact test. The generalized estimating equation (GEE) approach was performed using the binary distribution to study the presence of dormant conduction with IV steroid