Electrophysiological Findings in Adolescents With Atrial Fibrillation Who Have Structurally Normal Hearts

Kumaraswamy Nanthakumar, MD; Yung R. Lau, MD; Vance J. Plumb, MD; Andrew E. Epstein, MD; G. Neal Kay, MD

Background—Atrial fibrillation (AF) is uncommon in children, and its mechanisms are unknown. This study describes the electrophysiological findings in children and adolescents with AF and the outcome of catheter ablation.

Methods and Results—Nine adolescents with symptomatic, lone AF who failed antiarrhythmic drug therapy were evaluated. All patients had ECG-documented AF and underwent invasive electrophysiological testing. Intracardiac mapping was performed to determine the site of spontaneous onset of AF and rapidly firing atrial foci. Only the triggering focus was targeted for ablation or isolation. The patients’ mean age was 15.9 ± 3.3 years (range, 8 to 19 years). The most common finding was rapid, irregular atrial tachycardias in the region of the pulmonary veins (n = 5), left atrium (n = 2), or crista terminalis (n = 3). One patient had foci in both the pulmonary veins and crista terminalis. The cycle lengths ranged from 108 to 280 ms. Catheter ablation was acutely successful in 8 patients (88.9%), whereas 1 patient with multiple left atrium foci was treated with the surgical maze operation. Over a mean of 35 ± 22 months, 7 patients (77.8%) were arrhythmia free on no medications, while AF recurred in 2 patients who are controlled on antiarrhythmic medications. Two patients with tachycardia-induced cardiomyopathy had resolution of their left ventricular dysfunction after ablation.

Conclusions—AF in adolescents with structurally normal hearts is usually due to foci in the pulmonary veins, crista terminalis, or left atrium. These foci usually induce irregular atrial tachycardias. Catheter ablation of the foci is effective in eliminating recurrent AF. (Circulation. 2004;110:117-123.)

Key Words: atrial fibrillation • catheter ablation • pediatrics
enrollment. Initially, a quadripolar mapping and ablation catheter was placed in each of the PVs with ablative energy delivered to the site of earliest electrical activation. After a multielectrode circular mapping catheter was available (Lasso, Biosense Webster), this device was placed just inside the ostium of the PVs. If the patient was in AF after placement of catheters, cardioversion was performed, and the sites of earliest electrical activation were mapped during the spontaneous reinitiation of AF or the onset of rapidly firing atrial foci. Once a rapidly firing atrial or PV focus was identified, RF energy was delivered to the site demonstrating the rapidly firing atrial or PV focus for 60 seconds with a maximum power of 30 W and a target temperature of 50 °C. After a circular mapping catheter became available, segmental PV isolation was performed by application of RF energy to the ostium of the PV guided by the site of earliest PV activation on the circular mapping catheter. After ablation, isoproterenol was administered in a dose of 2 to 4 μg/min, and/or rapid atrial pacing was performed at cycle lengths as low as 180 ms as a method for reinduction of AF or rapidly firing foci. Acute procedural success was defined as noninducibility of AF with programmed atrial stimulation and rapid atrial pacing during isoproterenol infusion. This patient remained free of AF during follow-up. Figure 2 illustrates recordings made during persistent AF of 2 years’ duration. After cardioversion, salvos of an irregular atrial tachycardia were recorded (Figure 3) with earliest activation within the right superior PVs, sinus rhythm was restored (Figure 4). Figure 5 illustrates premature atrial beats originating from within the right inferior PV and patient 9. The Lasso catheter within the right inferior PV recorded earliest activation during premature beats. Segmental ostial ablation of this vein resulted in resolution of premature beats and has prevented recurrent AF. One patient with multiple LA foci was not treated with catheter ablation and was referred for a surgical maze operation. She has had no recurrence of arrhythmias over a follow-up period of >4 years.

Over a mean follow-up of 35±22 months (range, 3 to 65 months), 2 patients experienced a recurrence of AF. Patient 5 has had a single recurrence of AF and has been without recurrence while receiving flecainide. Patient 7 had multiple recurrences and was treated with verapamil with good control. Both patients with tachycardia-induced cardiomyopathy

### Results

The Table shows the clinical characteristics, sources of rapidly firing foci, and long-term outcome of the study population. There were 4 girls and 5 boys with a mean age of 15.9±3.3 years (range, 8 to 19 years). AF was permanent in 3 patients and paroxysmal in 6 patients. Two patients with permanent AF had a tachycardia-induced cardiomyopathy. All patients had failed at least 1 type 1 or type 3 antiarhythmic medication and were highly symptomatic during AF.

### Electrophysiological Findings

The initial cardiac rhythm was AF in 3 patients (all of whom were cardioverted after placement of catheters) and sinus rhythm with salvos of rapidly firing irregular atrial tachycardia in 6 patients. In 7 patients, the site of irregular, rapidly firing atrial beats was in the PVs (5 patients) or left atrium (LA) (2 patients). The mean cycle lengths of these foci ranged between 108 and 280 ms. The irregularity of these foci, quantified as the difference between the longest and shortest atrial intervals within a single firing, ranged between 26 and 97 ms.

The site of earliest atrial activation during rapid irregular atrial firing was from the crista terminalis in 3 patients, and 1 patient had foci in both a PV and the crista terminalis. Of the 5 patients with PV foci, 4 patients had a single focus (right inferior PV in 2 patients, right superior PV in 2 patients). The other patient had foci within 2 PVs (right superior and right inferior). In the 2 patients with LA foci, 1 had a single focus near the ostium of the right superior PV, and the other patient had multiple non-PV foci within the LA. Even though patients with foci from the LA and PVs had clinical ECGs demonstrating AF, mapping recorded only rapid, irregular atrial tachycardias rather than AF. All 3 patients with right atrial foci had initiating beats mapped to the lower portion of the crista terminalis.

### Ablation Results and Long-Term Outcome

Catheter ablation was acutely successful in eliminating all spontaneous atrial firing and inducible AF in 8 of the 9 patients. Figure 1 demonstrates spontaneous onset of a rapid, irregular atrial tachycardia arising from the crista terminalis. The application of RF current in the right atrium between the crista terminalis and the tricuspid annulus eliminated all inducible arrhythmias with programmed atrial stimulation and rapid atrial pacing during isoproterenol infusion. This patient remained free of AF during follow-up. Figure 2 illustrates recordings made during persistent AF of 2 years’ duration. After cardioversion, salvos of an irregular atrial tachycardia were recorded (Figure 3) with earliest activation in the LA just outside the ostium of the right superior PV. After 3 applications of RF current at a site outside the ostium of the right superior PVs, sinus rhythm was restored (Figure 4). Figure 5 illustrates premature atrial beats originating from within the right inferior PV in patient 9. The Lasso catheter within the right inferior PV recorded earliest activation during premature beats. Segmental ostial ablation of this vein resulted in resolution of premature beats and has prevented recurrent AF. One patient with multiple LA foci was not treated with catheter ablation and was referred for a surgical maze operation. She has had no recurrence of arrhythmias over a follow-up period of >4 years.

Over a mean follow-up of 35±22 months (range, 3 to 65 months), 2 patients experienced a recurrence of AF. Patient 5 has had a single recurrence of AF and has been without recurrence while receiving flecainide. Patient 7 had multiple recurrences and was treated with verapamil with good control. Both patients with tachycardia-induced cardiomyopathy
had rapid resolution of left ventricular dysfunction after control of AF and had maintained normal left ventricular systolic function at the last follow-up. There were no procedural complications. No patient developed signs or symptoms suggestive of PV stenosis, and all had normal functional status at last follow-up.

**Discussion**

AF in adults is usually initiated by rapidly firing foci with the PVs. The present study indicates that adolescents with AF and no structural heart disease usually have rapidly firing irregular foci in the PVs, LA, or crista terminalis. Eight of 9 patients had a focal source that was treated by catheter...
ablation, and 6 of these patients have had no recurrences while off medications. These findings support the potentially curative nature of catheter ablation to treat lone AF in adolescents. The favorable outcome of catheter ablation after a mean follow-up of 35 months in these adolescents underscores the importance of identifying focal sources of AF in adolescents who are symptomatic and have failed antiarrhythmic drug therapy. Although there were no acute or long-term complications from catheter ablation in this study, the number of patients was small, and long-term effects of ablation in or near the PVs have not been definitively determined.

Although all the patients in our study had clinical AF, most of them demonstrated repetitive nonsustained atrial firing with rapid, irregular cycle lengths that did not precipitate AF during mapping. This observation may distinguish adolescents from adults (in whom rapidly firing foci more commonly degenerate to AF during mapping). Adolescents may be less likely than adults to demonstrate degeneration from rapid atrial firing to AF because of a lower burden of atrial fibrosis, less dispersion of atrial refractoriness, or reduced atrial volume. Nevertheless, all the patients in this study had clinical episodes of AF, including permanent AF in 3 patients. This fact indicates that at least some of the rapid, irregular atrial tachycardia episodes were capable of degenerating to AF.

**PV Foci**

The landmark publication by Haïssaguerre et al in adults described 69 ectopic foci triggering AF. A single origin of ectopic beats was identified in 29 patients, 2 foci were identified in 9 patients, 3 foci were identified in 6 patients, and 4 were found in 1 patient. Ectopic beats originated in the atrial muscle in 4 patients. Of these, 3 were in the right atrium in 3 patients and 1 in the LA. PVs constituted 94% of the foci in that series. Our results are concordant in that most patients had a single triggering focus. The number of patients was too small in the present series to draw any conclusions regarding the sites of PV foci in children. Nevertheless, the relatively high proportion of extra-PV foci is suggestive of a difference between adolescents and adults.

A recent study by Kistler et al documented a high long-term success rate for ablation of regular atrial tachycardias originating from the PVs. Those PV tachycardias represented 16% of all focal atrial tachycardias and 78% of all LA tachycardias at a single center. Those investigators used a focal approach with a low incidence of recurrent atrial tachycardia, with no patients developing late AF, in concordance with our findings. Although patients with a regular, organized atrial tachycardia usually do not have AF, the atrial rhythm may degenerate to AF if the atrial rate is rapid enough. Our population may represent a continuum between the findings described by Kistler et al of regular tachycardias from the PVs and the typical findings of rapidly firing PV foci that quickly degenerate to AF more commonly observed in adults. However, a sustained regular atrial tachycardia was not documented in any of our patients because we specifically excluded patients who had organized atrial rhythms as their clinical arrhythmia. All patients in our series had, at some point, typical disorganized atrial electrograms of AF similar to that demonstrated in Figure 2.

Walsh et al described 12 young patients with drug-resistant ectopic atrial tachycardia who were treated with catheter ablation of the ectopic focus. In that series, the ectopic atrial tachycardia was mapped to the LA in 7 cases and to the right atrium in 5. LA cases were around the PV ostium in most patients. However, most of the right atrial cases were localized to the appendage and not to the crista terminalis. In the study by Walsh et al, no episodes of AF were reported.

**Figure 2.** Spontaneous AF before ablation. Surface ECG leads 1, aVF, and V1 and bipolar intracardiac electrogroms in patient with persistent AF (patient 3). Ablation catheter proximal (LA p) and distal (LA d) electrode pairs recorded at site in LA near ostium of right superior PV. Bipolar intracardiac electrogroms are displayed from catheters in His bundle region (His p and His d), coronary sinus (CS 9/10) through distal (CS 1/2), and right atrium (RA p and RA d). Note typical disorganized electrograms of AF in CS and LA electrogroms with higher frequency than in RA.
Non-PV Foci
Although foci in the PVs were most common (5 of 9 patients), non-PV foci were also common in this study. The crista terminalis is a frequent source of atrial tachycardia in both children and adults.\textsuperscript{9,10} The spectrum of non-PV foci in adults was well described in an extensive report by Lin et al.\textsuperscript{10} These investigators found that 28% of patients from their series had AF initiated by ectopic beats from the non-PV areas, including the LA posterior free wall (38.3%), superior vena cava (37.0%), crista terminalis (3.7%), ligament of Marshall (8.2%), coronary sinus (1.4%), and interatrial septum (1.4%). In contrast, we did not find foci in the ligament of Marshall, superior vena cava, or coronary sinus. During a follow-up period of 22±11 months in that series, 63.2% were free of antiarrhythmic drugs without AF recurrence. Doshi et al\textsuperscript{11} detailed the role of the sympathetic nervous system in AF that is triggered from the ligament of Marshall. The superior vena cava has also been implicated as a non-PV focus in adults and is thought to be responsible for a significant proportion of non-PV foci.\textsuperscript{10,12} We did not find foci originating from this region in adolescents.
Clinical Significance
Ablation directed only at the arrhythmogenic PVs is associated with high recurrence rates in adults, often because of the emergence of a focus in another PV. Therefore, in adults, the procedure has evolved to include empirical isolation of all 4 PVs, usually with wide area circumferential LA ablation. Only long-term follow-up will reveal whether foci will arise in other veins and lead to recurrences of AF. Although isolation of all 4 PVs may reduce the risk of recurrent AF, it may also increase the risk of complications. In addition, the effects of ablation on growing cardiac tissue may be different in adolescents than in adults and lead to an increased risk of PV stenosis. From our experience, we think it may be prudent to minimize the risk of complications by limiting ablation to the affected regions in adolescents.

AF in adolescents is rare but can have significant consequences, as evidenced by the incidence of tachycardia-induced cardiomyopathy in this series and the interference with physical activity. The cure for AF may have a significant impact on the long-term morbidity of this arrhythmia and the quality of life of these patients. The resolution of LV dysfunction in tachycardia-induced cardiomyopathy after curative therapy with ablation has been previously published and is concordant with our findings.

Study Limitations
Because patients with secondary causes for AF were excluded, we cannot comment on the occurrence of focal sources of AF among adolescents with other forms of heart disease, especially congenital heart disease. In addition,

Figure 4. RF application and cessation of irregular atrial tachycardia. This tracing is from same patient as in Figures 2 and 3. Ablation catheter was positioned in LA near ostium of right superior PV. Incessant, irregular atrial tachycardia resolved within 4 seconds after application of RF current with resumption of normal sinus rhythm. (25 mm/s). This patient with persistent AF lasting 2 years maintained normal sinus rhythm over follow-up period of 14 months without medications. CS indicates coronary sinus.

Figure 5. Premature atrial contractions originating from PVs. Patient 9. Surface ECG leads I, aVF, and V1 with simultaneous bipolar intracardiac electrograms from ablation catheter outside ostium of right inferior PV (ABL p and ABL d), superior vena cava (SVC p and SVC d), proximal (CS 9/10) through distal (CS 1/2) coronary sinus, and circular (Lasso) catheter in right inferior PV (L 1/2 through L 9/10). First 2 sinus beats demonstrate left atrial (LA) followed by PV activation. Third and fourth complexes are premature atrial beats with earliest activation (asterisks) in right inferior PV. This patient was treated with segmental ostial ablation of right inferior PV.
because the follow-up interval in the last 2 patients in this series was only 6 months, firm conclusions regarding either the long-term risk of recurrent AF or late complications cannot be made. However, the general safety of RF catheter ablation in adolescents has previously been established.16

Acknowledgment

Dr Nanthakumar is supported by the Clinician Scientist Program of the Canadian Institute of Health Research.

References

Electrophysiological Findings in Adolescents With Atrial Fibrillation Who Have Structurally Normal Hearts
Kumaraswamy Nanthakumar, Yung R. Lau, Vance J. Plumb, Andrew E. Epstein and G. Neal Kay

Circulation. 2004;110:117-123; originally published online June 14, 2004; doi: 10.1161/01.CIR.0000134280.40573.D8
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2004 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/110/2/117

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/