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Is Pulmonary Vein Isolation Necessary for Curing Atrial Fibrillation?

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Background—Pulmonary veins (PVs) play a pivotal role in initiating and perpetuating atrial fibrillation (AF). We investigated if PV electrical isolation from the left atrium is required for curing AF.

Methods and Result—Fifty-one patients with paroxysmal or persistent AF underwent circumferential radiofrequency ablation of PV ostia performed with an anatomic approach. The end point of the ablation procedure was the recording of low peak-to-peak bipolar potentials (<0.1 mV) inside the lesions. Left atrium pacing was used to assess the conduction between the PVs and the left atrium. During a mean follow-up period of 16.6 ± 3.9 months, 41 patients (80.4%) were free of atrial arrhythmias. When patients with and without AF recurrence were analyzed, no significant difference was observed in the mean number of PVs in which the ablation end point was reached (3.4 ± 1.2 versus 3.7 ± 0.87) and PVs isolated (1.5 ± 1.4 versus 1.6 ± 1). We noted that, although in 29 of 41 patients (71%) without AF recurrence, the ablation end point was reached in all PVs mapped, it was only possible to demonstrate the isolation of all PVs mapped in 2 patients. On the other hand, in 7 of 10 patients (70%) with AF recurrence, the ablation end point was reached in all PVs mapped, whereas one patient had all PVs isolated.

Conclusions—Our findings show that with the use of a pure anatomic approach, it is possible to prevent AF in $>80\%$ of patients undergoing catheter ablation. Moreover, the isolation of PVs is not crucial for curing AF. (*Circulation*. 2003; 108:657-660.)

Key Words: atrial fibrillation ■ veins, pulmonary ■ ablation

Ectopic beats originating from the orifice or myocardial sleeve inside the pulmonary veins (PVs) can initiate atrial fibrillation (AF).¹ Elimination of these foci has been reported to be effective in preventing AF recurrences²; however, despite their short-term effectiveness, there are several limitations with focal ablation techniques. Therefore, ablation strategy has changed to electrical isolation of the PVs from the left atrium by creating segmental or complete lines of block at their ostia.³ Recently, as an alternative to this electrophysiologically guided approach, an anatomic approach that uses 3D electroanatomic guidance has been proposed⁴ to perform the circumferential radiofrequency ablation of PV ostia. The end point of the latter technique is the abrupt decrease of the bipolar potentials inside the lesions. The aim of our study was to evaluate if PV isolation is achieved with the anatomic approach and if PV isolation is required to obtain clinical freedom from arrhythmia.

Methods

Patient Population

Fifty-one consecutive patients undergoing radiofrequency catheter ablation for paroxysmal or persistent AF were enrolled in the study.

Inclusion criteria were (1) symptomatic, drug-refractory AF despite the use of at least 2 antiarrhythmic drugs; (2) paroxysmal AF with documented, monthly, sustained episodes; or (3) persistent AF in patients who had already undergone ≥ 3 electrical cardioversions.

Study Protocol

All patients gave informed, written consent to take part in the study. All patients were treated with oral anticoagulation (warfarin sodium [INR 2 to 3.5]) for at least 4 weeks before catheter ablation and underwent ablation while receiving the best antiarrhythmic therapy, which was continued for at least 7 months. After this period, the decision to continue antiarrhythmic medications was based not only on AF occurrence but also on the presence of other symptomatic arrhythmias (ie, ectopic beats) or heart disease. Clinical examination and 12-lead ECG were scheduled at 7, 14, and 28 days after hospital discharge and then every month for 12 months. Echocardiography and Holter monitoring were scheduled at 30 days and then every 3 months. Patients were instructed to obtain an ECG recording if symptomatic palpitations occurred.

Mapping and Ablation Procedure

Two quadripolar catheters were placed in the right ventricular apex and coronary sinus. Left atrium and PVs were explored with a transeptal approach. Real-time 3D left atrium maps were reconstructed with a nonfluoroscopic navigation system (CARTO, Biosense Webster). PV ostia were identified by fluoroscopic visualiza-

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tion of the catheter tip entering the cardiac silhouette with simultaneous impedance decrease and appearance of atrial potential. In patients in sinus rhythm at the beginning of the procedure, the maps were acquired during pacing from the coronary sinus. In patients in AF, maps were acquired to assess amplitude of local atrial electrograms. Electrical cardioversion to restore sinus rhythm was performed, at the end of the mapping, to allow stimulation maneuvers. Radiofrequency pulses were delivered with an 8-mm tip catheter, with a temperature setting of 60°C and radiofrequency energy up to 100 W, until local electrogram amplitude was reduced $\geq 80\%$ up to 120 seconds. Ablation lines consisted of contiguous focal lesion deployed at a distance ≥ 5 mm from the ostia of the PVs, creating a circumferential line of conduction block around each PV. If two PVs seem to share the same ostium or have two ostia too close to be separately isolated, we referred to one and not to two PVs. Remapping was performed in all patients in sinus rhythm, with the preablation map used for acquisition of new points. A minimum of 5 points per each circumferential line were sampled. The end point of the ablation procedure was the recording of low peak-to-peak bipolar potentials (<0.1 mV) inside the lesion, as determined by local electrogram analysis and voltage maps. To evaluate left atrium–PV connection, electrical stimulation at an amplitude of 2 mA plus stimulation threshold and a duration of 2 ms was performed inside the circumferential line of ablation. PV isolation was characterized by an electrical stimulus that was able to depolarize the local fibers but was not conducted through the atrium, as recorded inside the coronary sinus (Figure 1).

Statistical Analysis

Continuous variables are expressed as mean \pm SD and were compared with a 2-tailed Student's *t* test for paired and unpaired data. A value of $P<0.05$ was considered statistically significant. AF-free survival data were analyzed with Kaplan-Meier analysis.

Results

Patients' Characteristics

Twenty-nine men and 22 women were enrolled, with a mean age of 60.3 ± 11 years. Of the patients, 23 had paroxysmal AF and 28 persistent AF. The mean AF duration was 5.4 ± 3.5 years, and the mean number of previously used, ineffective antiarrhythmic drugs was 2.9 ± 0.8 . Most of the patients (78.4%) had an underlying heart disease: 29 had hypertension, 7 had coronary artery disease, and 4 had valvular disease. The mean left atrial diameter was 50.4 ± 5.3 mm, and the mean left ventricular ejection fraction was $49.8\pm 7.8\%$.

Mapping and Ablation Procedure

The mean number of separate PV ostia mapped per patient was 4 ± 0.5 (5 PV ostia in 6 patients, 4 in 40 patients, and 3 in 5 patients). Of 151 PVs, 135 were individually encircled, whereas in the remaining 16, a single lesion encircled two PVs. The mean procedure time was 145 ± 36 (range, 63 to 238) min, with a mean fluoroscopic time of 26 ± 17 (range, 6 to 79) min, and a mean number of radiofrequency pulses per patient of 72 ± 15 (range, 43 to 105). The mean number of separate PV ostia in which the ablation end point was reached was 3.6 ± 0.9 per patient (5 PV ostia in 5 patients, 4 in 28 patients, 3 in 11 patients, and 2 in 7 patients). The mean number of isolated PVs per patient was 1.6 ± 1.3 (4 PVs in 4 patients, 3 in 5 patients, 2 in 19 patients, 1 in 14 patients, and no PV in 9 patients). Two major complications were observed during the procedure: a transient ischemic attack and a cardiac perforation.

Clinical Outcome

During the first month of follow-up, 12 of 51 patients (23.5%) had an AF recurrence. Of those 12, only 5 patients required electrical cardioversion to restore the sinus rhythm. If we consider follow-up after the first month, during a period of 16.6 ± 3.9 (range, 11 to 25) months, 41 patients (80.4%) were free of atrial arrhythmias (Figure 2) (83% of patients with paroxysmal AF and 79% of patients with persistent AF; $P=NS$). Of the 51 patients, 32 were on previously ineffective antiarrhythmic drug therapy (16 patients had β -blockers, 13 amiodarone, 7 flecainide, and 5 verapamil), whereas 19 were free of any antiarrhythmic therapy. When patients with ($n=10$) and without ($n=41$) AF recurrence were analyzed, no significant difference was observed in the mean number of PVs mapped (4 ± 0.7 versus 4 ± 0.4), mean number of PVs in which the ablation end point was reached (3.4 ± 1.2 versus 3.7 ± 0.8), and mean number of PVs isolated (1.5 ± 1.4 versus 1.6 ± 1). Of note, although in 29 of 41 patients (71%) without AF recurrence the ablation end point was reached in all PVs mapped, it was possible to demonstrate isolation of all PVs mapped in only 2 patients. On the other hand, in 7 of 10 patients (70%) with AF recurrences, the ablation end point was reached in all PVs mapped, whereas one patient had all PVs isolated.

Discussion

Our findings show that it is possible, with the use of a pure anatomic approach, to prevent AF in $>80\%$ of patients who undergo catheter ablation. Although radiofrequency pulses were delivered all around the PV ostia, only 40% of mapped PVs were electrically isolated from the left atrium. Because only 2 of 41 patients without AF recurrence during follow-up had all the mapped PVs isolated, our results show that isolation of all PVs is not necessary for preventing AF recurrence. On the other hand, absence of AF recurrences in 6 of 9 patients (66%) in whom no PV was isolated suggests that PV isolation is not a major determinant of clinical success.

Haïssaguerre et al³ demonstrated that PV ostia disconnection by use of partial perimetric ablation is associated with clinical success in patients with paroxysmal AF who undergo catheter ablation. Similar data have been reported by Pappone et al,⁴ who used a pure anatomic approach to perform PV isolation. Although they stressed that the proportion of PVs with complete lesions was similar between patients with and without recurrence, no data were available about the PV–left atrium conduction. In our work, we demonstrate that, using an anatomic approach, PV isolation is not crucial in determining clinical success. Our findings are confirmed by surgical experiences in which $>70\%$ of patients were free of AF and in which intraoperative cryoablation⁵ or radiofrequency⁶ were used to connect and not to isolate the PVs.

Different hypotheses can justify the clinical success observed when delivering radiofrequency in the area surrounding the PV ostia without isolating them: (1) modification of the substrate of PV tachycardia⁷ or "mother waves,"⁸ making reentry pathways unsuitable; (2) a denervating effect leading to a parasympathetic predominance⁹; (3) damage to the Marshall's ligament or the Bachmann's bundle, which are

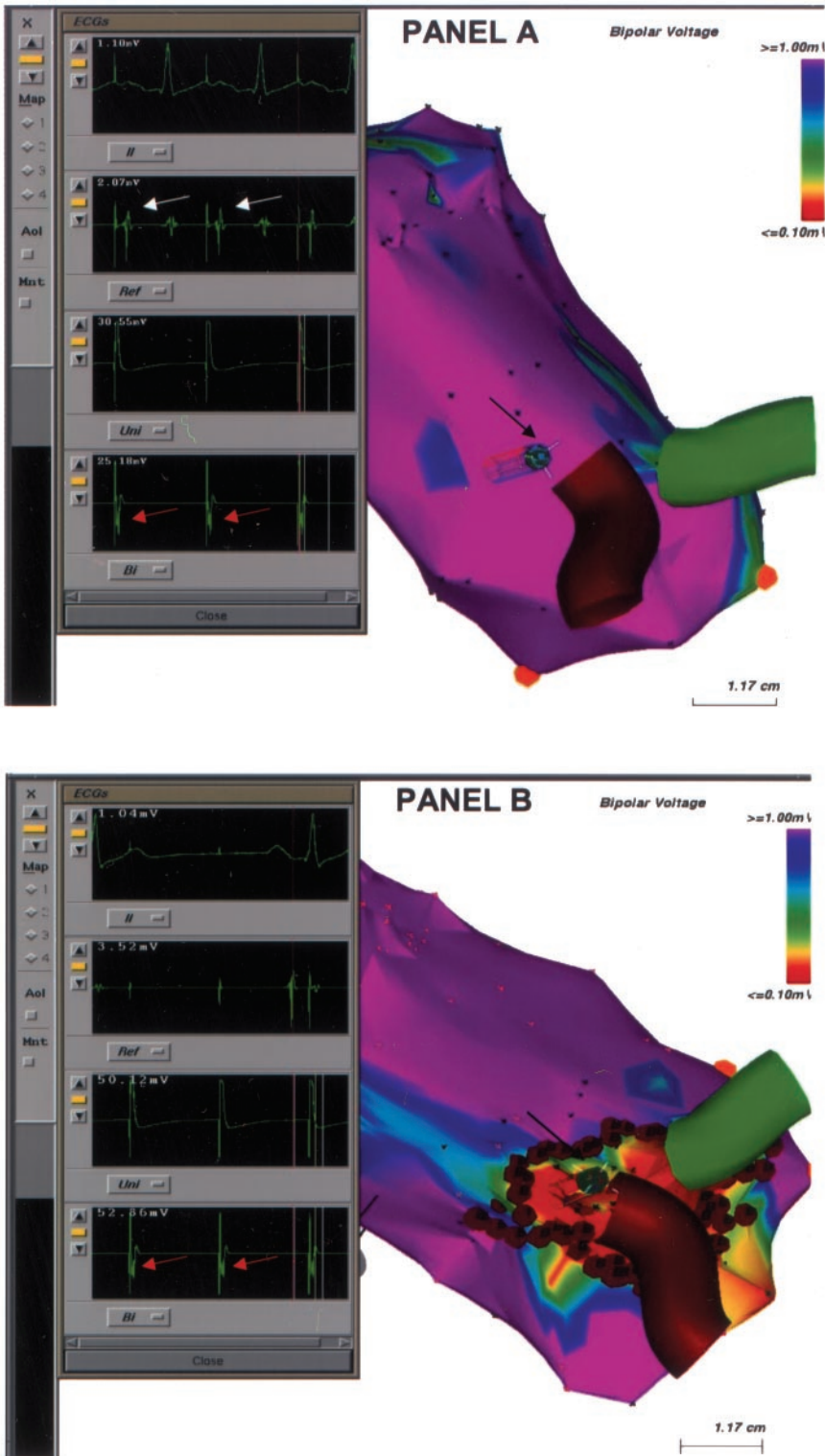


Figure 1. ECGs (left) and bipolar voltage maps (right), in a caudocranial view, acquired before (A) and after (B) ablation. On the left side, Bi and Uni channel show, respectively, bipolar and unipolar electrograms recorded by the tip of the ablation catheter; Ref channel shows coronary sinus electrograms; and II channel shows surface ECG. On the right side, red codes for low peak-to-peak bipolar potentials ($<0.1\text{ mV}$), and purple codes for high peak-to-peak bipolar potentials ($>1\text{ mV}$). Red tags point ablation sites. Red and green tubes are PVs. Panel A, Stimulation (green, vertical line on II, Uni, Bi, and Ref channels) from the mapping catheter (black arrow) is able to depolarize the atrium (red arrows) near the ostia of PVs, and then the stimulus is conducted through the atrium (white arrows) and recorded inside the coronary sinus. Panel B, Stimulation from a site near the PV ostia is still able to depolarize the local atrium (red arrows) but is not conducted through the coronary sinus.

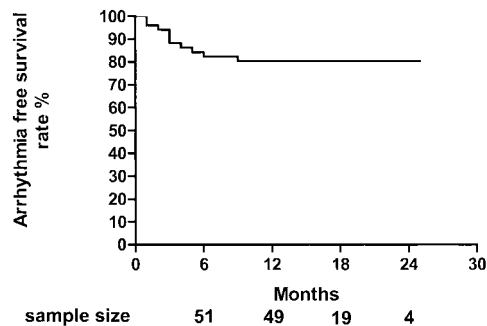


Figure 2. AF-free survival curve.

involved in the initiation and maintenance of AF^{10,11}; or (4) promotion of atrial electroanatomic remodeling involving the left atrium posterior wall to the point that the substrate for AF is no longer present.⁹

The present study has an important limitation: Many patients were being treated with an antiarrhythmic drug during follow-up. It is possible that medications would not have been necessary if the isolation had been complete.

References

- Haïssaguerre M, Jaïs P, Shah DC, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating from pulmonary veins. *N Engl J Med*. 1998;339:659–666.
- Jaïs P, Haïssaguerre M, Shah DC, et al. A focal source of atrial fibrillation treated by discrete radiofrequency ablation. *Circulation*. 1997;95:572–576.
- Haïssaguerre M, Shah DC, Jaïs P, et al. Electrophysiological breakthroughs from the left atrium to the pulmonary veins. *Circulation*. 2000;102:2463–2465.
- Pappone C, Rosanio S, Oreto G, et al. Circumferential radiofrequency ablation of pulmonary vein ostia. *Circulation*. 2000;102:2619–2628.
- Gaita F, Gallotti R, Calò L, et al. Limited posterior left atrial cryoablation in patients with chronic atrial fibrillation undergoing valvular heart surgery. *J Am Coll Cardiol*. 2000;36:159–166.
- Kottkamp H, Hindricks G, Autschbach R, et al. Specific linear left atrial lesions in atrial fibrillation: intraoperative radiofrequency ablation using minimally invasive surgical techniques. *J Am Coll Cardiol*. 2002;40:475–480.
- Oral H, Ozaydin M, Tada H, et al. Mechanistic significance of intermittent pulmonary vein tachycardia in patients with atrial fibrillation. *J Cardiovasc Electrophysiol*. 2002;13:645–650.
- Sueda T, Nagata H, Shikata H, et al. Simple left atrial procedure for chronic atrial fibrillation associated with mitral valve disease. *Ann Thorac Surg*. 1996;62:1070–1075.
- Pappone C, Oreto G, Rosanio S, et al. Atrial electroanatomical remodeling after circumferential radiofrequency pulmonary vein ablation. *Circulation*. 2001;104:2539–2544.
- Katritsis D, Ioannidis JPA, Anagnostopoulos CE, et al. Identification and catheter ablation of extracardiac and intracardiac components of ligament of Marshall tissue for treatment of paroxysmal atrial fibrillation. *J Cardiovasc Electrophysiol*. 2001;12:750–758.
- Mandapati R, Skanes AC, Berenfeld O, et al. Stable microreentrant sources as a mechanism of atrial fibrillation in the isolated sheep heart. *Circulation*. 2000;101:194–199.