Effects of Two Different Catheter Ablation Techniques on Spectral Characteristics of Atrial Fibrillation

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OBJECTIVES   The aim of this study was to determine the effects of circumferential pulmonary vein ablation (CPVA) and electrogram-guided ablation (EGA) on the spectral characteristics of atrial fibrillation (AF) and the relationship between changes in dominant frequency (DF) and clinical outcome.

BACKGROUND   Circumferential pulmonary vein ablation and EGA have been used to eliminate AF. Spectral analysis may identify high-frequency sources.

METHODS   In 84 consecutive patients, CPVA (n = 42) or EGA (n = 42) was performed for paroxysmal (n = 49) or persistent (n = 35) AF. During EGA, complex electrograms were targeted. Lead V_1 and electrograms from the left atrium and coronary sinus were analyzed to determine the DF of AF before and after ablation.

RESULTS   The left atrial DF was higher in persistent (5.83 ± 0.86 Hz) than paroxysmal AF (5.33 ± 0.76 Hz, p = 0.03). There was a frequency gradient from the left atrium to the coronary sinus (p = 0.02). Circumferential pulmonary vein ablation and EGA resulted in a similar decrease in DF (18 ± 17% vs. 17 ± 15%, p = 0.8). During a mean follow-up of 9 ± 6 months, the change in DF after CPVA was similar among patients with and without recurrent AF. An acute decrease in DF after EGA was associated with freedom from recurrent AF only in patients with persistent AF (19 ± 14% vs. 3 ± 6%, p = 0.02).

CONCLUSIONS   Both CPVA and EGA decrease the DF of AF, consistent with elimination of high-frequency sources. Whereas the efficacy of EGA is associated with a decrease in DF in patients with persistent AF, the efficacy of CPVA is independent of changes in DF. This suggests that CPVA and EGA eliminate different mechanisms in the genesis of persistent AF.   (J Am Coll Cardiol 2006;48:340–8) © 2006 by the American College of Cardiology Foundation

In experimental studies, atrial fibrillation (AF) displays spatiotemporal organization, reflecting high-frequency periodic sources, such as rotors, which may be an important mechanism of AF [1,2]. In the past few years, 2 different catheter ablation techniques, circumferential pulmonary vein ablation [3,4] (CPVA, also referred to as wide area circumferential ablation) and electrogram-guided ablation (EGA), both have been reported to be efficacious in eliminating AF [5]. The efficacy of these 2 techniques may be attributable, at least in part, to elimination of high-frequency sources. If so, this should be reflected in changes in the spatiotemporal organization of AF.

In an attempt to gain insight into the possible mechanisms by which catheter ablation eliminates AF, this study compared the effects of CPVA and EGA on the spectral characteristics of AF.

METHODS

Study subjects. The subjects of this study were 84 consecutive patients who underwent catheter ablation of paroxysmal (n = 49) or persistent (n = 35) AF. Their mean age was 57 ± 9 years, and 70 were men. The mean left atrial size was 43 ± 7 mm, and the mean left ventricular ejection fraction was 0.57 ± 0.10. The demographic and clinical characteristics of the patients in each group were similar except for left atrial diameter, which was larger in patients with persistent AF (Table 1).

Electrophysiologic study. Antiarrhythmic drug therapy was discontinued at least 5 half-lives before the ablation procedure except in 15 patients with persistent AF who were being treated with amiodarone. All patients provided written informed consent. Using femoral venous access, a quadripolar electrode catheter (EP Technologies, Sunnyvale, California) was positioned in the coronary sinus. Transseptal catheterization was performed, and systemic anticoagulation was initiated to maintain an activated clotting time of 300 to 350 s. A temperature-controlled 8-mm tip quadripolar catheter (Navistar, Biosense-Webster, Diamond Bar, California) was advanced into the left atrium and used for mapping and ablation. Electrograms were displayed at filter settings of 30 to 500 Hz (for the electrophysiologic

Abbreviations and Acronyms

AF = atrial fibrillation
CPVA = circumferential pulmonary vein ablation
DF = dominant frequency
EGA = electrogram-guided ablation
FFT = fast Fourier transformation

study) and were also recorded 0 to 200 Hz (for off-line spectral analysis). All recordings were stored on optical discs (EP-Workmate, EPMed Systems, West Berlin, New Jersey).

Radiofrequency catheter ablation. Atrial fibrillation was induced by rapid pacing in the coronary sinus at 10 mA, down to a cycle length of loss of 1:1 atrial capture in 38 of the 84 patients (45%) who presented in sinus rhythm. Circumferential pulmonary vein ablation was performed in 42 patients in the study, as previously described (Fig. 1) (3). The mean duration of radiofrequency energy application was 42 ± 11 min. If the patient still was in AF after completion of this lesion set, sinus rhythm was restored by infusion of 1 mg of ibutilide or transthoracic cardioversion.

Electrogram-guided ablation was performed in 42 patients. The left atrium was mapped, and focal ablation was performed at sites of complex electrograms characterized by a short cycle (relative to the cycle length recorded within the coronary sinus), fractionation and/or continuous electrical activity (5,6). Linear ablation was not performed (Fig. 2). The end point of EGA was termination of AF and the inability to reinduce AF. Whenever AF terminated during ablation, reinduction was attempted by rapid atrial pacing at a cycle length of 180 to 200 ms for 10 s. Induction was attempted 5 times, and inducible AF was defined as AF that lasted >1 min. If AF was reinduced, ablation was continued until it became noninducible or until all identified complex electrograms were ablated. If AF still was present, sinus rhythm was restored by infusion of ibutilide or transthoracic cardioversion. The mean duration of radiofrequency energy application was 35 ± 28 min.

After the ablation procedure, patients were monitored in a hospital bed overnight and anticoagulated with heparin. All patients were anticoagulated with warfarin for ≥3 months after the procedure. The antiarrhythmic drug therapy that was used before ablation was restarted and contin-

ued for 3 months. There were no complications in any of the study patients.

Study protocol. The study protocol was approved by the institutional review board. Electrograms recorded at the anterior base of the left atrial appendage and within the distal coronary sinus, along with each of the 12 leads of the electrocardiogram (ECG), were used for signal processing. In this study, left atrial electrograms indicate electrograms recorded at the base of the left atrial appendage on the anterior left atrial wall; 1-min segments recorded during AF before and after ablation were analyzed. Because site-specific electrograms recorded in the left atrium and coronary sinus may not be representative of the entire atrium, simultaneous recordings of the 12-lead ECG also were analyzed. Because atrial signals are best recognized in lead V_1 (7), only this lead was analyzed.

The coronary sinus catheter was kept in the same position throughout the procedure. The left atrial recording site was tagged on the electroanatomic mapping system to allow recordings at the same site before and after ablation. After ablation, left atrial electrograms were recorded only at sites that had not been ablated. If AF became noninducible after ablation (24 patients), then electrograms recorded during AF just before conversion were used for analysis. When AF terminated during ablation and was noninducible (24 patients), then left atrial recordings were acquired at the site of last termination. When the end point of noninducibility was not reached, recordings of the AF before ibutilide administration or transthoracic cardioversion were used for analysis. Recordings were stored on optical discs in digital format for off-line analysis.

Digital signal processing. Data were analyzed by fast Fourier transformation (FFT, MatLab, MathWorks, Inc., Natick, Massachusetts). First, the QRS complex in each signal was subtracted from the digitized recordings as described previously (8). For analysis of lead V_1, QRST subtraction was used (Fig. 3). In each patient, the longest QT interval within the 1-min sample was used as the duration of the subtracted signal (Fig. 3). Briefly, the locations of the QRST complexes were determined from a surface ECG. Thresholds for QRS detection were set at 75% of the maximum point of the signal (upper threshold) and 75% of the minimum point (lower threshold). For the

Table 1. Demographic and Clinical Characteristics

	CPVA			EGA			P_1	P_2
	All Patients	Paroxysmal AF	Persistent AF	All Patients	Paroxysmal AF	Persistent AF		
n	42	24	18	42	25	17	—	0.8
Age (yrs)	57 ± 10	58 ± 10	56 ± 10	57 ± 9	57 ± 8	59 ± 10	0.8	0.8
Gender (M/F)	35/7	19/5	16/2	35/7	20/5	15/2	1.0	0.8
LA diameter (mm)	44 ± 7	41 ± 6	46 ± 6	42 ± 7	40 ± 6	45 ± 8	0.3	0.02
LVEF	0.58 ± 0.11	0.61 ± 0.08	0.55 ± 0.13	0.56 ± 0.09	0.59 ± 0.06	0.52 ± 0.11	0.4	0.1
Duration of AF (yrs)	7 ± 6	7 ± 6	6 ± 5	6 ± 6	5 ± 5	6 ± 6	0.5	0.9

Continuous variables expressed as mean ± 1 SD. P_1 refers to comparisons among all patients in the CPVA and EGA groups; P_2 refers to comparisons among the 4 groups of patients with paroxysmal and persistent AF in the CPVA and EGA groups. For P_2, continuous and categorical variables were compared with analysis of variance and chi-square, respectively. Left atrial diameter was significantly larger in patients with persistent than with paroxysmal AF in both groups.

AF = atrial fibrillation; CPVA = circumferential pulmonary vein ablation; EGA = electrogram-guided ablation; LA = left atrium; LVEF = left ventricular ejection fraction.
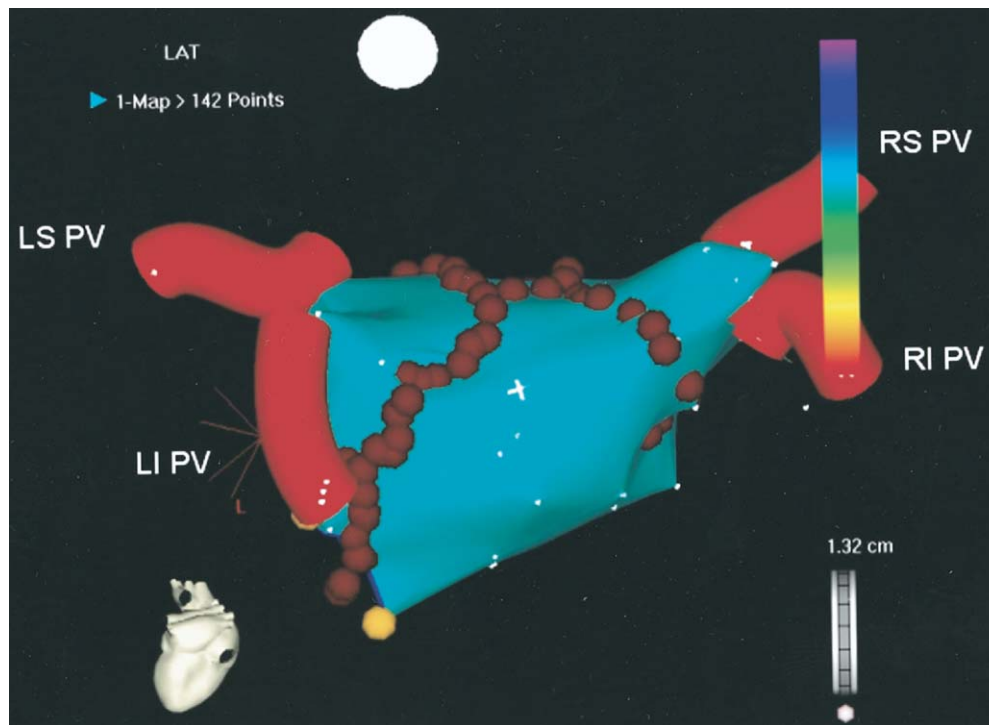
Figure 1. Circumferential pulmonary vein ablation. Shown is a posteroanterior projection of a 3-dimensional construction of the left atrium and the pulmonary veins (PV). **Red tags** indicate ablation sites. The PVs were encircled 1 to 2 cm from their ostia, with additional ablation lines in the mitral isthmus and roof. LI = left inferior; LS = left superior; RI = right inferior; RS = right superior.

complex to be recognized, the signal was required to track through the following series of states, in the specific order of: 1) pass above the upper threshold; 2) pass below the upper threshold; and then 3) pass below the lower threshold. The maximum and minimum points were defined as the 95th and 7th percentile values of the signal histogram, respectively. After a QRST complex was identified, a window was set during which another QRST complex could not be detected. In each electrogram, the longest QT was detected and was adjusted accordingly. The ideal QRST was determined by averaging all of the detected QRST complexes in the electrogram; it was then subtracted out of the electrogram signal in the intervals in which QRST complex detection occurred. After QRST subtraction using the nominal values, the success of QRST subtraction was manually checked.

Fast Fourier transformation of the digitized bipolar electrograms (60,000 points) was performed to analyze the content in the 0.5 to 80 Hz band. Firstly, the mean of each signal was subtracted in order to make the signal zero mean. Next, a split cosine bell-tapering window was applied with 5% of the data points being tapered. An estimate of the signal spectrum was then obtained by using a smoothed periodogram with a smoothing parameter of M (9). M was determined semiautomatically (10) using an unbiased risk estimator method to choose the tuning parameter M in the smoothed periodogram method (9,11). The dominant frequency (DF) was defined as the frequency of the highest peak of the smoothed periodogram in the interval of 0.5 to 60 Hz.

Follow-up. All patients were seen in an outpatient clinic 3 months and then every 3 to 6 months after the ablation procedure. In addition, patients were questioned by telephone by a nurse practitioner at bimonthly intervals and were instructed to call whenever they experienced symptoms. In the event of symptoms suggestive of an arrhythmia, 30-day transtelephonic event monitors were used to document the cause of symptoms. The mean duration of follow-up was 9 ± 6 months. No patient was lost to follow-up.

One of the aims of this study was to determine the relationship between acute changes in spectral characteristics after ablation and recurrent AF during follow-up. Therefore, clinical efficacy in this study was based only on the presence or absence of any episode of AF, asymptomatic or symptomatic, during follow-up, not atrial flutter. Because early recurrences of AF after ablation may be transient (12), a blanking period of 6 weeks was employed.

Statistical analysis. Continuous variables are expressed as mean ± 1 SD and were compared with Student t test. A paired t test was used to compare the simultaneous DFs at different sites in the same patient, and also to determine the effect of ablation on the DF at different sites in the same patient. Differences in groups of continuous variables were compared with analysis of variance. Categorical variables were compared by chi-square analysis or with Fisher exact test when $n < 10$. A value of $p < 0.05$ indicated statistical significance.

RESULTS

Spectral analysis in patients with paroxysmal and persistent AF. The mean left atrial DF was significantly lower in patients with paroxysmal AF, 5.4 ± 0.7 Hz, than in patients
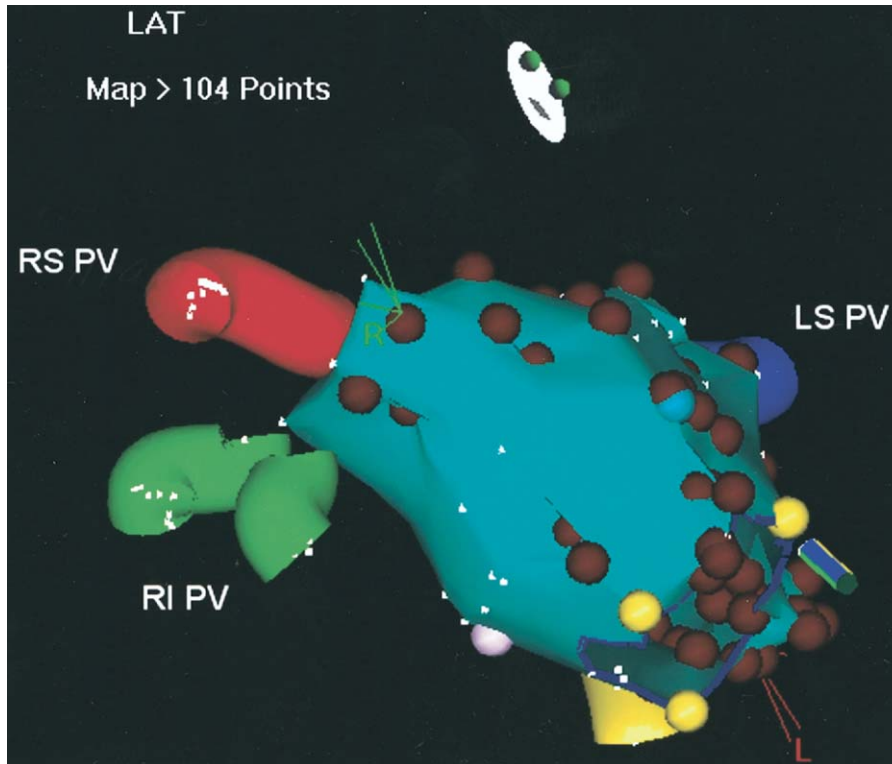
Figure 2. Electrogram-guided ablation. Shown is a right anterior-oblique projection of a 3-dimensional construction of the left atrium with caudal angulation. Focal applications of radiofrequency energy were delivered at sites that displayed complex electrograms. No linear lesions were created. **Red tags** indicate ablation sites. Abbreviations as in Figure 1.

with persistent AF, 5.8 ± 0.8 Hz ($p = 0.02$). The mean DFs recorded in the coronary sinus did not differ significantly in patients with paroxysmal and persistent AF (5.1 ± 0.9 Hz and 5.4 ± 0.8 Hz, respectively, $p = 0.2$). The DF in lead V_1 was 5.4 ± 0.9 Hz in patients with paroxysmal AF and 5.6 ± 1.1 Hz in patients with persistent AF ($p = 0.4$).

There was no significant difference in the DF of electrograms recorded from the left atrium (5.3 ± 0.7 vs. 5.6 ± 0.9, $p = 0.3$), coronary sinus (5.1 ± 0.8 vs. 5.4 ± 1.0, $p = 0.2$), or lead V_1 (5.3 ± 0.9 vs. 5.6 ± 0.9, $p = 0.3$) among patients who presented in sinus rhythm (38) and had AF induced before ablation and who presented in spontaneous AF (46), respectively.

Frequency gradients. Among patients with paroxysmal AF, the mean DF was significantly greater in the left atrium, 5.3 ± 0.7 Hz, than in the coronary sinus, 5.0 ± 0.7 Hz ($p = 0.002$), whereas the DF in lead V_1 was not significantly different than the DF in the left atrium ($p = 0.2$) or the coronary sinus ($p = 0.2$). Among patients with persistent AF, the mean DF in the left atrium, 5.8 ± 0.8 Hz, also was greater than in the coronary sinus, 5.4 ± 0.7 Hz ($p = 0.02$). There was a trend for a higher DF in lead V_1 than in the coronary sinus in patients with persistent AF ($p = 0.06$) whereas there was no significant difference in the DF in lead V_1 and in the left atrium ($p = 0.7$).

Effects of CPVA. In a combined analysis of patients with paroxysmal and persistent AF, CPVA significantly decreased the mean DF in the left atrium from 5.6 ± 0.8 Hz

to 4.5 ± 0.9 Hz ($p < 0.001$) (Fig. 4). Circumferential pulmonary vein ablation also significantly decreased the mean DF in the coronary sinus from 5.2 ± 0.9 Hz to 4.6 ± 1.1 Hz ($p < 0.001$).

Among patients with paroxysmal AF, the mean left atrial DFs before and after CPVA were 5.2 ± 0.5 Hz and 4.4 ± 0.6 Hz, respectively ($p = 0.03$) (Fig. 4). In the coronary sinus, there was no significant difference in the mean DF before, 5.1 ± 1.0 Hz, and after CPVA, 4.8 ± 1.0 Hz ($p = 0.1$).

Among patients with persistent AF, the mean left atrial DF decreased significantly after CPVA from 5.9 ± 0.9 Hz to 4.6 ± 1.1 Hz ($p = 0.003$) (Fig. 4). The mean DF in the coronary sinus also decreased significantly from 5.3 ± 0.8 Hz to 4.5 ± 1.2 Hz after CPVA ($p = 0.008$).

Effects of EGA. In a combined analysis of patients with paroxysmal and persistent AF, the mean left atrial DFs were 5.5 ± 0.8 Hz and 4.5 ± 0.9 Hz before and after EGA ($p < 0.001$) (Figs. 4 and 5). Electrogram-guided ablation also resulted in a significant decrease in the mean DF within the coronary sinus from 5.3 ± 0.7 Hz to 4.6 ± 0.9 Hz ($p < 0.001$).

Among patients with paroxysmal AF, the mean left atrial DFs before and after EGA were 5.4 ± 0.8 Hz and 4.3 ± 0.8 Hz ($p < 0.001$) (Fig. 4). The mean DFs within the coronary sinus were 5.1 ± 0.7 Hz before and 4.4 ± 0.7 Hz after EGA ($p < 0.001$).

Among patients with persistent AF, the mean left atrial DFs before and after EGA were 5.7 ± 0.8 Hz and $5.0 \pm$
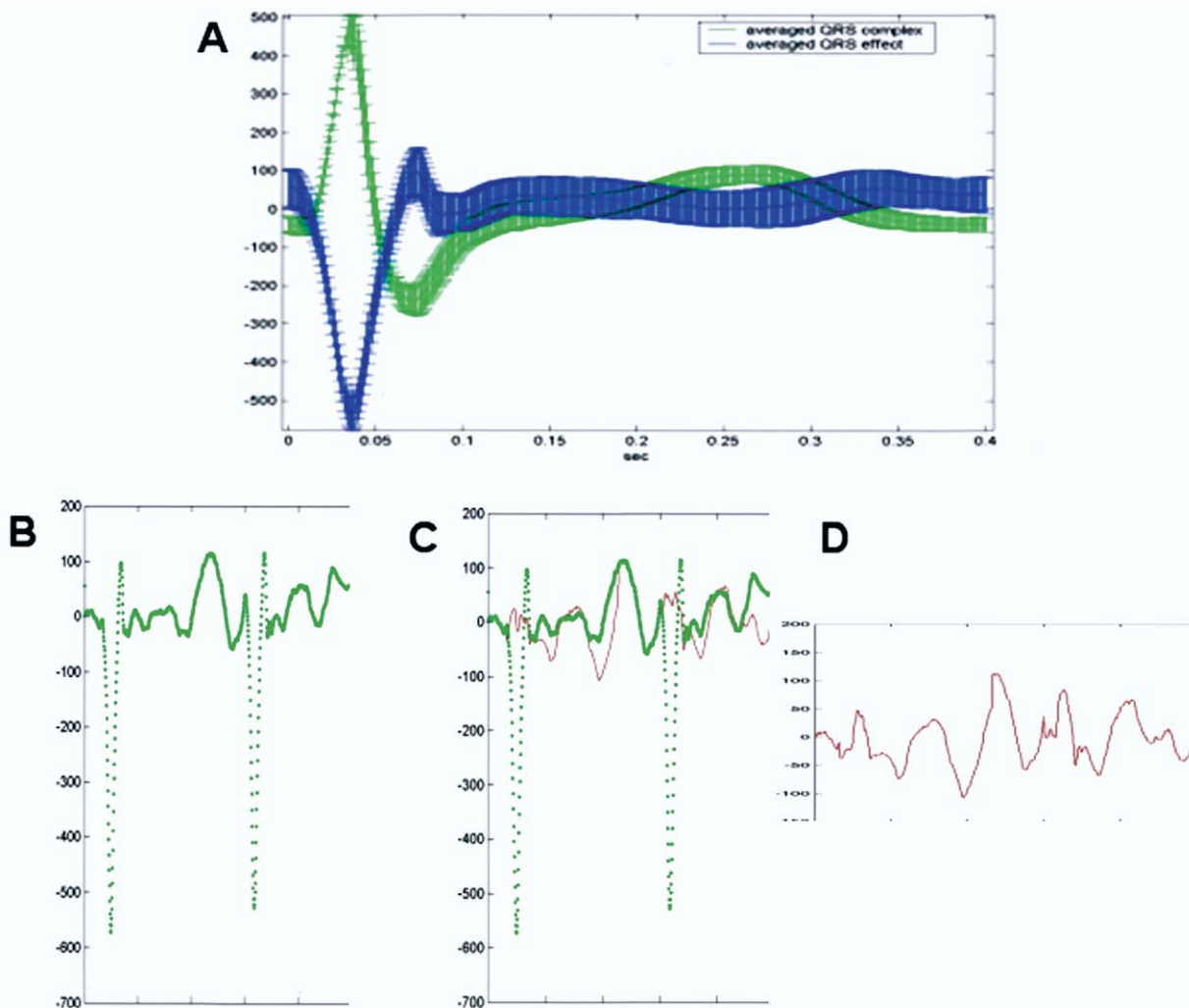
Figure 3. QRST subtraction. On digitized signals, QRST subtraction was performed as described in the Methods section. The **green line** represents an averaged QRST complex, and the **blue line** illustrates the averaged QRST effect **(A)**. Incoming electrocardiogram signal is depicted in **panel B**. **(C)** Superimposed incoming electrocardiogram signal **(green line)** and the electrocardiogram signal after subtraction **(red line)** are shown. **(D)** The electrocardiogram signal after QRST subtraction is shown.

0.9 Hz (p = 0.006) (Fig. 4). The mean DFs within the coronary sinus were 5.5 ± 0.8 Hz before and 5.0 ± 1.0 Hz after EGA (p = 0.003).

Effect of ablation on spectral characteristics of lead V_1. Circumferential pulmonary vein ablation was associated with a significant decrease in the DF in lead V_1 (5.4 ± 0.9 vs. 4.5 ± 1.1, p < 0.001) (Fig. 6). The DF in lead V_1 also was significantly lower after, 4.6 ± 1.0 Hz, than before EGA, 5.5 ± 1.0 (p < 0.001). The magnitude of reduction in DF in lead V_1 was similar among patients with paroxysmal and persistent AF after both CPVA (p = 0.9) and EGA (p = 0.5).

Differential effects of CPVA and EGA. Circumferential pulmonary vein ablation and EGA resulted in a similar magnitude of reduction in DF in the left atrium (18 ± 17% vs. 17 ± 15%, p = 0.8), in the coronary sinus (9 ± 19% vs. 12 ± 12%, p = 0.3), and in lead V_1 (17 ± 19% vs. 14 ± 15%, p = 0.5).

Termination of AF and DF. Atrial fibrillation terminated during ablation in 20 of the 42 patients (48%) who under-

went CPVA, and in 21 of the 42 patients (50%) who underwent EGA (p = 0.8). Among the 49 patients with paroxysmal AF, AF terminated during CPVA in 54% of the 24 patients and during EGA in 68% of the 25 patients (p = 0.4, Fisher exact test). Among the 35 patients with chronic AF, AF terminated during CPVA in 39% of the 18 patients and during EGA in 24% of the 17 patients (p = 0.5, Fisher exact test). There was no significant difference in the percent change in the DF in the left atrium (16 ± 13% vs. 19 ± 18%, p = 0.6), coronary sinus (11 ± 15% vs. 10 ± 16%, p = 0.5), or lead V_1 (14 ± 15% vs. 17 ± 19%, p = 0.5) when AF terminated during ablation and when it did not.

Spectral characteristics and freedom from AF. During a mean follow-up of 9 ± 6 months, among all patients with paroxysmal and persistent AF, 28 of the 42 patients (67%) who underwent CPVA and 30 of the 42 patients (71%) who underwent EGA were free from recurrent AF in the absence of antiarrhythmic drug therapy after a single ablation procedure (p = 0.6).
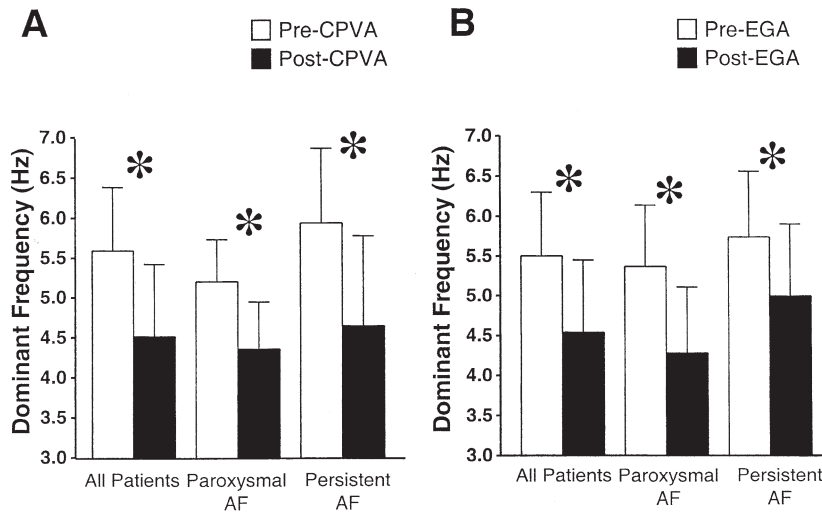
Figure 4. Effect of ablation on dominant frequency. The dominant frequencies recorded in the left atrium in all patients and in patients with paroxysmal and persistent atrial fibrillation (AF) are shown before **(open bars)** and after **(solid bars)** circumferential pulmonary vein ablation (CPVA) **(A)** and electrogram-guided ablation (EGA) **(B)**, respectively. Similar significant reductions in dominant frequency were also observed in the coronary sinus and electrocardiogram lead V_1. *p < 0.05 (paired *t* test).

There was no significant difference in the percent decrease in the DF in the left atrium ($17 \pm 18\%$ vs. $22 \pm 17\%$, p = 0.5), coronary sinus ($7 \pm 19\%$ vs. $12 \pm 18\%$, p = 0.4), or lead V_1 ($15 \pm 18\%$ vs. $20 \pm 21\%$, p = 0.7) between patients with paroxysmal or persistent AF who remained free from AF and patients who had recurrent AF after CPVA. There also was no significant difference in the percent decrease in the DF in the left atrium ($19 \pm 16\%$ vs. $23 \pm 9\%$, p = 0.4), coronary sinus ($14 \pm 12\%$ vs. $19 \pm 11\%$, p = 0.4), or lead V_1 ($16 \pm 18\%$ vs. $13 \pm 13\%$, p = 0.7) between patients with paroxysmal AF who remained free from AF and patients who had recurrent AF after EGA. In contrast, in patients with persistent AF, freedom from recurrent AF after EGA was associated with a greater percent reduction in the DF in the coronary sinus ($16 \pm 10\%$ vs. $1 \pm 6\%$, p = 0.002) and in lead V_1 ($19 \pm 14\%$ vs. $3 \pm 6\%$, p = 0.02), but not in left atrium ($18 \pm 16\%$ vs. $9 \pm 11\%$, p = 0.28).

DISCUSSION

Main findings. This study demonstrates that: 1) the DF in the left atrium is higher during persistent AF than during paroxysmal AF; 2) there is a DF gradient between the left atrium and the coronary sinus during AF; 3) both CPVA and EGA decrease the DF of AF; 4) during mid-term follow-up, the efficacy of CPVA does not appear to be related to an acute post-ablation decrease in DF; and 5) freedom from recurrent AF is associated with an acute reduction in DF in the coronary sinus and lead V_1 after EGA, but only in patients with persistent AF.

Paroxysmal versus persistent AF. In this study, the DF in the left atrium was higher during persistent AF than during paroxysmal AF. This may be explained by a greater degree of atrial electroanatomical remodeling in persistent AF, resulting in a more pronounced reduction in atrial refractoriness (13,14), and the maintenance of drivers that have a higher DF.

Consistent with this finding, a prior experimental study demonstrated that the left atrial DF was higher in chronic AF induced by mitral regurgitation than in pacing-induced episodes of acute AF (15).

DF gradient from the left atrium to the coronary sinus. The DF was significantly higher in the left atrium than in the coronary sinus during AF. A similar difference in DF was found in prior experimental studies (16–18) and in a prior clinical study (19).

The presence of a DF gradient between the left atrium and coronary sinus suggests that the primary drivers of AF originate in the left atrium and that activation of the coronary sinus probably is mostly passive during episodes of paroxysmal AF. It is widely accepted that the majority of the drivers of AF and rotors do originate within the pulmonary veins and/or left atrium (20,21).

Effect of CPVA and EGA on spectral analysis. Both CPVA and EGA resulted in a significant decrease in DF in the left atrium and coronary sinus. However, analysis of electrograms recorded from 2 sites inside the left atrium and coronary sinus may not provide detailed information on the spatial organization of AF. Spectral analysis of lead V_1, therefore, also was performed, because this lead may reflect global activation of both atria (7). A similar effect of CPVA and EGA was observed in lead V_1, suggesting that the effects of ablation were not specific to the intracardiac recording sites but represented a global effect in the atria.

The goal of EGA is elimination of complex electrograms characterized by a short cycle length, fractionation, and/or continuous electrical activity (5). Sites with a short cycle length by definition have a higher frequency content. Fractionation and/or continuous electrical activity may be caused by slow conduction, wave front collision, wave break, or pivot points that facilitate re-entry (6).
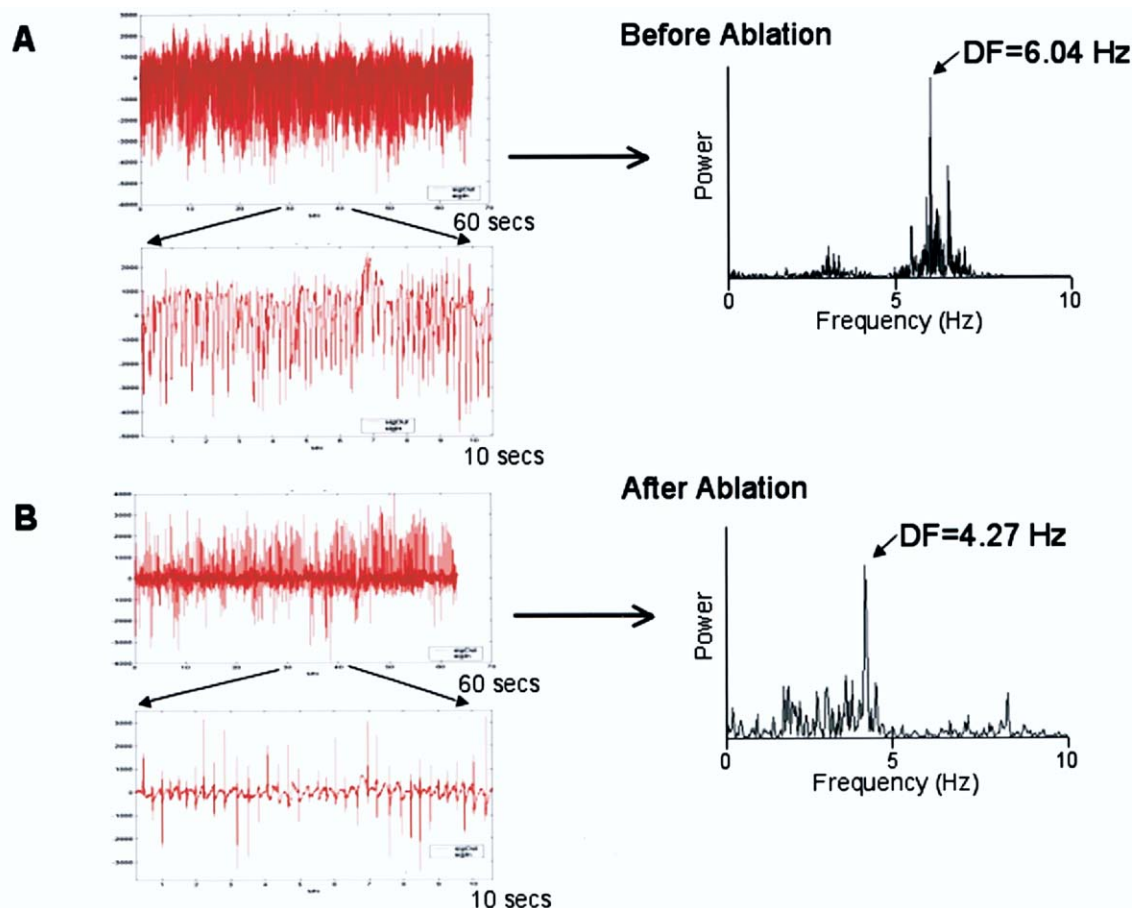
Figure 5. Effect of electrogram-guided ablation on dominant frequency (DF). A representative example of fast Fourier transformation analysis of left atrial electrograms before **(A)** and after **(B)** electrogram-guided ablation is shown. A 10-s fragment of the 60-s sample was magnified to better illustrate the electrograms in both panels. As described in the text, fast Fourier transformation analysis was performed using samples 60-s long. There was a marked decrease in the DF after electrogram-guided ablation.

During CPVA, the pulmonary veins are encircled without reference to the complexity of electrograms. Nevertheless, CPVA also was associated with a decrease in DF. Circumferential pulmonary vein ablation may decrease the DF by elimination of pulmonary vein tachycardias, ablation of rotors that have anchor points near a pulmonary vein (16), debulking of the left atrium with subsequent shortening of the potential wavelengths that can propagate (22), and/or by ablation of ganglionated plexi (23).
Spectral characteristics after ablation and clinical outcome.
An acute decrease in the DF of AF after EGA was associated with a favorable clinical outcome in patients with persistent AF. This may suggest that ablation of complex electrograms resulted in elimination of triggers and/or other driving mechanisms of AF and also possibly sites of ganglionated plexi. In contrast, there was no relationship between the acute change in DF and the clinical outcome after EGA for paroxysmal AF or after CPVA for paroxysmal or persistent AF.

In patients with persistent AF, rotors that have a high DF have been proposed as a potential dominant mechanism of the AF (7,13,14). Elimination of these rotors by EGA may explain why the efficacy of EGA was associated with an acute reduction in DF. However, it should be noted that

this study does not provide any data that prove the presence of rotors in the human left atrium. The major finding of this study is that there was an acute decrease in DF after both CPVA and EGA. Based on prior experimental studies (16,17,24), it may be inferred that elimination of rotors resulted in the decrease in DF. However, DF also may have decreased due to the other mechanisms discussed in the preceding text.

The efficacy of CPVA was not associated with an acute decrease in DF (i.e., a reduction in DF after CPVA did not necessarily result in a more favorable clinical outcome). It is possible that not all high-frequency sources may play the same role in perpetuation of AF, and there may be site-specific differences. During EGA, all of the pulmonary veins and the left atrium were mapped, and all complex electrograms were targeted for ablation until all target sites were eliminated and/or AF became noninducible. However, during CPVA, only those high-frequency drivers that happen to be located along the path of encircling lesions around the pulmonary veins are eliminated. It is possible that, in addition to eliminating rotors, CPVA exerts its therapeutic effect through other mechanisms such as atrial debulking, autonomic denervation, and elimination of pulmonary vein
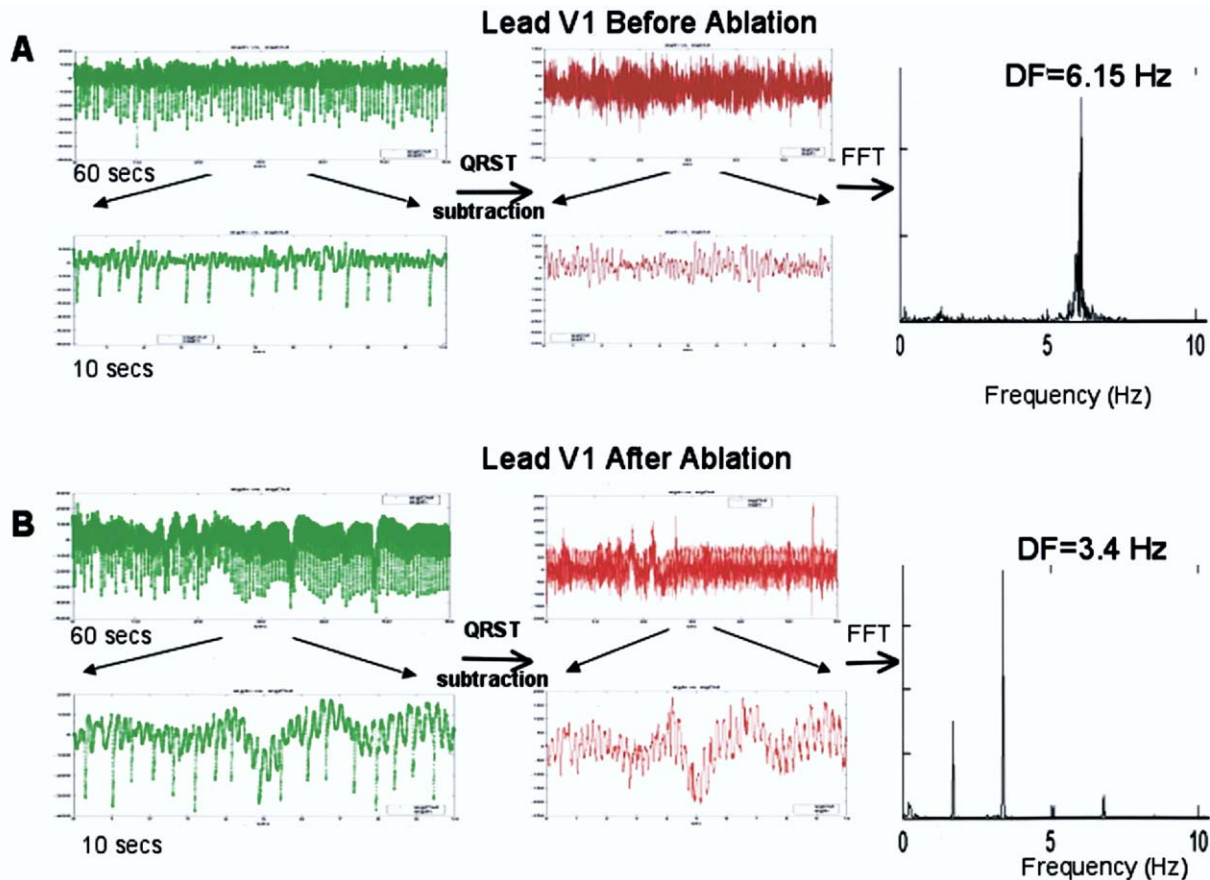
Figure 6. An example of fast Fourier transformation (FFT) analysis of lead V_1 before **(A)** and after **(B)** electrogram-guided ablation. A 10-s fragment of the 60-s sample was magnified to better illustrate the electrograms in both panels. Electrograms before QRST subtraction are shown in **green**. After the QRST subtraction, the electrograms are shown in **red**.

tachycardias. This may explain why the efficacy of CPVA was not associated with an acute reduction in DF.

In patients with paroxysmal AF, there was no association between an acute decrease in DF after CPVA or EGA and clinical outcome. During both CPVA and EGA, pulmonary vein tachycardias are targeted. In the majority of patients with paroxysmal AF, ablation of pulmonary vein tachycardias may be sufficient to eliminate AF. However, pulmonary vein tachycardias may not have the highest DF and may serve to trigger and maintain secondary drivers and/or rotors in the atrium. It also is possible that the frequency content of pulmonary vein tachycardias may have been underestimated because recordings were made at the base of the left atrial appendage and in the coronary sinus.

In this study, only the acute effects of ablation on the spectral characteristics of AF were analyzed. It is possible that progressive fibrosis and lesion maturation resulted in a further decrease in DF late after ablation in some patients, whereas DFs may have increased in others due to recovery of conduction in previously ablated sites. Therefore, an acute reduction in DF may not necessarily be predictive of long-term clinical outcome.

Prior studies. Spectral analysis of AF from electrocardiographic recordings has been reported previously by QRST cancellation techniques similar to the techniques

used in this study, and the reproducibility of spectral analysis over time has been validated in patients with AF (7,25,26).

In a study that analyzed intracardiac atrial electrograms in 14 patients with AF, no association between spontaneous termination of AF and a decrease in DF was demonstrated. Therefore, the decreases in DF observed in this study most likely occurred as a result of the effects of ablation on rotors and were not simply a nonspecific finding associated with conversion of AF (27).

Detailed intraoperative mapping of the atria was performed in 9 patients with chronic AF (28). Consistent with the findings of this study, a high-frequency source that displayed monomorphic electrograms was identified almost exclusively in the left atrium, whereas irregular electrograms suggestive of fibrillatory conduction were recorded from the rest of the atria in the majority of the patients.

In a recent study, catheter ablation of AF was performed under the guidance of online spectral analysis to target "AF-nests" or "fibrillar myocardium," identified by a rightward shift of the FFT in 34 patients with paroxysmal or persistent AF (29). During a mean follow-up of 10 months, 94% of patients were reported to be in sinus rhythm. It appears that the morphologic and spectral characteristics of AF-nests targeted in that study are similar to the complex

electrograms targeted during EGA in this study. In another recent study, online spectral analysis was utilized to ablate sites of cardiac autonomic innervation during "cardiac neuroablation" in patients with neurocardiogenic syncope, functional atrioventricular block, or sinus node dysfunction (30).

Study limitations. A limitation of this study is that the spectral analysis of intracardiac electrograms was performed on electrograms recorded at only 2 intracardiac sites and high-density analysis of the spatial organization of AF was not feasible. However, the effects of ablation on DF were also demonstrated with spectral analysis of the lead V_1, which may reflect global activation of the atria (7).

A second limitation is that some of the patients with persistent AF were being treated with amiodarone, which may decrease the DF. However, in this study, each patient served as his/her own control, and the change in DF after ablation was unlikely to be influenced by amiodarone.

This was not a randomized study. However, the patients were consecutive, and the clinical characteristics of patients in both treatment groups were similar. Furthermore, each patient served as his/her own control in the analysis of the effects of CPVA or EGA on DF.

Conclusions. By determining the effects of CPVA and EGA on the spectral characteristics of AF, this study provides evidence that both CPVA and EGA results in an acute decrease in the DFs recorded from select sites in the left atrium and also lead V_1, suggesting that high-frequency sources may have been eliminated. However, there is an association between an acute reduction in DF after EGA and clinical outcome only in patients with persistent AF, and the clinical efficacy of CPVA is not associated with a reduction in the DF of AF either in patients with paroxysmal or persistent AF. These findings suggest that different mechanisms play a role in the genesis of paroxysmal and persistent AF, and that CPVA and EGA exert their therapeutic effects by different mechanisms.

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