Epicardial Mapping of Chronic Atrial Fibrillation in Patients
Preliminary Observations

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Background—The mechanisms of chronic atrial fibrillation (AF) are not well understood. We performed epicardial mapping of chronic AF in patients undergoing open heart surgery to test the hypothesis that chronic AF is due to a left atrial “driver” with a regular, short cycle length, resulting in fibrillatory conduction to the rest of the atria.

Methods and Results—Nine patients with chronic AF (1 month to >15 years’ duration) were studied at open heart surgery, 8 before and 1 during cardiopulmonary bypass. During AF, atrial electrograms (AEGs) were recorded for 1 to 5 minutes from 404 epicardial electrodes arranged in bipoles along with ECG lead II or ventricular electrogram. Four-second segments of each bipolar AEG were also subjected to fast Fourier transform analysis. Two patterns of atrial activation were present during AF. In pattern 1 (7/9 patients), AEGs from parts of the atria demonstrated a short, regular cycle length with identical beat-to-beat morphology, and the rest of the atria were activated irregularly, and AEGs that demonstrated constant morphology and cycle length were localized to parts of the left atria (5/7), the right atria (1/7), or both atria (1/7). In pattern 2 (2/9 patients), AEGs showed no evidence of regular activation or constant morphology.

Conclusions—In 9 patients with chronic AF, the commonest recorded AEG pattern showed an area of regular, rapid rhythm, consistent with the possibility that a driver causing fibrillatory conduction is one mechanism of AF in these patients. (Circulation. 2004;110:3293-3299.)

Key Words: fibrillation ■ atrium ■ Fourier analysis ■ mapping ■ surgery

Several mechanisms of atrial fibrillation (AF) have been described in animal models. They include a single focus firing rapidly that causes fibrillatory conduction,1 multiple reentrant wavelets,2,3 and stable or unstable reentrant circuits of very short cycle length (CL) that generate fibrillatory conduction.4-6 In patients, the mechanisms of AF are poorly understood. For a long time, it was assumed, primarily on the basis of the work of Moe et al2 and Allessie et al,3 that AF in chronic AF, a “driver,” ie, a regular rhythm of very short CL in the LA, generates fibrillatory conduction to the right atrium (RA) and parts of the LA.

Methods
We studied 9 patients with chronic AF during OHS for valvular and/or CABG surgery (Table 1). The research protocol, in part a pilot study to develop and improve techniques in order to record from large numbers of atrial epicardial electrodes in patients during OHS, was approved by the committee on the conduct of human research at University Hospitals of Cleveland. All patients gave written informed consent before their surgery.

During the scheduled OHS, and after the heart was exposed under general anesthesia, either before (8 patients) or during (1 patient) cardiopulmonary bypass, arrays that contained 404 electrodes arranged in pairs were placed on the atrial epicardial surface (RA 188 electrodes; LA 156 electrodes; Bachmann’s bundle [BB] 60 electrodes; Figure 1) as described previously.5 The interelectrode distance of each electrode pair in the array was 1.2 mm; the distance between the center of each bipolar electrode pair and its neighbor is shown in Figure 1. Atrial electrograms (AEGs) were recorded simultaneously for 1 to 5 minutes from the LA and RA in 8 patients and sequentially from 1 patient (patient 1), along with surface ECG lead II or a ventricular electrogram. Because the electrode array initially placed on the inferior LA free wall (region B in Figure 1) did not overlie the LA appendage (LAA) and the region immediately lateral to the left superior and inferior pulmonary veins (region A in

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the sampling rate to 250 Hz. DC offset was removed by subtraction of its mean data value, and any linear trend was removed from the data segments to make them stationary. To prevent “leakage effect” due to the power in larger peaks of the spectrum, a Hamming window was applied before the FFT analysis was performed. Additional filtering (bandpass of 5 to 250 Hz) was applied to reduce respiration-induced fluctuation in the baseline and electrical noise. The signal was then subjected to a 4096-point discrete Fourier transform, which provided a resolution of 0.06 Hz displayed as a power spectrum. The region between 1 and 15 Hz was retained for analysis. The dominant peak frequency, defined by the peak frequency with the strongest power in the power spectrum, was automatically detected. The mean atrial CL was then calculated from the reciprocal of the dominant peak frequency. When multiple peaks were present, the range of atrial CLs was calculated. We5 and others4 have shown this method to be a valid method for characterizing the organization of atrial activity in the atria. All signal processing and analyses were done in the MATLAB environment (The Mathworks, Inc).

Results

Activation Patterns

Two patterns of atrial activation were noted during our recordings of chronic AF. In pattern 1, seen in 7 of the 9 patients (patients 2 through 8; Tables 1 and 2), parts of the atria were activated at remarkably constant intervals of relatively short CL, and the AEGs recorded from these sites demonstrated identical beat-to-beat morphology (Figure 2). The rest of the atria were activated irregularly and at intervals with longer CLs in 6 of these 7 patients (patients 2 through 6 and patient 8). Also, sometimes sites not in the area of regular activation showed fractionated AEGs, but no double potentials were observed. In patients 2, 4, 5, and 6, regular AEGs were recorded from parts of the LA, and in patients 2, 4, and 5, they were also recorded from the LA portion of BB, with
longer and irregular CLs elsewhere (Table 2). In patient 8, regular AEGs at the same short CLs were recorded in large parts of both atria, and in patient 3, AEGs with regular, short CLs were recorded in part of the RA, including the right side of BB, with no activation recorded from the LA, including the left side of the BB. In patient 7 (Tables 1 and 2), parts of the LA were activated at a regular CL that was longer (by a mean of 30 ms) than parts of the RA activated at irregular but shorter CLs (Figure 3). Although the CLs recorded from the regular areas in patients 2 through 8 were remarkably constant, with beat-to-beat CL variation of only 4 ms, the actual CLs had quite a wide range from patient to patient, from 137 to 288 ms (Table 2). In pattern 2, seen in patients 1 and 9, no evidence of regular activation in either atrium was present (Figure 4). Rather, AEGs from both atria varied in both morphology and CL.

Figure 2 shows a representative example of pattern 1 from patient 2 (Tables 1 and 2), who had AF of 10 years’ duration. The right panel shows selected bipolar AEGs simultaneously recorded from sites a through h (shown in the left panel), along with a ventricular electrogram. The left panel is a diagrammatic representation of the right and left atrial epicardial surfaces, with the FFT analyses of the bipolar AEGs from sites a through h placed at each site. The box below the diagram in the left panel shows AEGs and FFT analyses from sites b and c recorded 4 minutes earlier than that demonstrated in the other panels. Note that AEG morphology, CL, of BB, with no activation recorded from the LA, including the left side of the BB. In patient 7 (Tables 1 and 2), parts of the LA were activated at a regular CL that was longer (by a mean of 30 ms) than parts of the RA activated at irregular but shorter CLs (Figure 3). Although the CLs recorded from the regular areas in patients 2 through 8 were remarkably constant, with beat-to-beat CL variation of only 4 ms, the actual CLs had quite a wide range from patient to patient, from 137 to 288 ms (Table 2). In pattern 2, seen in patients 1 and 9, no evidence of regular activation in either atrium was present (Figure 4). Rather, AEGs from both atria varied in both morphology and CL.

Figure 2 shows a representative example of pattern 1 from patient 2 (Tables 1 and 2), who had AF of 10 years’ duration. The right panel shows selected bipolar AEGs simultaneously recorded from sites a through h (shown in the left panel), along with a ventricular electrogram. The left panel is a diagrammatic representation of the right and left atrial epicardial surfaces, with the FFT analyses of the bipolar AEGs from sites a through h placed at each site. The box below the diagram in the left panel shows AEGs and FFT analyses from sites b and c recorded 4 minutes earlier than that demonstrated in the other panels. Note that AEG morphology, CL,

### Table 2. Range of Dominant Frequencies Seen in Both Atria With FFT Analysis and Range of CLs at Sites With Electrograms Showing Constant Morphology and Regular (Within 4 ms) Beat-to-Beat CLs

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>RA FFT, Hz Range</th>
<th>LA FFT, Hz Range</th>
<th>Range of CL (ms)/FFT (Hz) at Regular Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.42–6.96</td>
<td>4.12–6.82</td>
<td>NA</td>
</tr>
<tr>
<td>2</td>
<td>3.30–6.47</td>
<td>4.88–6.47</td>
<td>154–156/6.47</td>
</tr>
<tr>
<td>3</td>
<td>3.50</td>
<td>NA</td>
<td>285–288/3.50</td>
</tr>
<tr>
<td>4</td>
<td>3.66–4.88</td>
<td>4.27–4.88</td>
<td>203–206/4.88</td>
</tr>
<tr>
<td>5</td>
<td>4.03–7.20</td>
<td>4.64–7.20</td>
<td>137–140/7.20</td>
</tr>
<tr>
<td>6</td>
<td>3.30–5.98</td>
<td>3.54–6.44</td>
<td>154–156/6.44</td>
</tr>
<tr>
<td>7</td>
<td>3.42–5.37</td>
<td>3.54–4.64</td>
<td>215–219/4.64</td>
</tr>
<tr>
<td>8</td>
<td>2.93–3.66</td>
<td>3.05–3.66</td>
<td>271–274/3.66</td>
</tr>
<tr>
<td>9</td>
<td>3.17–4.39</td>
<td>3.05–4.52</td>
<td>NA</td>
</tr>
</tbody>
</table>

NA indicates not applicable (ie, only irregular beat-to-beat CLs with variable beat-to-beat morphology).

![Figure 2](https://example.com/figure2.png)

Figure 2. Representative example of pattern 1 from patient 2 (Tables 1 and 2) with selected bipolar AEGs and FFT analyses separated by 4 minutes. Numbers between AEGs indicate beat-to-beat CL in milliseconds. See text for discussion. EG indicates electrogram; V, ventricular activation; LAA, LA appendage; RAA, RA appendage; PV, pulmonary vein; SVC, superior vena cava; and IVC, inferior vena cava.

![Diagram](https://example.com/diagram.png)

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and FFT analyses were comparable, which demonstrates the stability of these data over the recording period. FFT analyses from sites a, b, and c demonstrated a single, narrow peak (6.47 Hz), which corresponded to the regular CL (154 to 156 ms) of the AEGs recorded at these sites. These sites had the shortest CLs recorded, consistent with but not proof of their being a “driver.” FFT analyses from sites d, e, f, g, and h demonstrated a broad band with multiple peaks, which corresponded to the irregular CLs of the AEGs recorded from these sites. Also apparent are the dominant peaks at sites d, e, f, g, and h that occurred at a lower frequency (ie, longer and irregular CLs), consistent with their being due to fibrillatory conduction produced by an LA driver.

Figure 4 shows a representative example of pattern 2 from patient 1 (Tables 1 and 2), who had AF of 15 years’ duration. Figures 4A and 4B illustrate representative AEGs and their FFT analyses seen in this patient, in whom sequential recordings from the LA and RA were obtained. Figure 4A shows selected bipolar AEGs recorded with ECG lead II from sites a through i, and Figure 4B shows the corresponding FFT analysis from these sites. In Figure 4A, tracings a and b were recorded from a region that demonstrated a relatively slow, irregular rhythm. Tracings b and c are neighbors. Tracings c and d show variable abnormal signals, including fractionation. Tracings e and g show continuous activation, and tracing f shows low-amplitude signals that occur at long, irregular CLs. Sites e and f are neighbors. Sites h and i show recordings from the LA sites with a higher dominant frequency than the recordings from the RA. The relative complexity of these recording patterns is obvious and not easily understood, but no potential driver was seen.

Discussion

Major Findings
In this study of chronic AF, 7 of the 9 patients manifested a rapid, regular rhythm, most often in the LA. In 6 of 7, this rapid, regular rhythm may have served as a driver, producing fibrillatory conduction and thereby clinical AF, because the CL of the regular rhythm was shorter than that of the large areas of irregular activation. However, in 1 of 7 patients, the area of regular activation in the LA demonstrated a longer CL than parts of the RA. An explanation for this is not evident,
but clearly, not all the data from these patients with chronic AF are consistent with a driver possibly causing fibrillatory conduction, because in 2 of 9 patients, there was irregular and widely disparate type activation of both atria. Furthermore, for patients demonstrating regular activation of very short CLs, there were several variations, including 1 patient with regular activation in a portion of the RA and no activation of large parts of the LA and another patient with regular activation of most parts of both atria with small portions of both atria showing irregular activation of longer CL.

Additionally, it is of interest that as shown in Table 2, the range of CLs in the areas with a regular rhythm is quite wide (137 to 288 ms). In fact, 1 of the patients demonstrated CLs in the range of typical atrial flutter, and 2 patients demonstrated rates in the range of atrial tachycardia, ie, CLs during which 1:1 atrial activation normally would be expected. If these sites of regular activation were acting as drivers, we would have to explain why relatively “slow” rates could still cause fibrillatory conduction. The data from the present study do not provide the answer.

**Patterns of Activation During AF in Humans**

Limited intraoperative mapping studies of induced AF in patients after surgical ablation of an accessory AV connection in patients with Wolff-Parkinson-White syndrome have not been definitive in demonstrating a mechanism of AF. However, the studies by Cox et al did demonstrate the presence of unstable reentrant circuits, principally in the RA, which could be interpreted as causing fibrillatory conduction to the LA and parts of the RA. Likewise, the studies by Konings et al demonstrated 3 activation patterns in the RA, 1 of which included the presence of an unstable reentrant circuit of short CL that may have served as a driver, causing fibrillatory conduction. Harada et al performed epicardial mapping sequentially from limited portions of each atrium using a card-type electrode array of 30 unipolar electrodes in 12 patients with chronic AF and isolated mitral valve disease. These investigators found relatively regular (the beat-to-beat CLs appear to vary) and repetitive activation with short CLs in a portion of the LA (at the base of the LA appendage and lateral to the left pulmonary veins, or at the posterior wall of the isthmus).
adjacent to the AV groove) with irregular activity of the RA. Surgical procedures, including resection of the LA appendage and cryoablation performed at sites suggested by the mapping findings, eliminated AF. These investigators concluded that these relatively organized sites in the LA acted as a driver causing the AF. Sueda et al performed simultaneous epicardial mapping from limited portions of the RA and LA also using a card-type electrode array, but one that consisted of 24 bipolar electrodes, in 11 patients with chronic AF and isolated mitral valve disease. These investigators found rapid, repetitive activation characterized by slightly varying CLs and AEG morphologies in a portion of the LA (the base of the LA appendage and the posterior wall lateral to the left pulmonary veins) compared with irregular activation of the RA in 7 of 11 patients. A nondirected LA ablative procedure was effective in eliminating chronic AF. Wu et al performed simultaneous computerized mapping of a small portion of the RA and LA of 6 patients with permanent AF and organic heart disease. They found rapid, repetitive activity with variable CLs and AEG morphologies in the LA between the 4 pulmonary veins. This activation was faster (of shorter CL) than that observed in the RA. Yamauchi et al performed sequential epicardial mapping of portions of the RA and LA using a card-type electrode array of 60 unipolar electrodes in 40 patients with chronic AF and isolated valve disease. Recorded AEGs showed a similar sequence (it was not possible to assess beat-to-beat AEG morphology and CL characteristics from the data provided), but with irregular activity of the RA. LA ablative procedures, guided by the mapping data when possible, were effective in eliminating AF. It was concluded that the LA was the driving chamber of chronic AF. In sum, previous limited epicardial mapping studies of AF in patients have provided similar data despite recognized limitations: (1) during mapping of induced AF after postsurgical ablation of an accessory AV connection (Wolff-Parkinson-White), the data did show RA reentry of very short CL that could have generated fibrillatory conduction; and (2) during mapping of chronic AF in patients with valvular heart disease, many patients manifested relatively regular, repetitive activity from an area of the LA, usually at the base of the LA appendage and lateral to the left pulmonary veins, which had very short CLs and which could have generated fibrillatory conduction to the rest of the atria. In some of the studies, ablative techniques directed to this area appear to have been relatively effective in restoring sinus rhythm.

Comparison of Present Study With Prior Studies

The data from the present study add to the above studies in several ways. First, we recorded from much larger areas of both atria, and in all but 1 patient, we recorded simultaneously from both atria. Second, we found localized areas in either atrium, but principally in the LA, with rapid activation at very regular CLs with constant beat-to-beat morphology. In all but 1 instance, the CLs were shorter than those found in the rest of the atria. These areas were most often present in the LA in the same region described by others, namely, at the base of the LA appendage and lateral to the left pulmonary veins. The examples recorded by these other investigators did not appear to show completely regular beat-to-beat CL or morphology, but they did appear to show a repetitive activation sequence. We also uniformly found regular activity on the left side of BB whenever regular activity was found in the LA. Third, we found patients in whom all AEGs in both the LA and RA were irregular in CL and morphology. Fourth, we also found a variety of abnormal, widely scattered AEG recordings, including fractionated AEGs, absence of conduction to an area, areas of apparent independent activation patterns, and absence of activation of the whole LA including the left side of BB.

Implications

There is little information regarding the mechanism of chronic AF in patients. In the majority of our patients, the mechanism of AF appears unlikely to be explained by either multiple randomly reentrant wavelets or unstable reentrant circuits of short CL, because in either instance, areas of regular activation of short CL and constant electrogram morphology would not be expected. As suggested above, these observations are more consistent with another mechanism, namely, fibrillatory conduction produced by a regular driver whose CL is too short to permit activation of the rest of the atria in a 1:1 fashion. Actually, this is an old idea that is supported by studies in animal models in which AF is generated either by a single focus firing rapidly or by a reentrant circuit of very short CL. In short, the results of the present study suggest that one of the mechanisms of chronic AF may be secondary to a driver that causes fibrillatory conduction.

This suggested explanation, however, does not appear to explain the mechanism for all of the cases of chronic AF we studied. One patient (patient 7) had an area of regular rhythm, but areas of irregular rhythm with shorter CLs were also present. In addition, in 2 patients, there was no evidence of a driver. In the latter 2 patients, no obvious mechanism of AF is suggested.

Study Limitations

We did not record from any portion of the atrial endocardium or the pulmonary veins. We did not perform ablation of any of the areas that demonstrated rapid, regular activity to determine whether it would eliminate the AF. In this pilot study, because of the need to move our LA electrode array to record sequentially from regions A and B simultaneously with the BB and RA, and because of decreased signal-to-noise ratio of some recordings (mainly due to problems with electrode contact or the operative room environment), which led to scattered noisy AEG recordings, we were unable to provide reliable sequence of activation maps. We did not perform cardioversion in these patients to ascertain whether the chronic AF was persistent or permanent. We also did not record for a second 5-minute period, which would have permitted assessment of the constancy of the location, CL, and electrogram morphology of areas of regular activation.

Conclusions

We found several AEG patterns during chronic AF. The most common pattern showed AEGs of constant, short CLs and
morphology recorded over a relatively large area, principally, but not exclusively, in the LA, with slower and irregular activity in the rest of the atria. These findings are consistent with the possibility that a driver that causes fibrillatory conduction is one mechanism of AF in these patients. We also found patients with no regular activity in either atrium and for whom no obvious AF mechanism was suggested.

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