Separating Atrial Flutter From Atrial Fibrillation With Apparent Electrocardiographic Organization Using Dominant and Narrow F-Wave Spectra

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OBJECTIVES
The purpose of this study was to separate atrial flutter (AFL) with atypical F waves from fibrillation (AF) with “apparent organization.”

BACKGROUND
We hypothesized that F-wave spectra should reveal a dominant and narrow peak in AFL, reflecting its single macro–re-entrant wave front, but broad spectra in AF, reflecting multiple wave fronts.

METHODS
We identified 39 patients with electrocardiograms (ECGs) of “AFL/AF” or “coarse AF” from 134 consecutive patients referred for ablation: 21 had AFL (18 atypical, 3 typical), 18 had AF, and all were successfully ablated. Filtered atrial ECGs were created by cross-correlating F waves to successive ECG time points. Dominant peaks between 3 and 10 Hz were identified from power spectra of X (lead V5), Y (aVF), and Z (V1) axes, and for each, we calculated height (relative to two adjacent spectral points) and area ratio to envelopes of bandwidth 0.625, 1.25, 2.5, 3.75, and 5 Hz (range 0 to 1, where higher ratios reflect narrower peaks).

RESULTS
Dominant peaks had greater relative height for AFL than AF (three-axis mean: 14.2 ± 6.4 dB vs. 6.6 ± 2.1 dB; p < 0.001). Peak area ratios were also higher for AFL than AF for all envelopes (p < 0.001). For the 2.5-Hz envelope, the separation (0.61 ± 0.14 vs. 0.35 ± 0.05, respectively; p < 0.001) enabled a ratio ≥0.44 to identify all cases of AFL from AF (p < 0.001). A panel of seven cardiologists blinded to clinical data provided lower diagnostic accuracy (82.1%; p < 0.01).

CONCLUSIONS
In ambiguous ECGs with atypical F waves, spectral evidence for a solitary activation cycle separates AFL from AF with “apparent organization.” This approach might improve bedside ECG diagnosis and shed light on intra-atrial organization of both rhythms. (J Am Coll Cardiol 2005;46:2079 – 87) © 2005 by the American College of Cardiology Foundation

Although atrial fibrillation (AF) (1,2), atypical (non-subeustachian isthmus-dependent) atrial flutter (AFL) (3), and typical (isthmus-dependent) AFL (4) have increasingly different management, the precise separation of atypical AFL from AF, in particular, is often not made until invasive electrophysiologic study (EPS) (5,6).

Traditional electrocardiography (ECG) diagnosis is limited, because only the classic F waves of typical AFL are defined. In their absence, “atypical” F waves might represent atypical AFL (6), variants of typical AFL (5), or AF (7). In fact, atypical ECG F waves that are quasi-regular in one lead (often V1) are frequently classified as AFL (8,9), even though AF with regional intra-atrial organization might present this way (10). Conversely, low-amplitude F waves or irregularly irregular RR-intervals are often classified as AF (8,9), although both might occur in AFL, particularly when atypical (6). These facts explain why the ECG diagnosis of “AFL/AF” is still encountered.

We reasoned that mechanistic differences between AFL and AF should be reflected on the ECG. Atrial flutter is generally characterized by a macro–re-entrant circuit capturing both atria (4), whereas AF, even with regional organization (10–12) or possible focal drivers (13,14), activates the atria via multiple wave fronts. We hypothesized that the solitary macro–re-entrant wave front of AFL should produce a narrow, dominant F-wave spectral peak, whereas AF, even if organized, should result in broadband contributions to power spectra. We tested this hypothesis in patients referred for ablation with ECGs of “AFL/AF” or “coarse AF” by establishing the diagnostic accuracy of novel algorithms, extending our prior work (15) in comparison with the “gold standard” diagnosis at EPS.

METHODS
We screened 134 consecutive patients referred to the arrhythmia service of the University of California (UCSD) and Veterans Affairs (VAMC) Medical Centers, San Diego, for ablation of AFL or AF. We prospectively identified 39
patients in whom 12-lead ECGs (standard 8- to 10-s duration) showed organized F waves (≥0.2 mV in leads III and V₁) (8) without a “typical” appearance (4) and were labeled “AFL/AF” or “coarse AF.” This study was approved by the joint UCSD/VAMC Institutional Review Board. All patients had been anti-coagulated or lacked thrombus on transesophageal echocardiography, and many had failed one or more anti-arrhythmic medications (Table 1).

**EPS diagnosis and ablation.** Patients underwent EPS in the fasting sedated state, after discontinuing all anti-arrhythmic drugs (except amiodarone) for >5 half-lives. Catheters were advanced transvenously to the coronary sinus (6-F decapolar), His bundle position (6-F quadrapolar), and right atrium (RA) (6-F quadrapolar). For AFL, a 7-F duodecapolar (“Halo”) catheter was positioned parallel to the tricuspid annulus lying across the cavitricuspid isthmus (CTI). For cases of AF and left-sided atypical AFL, catheters were advanced transeptally to the left atrium (LA).

Typical AFL was diagnosed by counter-clockwise tricuspid annular activation (clockwise in reverse typical), concealed entrainment during CTI pacing, and inability to re-induce AFL after creating bi-directional CTI conduction block by ablation. Atypical AFL was diagnosed from distinct atrial activation, concealed entrainment at sites of earliest atrial activation or slow conduction (i.e., double potentials or fragmented electrograms), and tachycardia termination during ablation at sites outside the CTI. Mapping and identification of ablation sites was aided by electroanatomic mapping (Carto; Biosense Webster, Diamond Bar, California) in 12 cases of AFL. Atrial fibrillation was diagnosed from electrograms lacking 1:1 capture between atrial regions, varying electrograms, and inability to entrain the tachycardia. Ablation for AF was performed by pulmonary vein (PV) segmental ostial isolation or linear lesions, individualized for each patient (2). Atrial cycle lengths (CL) were measured as the mean of 20 atrial cycles at Halo, coronary sinus, or PV sites at 200-mm/s scale. For AF, cycles ≤30 ms apart were considered as one fractionated electrogram (1).

**ECG evaluation by expert readers.** A standard 12-lead ECG, simultaneous with intracardiac tracings, was printed from the physiologic recorder (Bard Inc., Billerica, Massachusetts) at 25-mm/s speed and 1-mV/cm amplitude, avoiding regions of extreme noise or possible transitions between AFL and AF. Seven cardiologists from UCSD/VAMC (including three electrophysiologists) coded each ECG as AF or AFL, blinded to EPS and all clinical data. The majority diagnosis was determined for each ECG.

**Quantitative ECG analysis: extraction of atrial activity.** The identical ECG was exported digitally to a PC (filtered 0.05 to 100 Hz; digitized at 1 kHz to 16-bits). The ECGs were analyzed with software written in LabView (National Instruments, Austin, Texas) by Dr. Narayan (16), blinded to all clinical data. This software takes 5 to 10 s to complete analysis on a Pentium III PC.

We created filtered atrial ECGs to analyze F waves, even if superimposed on QRST complexes. For each ECG lead, a 120-ms non-isoelectric F-wave was selected by software, preceding the second or subsequent QRS complex; this was adjusted manually, if necessary, to avoid T waves (Fig. 1). Each sample was cross-correlated to its parent ECG lead at successive time points with the Pearson coefficient (16). Templates overlay simultaneous time points in each ECG lead (Figs. 2 and 3). Figure 1 shows this analysis in AFL, for which correlation r is approximately equal to 1 when F waves recur, and ranges from +1 to −1 elsewhere. The resulting correlation time-series normalizes F-wave amplitude and, thus, reduces magnitude variations during the arrhythmia (e.g., AF) or from noise (e.g., breathing), unlike QRS subtraction algorithms (17).

**ECG correlation spectra: relative peak height.** Filtered atrial ECG power spectra were computed with Fast Fourier Transforms over 8.192 s (2¹³ ms) for each lead (lower panels in Figs. 2 and 3), modified slightly from our prior work (16) and including a Hanning window. The dominant peak was defined as the largest spectral magnitude between 3 and 10 Hz, a bandwidth selected a priori to reflect reasonable longest CL (≥333 ms in AFL) (4) and shortest CL (≥100 ms in AF) (1) for this population. Relative peak height was expressed in dB compared with the mean of one adjacent spectral point on either side (16).

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**Table 1.** Patient Demographics EPS Diagnosis (n = 39)

<table>
<thead>
<tr>
<th>EPS Diagnosis</th>
<th>Age, yrs</th>
<th>Gender, M/F</th>
<th>EF, %</th>
<th>LA Size, mm</th>
<th>Structural Dis/Anti-Arrhythmic Surgery</th>
<th>Drug Therapy*</th>
</tr>
</thead>
<tbody>
<tr>
<td>AF, n = 18</td>
<td>51.7 ± 8.4</td>
<td>18/2</td>
<td>62.5 ± 11.4</td>
<td>41.1 ± 3.9</td>
<td>6/18</td>
<td>15/18</td>
</tr>
<tr>
<td>AFL, n = 21</td>
<td>55.8 ± 15.5</td>
<td>21/7</td>
<td>58.1 ± 12.1</td>
<td>41.4 ± 8.1</td>
<td>8/21</td>
<td>10/21</td>
</tr>
</tbody>
</table>

* p < 0.05.

AF = atrial fibrillation; AFL = atrial flutter; EF = ejection fraction; EPS = electrophysiologic study; LA = left atrium.
ECG correlation spectra: dominant peak width (area ratio). We reasoned that atrial activity in AFL should be represented as a singular frequency with a dominant peak distinct from other spectral components, whereas the dominant peak in AF should lie within a broader envelope. We expressed the narrowness of each peak as the ratio of peak area (width 0.25 Hz) to the area of an encompassing envelope centered at this peak of widths 0.625 Hz, 1.25 Hz, 2.5 Hz, 3.75 Hz, and 5 Hz. Regular AFL circuits should produce a larger area ratio than circuits that vary in rate or number (as in AF). Envelope widths should thus avoid harmonic frequencies. For AFL with dominant peak >3 Hz (i.e., CL approximately equal to 300 ms), the maximum envelope width (centered at 3 Hz) should be <5 Hz to avoid the first harmonic at 6 Hz. Because AFL spectra might have additional peaks (18), we also compared narrower envelopes to optimally identify AFL from AF. The focus on the dominant peak, ignoring harmonic and additional peaks outside the envelope, separates this method from prior organizational indexes (19).

Spatial analyses and comparison with clinical diagnosis. Dominant relative peak heights and area ratios were compared between lead-axes and as three-axis means for each patient group. Receiver-operating characteristic (ROC) curves were then derived for ECG relative peak height and peak area ratio. We compared the diagnostic accuracy of each ECG index, using ROC-derived cutpoints, with the consensus diagnosis from our expert panel.

Statistical analyses. Continuous data are presented as mean ± SD. Two-tailed t tests were used to compare continuous variables between groups. The McNemar test was used to compare paired diagnoses (physician vs. algorithmic) for each ECG, judged against the diagnostic gold standard at EP study. A probability level of 5% (p < 0.05) was considered statistically significant.

RESULTS

Our population comprised 21 cases of AFL (15 atypical, 5 typical, 1 reverse typical) and 18 cases of AF (Table 1). Atypical AFL was ablated at the crista terminalis (n = 2), lateral RA scar (n = 6), lower loop re-entry (n = 1), superior vena caval baffle (n = 1), and LA (n = 5). Mean CL for AFL was 278 ± 46 ms and, for AF, 173 ± 29 ms (p < 0.001) (Table 2).

ECG evidence for dominant and solitary wave fronts in AFL. The EPS-proven AFL had dominant peaks of significantly greater relative height than AF (three axis-means: 14.2 ± 6.4 dB vs. 6.6 ± 2.1 dB; p < 0.001) (Table 2). Dominant peaks for AFL also contained more relative power (i.e., were narrower), evidenced by higher peak area ratios, than AF for all envelope widths (Table 2).

Figure 2 shows an ECG with ventricular pacing that was coded as AF; however, correlation series spectra showed tall and narrow dominant peaks (Fig. 2C), suggesting AFL. Lower loop re-entry was confirmed and ablated in the RA. Figures 3A and 3B, respectively, show EPS-proven atypical AFL and AF, both showing variable F waves lacking a typical sawtooth and irregular RR intervals. The ECG in Figure 3A was read by the expert panel as AF. In correlation spectra, the dominant peak had relative height of 9.2 dB at 3.2 Hz (lower panel) with a peak area ratio of 0.48 (2.5 Hz envelope indicated by arrows), suggesting AFL. Predicted atrial CL (1/frequency = 1/3.2 = 0.312 s) approximated measured atrial CL (304 ms). AFL was ablated in the lateral RA.

Figure 3B shows an ECG read as AFL; however, its filtered atrial ECGs were irregular (middle panel), with broadband spectra (bottom panel). The dominant peak (in the 3- to 10-Hz band) had large absolute magnitude but a relative height of only 3.67 dB at 6.07 Hz and a peak area...
Atrial fibrillation was evident on PV and coronary sinus electrograms, and ECG-predicted CL (1000/6.07 = 165 ms) approximated mean PV CL (160 ms). Additional AF cases are shown below.

**Relative peak height versus area ratios.** Although relative peak heights were higher for AFL than AF (Fig. 4A), the optimum cutpoint for AFL (≥7.89 dB, from ROC analysis in Fig. 4C) misclassified two cases of AF with tall dominant peaks as AFL (Patients #30 and #34, Fig. 7D) and one case of AFL with a short peak as AF (Patient #11; Fig. 4B). The relative peak height ROC curve for AFL had area 0.94 (Fig. 4C).

Peak area ratios (Fig. 5) decreased progressively with increasing envelope width from 0.625 Hz to 5 Hz (Table 2, top row of Fig. 5) but remained significantly higher for AFL than AF, as expected. The ROC curves using peak area ratios to diagnose AFL had areas of 0.86 (for 0.625 Hz envelope, with optimum cutpoint ≥0.86), 0.99 (1.25 Hz, ≥0.56), 0.91 (3.75 Hz, ≥0.36), and 0.90 (5 Hz, ≥0.30; bottom row of Fig. 5). Against a 2.5-Hz envelope, peak area ratios ≥0.44 classified all cases of AFL and none of AF (Fig. 6A) with ROC area of unity (Fig. 6B). The tall peaks in AF Patients #30 and #34 were appropriately broad (area ratios <0.44), whereas the shorter peak in Patient #11 was narrow (area ratio = 0.51, three-axis means).

**Spatial characteristics of ECG indexes.** Relative peak height (Fig. 4B, Table 2) and peak area ratios (Fig. 6C, Table 2) varied between X-, Y-, and Z-axes for each individual but not consistently for either group (p NS for all axis-comparisons). Therefore, we used three-axis means for each parameter.

**Diagnostic accuracy of quantitative criteria versus clinical readers.** Expert readers had a sensitivity and specificity of 80.9% and 83.3% for AFL and 83.3% and 80.9% for AF referenced to EPS, respectively (seven misclassifications, accuracy 82.1%) (Table 3). Misclassifications using relative peak height and area ratios are notated in Figures 4 to 6. Notably, peak area ratio ≥0.44 (2.5-Hz envelope) identified all cases of AFL from AF (100% sensitivity and specificity; p < 0.01 versus expert readers).
DISCUSSION
This study shows that spectral ECG analysis identifies mechanistic differences in AFL versus AF even when visual separation is difficult. In patients with ambiguous ECGs notated as “AFL/AF” or “coarse AF,” evidence for a solitary wave front accurately identified AFL from AF and significantly improved upon conventional expert diagnosis. Unlike prior ECG studies, our comparisons were referenced to the objective gold standard diagnosis at EPS rather than physician diagnosis. This functional approach might better reflect intracardiac organization than ECG F-wave morphology or voltage, both of which vary with atrial size and other factors (5), and may help guide the approach to management and shed light on arrhythmia mechanisms.

AFL and F-wave regularity. A narrow and dominant ECG spectral peak successfully identified regular macro–re-entrant AFL, even when biological F-wave variability obscured its regularity in timing, from AF with “apparent organization.”

Although macro–re-entry in AFL should always yield temporally regular F waves, this distinction might be lost on

| Table 2. Spectral and Spatial Characteristics of EPS-Verified AFL Versus AF |
|---------------------------------|--------|--------|--------|
| Atrial CL, ms                   | 278.4±46.0 | 172.9±28.7 | <0.001 |
| Dominant peak height, dB        |         |        |        |
| 3-axis mean                     | 14.2±6.4 | 6.6±2.1 | <0.0001 |
| X-axis                          | 14.8±6.9 | 7.2±3.7 | <0.0002 |
| Y-axis                          | 14.0±7.3 | 6.0±2.6 | <0.0001 |
| Z-axis                          | 13.9±6.5 | 6.6±2.6 | <0.0001 |
| Dominant peak area ratios       |         |        |        |
| 0.625-Hz envelope, 3-axis mean  | 0.88±0.07 | 0.79±0.05 | <0.0001 |
| 1.25-Hz envelope, 3-axis mean   | 0.71±0.11 | 0.50±0.04 | <10^-8  |
| 2.5-Hz envelope, 3-axis mean    | 0.61±0.14 | 0.35±0.05 | <10^-8  |
| X-axis                          | 0.61±0.16 | 0.34±0.08 | <10^-6  |
| Y-axis                          | 0.60±0.18 | 0.37±0.09 | <0.0001 |
| Z-axis                          | 0.64±0.18 | 0.35±0.12 | <10^-5  |
| 3.75-Hz envelope, 3-axis mean   | 0.49±0.14 | 0.30±0.05 | <10^-5  |
| 5-Hz envelope, 3-axis mean      | 0.44±0.14 | 0.26±0.04 | <10^-5  |

CL = cycle length; other abbreviations as in Table 1.
visual ECG inspection (8). First, difficulties might arise if ECG F waves are small, as commonly seen in atypical AFL (6), or superimposed on QRS and T waves. The described sliding correlation approach magnifies F waves in relation to poorly-correlated waveforms (QRS and T) and, by normalization, increases the effective gain for low-amplitude F waves. Moreover, F waves spanning QRS complexes are detectable if the template (120-ms duration) also overspills the QRS, although correlation maxima then fall below unity (Figs. 1 and 4A of reference 18).

Second, F waves might vary in AFL, even when unobstructed (Figs. 2, 3A, 7A, and 7B) (6), likely reflecting vector and amplitude variations from breathing, ventricular systole (20), or, potentially, subtle intra-atrial wave front variability (18). Importantly, even AFL F waves in this study that varied morphologically showed tall and narrow

Figure 4. (A) Relative peak heights were higher in AFL than AF (p < 0.001), yet resulted in three misclassifications at the optimal cutoff (≥7.89 dB). (B) Spatial non-uniformities in relative peak heights for each patient were not consistent for either group (Table 2). (C) Receiver operating characteristic (ROC) (area 0.94). Other abbreviations as in Figures 1 and 2.

Figure 5. (A) Peak area ratio (three-axis mean) to varying envelope widths show that peak area ratios fall as envelopes widen from 0.625 to 5 Hz, although differences between AF and AFL were maintained (Table 2). Small icons represent individual patients and large icons represent the mean (± SD) for each group. (B) Receiver operating characteristic (ROC) curves for the diagnosis of AFL at each envelope width. The arrow indicates the optimum envelope width (2.5 Hz; Fig. 6). Other abbreviations as in Figures 1 and 2.
spectral peaks (e.g., Figs. 2, 3A, 7A, and 7B). Future studies should explore whether dominant peak width might actually define the interface between a single AFL wave front (with variability) and type I (organized) AF (21, 22).

Somewhat surprisingly, F-wave dominant peak heights and width in AFL did not show uniform spatial orientations (Table 2, Figs. 4B and 6C); however, individual patients showed spatial “preferences” in each index, suggesting that differing atypical AFL circuit locations might have obscured consistency for the group. Ongoing studies in our laboratory are quantifying whether “preferred” planes of ECG activation might help localize atypical AFL circuits.

Intra-atrial organization in AF and ECG spectral width.
Both atria activate via multiple wave fronts in AF, even if “organized” (11, 12), producing a range of atrial periodicities and broad spectra. Results from this study support the hypothesis that even when AF shows tall dominant peaks, such as in the two cases misclassified in Figure 4B, their broad widths (Fig. 6C) suggest multiple wave fronts. Broad spectral contributions are also consistent with suggestions that AF might be a chaotic rhythm (23), whereas narrow spectra in AFL reflect its periodicity. Area ratios are likely effective because they characterize narrowness or broadness of the dominant spectral peak without including its harmonics or additional frequencies (19) of less clear physiologic significance.

Recent evidence suggests that human AF is regionally organized, potentially driven by localized macro-re-entry (24) or focal “drivers” (13, 14). It is intriguing to speculate whether the two AF cases with large relative peak height (Patients #30 and #34; Figs. 4B and 7D) were driven by such mechanisms. High-resolution mapping (13, 14) could address this issue and identify, for example, whether the 11-Hz peak in Figure 3B represents a driver (although possibly too fast for human AF) (14). Although spectral peak narrowing precedes clinical termination of AF by ibutilide (17) and predicts pace termination of short-lived canine AF (19), corresponding intra-atrial changes in AF organization are unclear. High-resolution mapping could, thus, define the relationship between intra-atrial and ECG organization in AFL and AF.

Comparison with previous studies. Few studies have attempted to clarify the ECG coding of “AF/AFL,” and many were referenced to clinical interpretation (25), despite its limitations (8, 9). Spectral entropy was shown to separate AF from AFL with 91.8% accuracy but was not referenced to EPS (26). Although organized activation of trabeculated RA in human AF has been characterized spectrally (12) and causes large F waves in lead V1 (10), other features of ECG organization or indexes separating AF from AFL were not described. Elegant spectral analyses of the ECG (17) and intra-atrial electrograms (19, 27) have shown that distinct spectral peaks in AF suggest greater organization than one spectral envelope; however, that work did not define ranges for AFL, separate AFL from AF, or address the clinical dilemma of ambiguous ECGs. Our algorithm also differs from those approaches in that we focus on the dominant peak and ignore harmonics and additional peaks of unclear significance.

Clinical significance. Accurate ECG diagnosis of AF and AFL might help guide the approach to ablation, including the need for trans-septal catheterization, choice of catheters, and/or mapping systems. Precise ECG analyses might also
avoid the consequences of misdiagnosis (9) and help guide anti-arrhythmic drug selection because, for example, ibutilide might be more effective for AFL (28) or amiodarone for AF (29). Future studies with concomitant high-resolution mapping should determine whether these ECG indexes reflect specific intra-atrial organizational features in AF. If so, ECG spectra could have important prognostic implications and help guide AF ablation.

Study limitations. First, we enrolled only patients with ECGs of “AF/AFL” or “coarse AF” who underwent EPS mapping to confirm arrhythmia mechanism. This strengthens our work over studies relying upon clinical ECG diagnosis, although its prospective validation in a wider population is necessary. Second, the optimum peak area ratio cutpoint requires confirmation in larger studies. Third, it is important to emphasize that our AFL cases, some of
which exhibited varying F waves, did not reflect AF. We applied standard diagnostic criteria for AFL (4), often with electroanatomic mapping, and achieved successful ablation without LA compartmentalization or PV isolation. Fourth, since ECG diagnosis typically has to be made without the benefit of adenosine or vagal maneuvers to induce AV block and unmask F waves, we analyzed only 12-lead ECGs of standard duration without these interventions. Finally, a rhythm classified during EPS as AFL could conceivably disorganize to AF at the moment of ECG inscription or vice versa. Although none of our analyzed ECGs showed simultaneous electrograms suggesting transitions, this might explain some cases of AFL and AF that are spectrally similar and further motivates the need for high-spatial resolution mapping studies.

Conclusions. In ambiguous ECGs of “AFL/AF” or “coarse AF,” spectral evidence for a solitary macro–re-entrant circuit accurately identifies AFL, even with low amplitude or varying F waves, from AF with apparent organization. Referenced to the gold standard of EPS diagnosis, this approach improved diagnostic accuracy compared with a panel of experts and might shed light on the intra-atrial organization of AF.

Acknowledgments
The authors thank Paul Clopton, MS, for statistical assistance and Kathleen Mills, BA, and Nancy McCormick, RNP, for coordinating this study.

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