Termination of persistent atrial fibrillation by ablating sites that control large atrial areas

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Abstract

Aims: Persistent atrial fibrillation (AF) has been explained by multiple mechanisms which, while they conflict, all agree that more disorganized AF is more difficult to treat than organized AF. We hypothesized that persistent AF consists of interacting organized areas which may enlarge, shrink or coalesce, and that patients whose AF areas enlarge by ablation are more likely to respond to therapy.

Methods and results: We mapped vectorial propagation in persistent AF using wavefront fields (WFF), constructed from raw unipolar electrograms at 64-pole basket catheters, during ablation until termination (Group 1, N = 20 patients) or cardioversion (Group 2, N = 20 patients). Wavefront field mapping of patients (age 61.1 ± 13.2 years, left atrium 47.1 ± 6.9 mm) at baseline showed 4.6 ± 1.0 organized areas, each separated by disorganization. Ablation of sites that led to termination controlled larger organized area than competing sites (44.1 ± 11.1% vs. 22.4 ± 7.0%, P < 0.001). In Group 1, ablation progressively enlarged unablated areas (rising from 32.2 ± 15.7% to 44.1 ± 11.1% of mapped atrium, P < 0.0001). In Group 2, organized areas did not enlarge but contracted during ablation (23.6 ± 6.3% to 15.2 ± 5.6%, P < 0.0001).

Conclusion: Mapping wavefront vectors in persistent AF revealed competing organized areas. Ablation that progressively enlarged remaining areas was acutely successful, and sites where ablation terminated AF were surrounded by large organized areas. Patients in whom large organized areas did not emerge during ablation did not exhibit AF termination. Further studies should define how fibrillatory activity is organized within such areas and whether this approach can guide ablation.

Introduction

Mechanistic understanding of atrial fibrillation (AF) is unclear. Pulmonary Vein Isolation (PVI) is a cornerstone of AF ablation[1], but outcomes remain suboptimal with variability across centres. Several mechanisms are suggested that describe persistent AF as consisting of organized regions of high dominant frequency,[2] drivers, or passive activation[3,4] or, alternatively, disorganized sites[5] of colliding waves represented by complex electrograms. However, it is unclear how to reconcile these mechanisms to guide therapy.

One notable conceptual agreement between models is that AF exhibits a spectrum from relatively organized to disorganized activity. This spectrum was noted by Konings et al.[6] and, more recently, organized AF on the ECG has been associated with successful cardioversion and ablation[7] as measured in the coronary sinus (CS).[8] However, it is currently unclear how to map this spectrum of AF organization clinically to guide or assess the impact of therapy. We hypothesized that persistent AF comprises areas of organized activity interspersed with zones of disorganization.[5,6] We further reasoned that successful ablation may remove disorganized zones so that remaining organized areas cover progressively more of the atrial surface. Ultimately, this may result in the atria activating in a 1:1 fashion and no longer fibrillating, i.e. atrial tachycardia or sinus rhythm.

Methods

Patient inclusion: We recruited consecutive patients with persistent AF, resistant to one or more antiarrhythmic medications, at catheter ablation, in whom mapping with basket catheters was used throughout the procedure and in whom ablation acutely terminated AF during defined ablation ($n = 20$). In this same time frame, we identified consecutive patients without AF termination during ablation ($n = 0$).

Electrophysiology study: Patients were brought to the EP lab in the post-absorptive state. All antiarrhythmic medications were discontinued >5 half-lives (>30 days for amiodarone). Catheters were placed in the right atrium (RA), CS, and left atrium (LA) via transseptal puncture. Basket catheters (64 poles, FIRMap, Abbott) were placed in the right then left atria sequentially, or simultaneously ($N = 9$). Ablation was guided prospectively by a clinical mapping system (*RhythmView™, Abbott*). Regions of ablation were recorded relative to electrodes and in electroanatomic maps. Analysis in this study then focused on WFF streamlines blinded to sites of delivered ablation and outcome.

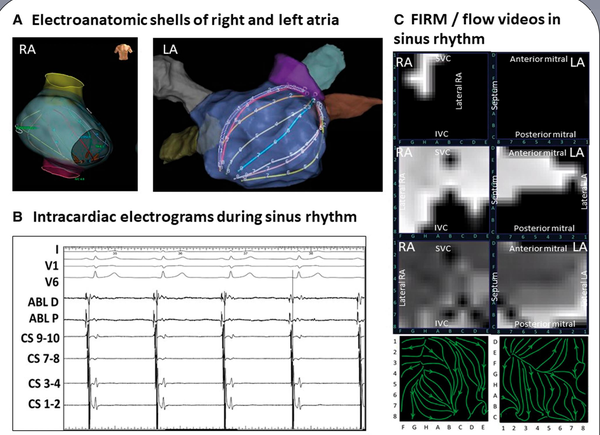

Figure 1: WFF mapping of sinus rhythm. Biatrial basket locations in the right (A) and left atria (B) demonstrating appropriate contact and coverage of the atrium. (B) Electrograms in sinus rhythm. (C) Successive snapshots of wavefront propagation over the atria in sinus rhythm, commencing in the sinus region (10 ms), proceeding to the posterior RA and across Bachmann's bundle (50 ms), then to the inferolateral LA. (D) WFF summary of the sinus wavefront displayed as stream lines (green) with arrows showing propagation direction. LA, left atrium; RA, right atrium; WFF, wavefront field.

Wavefront field mapping: We used a novel approach to map AF propagation globally[10]. Wavefront field mapping applies gradient matching to calculate dynamic vector fields that describe AF wavefront propagation over time. These vector fields represent the direction and velocity of conduction across the atrium at each point in time. Raw electrograms from panoramic recordings are used as the input, and vectors are calculated based on activation timings from any method, such as openly available methods online or clinical mapping systems. The process is displayed as an animated sequence of images.

Identification of organized areas in atrial fibrillation: Organized areas were defined when wavefront propagation activated the area in a repeatable, 1:1 fashion. Organized areas were quantified as proportions of the mapped field. Three trained observers examined a random sampling of 30 animated image sequences of AF and visually estimated the size of the largest organized area as a proportion of the mapped field. The temporal presence of each organized area was calculated by a trained observer as a proportion of the mapped time (0–100%).

Statistical analysis: The primary analysis was based on WFF for the largest organized area in the baseline minute and the minute prior to termination or cardioversion. Comparisons between two groups were made with Student's *t*-tests for independent samples or Welch's *t*-test if heterogeneity was present. Nominal values were expressed *n* (%) and compared with χ^2 tests or Fisher's exact tests as appropriate. A probability of <0.05 was considered statistically significant.

Results

Ablation causing termination to sinus rhythm: We applied WFF mapping during ablation of persistent AF. Overall, AF terminated to sinus rhythm in nine cases, in each of which eliminating organized areas caused enlargement of residual areas. Elimination of such primary organized areas terminated AF to sinus rhythm in each case.

Ablation with termination to atrial tachycardia: Overall, 6 of 11 cases where ablation terminated AF to atrial tachycardia ($n = 8$) or atrial flutter ($n = 3$) showed two competing primary areas controlling most of the atrium, with ablation of one area leaving the remaining area as an organized atrial tachycardia. Three of the 11 cases terminated to cavotricuspid atrial flutter, whose ablation resulted in sinus rhythm.

Cases where atrial fibrillation did not terminate by ablation: Of 20 cases in Group 2 without AF termination by ablation, 18 cases showed no expansion of organized areas. The remaining two cases showed progressive enlargement of an organized area that was not ablated because it was not identified prospectively by clinical mapping.

Organized areas between patients in whom atrial fibrillation did/not terminate by ablation: For Group 1 patients, that organized areas surrounding AF termination sites covered larger atria areas (44.1 ± 11.1%) than the average of cotemporaneous competing sites (22.4 ± 7.0%; $P < 0.00001$). The temporal presence for organized areas was also greater for terminating than competing sites (45.1 ± 23.4% vs. 26.1 ± 13.7% of mapped time; $P < 0.005$).

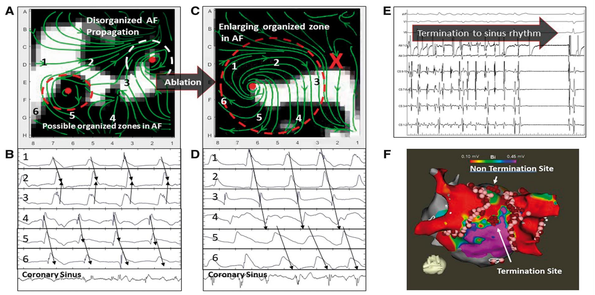

Figure 2: WFF of persistent AF in a 55-year-old man with termination to sinus rhythm. (*A*) WFF and corresponding electrograms. WFF shows two organized areas (coloured ellipses) separated by disorganization. Unipolar electrograms at precise points marked on WFF streamlines confirm 1:1 activation near the red ellipse, within disorganized activity seen on bipolar CS electrograms. The white ellipse area was ablated, but AF did not terminate. (*B*) WFF after ablation of white organized ellipse (marked X), shows enlargement of the residual organized area (red ellipse). Unipolar electrograms confirm 1:1 activation within the red ellipse. (*C*) Ablation at the centre of this primary area terminated AF to sinus rhythm. (*D*) Electroanatomic map. AF, atrial fibrillation; CS, coronary sinus; WFF, wavefront field.

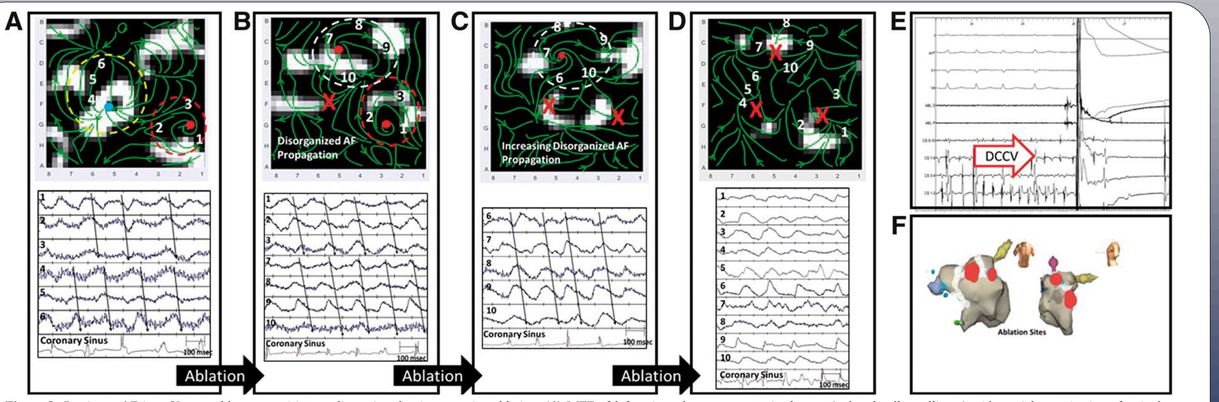

Figure 3: Persistent AF in a 62-year-old man requiring cardioversion despite extensive ablation. (*A*) WFF of left atrium shows two organized areas (red and yellow ellipses) with partial organization of unipolar electrograms. Ablation within these sites did not terminate AF. (*B*) WFF remapping of left atrium (ablation marked X) reveals a new organized area (white ellipse) with minimal change to the previous red labelled area, with unipolar electrograms showing partial organization. Ablation of the red ellipse did not terminate AF. (*C*) WFF remapping of left atrium (ablated area marked X) shows continuation of white organized area, and unipolar electrograms showing some organization. Ablation within the white area did not terminate AF. (*D*) WFF mapping after ablation of all organized areas; unipolar electrograms show no organized areas are present (*E*) AF cardioversion (red arrow labeled DCCV) to sinus rhythm. (*F*) Electroanatomic map showing ablation lesions within organized zones (red) and PVI (white). AF, atrial fibrillation; DCCV, direct current cardioversion; PVI, pulmonary vein isolation; WFF, wavefront field.

For Group 2 patients, in segments prior to cardioversion, there was no difference in the size of the largest organized area compared with the average organized area (16.6 ± 6.9% vs. 15.2 ± 5.6% of mapped area; $P = 0.376$).

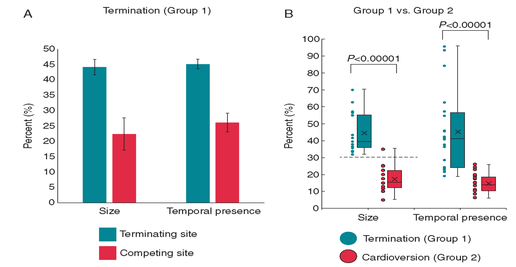

Figure 4: Comparison of organized areas leading to termination. (*A*) Bar graph showing organized area size (as % of mapped area) and temporal duration(as % of mapped duration) of sites that led to termination (terminating site, green) compared with the average of cotemporaneous competing areas (competing site, red) prior to termination. (*B*) Histogram of all organized area sizes and temporal duration that led to termination (green) compared with sites prior to cardioversion (red). Error bars represent standard error of means.

Limitations

First, this is a relatively small cohort of patients, although they were well mapped over a long duration. Prospective, larger studies will be needed to accurately predict termination based on atrial organized areas. Organized areas were estimated by blinded, visual analysis. Patients in this study were part of multiple protocols, and so long-term outcomes are not available. Global mapping is needed to define organized areas and basket catheters are limited by variable contact, electrode spacing, and movement. Nevertheless, they currently provide the highest available resolution for wide-area contact mapping. True assessment of areas of control is limited by 2-dimensional displays of the basket.

Conclusions

We use novel global mapping of AF propagation to show that AF can be represented as a dynamic interaction of organized areas of control, interspersed by disorganized activity. In successful cases, ablation enabled residual areas to enlarge, and sites surrounded by a critical atrial area were invariably sites where ablation terminated AF. Patients in whom atrial areas did not enlarge did not exhibit termination. Future studies should test if using these results to guide ablation can improve outcomes.

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