Biatrial Activation in Isthmus-Dependent Atrial Flutter

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Background—The aim of this study was to determine the biatrial activation pattern in isthmus-dependent atrial flutter (AFL) to understand the functional interatrial connections and the activation pattern of the left atrium (LA).

Methods and Results—Biatrial activation was performed, using an electroanatomic mapping system, in 10 patients undergoing right atrial isthmus ablation for counterclockwise (n=7) or clockwise (n=3) AFL. The AFL circuit was pericricuspid and propagated slowly (0.5±0.2 m/s) through the isthmus. LA was activated by two wave fronts, with discrete breakthroughs in the superior, mid, or inferior atrial septum. The activation of LA overlapped 50±16% of the AFL cycle length. In counterclockwise AFL, at least one breakthrough was located in the inferior atrial septum. LA activation began immediately after the exit of the flutter wave from the isthmus and was directed inferosuperiorly in all patients, being synchronous with the atrial septal activation. The septal breakthroughs in patients with clockwise AFL were variably located. The direction of LA activation was superoinferior in 2 and inferosuperior in 1 patient.

Conclusions—The circuit of isthmus-dependent AFL was entirely in the right atrium. LA activation was a bystander and followed trans-septal conduction across the inferior coronary sinus-LA connection, Bachmann’s bundle, and/or fossa ovalis. (Circulation. 2001;104:2545-2550.)

Key Words: atrial flutter ■ conduction ■ mapping

A detailed mapping of isthmus-dependent or typical atrial flutter (AFL) using multiple endocardial recordings, intracardiac echocardiography, electroanatomic CARTO, 64-electrode basket catheter, noncontact EnSite, and body surface mapping has shown a right atrial (RA) macroreentrant circuit around the tricuspid annulus. Although mapping of the right side of the atrial septum was performed in several of these studies, the site of interatrial connections and the pattern of left atrial (LA) activation have been described only in animal models. Our aim was: to construct a global biatrial activation pattern of isthmus-dependent AFL to determine the location of interatrial connections and the activation pattern of the LA.

Methods

Study Patients

Biatrial activation mapping was performed using the CARTO electroanatomic mapping system ( Biosense-Webster ) in 10 patients (60±10 years, 8 men) who underwent radiofrequency ablation of the right atrial isthmus (RAI) for typical AFL. All patients were symptomatic for 5.7±9.1 years for recurrent episodes of AFL. The polarity of the flutter wave was studied carefully during >2:1 AV block, spontaneous or induced, either by carotid sinus massage or by intravenous adenosine. Seven patients had counterclockwise (CCW) and the remaining 3 had clockwise (CW) AFL. In general, the inferior lead CCW flutter wave morphology showed a negative polarity followed terminally by a positive part and a downsloping plateau segment (Figure 1A). In the remaining 3 patients with CW AFL, two different morphologies were observed in inferior leads: a small initial negativity followed by a prominent and notched positive flutter wave (n=2, Figure 1B) and an almost flat flutter wave (n=1). Seven patients had in addition atrial fibrillation, which was paroxysmal in 3, persistent in 3, and required internal cardioversion to restore sinus rhythm in 1 patient. Two patients had diminished left ventricular function, which was attributable to ischemic heart disease in 1 patient and a tachycardiomypathy in the other. One other patient had long-standing hypertension. The remaining 7 patients had structurally normal hearts. The mean LA size was 4.8±1 cm (range, 2.8 to 5.8 cm). Present antarrhythmic drug therapy, including class Ic or III, was not stopped at the time of the electrophysiologic study.

Electrophysiologic Study

All procedures were performed in a postabsorptive state. The study was performed according to the ethical requirements of our institution after obtaining informed consent. Typical AFL was incessant in 7 patients since the beginning of the study and was induced in the other 3 patients. Three diagnostic catheters, a duodecapolar Halo catheter ( Cordis-Webster ) around the tricuspid annulus, a decapolar catheter in the coronary sinus (CS), and a quadripolar catheter in the His bundle region, were introduced during every procedure. Entrainment studies were not performed.

A three-dimensional reconstruction of the biatrial activation pattern of AFL was made using the CARTO electroanatomic mapping system. A revised 4.2 version of the software was used, with the Smooth algorithm used for three-dimensional reconstruction. A maximal positive/negative value of the bipolar CS atrial electrogram, generally in bipole 5 to 6, was used as a reference electrogram. An INR value ≤1 and absence of LA clot or spontaneous echo contrast on transesophageal echocardiography would exclude paradoxical embolism.

Received July 7, 2001; revision received August 16, 2001; accepted August 17, 2001.

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Radiofrequency Ablation

Ablation was performed during AFL (n=3) or after restoring sinus rhythm (n=7). A conventional 8-mm-tip (n=6) or 4-mm-tip (n=1) (Cordis-Webster) or a Sidewinder (Bard, n=3) ablation catheter was used to deliver radiofrequency pulses. Bidirectional isthmus conduction block and AFL noninducibility were confirmed under isoproterenol infusion\textsuperscript{13,14} after ablating the posterior (n=8) or the septal (n=1) RAI. In the remaining patient, bidirectional block was not obtained. The posterior isthmus was successfully ablated using a saline-irrigated-tip catheter (ThermoCool, Cordis-Webster) during a repeat procedure.

Statistical Analysis

All values were expressed as mean±SD and percentages. Mean values were compared by \( \chi^2 \) test. Results were considered to be significant at 5% critical level (\( P<0.05 \)).

Results

Global RA Activation Pattern of Isthmus-Dependent AFL

The mean AFL cycle length was 291±48 ms (range, 220 to 370 ms). The volume of the RA map, constructed by acquiring 80±37 points, was 153±44 mL. The flutter circuit was entirely in the RA and was mapped almost completely (283±45 ms) around the tricuspid annulus (Figures 2B and 2C).

During CCW-AFL (n=7), the flutter wave front propagated through the inferior RAI in an anterior-to-septal direction, then inferosuperiorly along the septum, further in a septal to anterior direction along the superior RA, and finally superoinferiorly along the anterior wall to reenter the isthmus (Figure 3). Superiorly, the flutter wave front propagated both anterior and posterior to the SVC, fusing superoanteriorly, before proceeding down the anterior RA wall. The posterior wall was activated inferosuperiorly as the flutter wave front turned around the septal end of the Eustachian ridge or valve (n=4), superoinferiorly by the activation wave front propagating posterior to the SVC (n=2), or in an anterior to septal direction after a superior crista breakthrough (n=1) (Figure 4).

The activation pattern of CW-AFL (n=3) was similarly along the tricuspid annulus but in a reverse direction (Figure 5). The posterior RA wall was activated superoinferiorly in 2 patients and inferosuperiorly in the remaining patient.

In either rotation of AFL, propagation was slowest through the RAI (0.5±0.2 m/s, \( P<0.0001 \)), followed by the septal (0.7±0.3 m/s), anterior (1.2±0.6 m/s), and superior (1.5±0.8 m/s) RA wall. An analysis of the available bipolar electrograms showed a polyphasic wide electrogram around the CS ostium in 5 patients and in the fossa ovalis in 2 patients. A double potential was recorded in the region of Bachmann’s bundle in 3 patients.

Global LA Activation Pattern of Isthmus-Dependent AFL

The volume of the LA map, constructed by acquiring 118±13 points, was 137±44 mL. The LA was activated, after one (n=6) or two (n=4) discrete breakthroughs, from the RA flutter circuit, noted on the left side of the atrial septum. When initiated by two distinct breakthroughs, these were within 19±23 ms of each other. Fluoroscopically, the breakthrough sites were identified in the superior, mid (near the

(TEE) were prerequisites to performing a trans-septal puncture. Trans-septal puncture, guided by TEE, was performed by a standard technique using the Brockenbrough needle.\textsuperscript{11} Heparin was then given systemically. First, mapping of the LA was performed by introducing a Navistar (Cordis-Webster) catheter through a 8F Mullins sheath (Medtronic Inc). After completion of LA mapping, the trans-septal sheath was withdrawn and mapping was continued in the RA. A global activation map of both the atria was thus constructed. Electrograms obtained from different atrial sites, identified fluoroscopically, were tagged. On the left side, these sites included the pulmonary veins, LA appendage, along the mitral annulus, and on the superior, mid, and inferior atrial septum. On the right side, these sites included the superior vena cava (SVC), inferior vena cava (IVC), RA appendage, Bachmann’s bundle, different levels on the septum (including the site of trans-septal puncture in the fossa ovalis), His bundle, CS ostium, and along the tricuspid annulus, including the isthmus. Double potentials or fractionated electrograms were analyzed retrospectively. The activation maps were edited manually for valid annotation of the reference electrogram (particularly when mapping close to the AV annulus) and for stability criteria and activation timing of the acquired atrial electrograms. Reannotation of the acquired atrial electrograms was done in the best possible manner using both bipolar and unipolar electrograms. The definitive biatrial map was displayed as a solid isochronal activation and propagation map, for a global understanding of the propagation of the activation wave front, with reference to the labeled anatomic structures.

Biatrial activation was described using a new anatomically correct nomenclature proposed recently by Cosio et al.\textsuperscript{13} In short, propagation of the flutter wave front along the AV anuli was described along superior, inferior, septal, and anterior (tricuspid/posterior (mitral) atrial walls (Figure 2A). Right and left sides of the atrial septum were mapped separately and described as such. Regional conduction times and velocities were determined.
trans-septal puncture site), or inferior septal region, respectively, in relation to Bachmann’s bundle, the fossa ovalis, and the CS ostium. The mean duration of LA activation was 165\pm67 ms (range, 87 to 287; median 156.5), occupying only 50\pm16% of the total flutter cycle length.

In every patient with CCW-AFL, the LA activation was initiated adjacent to the CS ostium in the inferior atrial septum. Three patients had an additional superior septal breakthrough in relation to Bachmann’s bundle. Globally, after a single inferior septal breakthrough, the activation wave front propagated over the LA in two directions: one along the inferior wall in a septal-to-posterior direction (0.7\pm0.3 m/s) and then speeding inferosuperiorly up the posterior wall (1.1\pm0.6 m/s) and the second up the septum and then along the superior LA in a septal-to-posterior direction (0.7\pm0.2 m/s). In the 3 patients who had an additional superior septal breakthrough, the overall LA activation was similar, except that the superior LA was activated via the second breakthrough in a septal to posterior direction. The two wave fronts then collided posterosuperiorly. Exceptionally, in one case, the activation wave front propagating along the inferior and then the posterior LA wall continued to propagate addition-
ally in a posterior-to-septal direction along superior LA and collided with the ascending septal wave front in the superior septal region. In sum, the major LA mass was activated always in a inferosuperior direction (Figures 2B, 3, and 4A).

Additional spread of activation was similar by two wave fronts. Both the inferior (1.1\pm0.1 m/s) and the superior (0.8 m/s) LA were activated in a septal-to-posterior direction, whereas the posterior wall activation was either superoinferior (n=2, 1.1 m/s) or inferosuperior (n=1, 2.1 m/s). The two wave fronts collided at different LA sites: posterosecond, postero inferior, or at two sites along the superior mitral annulus. (Figures 2C and 5)

**Discussion**

**RA Circuit of Isthmus-Dependent AFL**

A global biatrial map of isthmus-dependent AFL was constructed in 10 patients. The mean AFL cycle length was slow, 291\pm48 ms, because of the use of class Ic or III antiarrhythmic drug therapy. The macro-reentrant flutter circuit could be mapped almost completely and was located entirely in the RA. The endocardial activation sequence showed that the flutter pathway, irrespective of the rotation, was peritricuspid and bordered anteriorly by the tricuspid annulus. The more frequent occurrence of CCW-AFL (7 of 10 patients), compared with CW-AFL, has also been noted in other ablation studies. During both rotations of AFL, slow RAI conduction (0.5\pm0.2 m/s) supports the macro-reentrant circuit. Anatomically, the crista terminalis is a thick muscular ridge, which begins at the superior part of the atrial septal surface, passes anterior to the orifice of the SVC, and skirts the anterior RA wall to reach the septal side of the IVC orifice. It terminates as Eustachian ridge or valve. Our findings of faster conduction along the superior (1.5\pm0.8 m/s) and the anterior (1.2\pm0.6 m/s) RA wall and posterior RA wall activation, in 6
of 7 patients, by the flutter wave front after it has turned around the septal end of the Eustachian ridge or by the activation wave front, which travels posterior to SVC, support previous work, proposing an anchor role of the crista terminalis. The crista terminalis seems to form a posterior boundary of the flutter circuit, conduction being fast longitudinally and not transversely. In 1 patient, the posterior RA wall activation was seen after a breakthrough high along the crista terminalis. The heterogeneity of posterior RA wall activation observed in this study, inferosuperior, superoinferior, or in an anterior-to-septal direction, is in accordance with the observations of Shah et al but contradictory to a uniform superoinferior activation reported recently by Friedman et al. Also, the activation of posterior RA wall in patients with CW-AFL was not uniformly inferosuperior, as observed in this last mentioned study. We did not map specifically for double potentials in the posterior septal (sinus venosa) region. In the absence of entrainment studies, we could not be certain which of the two wave fronts propagating on either side of the SVC was part of the reentry circuit.

Role of Interatrial Connections
The sites of initial LA activation were recorded as discrete septal breakthroughs. They corresponded with the locations of the interatrial connections—Bachmann’s bundle, fossa ovalis, and the inferior CS-LA connection—that have been identified in the past, anatomically or electrically. The presence of discrete left septal breakthrough, at times more than one, considered together with the fact that the activation on the right and left side of the atrial septum (paraseptal activation), as clearly illustrated in Figure 5, was not always synchronous, suggests that the two sides of the atrial septum behave electrically as separate walls. This finding could be of potential importance in understanding the interatrial dependence of different atrial arrhythmias.

The proximity of the isthmic exit to the inferior CS-LA connection may be the reason why this was the preferred route of

Figure 3. Biatrial activation map of CCW-AFL shown in Figure 2B is displayed as a propagation map (A through E). A, Anterior to septal activation of the RAI. B, Inferosuperior septal activation with LA breakthrough in the inferior septum, suggesting trans-septal activation via the inferior CS-LA connection (23 ms after the exit). C, Continuation of inferosuperior septal activation followed by activation of the posterior RA wall as the flutter wave front turns around the septal end of the Eustachian ridge or valve. As shown, the major LA activation, along the posterior LA wall, is in inferosuperior direction. D, Activation propagates in a septal-to-anterior direction along the superior RA. Posterior RA wall activation is inferosuperior. E, Superoinferior activation of the anterior RA wall. The two wave fronts activating the LA, one along the septum and the other along the posterior wall, collide at the posterosuperior LA wall.
LA Activation in Isthmus-Dependent AFL

This is the first report in humans studying LA activation during isthmus-dependent AFL using high-resolution mapping. Activation was propagated by two wave fronts, along the inferior and superior LA wall, finally colliding with each other at posterosuperior LA. LA activation lasted 165±67 ms (87 to 287, median 156.5), occupying only 50% of the flutter cycle length. The lack of a circular activation pattern and a total LA activation time far shorter than the flutter cycle length confirm the bystander nature of LA activation. However, the high SD (67 ms) reflects a large interpatient variability in total LA activation time. This finding suggests that the LA contribution to electrocardiographic configuration of the flutter wave may not be the same in all patients.

In patients with CCW-AFL, experimental models,5,9 vectorcardiography,22 and CS activation sequence (proximal to distal)5,7,23 have long since suggested an inferosuperior activation of the major LA mass. In all of our patients with CCW-AFL, the inferior LA was activated in a septal-to-posterior direction and the posterior LA in an inferosuperior direction, thus confirming the indirect impression from previous studies. Faster conduction along the posterior wall ensured an inferosuperior LA activation. Synchronous inferosuperior septal RA and posterior LA activation can explain the negative polarity of the flutter wave in inferior leads.

In an experimental model of CW-AFL,4 LA activation was observed to be superoinferior. This has not been confirmed in a clinical setting. In fact, different sequences of CS activation have been reported by different authors.5,7,23 In this study, the overall LA activation in 3 patients with CW-AFL was superoinferior in 2 and inferosuperior in 1 patient. This variation in LA activation can be explained on the basis of differences in trans-septal conduction. However, the small number of patients with CW-AFL does not allow us to comment on typical pattern of LA activation. Therefore, the role of biatrial activation in determining the electrocardiographic morphology CW-AFL could not be clarified.

Conclusions

Our study demonstrates that the circuit of CCW and CW isthmus-dependent AFL is around the tricuspid annulus and entirely in the RA. The propagation was slowest through the RAl and faster along the crista terminals. LA activation occurred as a bystander after trans-septal conduction across the inferior CS-LA connection, Bachmann’s bundle, and/or the fossa ovalis.

References


Figure 5. Bilateral activation map of CW-AFL shown in Figure 2C is displayed as a propagation map (A through E). A, After exit from the anteroinferior RA, the flutter wave propagates up the anterior RA wall. The superior RA is activated in an anterior-to-septal direction. B, From the superior septal region, additional RA activation is observed in the LA at the corresponding level. B1 occurs 178 ms after the exit of the FW from the RAI. D, When the activation wave front reaches the CS ostium, another breakthrough is observed in the inferior LA septum (B2). B1 and B2 suggest trans-septal conduction through the fossa ovaris and the inferior CS-LA connection. Clearly, the right and left paraseptal activation is not synchronous. The RAI is activated in a septal-to-anterior direction. E, Slow conduction is present in the RAI. Major LA activation, along the posterior LA wall, is inferosuperior.
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Circulation. 2001;104:2545-2550
doi: 10.1161/hc4601.097996
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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