Use of Electroanatomic Mapping to Delineate Transseptal Atrial Conduction in Humans

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Background—Interaction between wave fronts in the right and left atrium may be important for maintenance of atrial fibrillation, but little is known about electrophysiological properties and preferential routes of transseptal conduction.

Methods and Results—Eighteen patients (age 44±12 years) without structural heart disease underwent right atrial electroanatomic mapping during pacing from the distal coronary sinus (CS) or the posterior left atrium. During distal CS pacing, 9 patients demonstrated a single transseptal breakthrough near the CS os, 1 patient in the high right atrium near the presumed insertion of Bachmann’s bundle and 1 patient near the fossa ovalis. The mean activation time from stimulus to CS os was 48±15 ms compared with 86±15 ms to Bachmann’s bundle insertion (P<0.01) and 59±23 ms to the fossa ovalis (P=NS and P<0.01, respectively). During left atrial pacing, the earliest right atrial activation was near Bachmann’s bundle in 5 and near the fossa ovalis in 4 patients. The activation time from stimulus to CS os was 70±15 ms compared with 47±16 ms to Bachmann’s bundle (P<0.01) and 59±25 ms to the fossa ovalis (P=NS). Whereas the total septal activation time was not significantly different during CS pacing compared with left atrial pacing (41±16 versus 33±17 ms), the total right atrial activation time was longer during CS pacing (117±49 versus 79±15 ms; P<0.05).

Conclusions—Three distinct sites of early right atrial activation may be demonstrated during left atrial pacing. These sites are in accord with anatomic muscle bundles and may have relevance for maintenance of atrial flutter or fibrillation. (Circulation. 1999;100:1791-1797.)

Key Words: atrium • conduction • mapping • arrhythmia

Anatomic examination of human and animal hearts suggests that atrial muscle bundles, such as Bachmann’s bundle,1,2 the rim of the fossa ovalis,3,4 and the coronary sinus (CS),5 form connections between the right and left atria. However, the actual sites of impulse propagation from the right to the left atrium and vice versa have not been studied in humans.

A better understanding of location and electrophysiological properties of interatrial connections may have clinical implications. It has been suggested that wavelet-to-wavelet interactions are required to sustain atrial fibrillation6 and that reduction of the degree of interaction by either surgical7 or catheter-based atrial compartmentalization8 may prevent sustained atrial fibrillation. Furthermore, either single-3 or dual-site10 atrial pacing has been proposed to prevent atrial fibrillation, and pacing at the sites of transseptal connection might further optimize such a modality.

In recent studies,11,12 a method for catheter-based electroanatomic mapping has been described that combines electrophysiological information, such as the sequence of cardiac activation, with a 3D image of the cardiac chamber. The aim of the present study was to define sites of earliest right atrial activation during pacing from the left atrium and the distal CS with this electroanatomic mapping system.

Methods

Patients

The study was performed in 18 patients (10 women; mean age 44±12 years) undergoing electrophysiological study for various indications after written informed consent was obtained according to the protocol approved by the Committee on Human Research of the University of California San Francisco. All antiarrhythmic medication was stopped ≥5 half-lives before the electrophysiological study; no patient was taking amiodarone. None of the patients had any evidence of underlying structural heart disease as assessed by transthoracic echocardiography.

Nonfluoroscopic Mapping System

The electroanatomic mapping system (CARTO, Biosense/Johnson & Johnson) has been described recently in detail.11,12 In short, the system consists of a low-intensity magnetic field generated by a location pad under the bed of the patient, 2 catheters instrumented...
with a sensor (a 7F catheter for endocardial mapping and ablation [STAR] and a reference catheter [REF] fixed externally to the back of the patient), and a graphic computer. The magnetic sensor in the distal part of the mapping catheter provides information about the 3D position and rotation of the distal catheter segment. From the catheter tip, unipolar and bipolar signals can be recorded. The timing is related to the reference signal (in our case, either the CS or left atrial pacing signal) and allows activation times to be recorded in relation to the position of the catheter in the heart. A real-time 3D color activation map is obtained by sequential recording of several points along the endocardium. The 3D map is displayed on the computer screen together with the catheter icon, which enables catheter manipulation in relation to the obtained map.

**Atrial Pacing Protocol**

In all patients, a 7F decapolar catheter (Daig Corp) was placed in the CS. The study patients were separated into 2 groups, depending on the site of pacing: group A (distal CS, pacing electrode bipole in a 2:30- to 4-o’clock position in the 45° left anterior oblique view) and group B (left atrium, pacing electrode bipole of a quadripolar catheter in a position on the posterior wall of the left atrium approximately midway between the ostia of the left and right upper pulmonary veins). Pacing was performed at twice diastolic threshold at a cycle length between 450 and 600 ms, which exceeded the underlying sinus rate by ≥100 ms.

**Right Atrial Mapping Procedure**

To generate a 3D map that correlated with specific anatomic landmarks, 3 reference points were obtained with the mapping catheter in the right atrium by use of fluoroscopy in combination with CARTO: the superior vena cava/right atrial junction, the inferior vena cava/right atrial junction, and the CS os. Additional catheter handling and serial collection of mapping points were guided by the catheter icon in the 3D image, usually displayed in a right anterior oblique (45°) and left lateral view. Care was taken to accomplish a high density of mapping points in the area of early activation. Measurements were included in the 3D map if the stability criteria in space (4 mm) and in local activation time (4 ms) were met.

**Measurements and Definitions**

After manual correction of the activation onset of each point by both bipolar and unipolar signals and after deletion of points with unfavorable signal quality or unreliable beat-to-beat atrial capture, the final map was used for data analysis. First, the color range of the right atrial map was compressed to include 30-ms isochrones to increase the spatiotemporal resolution. More than 1 right atrial breakthrough was considered present if (1) distinct early sites were activated within 15 ms and (2) an area spatially located between each early site was observed that was activated later than any early site. Subsequently, additional parameters were calculated for every right atrial endocardial map during CS or left atrial pacing: (1) the activation time from the pacing site to the point with the earliest activation in the region of the CS os; (2) the activation time from the pacing site to the point with the earliest activation on the high anterior right atrium, at the presumed insertion of Bachmann’s bundle; (3) the difference in activation times between CS os and Bachmann’s bundle; (4) the distance between early activation sites near the CS os and Bachmann’s bundle; (5) the activation time from the pacing site to the fossa ovalis in patients in whom the fossa was identified by intracardiac echocardiography or by the site of the transseptal sheath; (6) the total septal activation time, defined as the time from earliest septal activation during distal CS or posterior left atrial pacing to the latest activation of either of the surrogate sites of Bachmann’s bundle, fossa ovalis, or CS os; and (7) the total right atrial activation time, defined as the time from earliest septal activation to the latest right atrial activation, as well as the site of the latest right atrial activation.

**Intracardiac Echocardiography**

In 4 patients, a 9F, 9-MHz intracardiac ultrasound probe (Boston Scientific) was advanced into the right atrium via a 10F sheath in the left femoral vein. Right atrial anatomic structures including the crista terminalis, CS os, and fossa ovalis were identified. The fossa ovalis was marked as a point location on the right atrial activation map by echocardiographic visualization of the STAR mapping catheter while it was tenting the fossa ovalis. Furthermore, sites of earliest right atrial activation during pacing were visualized by intracardiac echocardiography.

**Statistical Analysis**

Values are expressed as mean±SD. Intergroup comparisons were performed by 1-way ANOVA for continuous variables followed by a Scheffé test if the ANOVA test was significant or Student t test, paired or unpaired as appropriate. A value of $P<0.05$ was considered statistically significant.

**Results**

**General Considerations**

Right atrial mapping by use of the CARTO system was performed in 9 patients during pacing from the distal CS, in 7 patients during pacing from the posterior wall of the left atrium, and in 2 patients during both distal CS and left atrial pacing. For all 20 right atrial maps (mean number of mapping points 94±33), the mean local activation time from the pacing site to the CS os, which was found to be activated earliest in 9 activation maps, was 58±19 ms. The mean activation time to the insertion of Bachmann’s bundle, which was found to be activated earliest in 6 activation maps, was 68±25 ms ($P=NS$). The mean distance between these points was 45±7 mm. The mean activation time from the pacing site to the fossa ovalis, which was found to be activated earliest in 5 activation maps, was 59±24 ms ($P=NS$). The total septal activation time for all acquired maps was 37±17 ms, and the total right atrial activation time was 100±41 ms.

**Transseptal Activation During Distal Coronary Sinus Pacing**

Right atrial mapping during CS pacing revealed a single transseptal breakthrough near the CS os in 9 of 11 patients (Table; Figure 1). One patient demonstrated a single breakthrough in the high right atrium near the area of the presumed insertion of Bachmann’s bundle, and 1 patient demonstrated a breakthrough near the fossa ovalis. The mean activation time from the distal CS stimulus to the CS os was 48±15 ms compared with 86±15 ms to the insertion site of Bachmann’s bundle ($P<0.01$) and 59±23 ms to the fossa ovalis ($P<0.01$ compared with the insertion of Bachmann’s bundle, $P=NS$ compared with the CS os). The total septal activation time for all acquired maps during distal coronary sinus pacing was 41±16 ms, and the total right atrial activation time was 117±49 ms. The site of the latest right atrial activation was found to be in the high lateral right atrium in 8 patients (Figure 1), in the mid lateral right atrium in 2 patients (Figure 3A), and in the low lateral right atrium in 1 patient.

**Transseptal Activation During Left Atrial Pacing**

Right atrial mapping during pacing from the posterior wall of the left atrium revealed a single transseptal breakthrough in the high right atrium near the presumed insertion of
Bachmann’s bundle in 3 patients (Table; Figure 2A). Intra-cardiac echocardiography demonstrated the site of earliest activation slightly below the junction between superior vena cava and right atrium, at the septal margin of the crista terminalis (Figure 2, B and C). Two patients demonstrated an almost simultaneous activation of high right atrium and CS os, with the high right atrium being activated slightly earlier (11 and 9 ms, respectively; Figure 3). In 2 patients, right atrial mapping revealed a single early activation near the fossa ovalis (Figure 4). One patient demonstrated an almost simultaneous activation of fossa ovalis and insertion site of Bachmann’s bundle, with the fossa being activated slightly earlier (6 ms). Finally, 1 patient demonstrated an almost simultaneous activation of fossa ovalis, CS, and Bachmann’s bundle (activation over a distance of 52 mm within 15 ms; Figure 5). The mean activation time from stimulus to CS os was 70±615 ms compared with 47±616 ms to the insertion site of Bachmann’s bundle (P<0.01) and 59±25 ms to the fossa ovalis (P=NS).

In the 2 patients in whom mapping was performed during both CS and posterior left atrial pacing, the earliest right atrial activation during CS pacing occurred in the region of the CS os, whereas during posterior left atrial pacing, the earliest activation occurred near the fossa ovalis or the insertion of Bachmann’s bundle, respectively.

The total septal activation time for all acquired maps during posterior left atrial pacing was 33±17 ms, which was not significantly different than in the maps acquired during distal CS pacing. However, total right atrial activation time during posterior left atrial pacing was 79±15 ms, which was significantly shorter than for the maps acquired during distal CS pacing (117±49 ms; P<0.05). The site of the latest right atrial activation was found to be in the low lateral right atrium in 7 patients (Figure 3B), in the mid lateral right atrium in 1 patient, and in the high lateral right atrium in 1 patient.

### Discussion

**Main Findings**

In this study, we performed right atrial activation mapping during pacing from the distal CS or the posterior wall of the left atrium to assess preferential routes of conduction from the left to the right atrium. Three sites of transseptal breakthrough (the region of the CS os, the fossa ovalis, and the high anterosetal right atrium at the putative insertion of Bachmann’s bundle) have been clearly discerned. The CS os was the earliest right atrial site to be activated in 9 of 11 patients during pacing from the distal CS. During posterior left atrial pacing, Bachmann’s bundle region was the single earliest activation site, or was activated simultaneously with the CS.
os or fossa ovalis, in 7 of 9 patients. Intracardiac ultrasound allowed visual identification of the presumed right atrial endocardial insertion site of Bachmann’s bundle to be at the medial septal margin of the crista terminalis as it crosses in front of the superior vena cava. The total septal activation time was not significantly different in patients with either distal CS or posterior left atrial pacing. However, the total right atrial activation time was significantly longer during CS pacing than during left atrial pacing.

Previous Studies
The present understanding of atrial transseptal activation is mainly based on anatomic studies of the architecture of atrial musculature in humans\(^2\) and on studies of cellular conduction properties in experimental settings.\(^3,4\) Circumferential and longitudinal muscle bundles have been demonstrated to provide preferential pathways for impulse propagation\(^2\) but were not considered to be part of a specialized conduction system.\(^4\)

The interatrial band, a circumferential muscle bundle that is located at the anterior wall of the left atrium, was proposed by Bachmann\(^1,2\) as the primary pathway for conduction from the right to the left atrium. A secondary pathway for impulse propagation has been thought to reside along the rim of the fossa ovalis.\(^3,4\) Recent anatomic and electrophysiological findings in dogs\(^5\) suggest that the media of the CS form another electrical connection between the right and left atria. Our findings support both human and animal data showing that the CS is a preferential pathway for left-to-right atrial conduction primarily during CS pacing. However, the putative insertion site of Bachmann’s bundle and the fossa ovalis are the preferential pathways for conduction during left atrial pacing. All the studied patients demonstrated ≥1 of the 3 preferred pathways suggested by prior anatomic studies.\(^1,2,5\)

Clinical Implications
Attempts to control atrial fibrillation by nonpharmacological means such as pacing\(^10\) and ablation\(^8\) formed the impetus of the present study. Mapping studies in both animals\(^14\) and
humans\textsuperscript{15} have found that endocardial activation is far more disorganized in the left atrium than in the right atrium. Thus, it may be hypothesized that in some patients, a left atrial circuit is primarily responsible for perpetuation of atrial fibrillation, whereas the right atrium is activated more passively\textsuperscript{16} or behaves as an innocent bystander. Limited radiofrequency applications in the area of Bachmann’s bundle or the mid septum\textsuperscript{17} have been found to successfully terminate atrial fibrillation in animals. One reason may be that interruption of a preferential electrical connection between the left and right atria reduced the degree of wavelet-to-wavelet interaction critical for sustenance of atrial fibrillation.\textsuperscript{6} Likewise, Cox et al\textsuperscript{7} emphasized the importance of cryoablation around the CS for the success of the Maze procedure as a surgical therapy for atrial fibrillation, which may be due to the role of the CS as a connection between right and left atria.

Dual-site pacing from the high right atrium and CS os has recently been found to be effective in some patients with drug-refractory atrial fibrillation, possibly owing to a reduction in interatrial conduction delay and synchronization of left and right atrial activation.\textsuperscript{10,18,19} Pacing from the CS os may be effective in patients in whom the CS os is a preferential site of transseptal conduction,\textsuperscript{10} whereas a failure to respond may imply that the preferential transseptal connection is at a different site. In the present study, the total right atrial activation time was significantly shorter during posterior left atrial pacing with a preferential right atrial breakthrough at the insertion of Bachmann’s bundle than during distal CS pacing with a preferential breakthrough at the CS os. If the reverse is true for conduction from the right to the left atrium, multisite pacing including Bachmann’s bundle may cause a further reduction in interatrial conduction delay, but additional studies are required to test this hypothesis.

Finally, despite a high success rate for a catheter-based cure of typical atrial flutter,\textsuperscript{20} some atypical forms of atrial flutter are still poorly understood.\textsuperscript{21} Multiple disparate con-
atrial activation times in a limited number of patients, closer to the septum. Owing to the considerable variability in pacing from different sites in the left atrium, especially sites conceivably, different activation patterns may be found during posterior wall and only in 2 patients from both sites. Con-

has been performed only from the distal CS and the left atrial pattern of right-to-left atrial activation. Furthermore, pacing conduction routes do not necessarily translate into a similar only in the right atrium. Therefore, the preferential transseptal or faster heart rates. Activation mapping has been performed

ations between the right and left atria may allow for the substrate for biatrial flutter, entering the left atrium from the CS, travelling around the pulmonary veins to Bachmann's bundle, reentering the right atrium over this bundle, and travelling down the right atrial septum to link again with the CS, as suggested by Olgin et al.22

Study Limitations

Because the present study was performed with patients with normal hearts at slow rates, our findings cannot be extrapo-
lated to patients with structural heart disease, enlarged atria, or faster heart rates. Activation mapping has been performed only in the right atrium. Therefore, the preferential transseptal conduction routes do not necessarily translate into a similar pattern of right-to-left atrial activation. Furthermore, pacing has been performed only from the distal CS and the left atrial posterior wall and only in 2 patients from both sites. Conceivably, different activation patterns may be found during pacing from different sites in the left atrium, especially sites closer to the septum. Owing to the considerable variability in atrial activation times in a limited number of patients,

individual isochrone densities were used to display the primary interatrial pathways. Therefore, the discreteness of interatrial coupling was not evaluated, although it may have important clinical implications.

Conclusions

Right atrial activation mapping during left atrial and distal CS pacing demonstrated preferential sites of transseptal conduction in patients without structural heart disease. The earliest right atrial activation is found near the CS os, the insertion of Bachmann’s bundle, and the fossa ovalis. These findings confirm prior anatomic studies suggesting that the activation spreads along circumferential or longitudinal muscle bundles and may have major implications for a catheter-based cure of atrial fibrillation and some forms of atypical atrial flutter or for alternative pacing sites for prevention of atrial fibrillation.

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