Interatrial conduction can be accurately determined using standard 12-lead electrocardiography: validation of P-wave morphology using electroanatomic mapping in man.

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- Validation of P wave morphology using electroanatomical mapping in human

Holmqvist et al. "Comparison between ECG and electroanatomical mapping"

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Abstract

Background: It has been postulated that different P wave morphologies during sinus rhythm, as displayed on standard ECGs, correspond to differences in interatrial conduction.

Objective: The objective of the present study was to evaluate this hypothesis by comparing P wave morphologies with left atrial activation maps.

Methods: Twenty-eight patients (mean age 49 ± 9 years) admitted for ablation of paroxysmal atrial fibrillation were studied. Electroanatomical mapping of left atrial activation was performed at baseline during sinus rhythm simultaneously with standard 12-lead ECG. Unfiltered signal-averaged P waves were analyzed to orthogonal determine P wave morphology. The morphology was subsequently classified into one of three predefined types. All analyses were blinded.

Results: The fossa ovalis (FO) was the primary left atrial breakthrough site in 8 patients, Bachmann's bundle (BB) in 18, and the coronary sinus (CS) in two. Type 1 P wave morphology was observed in 9 patients, Type 2 in 17 patients and Type 3 in 2 patients. Seven of 8 patients with FO breakthrough were found to have Type 1 P wave morphology, whereas 16 of 18 patients with BB breakthrough exhibited Type 2 morphology, and both cases with CS breakthrough showed Type 3 P wave morphology. Overall, the P wave morphology criteria correctly identified the site of left atrial breakthrough in 25 of the 28 patients (89%).

Conclusions: The P wave morphology derived from a standard 12-lead ECG correctly identified left atrial breakthrough site and the corresponding route of interatrial conduction in the vast majority of the patients studied.

Keywords: computers; conduction; mapping; electrocardiography; atrium

Introduction

Interatrial conduction defects are increasingly being considered a vital contribution to supraventricular arrhythmogenesis. However, knowledge about normal interatrial conduction during sinus rhythm in the intact human heart is based on a few reports on patients with clinical arrhythmia, using various invasive techniques.[1-5] The results are to a certain degree conflicting, with the proportion of patients showing activation of the left atrium via Bachmann's bundle being lower in some reports[1, 5] than in others.[2-4] Nevertheless, based on the data available, it seems reasonable to conclude that Bachmann's bundle is the most common interatrial conductive route, although other routes, located posteriorly[6, 7] and inferiorly,[8-10] also participate in interatrial conduction in most patients.

Impairment of the interatrial conduction can be observed on a standard 12-lead ECG as prolongation of the P wave.[11, 12] This is primarily thought to be mediated by a delay in the conduction over Bachmann's bundle.[13] Advanced interatrial block, which has been shown to be caused by complete blockage of Bachmann's bundle,[14] is seen as a prolonged, biphasic P wave in the inferior leads.[15, 16] Interatrial block of any degree has been shown to be associated with a high propensity for atrial arrhythmia, including atrial fibrillation.[14, 17, 18] However, the risk of developing atrial arrhythmia is substantially higher in cases of advanced interatrial block.[18] With the exception of these rather crude indices of impaired interatrial conduction, it has not until now been possible to extract any further information regarding interatrial conduction from the standard 12-lead ECG.

Analysis of unfiltered, signal-averaged P waves has been shown in several publications to reveal differences other than those in P wave duration between patient groups.[19-21] It was recently suggested that the three different P wave morphology classes that have been identified (Figure 1),[19-21] arise from differences in interatrial conduction.[20] If confirmed, this

may vastly improve clinical diagnostic abilities in the case of atrial arrhythmia. The differences between the observed P wave morphology classes are primarily seen in the terminal portion of the P wave, and are therefore likely to reflect foremost differences in left atrial activation.[22] To test this hypothesis, the present study was performed to investigate the relationship between detailed descriptions of interatrial conduction derived from unfiltered, signal-averaged P waves and simultaneously obtained invasive electroanatomical maps.

Methods

Patient population

Patients referred for catheter ablation of atrial fibrillation at two tertiary care centers were studied. The indications for catheter ablation were diagnosis of paroxysmal or persistent atrial fibrillation with invalidating symptoms, structurally normal heart, failure of more than two antiarrhythmic drugs in the treatment of atrial fibrillation, and an age below 70 years. Only patients with sinus rhythm at the time of electroanatomical mapping were included. The study was approved by the local ethics committees and complied with the Declaration of Helsinki. All subjects gave informed consent to participation.

Data acquisition and analysis

The electroanatomic mapping was performed with CARTO system (Biosense Webster, Diamond Bar, CA, USA), using either a 7F Navistar or ThermoCool catheter (Biosense Webster, Diamond Bar, CA, USA). A decapolar 6F diagnostic catheter was placed in the CS for time reference. The electrophysiological study was performed using standard techniques with CardioLab system (Prucka Engineering, GE Healthcare, WI, USA) or Bard LabSystem DUO (Bard Electrophysiology, Billerica, MA, USA).

Three-dimensional isochronal activation maps were generated in sinus rhythm, gated to a stable Coronary sinus reference signal. All the points and the respective ECG and intracardiac recordings in the maps were visually inspected, and the activation time was corrected manually when needed. The local activation time was defined as the maximum/minimum of the first sharp deflection of the bipolar signal at the distal electrode pair of the catheter. P wave morphology was examined in order to ensure sinus origin. If the beat was of non-sinus origin, the intracardiac signal was less than 0.1 mV in amplitude, or signs of artifacts or catheter instability were seen, the respective point was rejected. If more than one P wave morphology was seen, the predominant one was chosen. Not only had the three main areas of interatrial routes be represented in the maps, but also the points had to be evenly scattered in the LA. When double potentials were found, the first potential was used except for cases when the first potential could be clearly defined as low frequency far field. All intracardiac ECG data was gathered before starting the ablation procedure. The site of earliest activation was recorded. The activation routes were classified as Bachmann's bundle, Fossa ovalis or Coronary sinus (examples illustrated in Figure 2, left column). If separate early sites were seen during the first 15 ms of the LA activation, two activation routes were considered to be present.[23] This classification was done independently in both the centers, and ambiguous maps were crosschecked in each center, and the final classification was achieved by consensus.

Standard 12-lead ECG data, of at least 10 seconds duration[24] were recorded using a Prucka CardioLab EP system (GE Healthcare) or a Bard LabSystem DUO (Bard Electrophysiology, Billerica, MA, USA). To enable the analysis of orthogonal P wave morphology, orthogonal-lead ECG data were derived from the 12-lead ECG using the inverse Dower transform.[25, 26] Unfiltered, signal-averaged P waves were analyzed to determine P wave morphology.[19, 20, 24, 25] Following high-pass (0.5 Hz) and bandstop (50 Hz) filtering the QRS complexes were

automatically identified and grouped according to similarity (a cross-correlation coefficient, $\rho > 0.9$). P waves were extracted using 250 ms wide signal windows preceding each QRS complex. The signal windows were then shifted in time to estimate the maximal correlation in each lead. P waves with a cross-correlation coefficient of $\rho > 0.9$ (analyzed separately in all leads) were grouped together and averaged. The actual P waves were defined by manual setting of the onset and end. The method used is described in detail elsewhere.[19, 20, 25] The morphology was subsequently classified into one of three predefined classes (Type 1: positive Leads X and Y and negative Lead Z; Type 2: positive Leads X and Y and biphasic Lead Z (-/+); and Type 3: positive Lead X and biphasic signals in Leads Y (+/-) and Z (-/+)).[20] The three different types are schematically illustrated in Figure 1. All analyses were carried out in a blinded fashion. Standard transthoracic echocardiography was performed in association with ablation.

Statistics

Data are expressed as the mean ± standard deviation. Kendall's tau-b was used to evaluate the relationship between P wave morphology and the electroanatomical maps. All tests were two-sided and $P < 0.05$ was considered statistically significant. All statistical analyses were performed using STATISTICA for Windows, version 6.1 (StatSoft, Inc., Tulsa, OK, USA).

Results

Twenty-eight patients (age 49±9 years, 23 men (83%)) were studied. All patients suffered from either paroxysmal (86%) or persistent (14%) atrial fibrillation. The majority of the patients (n=23, 82%) were taking one or more antiarrhythmic agents. Baseline echocardiographic parameters revealed a left atrial diameter of 41±6 mm and a left ventricular

ejection fraction of 62±7 %. A detailed description of the patient characteristics is given in Table 1.

The average time between P wave onset and earliest left atrial activation was 46±17 ms. Sixteen patients (57%) exhibited a single left atrial breakthrough, with Bachmann's bundle being the most common site (13/16). A single fossa ovalis breakthrough was noted on one occasion and coronary sinus breakthrough on two. The remaining twelve patients exhibited two simultaneous breakthrough sites. All but one of these included Bachmann's bundle (six Bachmann's bundle and fossa ovalis combined, five Bachmann's bundle and coronary sinus). Twenty-four of the patients (86%) exhibited some interatrial conduction via Bachmann's bundle, eight (29%) via the fossa ovalis and eight (29%) via the coronary sinus.

The average P wave duration, estimated using unfiltered, signal-averaged P wave analysis was 148±17 ms. The average heart rate during the investigation was 63±10 beats per minute. Nine patients (32%) were found to have Type 1 P wave morphology, whereas Type 2 morphology was found in 17 patients (61%), and Type 3 in two (7%).

Seven of the eight patients (88%) with conduction via the fossa ovalis (regardless of other simultaneous interatrial conduction sites) exhibited Type 1 P wave morphology. Sixteen of the 18 patients (89%) with interatrial conduction via Bachmann's bundle (with or without simultaneous conduction via the coronary sinus) exhibited Type 2 P wave morphology. Both patients with single pathway interatrial conduction via the coronary sinus exhibited Type 3 P wave morphology (Kendall's tau-b = 0.8082, $P < 0.0001$, overall percentage agreement in categories, 89.3%). The relationship between primary breakthrough site and P wave morphology is presented in Table 2. Typical examples of the relationship between left atrial breakthrough site and P wave morphology obtained via unfiltered, signal-averaged P wave analysis are shown in Figure 2.

Discussion

The present study demonstrates, for the first time, a robust agreement between the P wave morphology obtained from a standard 12-lead ECG and left atrial breakthrough site determined using invasive mapping. This implies that accurate information regarding interatrial activation can be routinely obtained in everyday clinical practice.

Findings in relation to previous studies

The finding in the present study that Bachmann's bundle is the most common interatrial route, alone or in combination with other routes, is well in line with the findings of previous studies.[1-5] However, the non-negligible proportion of the study population without detectable Bachmann's bundle conduction, or conduction via other routes in conjunction with Bachmann's bundle, illustrates that other routes (i.e. the fossa ovalis and coronary sinus) are important in a substantial proportion of the patients, again in line with previous studies.[1, 5, 10]

The analysis of unfiltered, signal-averaged P waves has previously been shown to provide more detailed information on atrial electrophysiology than the analysis of P wave duration alone.[21, 24] The method has been shown to be robust, even when short-duration recordings are analysed.[24] The distribution of P wave morphologies found/reported in the present study is in agreement with the findings of previous studies using the same method in comparable patient groups.[20, 21] The distribution of P wave morphology has been shown to shift towards Type 2 (and 3) with advancing age[19] and increased susceptibility for[20] or increased prevalence[21] of atrial fibrillation. Thus, the high prevalence of Type 2 P wave morphology in the present study is expected. The exact prevalence of advanced interatrial block[16, 27] (Bachmann's bundle; Type 3 P wave morphology) has, to the best of our knowledge, not been reported, but

since it has been shown to be associated with a high risk of atrial arrhythmia including atrial fibrillation,[18] the two cases found in the present study were not unexpected.

The P wave morphology and its possible invasive correlate

The sequential activation of the atrial chambers and its relative contribution to the genesis of the P wave (Lead II, standard 12-lead ECG) was recently reported.[22] In that study, it was reported that the mid-third of the P wave represented equal contributions from the right and left atria, while the initial and terminal thirds foremost represented the right atrium and left atrium, respectively.

Based on the findings in a group of patients with hypertrophic cardiomyopathy, it was recently proposed [20] that since Type 1 morphology must be generated by a right-to-left (positive Lead X), superior-to-inferior (positive Lead Y) and posterior-to-anterior activation pattern (negative Lead Z), and the sinus node located posteriorly, superiorly in the right atrium,[28] the observed vector (i.e., predominantly negative Lead Z) was most likely to be generated by activation of the left atrium with participation of connections located posteriorly (i.e., the fossa ovalis).[9, 10, 29] Although concomitant conduction via Bachmann's bundle could not be excluded, it was considered unlikely that the main activation sequence of the left atrium (posterior-to-anterior) would be the result of conduction exclusively via Bachmann's bundle. Consequently, Type 2 morphology is generated by a right-to-left, superior-to-inferior and posterior-to-anterior-to-posterior activation pattern (biphasic Lead Z). This means that the activation wave front is probably spread to the left atrium via connections located anteriorly and superiorly, i.e., the Bachmann's bundle area, without noticeable contributions from posterior or inferior connections (coronary sinus).

As mentioned previously, biphasic P waves in the inferior leads have been shown to be indicative of a block in Bachmann's bundle.[14, 16, 27] It was noted that the presence of a

biphasic signal in Lead Y (Type 3) was always accompanied by a biphasic Lead Z (as illustrated in Figures 1 and 2), hence the activation direction in Type 3 morphology was not only characterized by the superior-to-inferior-to-superior route, but also posterior-to-anterior-to-posterior propagation, indicating not only a Bachmann's bundle block, but also a block or delayed conduction in the posterior route. In other words, it was hypothesized that Type 1 morphology corresponds to conduction via the fossa ovalis with or without simultaneous conduction via other routes; that Type 2 morphology corresponded to Bachmann's bundle conduction with or without simultaneous conduction via the coronary sinus, and finally, that Type 3 morphology was the result of conduction via the coronary sinus without any other noticeable interatrial conduction.

Direct comparison of surface ECG with electroanatomical mapping

The agreement between the three categories when comparing the P wave morphology with the atrial activation map in each patient was high in the present study (89%, or 25 of 28 patients), demonstrating that the left atrial breakthrough site was correctly identified in about 9 out of 10 patients. The three patients in whom there was a discrepancy between the two methods (one patient with Type 2 morphology with conduction via the fossa ovalis, and two patients with Type 1 morphology without conduction via the fossa ovalis) may represent patients with several atrial activation patterns and consequently several P wave morphologies, where the ECG data did not correspond in time with the activation map. Overall, the positive findings are strongly supportive of the suggested hypothesis, and imply that unfiltered, signal-averaged P wave analysis can be used as a non-invasive tool for assessing interatrial conduction.

Clinical implications

The findings of the present study may affect clinical practice in more ways than one. Firstly, it offers a simple, non-invasive method of determining interatrial conduction, which is likely to reflect the propensity for atrial arrhythmia[14, 17, 18] in large patient cohorts. It is also likely to offer a means of optimizing the choice of septal pacing site in order to resynchronize the atria when pacemaker therapy is chosen for treatment of patients with severe paroxysmal atrial fibrillation.[30]

Limitations of the study

For ethical reasons the invasive atrial activation maps were only recorded in patients with a clinical indication thereof. Therefore, patients without a history of atrial fibrillation were not included. However, it is reasonable to assume that the agreement between the methods is comparable in other patient cohorts. ECG data were recorded throughout the invasive procedure, but the segments analyzed using unfiltered, signal-averaged P wave analysis, represent only part of this data. Therefore, there may be a discrepancy between the two methods in patients with multiple atrial activation patterns. However, if this were the case, the true agreement between the two methods would have been even higher than that reported here.

Conclusions

For the first time, detailed description of orthogonal P wave morphology is evaluated in detail, using electroanatomical mapping of atrial activation during sinus rhythm. The results indicate that, in the vast majority of the patients, P wave morphology derived from a standard 12-lead ECG may be used to correctly identify the type of interatrial block, left atrial breakthrough site, and the corresponding route of interatrial conduction.

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Tables

Table 1 Patient characteristics

	Subjects (n=28)
Age (years)	49±9
Male/Female	23/5
Paroxysmal AF	24 (86%)
Persistent AF	4 (14%)
LA diameter (mm)	41±6
LVEF (%)	62±7
Cardioactive drugs	
None	5 (18%)
β-blocker	17 (65%)
Sotalol	2 (8%)
Class I	13 (46%)
Class III	4 (15%)
Digitalis	2 (8%)
Ca^{2+}- channel blocker	1 (4%)
Heart rate (bpm)	63±10
P wave duration (ms)	148±17

AF = atrial fibrillation; LA = left atrial; LVEF = left ventricular ejection fraction.

Table 2 The relationship between primary left atrial breakthrough site and P wave morphology.

	Type 1	**Type 2**	**Type 3**
Fossa ovalis	7	1	
Bachmann's bundle	2	16	
Coronary sinus			2

Shaded cells indicate the expected distribution according to the tested hypothesis.

Figure legends

Figure 1

Schematic illustration of the three P wave morphology classes. Type 1 is characterized by a right-to-left (positive Lead X), superior-to-inferior (positive Lead Y) and posterior-to-anterior activation pattern (negative Lead Z). Type 2 is also characterized by positive signals in Lead X and Y, but the biphasic signal in Lead Z indicates a more complex activation pattern (posterior-to-anterior-to-posterior). Type 3 P wave morphology also exhibits a positive signal in Lead X, and a biphasic signal in Lead Z , as does Type 2, but the signal in Lead Y reflects the retrograde activation of the left atrium[14] (superior-to-inferior-to-superior).

Figure 2

Three examples, illustrating the different left atrial breakthrough sites and their corresponding P wave morphologies. The electroanatomical maps (anteroposterior view) are shown in the left column. The different left atrial breakthrough sites are illustrated (fossa ovalis (A), Bachmann's bundle (B) and coronary sinus (C)). Various combinations of these breakthrough sites were commonly seen (see text), but are not illustrated in the Figure. The corresponding P wave morphology types (Type 1, 2 and 3) are illustrated in the right column.

Figure1

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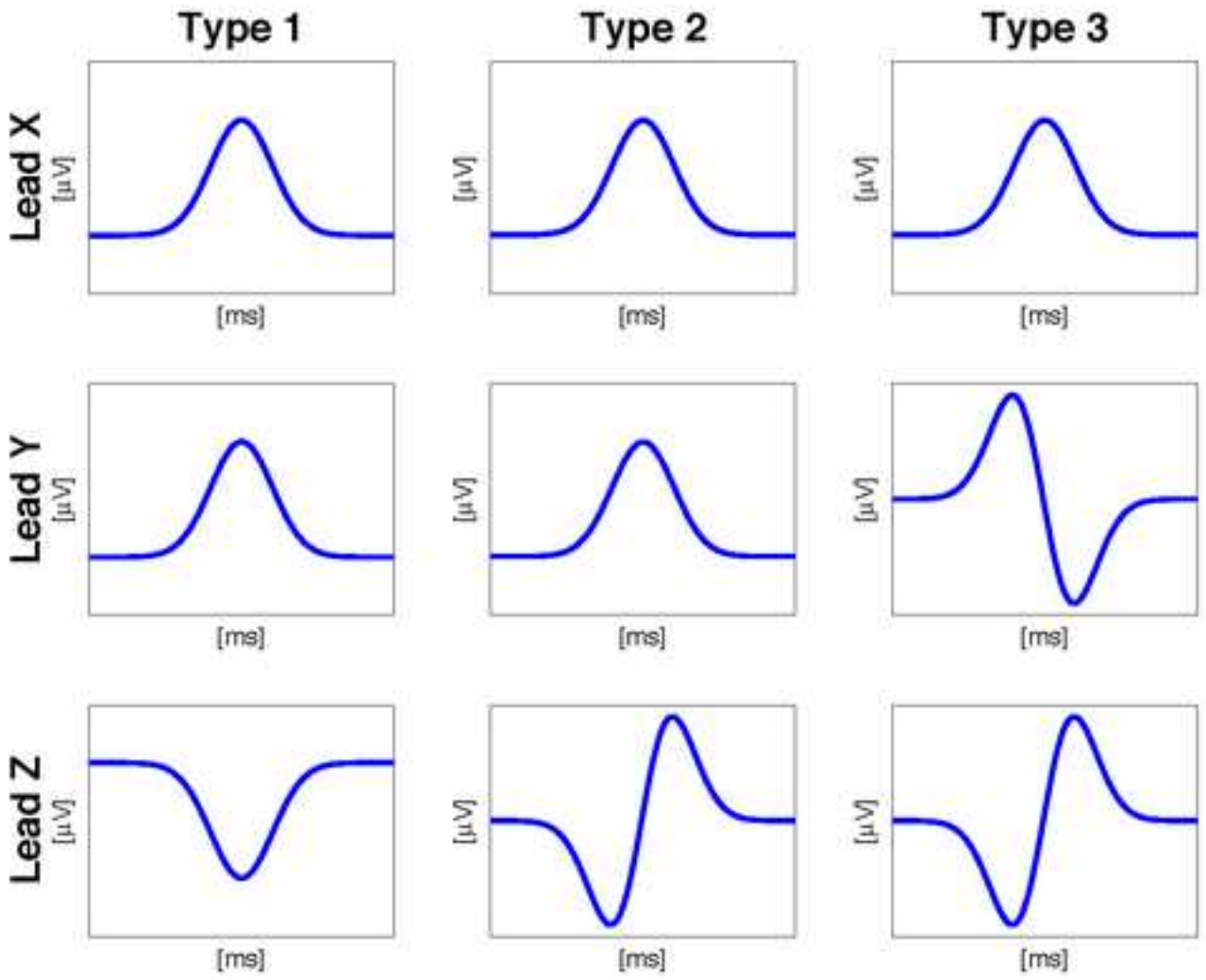

Figure2

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