Detection of Patients at Risk for Paroxysmal Atrial Fibrillation During Sinus Rhythm by P Wave–Triggered Signal-Averaged Electrocardiogram

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To determine whether patients at risk for paroxysmal atrial fibrillation could be detected while in sinus rhythm, the signal-averaged electrocardiogram triggered by P waves was recorded in 42 patients with paroxysmal atrial fibrillation (Paf group) and in 50 control patients. The root mean square voltages (LP₁₀, LP₂₀, and LP₃₀) for the last 10, 20, and 30 msec and the duration (Ad) of filtered (40–300 Hz) P wave of the spatial magnitude were measured. LP₁₀ and LP₂₀ were significantly lower in the Paf than in the control group (LP₁₀ 1.92±0.58 versus 2.49±0.78 μV, p<0.001; LP₂₀ 2.47±0.78 versus 3.46±1.20 μV, p<0.0001), although no significant difference in LP₃₀ was found between groups. Ad was also significantly longer in the Paf than in the control group (137.0±14.3 versus 118.6±11.3 msec, p<0.001). These differences between the Paf and control groups remained significant even after dividing by the presence or absence of organic heart diseases. The criteria of “LP₃₀=3.5 μV or less” and “Ad>120 msec” as defining “atrial late potential” gave a sensitivity of 91% and a specificity of 76%. These findings suggest that patients at risk for paroxysmal atrial fibrillation could be detected while in sinus rhythm by using the P wave–triggered signal-averaged electrocardiogram. (Circulation 1991;83:162–169)

The signal-averaged electrocardiogram has been increasingly recognized as a useful means in identifying patients at risk for ventricular tachycardia1–5 or sudden cardiac death6,7 after myocardial infarction. On the other hand, analysis of the P wave on the signal-averaged electrocardiogram has failed to detect patients with paroxysmal atrial fibrillation or flutter,8 probably because electrocardiography was performed with an R wave–triggered signal-averaging method that has some problems associated with analysis of atrial activity. Therefore, we recently developed a P wave–triggered signal-averaging system9 that eliminates the effects of ectopic atrial beats and overcomes a substantial problem of the variation of the PQ interval inevitably induced by the conventional R wave–triggering system during signal averaging. Using this newly developed system, we attempted to detect patients, during sinus rhythm, who are at risk for paroxysmal atrial fibrillation, which is known to be a potential risk for systemic thromboembolisms10–12.

Methods

Patients

The study population consisted of two groups of patients: 42 consecutive patients (27 men and 15 women; average age, 60.3±13.0 years; age range, 28–78 years; group 1) who had paroxysmal atrial fibrillation documented on the electrocardiogram but had not received antiarrhythmic drugs for at least 1 week before undergoing signal-averaged electrocardiography; and 50 control patients (27 men and 23 women; average age, 60.8±12.0 years; age range, 31–80 years; group 2) without paroxysmal atrial fibrillation. There were no significant differences in age and sex between the two groups. Group 1 was composed of 22 patients with organic heart diseases (group 1A: eight with mitral valvular disease, eight with ischemic heart disease, one with hypertrophic cardiomyopathy, three with hypertensive heart disease, and two with congenital heart disease) and 20 patients without organic heart diseases (group 1B).
Similarly, group 2 was composed of 14 patients with organic heart diseases (group 2A: two with mitral valvular heart disease, 10 with ischemic heart disease, one with dilated cardiomyopathy, and one with hypertensive heart disease) and 36 patients without organic heart diseases (group 2B). Also, none of the group 2 patients had received any antiarrhythmic drugs. Each patient gave informed consent to participate in the study.

Signal-Averaged Electrocardiogram Recording

In an electrically shielded room, which minimized noise, a signal-averaged electrocardiogram was recorded from a modified X, Y, and Z lead system using the VCM-3000 (Fukuda Denshi), which was recently developed for P wave signal averaging as well as for conventional R wave–triggered signal averaging. The X lead was between the right and left shoulders, meaning the standard I lead. The aVF lead was used as the Y lead. The precordial V1 lead was used as the Z lead. The total gain was 200,000, and noise was 0.6 μV, which referred to input. The signal from each lead was amplified up to 5 μV/cm and passed through a low-pass filter of 300 Hz (the slope; 12 dB/oct) and a high-pass filter of 40 Hz (the slope; 18 dB/oct), and then converted from analog to digital data to a 12-bit accuracy at the sampling rate of 1 kHz. In nine patients, 20, 30, 60, and 80 Hz, as well as 40 Hz, were used to evaluate the effect of the high-pass filter on the late potential indexes.

Signal Averaging

All digital data were stored on floppy disk. Ventricular ectopic beats and gross noise were eliminated by a conventional QRS template-matching program before proceeding to the P wave recognition program. The algorithm for the P wave–triggering system is depicted in Figure 1. A specially filtered P wave derived from the dominant P wave of the standard II lead served as a reference signal for all processing. The signals were averaged on a trigger point within a specially filtered P wave, after passing through a P wave template recognition program to eliminate ectopic atrial beats. The signals of 200 beats were usually averaged. If the noise level remained at more than 1 μV even after averaging of 200 beats, then the averaging was continued until the noise level was reduced to less than 1 μV.

In addition to the P wave–triggered signal-averaged electrocardiogram, the conventional R wave–triggered signal-averaged electrocardiogram was also recorded in 17 patients.

Data Analysis

Only the X, Y, and Z lead signals were analyzed in this study. The filtered signals for the X, Y, and Z leads were combined into a spatial magnitude, \( \sqrt{X^2 + Y^2 + Z^2} \), that allowed the detection of high-frequency voltage in any lead. Voltages are the root mean square (RMS) in microvolts. The onset and offset of the filtered P wave were determined by defining the filtered P wave as signals within the interval showing a persistent level of more than 1 μV and as the noise signals when showing a persistent level of less than 1 μV. Incidentally, the interobserver’s variation to measure the duration of filtered P wave was 2.18±6.70%. The RMS voltage is the RMS of the spatial magnitude over an interval. We measured the RMS voltages (LP_{10}, LP_{20}, and LP_{30}) for the last 10, 20, and 30 msec of the filtered P wave of the spatial magnitude and its duration.

Comparisons With Variables Other Than Those From Signal-Averaged Electrocardiogram

In all patients, P wave width was measured in standard II lead of the scalar electrocardiogram recorded at a chart speed of 200 mm/sec and was compared with duration of filtered P wave. In patients who were examined by echocardiography, the left atrial dimension was measured by the standard method and was also compared with duration of filtered P wave.

Statistical Analysis

Variables were compared between groups 1 and 2, 1A and 2A, or 1B and 2B. Data are presented as the mean±SD. Statistical analysis was performed with the unpaired or paired t test; the level of significance was determined at a p value of 0.05.

Results

Figure 2 depicts two original tracings of the signal-averaged electrocardiogram in representative patients with and without paroxysmal atrial fibrillation. Of note, the terminal portion of filtered P wave is lower in amplitude and longer in duration in a patient with paroxysmal atrial fibrillation than that in a control patient. Table 1 summarizes data on four variables, that is, LP_{10}, LP_{20}, LP_{30} and duration of filtered P wave, for atrial late potential and P wave width in standard II lead, as well as left atrial dimension, assessed by echocardiography in each group.
RMS Voltages for the Last Portion of Filtered P Waves

Figure 3 shows the comparison of LP_{10}, LP_{20}, and LP_{30} between groups 1 and 2. LP_{10} (1.92±0.58 μV) and LP_{20} (2.47±0.78 μV) in group 1 were significantly (p<0.001) lower than those (LP_{10}, 2.49±0.78; LP_{20}, 3.46±1.20 μV) in group 2, although the difference in LP_{30} was not significant between the two groups. Moreover, in patients without organic heart diseases, LP_{10} was not useful in discriminating patients with from those without paroxysmal atrial fibrillation. In Figure 3, LP_{10}, LP_{20}, and LP_{30} were also compared between groups 1A and 2A with organic heart diseases and between groups 1B and 2B without organic heart diseases. These results were also similar to the results of the previous comparison between groups 1 and 2 before dividing patients by the presence of organic heart diseases.

Duration of Filtered P Waves

Figure 4 demonstrates the duration of filtered P wave in patients with and without paroxysmal atrial fibrillation and in those with and without organic heart diseases. The duration of filtered P wave was significantly (p<0.0001) longer in patients with paroxysmal atrial fibrillation (137.0±14.3 msec) than in those without it (118.6±11.3 msec), irrespective of

TABLE 1. Variety of Variables for Atrial Late Potential in Patients With or Without Paroxysmal Atrial Fibrillation and With or Without Organic Heart Diseases

<table>
<thead>
<tr>
<th></th>
<th>Paf group with OHD (n=42)</th>
<th>Paf group without OHD (n=20)</th>
<th>Control group with OHD (n=50)</th>
<th>Control group without OHD (n=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LP_{10} (μV)</td>
<td>1.92±0.58*</td>
<td>2.03±0.52*</td>
<td>2.49±0.78</td>
<td>2.65±0.79</td>
</tr>
<tr>
<td>LP_{20} (μV)</td>
<td>2.47±0.78*</td>
<td>2.68±0.89†</td>
<td>3.46±1.20</td>
<td>3.61±1.27</td>
</tr>
<tr>
<td>LP_{30} (μV)</td>
<td>3.83±1.81</td>
<td>3.97±1.88</td>
<td>4.60±1.84</td>
<td>4.99±2.24</td>
</tr>
<tr>
<td>Ad (msec)</td>
<td>137.0±14.3‡</td>
<td>139.2±15.5*</td>
<td>118.6±11.3</td>
<td>123.1±7.9</td>
</tr>
<tr>
<td>P_{11} (msec)</td>
<td>105.2±14.5</td>
<td>108.7±15.4</td>
<td>101.8±12.1</td>
<td>108.4±14.6</td>
</tr>
<tr>
<td>LAD (mm)</td>
<td>36.4±1.0</td>
<td>37.5±1.6</td>
<td>32.8±1.1</td>
<td>34.2±1.5</td>
</tr>
</tbody>
</table>

Values are mean±SD.
Paf, paroxysmal atrial fibrillation; LP_{10}, LP_{20}, and LP_{30}, root mean square voltages for the last 10, 20, and 30 msec of filtered P wave; Ad, duration of filtered P wave; P_{11}, P wave width in standard II lead; LAD, left atrial dimension.

* p<0.001, † p<0.02, versus control, ‡ p<0.0001.
the presence of organic heart diseases. Although there was a significant correlation ($r=0.36$, $n=58$, $p<0.01$) between filtered P wave duration and left atrial dimension assessed by echocardiography, the information on left atrial dimension failed to identify patients suffering from paroxysmal atrial fibrillation (Table 1). Moreover, we examined the relation between the filtered P wave duration and P wave width in standard II lead. Although there was a significant correlation ($r=0.44$, $p<0.01$), the relation again failed to distinguish patients with from those without paroxysmal atrial fibrillation.

Effect of High-Pass Filter on Atrial Late Potential

Figure 5 depicts the relation between high-pass filter and the total duration of filtered P wave. The higher the high-pass filter, the less was the filtered P duration. In particular, at the 20- and 30-Hz high-pass filters, consistently determining the end point of filtered P wave was difficult (Figure 5) because the P wave signal sometimes over-lapped the QRS signal. Accordingly, the 20- or 30-Hz high-pass filter was thought to be inappropriate for the aim of this study. On the other hand, Figure 6 shows the comparisons of the 40- and 80-Hz high-pass filtering in terms of RMS voltage ($LP_{30}$) during the last 20 msec and the total duration of filtered P wave. In both, 40 Hz was superior to 80 Hz, probably because the signal through the 80-Hz high-pass filter would be closer to that of the standard electrocardiogram.
Comparison of P Wave–Triggered and R Wave–Triggered Signal Averagings

Figure 7 depicts the original tracings of filtered P waves by P wave– and R wave–triggered signal averagings in a patient on the same day. It is clear that the P wave–triggered signal peak is higher than the R wave–triggered signal peak. Figure 8 shows significant differences in both filtered P wave duration and peak amplitude of the signal between P wave– and R wave–triggered signal averagings.

Criteria as a Screening Test for Detection of Patients With Paroxysmal Atrial Fibrillation During Sinus Rhythm

A need exists to identify patients at risk for paroxysmal atrial fibrillation during sinus rhythm, which is a risk factor for systemic thromboembolism, using the above-mentioned two variables: One is the RMS voltage for the last 20 msec of filtered P wave, LP20; the other is the filtered P wave duration, Ad. When the criterion “LP20≤3.5 μV” was used, the sensitivity, specificity, and predictive value were 95%, 54%, and 73%, respectively. On the other hand, when the criterion “Ad>120 msec” was used, sensitivity, specificity, and predictive value were 95%, 48%, and 70%, respectively. When both criteria “LP20≤3.5 μV” and “Ad>120 msec” were combined, the sensitivity, specificity, and predictive accuracy became 91%, 76%, and 83%, respectively. Moreover, when the presence of organic heart diseases was considered, the sensitivity, specificity, and predictive accuracy improved (91%, 86%, and 89% in the patients with organic heart diseases).

Discussion

We have been searching for a method to identify patients at risk for systemic thromboembolism, with either indium-111 platelet scintigraphy for detecting an intracardiac thrombus or plasma D-dimer assay for determining a high-clotting state.13–17 In the Framingham study,11 chronic atrial fibrillation induced systemic embolism five times more often than in the control. On the other hand, even though paroxysmal atrial fibrillation has been reported as frequently, the relative risk of inducing embolism would be five times higher,12 and it remains difficult to diagnose during normal sinus rhythm.

The present study indicates that the P wave–triggered atrial signal-averaged electrocardiogram could be of clinical use to distinguish the patients with from those without paroxysmal atrial fibrillation during sinus rhythm whether or not they had organic heart diseases. In particular, the RMS voltage for the last 20 msec and the total duration of the filtered P wave in the signal-averaged electrocardiogram were worthwhile measurements as screening tests for paroxysmal atrial fibrillation. Furthermore, we compared data (1A versus 1B, 2A versus 2B) after categorizing patients by the presence of organic heart diseases; the comparison showed that the presence or absence of organic heart diseases did not matter, although the presence of organic heart diseases improved the sensitivity, specificity, and predictive value for paroxysmal atrial fibrillation. We also found that there was no significant difference in the left atrial diameter assessed echocardiographically between patients with or without organic heart diseases and between patients with or without paroxysmal atrial fibrillation (Table 1).

Engel et al9 reported that the signal-averaged P wave did not identify the patient with paroxysmal atrial fibrillation or flutter, although they included some patients with persistent atrial fibrillation or flutter who had responded to cardioversion and who were administered antiarrhythmic drugs to maintain sinus rhythm. They tried in vain to predict atrial fibrillation analogously to ventricular late potential18,19 because only a few studies20–22 reported a slowly conducted atrial activity in the intracardiac electrogram in patients who had previously demonstrated atrial fibrillation or flutter. In their study, however, P wave signal was averaged on the point triggered by R wave, which inevitably results in two problems. One is that the PQ interval varies during signal averaging, and the other is that R wave–triggered signal averaging cannot eliminate atrial ectopic beats, which are often observed in patients with paroxysmal atrial fibrillation. Patients with atrial flutter were not included in our study. It is natural to
think that atrial tachycardia or flutter is an analog of ventricular tachycardia because atrial fibrillation corresponds to ventricular fibrillation, which is known not to show late potential. However, atrial late potential does not seem to be detected as often in atrial tachycardia as in paroxysmal atrial fibrillation, although this has not been confirmed by published studies. The reasons are unclear. We speculate that myocardial fragmented activity was not sufficient in quantity to make late potential in atrial tachycardia but that the sum of fragmented activity was sufficient in atrial fibrillation.

Therefore, we recently developed a P wave–triggered signal-averaging method for the analysis of filtered P wave. Figure 7 shows the comparison of P wave– and R wave–triggered signal-averaged waves in the original tracing. In each peak of the filtered P wave, the P wave–triggered electrogram has a higher amplitude than that triggered by R wave. In other words, each peak of R wave–triggered P wave is more attenuated. Figure 8 demonstrates that the P wave–triggered P wave peak amplitude was significantly higher than that triggered by R wave. Incidentally, attenuation by averaging in peak amplitude of the filtered P wave, in terms of percent reduction from 20- to 200-times signal averagings, was 1.94±6.86% (n=6) in the P wave–triggered method and 22.61±17.61% (n=6) in the R wave–triggered method. Such a difference can be attributed not only to inclusion of ectopic beats but also to variable PQ interval (coefficient of variance for consecutive 100 beats: 3.99±2.26%, n=5) during signal averaging in the R wave–triggered method. We have also reported previously that the P wave–triggered method was superior to that triggered by the R wave for detecting patients with paroxysmal atrial fibrillation in terms of LP20 (p<0.001 versus p>0.01) and filtered P wave duration (p<0.001 versus p<0.01). As for the reproducibility of measurements in the P wave–triggered signal-averaged electrocardiogram, interobserver’s
percent variation was sufficiently small (2.18±6.70%, n=14). Moreover, the reproducibility of intraindividual recordings was subtle (day-to-day variation, 5.8±5.9%, n=8).

To our knowledge, there have been no published data on the filtering for recording the signal-averaged P wave. The 40–300-Hz filter was selected in this study, as a result of evaluating the effect of filtering on these variables, similar to the QRS complex. This might be conceivable from the viewpoint of the presence of delayed atrial activity in the intracardiac electrogram similar to ventricular fragmented activity. Figure 5 shows the effect of high-pass filters on the filtered P wave duration. When we use a high-pass filter of 20–30 Hz, in the terminal portion of the P wave signal, QRS signal could sometimes be overlapped. For this reason, some data on 20 or 30 Hz were missing (Figure 5). On the other hand, when 60–80 Hz were used, the signal probably approximates the standard electrocardiogram. Therefore, we found that a high-pass filter of 40 Hz but not of 80 Hz was useful in classifying patients with and without paroxysmal atrial fibrillation (Figure 6). As for the effect of unidirectional filtering reported by Simson on the low-amplitude signal of the terminal portion of the filtered P wave, we did not address these findings because we did not compare the results between unidirectional and bidirectional filtrings. However, the ringing effect may be negligible because P wave voltage is relatively low compared with that of the QRS complex. Actually, even if the ringing effect were significant, these data would be acceptable because these are based on the controlled study.

In conclusion, we reported in this study that the criterion "the RMS voltage for the last 20 msec of the filtered P wave 3.5 or less μV and the total duration of the filtered P wave more than 120 msec" in P wave-triggered atrial averaging is of clinical use for detecting patients with paroxysmal atrial fibrillation. Therefore,
further study is needed to elucidate the relation between “atrial late potential” and atrial dysrhythmias.

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References


KEY WORDS • thromboembolism • atrial electrical activity, fragmented • late potential, atrial • electrocardiogram, signal averaged
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