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Characteristics of Frequency Content of Atrial Signal-Averaged Electrocardiograms During Sinus Rhythm in Patients With Paroxysmal Atrial Fibrillation

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To clarify the characteristics of the frequency content of atrial signal-averaged electrocardiograms (ECGs) during sinus rhythm in patients with paroxysmal atrial fibrillation, P wave-triggered signal-averaged ECGs were recorded in 28 patients with and 34 control patients without paroxysmal atrial fibrillation. Fast Fourier transform analysis was performed on the 100-ms segment starting 75 ms before the end of the P wave. An area ratio (AR_{50}) was calculated by dividing the area under the spectrum curve between 20 and 50 Hz, multiplied by 100, by the area between 0 and 20 Hz. Magnitude ratios (MR_{20}, MR_{30}, MR_{40} and MR_{50}) were calculated by dividing the magnitude at 20, 30, 40 and 50 Hz, respectively, multiplied by 100, by the maximal magnitude of the entire signal.

AR_{50} was significantly greater in patients with than without paroxysmal atrial fibrillation (62.3 ± 34.2 vs. 42.4 ± 18.4). MR_{20} and MR_{30} were also significantly greater in patients with than without paroxysmal atrial fibrillation (MR_{20} 76.1 ± 15.2 vs. 60 ± 20.2; MR_{30} 41 ± 18.8 vs. 26.6 ± 14.4), although no significant differences in MR_{40} or MR_{50} were observed between the two patient groups. The difference in MR_{30} between groups remained significant even after taking into account the presence of organic heart disease.

It is concluded that, irrespective of the presence of organic heart disease, the terminal portion of the P wave contained significantly more components in the 20- to 50-Hz range, especially around 30 Hz, in patients with than in patients without paroxysmal atrial fibrillation. These results suggest that frequency analysis could characterize atrial signal-averaged ECGs of patients at risk for paroxysmal atrial fibrillation.

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In recent years, ventricular late potentials, which are recognized in time domain analysis of the noninvasive signal-averaged electrocardiogram (ECG), have been used to identify patients at risk for ventricular tachycardia after myocardial infarction (1–5). Some investigators (6–10) have also found frequency domain analysis of the terminal QRS complex and ST segment useful in identifying patients with ventricular tachycardia.

More recently, P wave analysis for detecting patients with paroxysmal atrial fibrillation, a known potential risk factor for systemic thromboembolism, has also focused on "atrial late potentials" in analogy to ventricular late potentials (11). We (12) reported that time domain analysis of the P wave on the signal-averaged ECG triggered by the P wave could be useful for detecting patients at risk of paroxysmal atrial fibrillation. However, such analysis has some problems associated with a band-pass filter in determining the end of the P wave, a point important to the definition of atrial late potentials. Therefore, frequency analysis of the P wave is needed for the reason similar to the need for analysis of the QRS complex.

The purpose of this study was to clarify the characteristics of the frequency content of the atrial signal-averaged ECG during sinus rhythm in patients with paroxysmal atrial fibrillation, before attempting to assess the clinical significance of frequency analysis of the atrial signal-averaged ECG.

Methods

Patient selection. The study patients constituted two groups of patients: group 1, 28 consecutive patients (15 men and 13 women; mean age [± SD] 60.1 ± 15.8 years [range 28 to 82]) who had paroxysmal atrial fibrillation documented on the ECG; and group 2, 34 control patients (20 men and 14 women; mean age 60.3 ± 11.4 years [range 26 to 83]) without paroxysmal atrial fibrillation. No patient had received antiarrhythmic drugs for ≥1 week before undergoing signal-averaged electrocardiography. There were no significant differences in age and gender between the two groups. Groups 1 and 2 were each divided into two subgroups based

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on the presence or absence of organic heart disease. Group 1A comprised 17 patients with organic heart disease (5 with ischemic heart disease, 4 with mitral valve disease, 3 with hypertrophic cardiomyopathy, 1 with dilated cardiomyopathy, 2 with hypertensive heart disease and 2 with congenital heart disease) and group 1B comprised 11 patients with no organic heart disease. Group 2A comprised 26 patients with organic heart disease (18 with ischemic heart disease, 2 with mitral valve disease, 1 with hypertrophic cardiomyopathy, 4 with dilated cardiomyopathy and 1 with congenital heart disease) and group 2B comprised 8 patients with no organic heart disease. Each patient gave informed written consent to participate in this study.

Signal-averaged ECG recording. A signal-averaged ECG was recorded from a modified X, Y and Z lead system in an electrically shielded room, to minimize noise, with use of the Multicardiner VCM-3000 (Fukuda Denshi), which was recently developed for P wave-triggered signal averaging. The X lead was between the right and left shoulders (standard lead I); Lead aVF was used as the Y lead and precordial lead V_1 was used as the Z lead. The gain of the amplifier was 1,000 and the noise input was <0.6 μV. The signal from each lead was recorded at a band width of 0.08 to 250 Hz and was then converted from analog to digital data with 12-bit accuracy at a sampling rate of 1 kHz.

Signal averaging. All of the 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 according to the algorithm for the P wave-triggering system previously reported (12). Briefly, a specially filtered P wave derived from the dominant P wave of the Z 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 100 beats were usually averaged to reduce the noise level to <1 μV.

Fast Fourier transform analysis of the atrial signal-averaged ECG. Frequency domain analysis was performed on a 100-ms segment from 75 ms before to 25 ms after the end of the P wave on the signal-averaged Z lead. This component was identified with the use of a computer graphics cursor and standard ECG criteria. These data were multiplied by the Blackmann-Harris four-term window function to reduce spectral leakage from edge discontinuities after a direct-current component was removed from the data. The data were padded with zeros to fill a 512-point array and the fast Fourier transform was applied to determine frequency content. After the analysis, the magnitude versus frequency plot curve was obtained.

Data analysis. An area ratio (AR_{50}) was calculated by dividing the area under the curve between 20 and 50 Hz, multiplied by 100, by the area between 0 and 20 Hz. Another area ratio (AR_{100}) was calculated by dividing the area between 50 and 100 Hz, multiplied by 100, by the area between 0 and 50 Hz. On the spectrum curve the magnitude at each frequency was not described as the absolute value but as the ratio of the magnitude at each frequency to maximal magnitude of the entire signal; the preceding areas were calculated on the curve where the magnitude was expressed as the absolute value. In addition to area ratio, magnitude ratios (MR_{20}, MR_{30}, MR_{40} and MR_{50}) were also calculated by dividing the magnitude at 20, 30, 40 and 50 Hz, respectively, multiplied by 100, by the maximal magnitude of the entire signal.

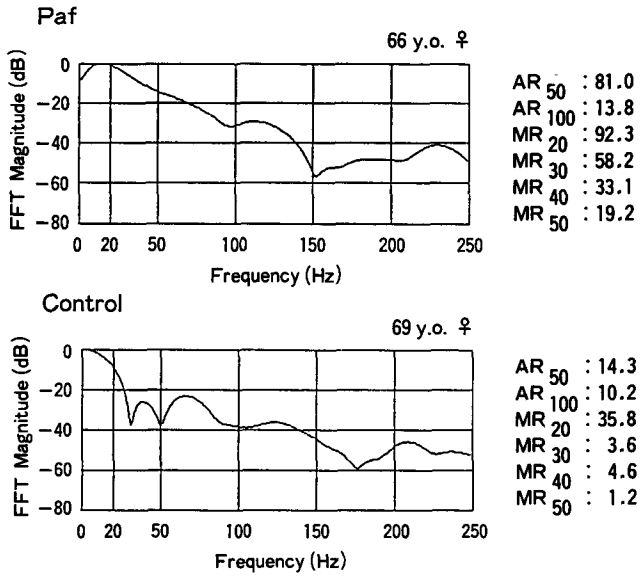


Figure 1. Representative fast Fourier transform (FFT) analysis of the 100-ms segment starting 75 ms before the end of the P wave in the signal-averaged Z lead from a patient with (Paf) and without (Control) paroxysmal atrial fibrillation. AR_{50} = a ratio calculated by dividing the area under the spectrum curve between 20 and 50 Hz, multiplied by 100, by the area between 0 and 20 Hz. AR_{100} = a ratio calculated by dividing the area between 50 and 100 Hz, multiplied by 100, by the area between 0 and 50 Hz. MR_{20}, MR_{30}, MR_{40} and MR_{50} = ratios calculated by dividing the magnitude at 20, 30, 40 and 50 Hz, respectively, multiplied by 100, by the maximal magnitude of the entire signal. The segment from the 66-year old woman with paroxysmal atrial fibrillation contains relatively more high frequency components in the 20- to 100-Hz range than that from the 69-year old woman without paroxysmal atrial fibrillation.

Statistical analysis. Variables were compared between groups 1 and 2, 1A and 2A and 1B and 2B. Data are presented as mean values ± SD. Statistical analysis was performed with an unpaired Student *t* test after a one-way analysis of variance; significance was detected at p = 0.05.

Results

Representative plots of results of fast Fourier transform analysis from patients with and without paroxysmal atrial fibrillation are shown in Figure 1. Each panel depicts magnitude versus frequency plots during the segment from before 75 ms to after 25 ms of the end of the P wave on the Z lead. The segment from the patients with paroxysmal atrial fibrillation contained relatively more high frequency compo-

Table 1. Summary of Results Obtained With Frequency Analysis in Patients With and Without Paroxysmal Atrial Fibrillation

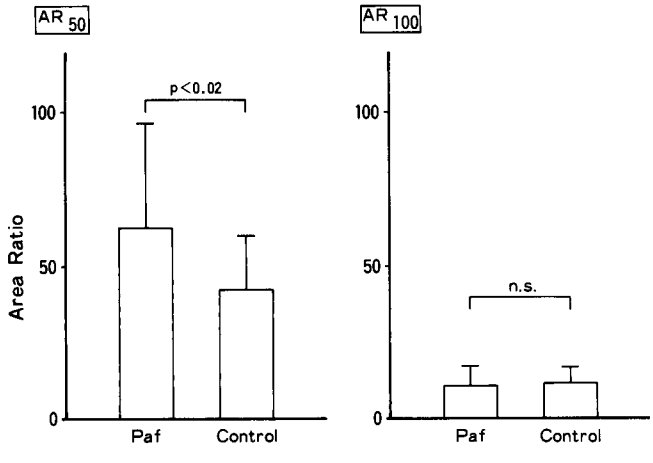
	Paf Group			Control Group		
	Total (n = 28)	With HD (n = 17)	Without HD (n = 11)	Total (n = 34)	With HD (n = 26)	Without HD (n = 8)
AR_{50}	62.3 ± 34.2*	64.2 ± 39.9†	59.4 ± 24.5	42.4 ± 18.4	42.3 ± 19.6	42.7 ± 15
AR_{100}	10.8 ± 6.4	11 ± 5.6	10.7 ± 7.8	11.2 ± 5.8	11 ± 6.1	12.9 ± 5
MR_{20}	76.1 ± 15.2‡	77 ± 12.8§	74.7 ± 19	60 ± 20.2	60 ± 21.8	60.1 ± 14.9
MR_{30}	41 ± 18.8‡	41.5 ± 22.1*	40.3 ± 13.1†	26.6 ± 14.4	26.9 ± 15.4	26.1 ± 11.1
MR_{40}	21.4 ± 13.6	21.5 ± 14.4	21.3 ± 12.8	16.8 ± 8.7	16 ± 8.7	19 ± 9
MR_{50}	11.4 ± 7.1	11.6 ± 6.7	11.2 ± 8.1	10 ± 6.6	9.9 ± 6.2	10.6 ± 8.2
Ad (ms)	143.1 ± 19.1‖	144.9 ± 23.3‡	140 ± 9.0‡	125.1 ± 9.7	125.6 ± 9.8	123.1 ± 9.6
LP_{20} (μV)	2.19 ± 1.12*	2.14 ± 0.78†	2.28 ± 1.58	3.14 ± 1.74	2.94 ± 1.67	3.78 ± 1.9

All values are mean ± SD. *$p < 0.02$, †$p < 0.05$, ‡$p < 0.005$, §$p < 0.01$, ‖$p < 0.0001$ vs control. Ad = duration of filtered (40 to 300 Hz) P wave; AR_{50} = a ratio calculated by dividing the area under the spectrum curve between 20 and 50 Hz, multiplied by 100, by the area between 0 and 20 Hz; AR_{100} = a ratio calculated by dividing the area under the spectrum curve between 50 and 100 Hz, multiplied by 100, by the area between 0 and 50 Hz; LP_{20} = root-mean-square voltage for the last 20 ms of filtered P wave; MR_{20}, MR_{30}, MR_{40} and MR_{50} = ratios calculated by dividing the magnitude at 20, 30, 40 and 50 Hz, respectively, multiplied by 100, by the maximal magnitude of the entire signal; Paf = paroxysmal atrial fibrillation; With HD = patients with organic heart disease; Without HD = patients without organic heart disease.

nents in the 20- to 100-Hz range than that from the patients without paroxysmal atrial fibrillation, as reflected by the greater values for area and magnitude ratios. Table 1 summarizes data on six variables from frequency domain analysis—that is, AR_{50}, AR_{100}, MR_{20}, MR_{30}, MR_{40} and MR_{50}—with the root-mean-square voltage for the last 20 ms of the filtered P wave and its duration from time domain analysis that we previously reported (12).

Area ratios in patients with and without paroxysmal atrial fibrillation (Table 1, Fig. 2). AR_{50} was significantly greater in group 1 than in group 2; the difference in AR_{100} was not significant between the two groups. AR_{50} in group 1A was also significantly greater than that in group 2A, but AR_{50} in group 1B tended to be greater than that in group 2B. Therefore, we compared magnitude ratios from 20 to 50 Hz in patients with and without paroxysmal atrial fibrillation.

Figure 2. Comparisons of area ratios (AR) between patients with (Paf) and without (Control) paroxysmal atrial fibrillation. The AR_{50} **(left)** in patients with paroxysmal atrial fibrillation is significantly greater than that in control patients; the difference in AR_{100} **(right)** between the two groups is not significant. Definitions as in Figure 1.

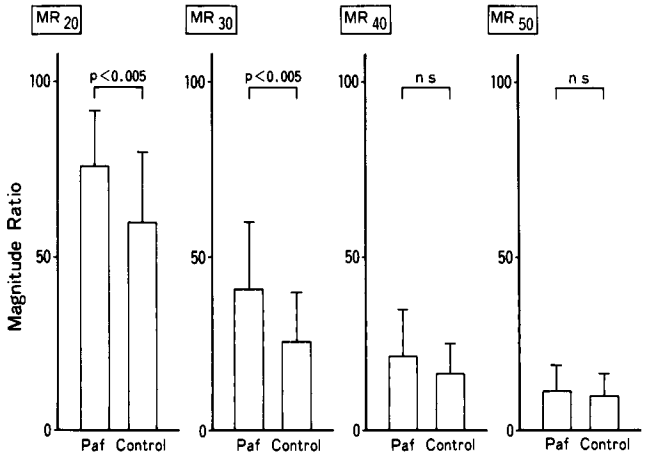


Magnitude ratios in patients with and without paroxysmal atrial fibrillation (Table 1, Fig. 3). MR_{20} and MR_{30} were significantly greater in group 1 than in group 2. Although the differences in MR_{40} or MR_{50} between the two groups were not significant, MR_{40} in group 1 tended to be greater than that in group 2. Each magnitude ratio was also compared after taking into account the presence of organic heart disease. The difference in MR_{20} was significant between groups 1A and 2A but not between groups 1B and 2B; however, the difference in MR_{30} was significant in both comparisons.

Discussion

Detection of paroxysmal atrial fibrillation. Atrial fibrillation, whether chronic or paroxysmal, is a potential risk

Figure 3. Comparisons of magnitude ratios (MR) between patients with (Paf) and without paroxysmal atrial fibrillation (Control). The MR_{20} and MR_{30} in patients with paroxysmal atrial fibrillation are significantly greater than those in control patients; neither difference in MR_{40} or MR_{50} between the two groups is significant. Definitions as in Figure 1.



factor for systemic thromboembolism (13,14). We (15) also demonstrated that atrial fibrillation itself may be more important than factors predisposing to atrial fibrillation in the development of intracardiovascular clotting. However, it remains difficult to diagnose paroxysmal atrial fibrillation during sinus rhythm. We (12) previously reported that analysis of the atrial signal-averaged ECG could be useful in detecting patients with paroxysmal atrial fibrillation. Such time domain analysis has some inherent problems: the filtered P wave signal at the 20- and 30-Hz high pass filter sometimes overlaps the QRS signal, so that it is difficult to consistently determine the end of the filtered P wave (12). Furthermore, when the signal is passed through a bandpass filter, especially a high pass filter, prior knowledge of the frequency distribution of the signals of interest is needed, because the use of filtering may potentially exclude those signals. Therefore, in this study we examined the difference in the frequency content of the atrial signal between patients with and without paroxysmal atrial fibrillation by frequency analysis.

Electrophysiologic basis of paroxysmal atrial fibrillation. Electrophysiologic studies (16–18) in patients who had previously demonstrated atrial fibrillation recorded a slowly conducted atrial activity, a widening of the fragmented activity zone in response to atrial extrastimuli and a fragmented right atrial electrogram during sinus rhythm related to the development of paroxysmal atrial fibrillation. These findings suggest that reentrant activity is associated with the genesis of atrial fibrillation. Although the electrophysiologic alterations responsible for the abnormal signals detected in this study by frequency domain analysis remain unclear, our results are supported by the data that most energy of the normal P wave is in <20 Hz (19,20). In contrast, ventricular fragmented signals, of which local myocardial areas were reported to function as a source of reentrant arrhythmia (21,22), were shown to have a peak frequency in the 25- to 50-Hz range. Several investigators (6–10) recently reported that the terminal QRS complex and ST segment contained more components in the 20- to 50-Hz range in patients with than in patients without ventricular tachycardia. Therefore, we speculate that the frequency distribution of atrial fragmented signals might be approximately similar to that of ventricular signals and that the altered frequency components detected in this study might reflect slow fragmented atrial activity.

Identifying patients with paroxysmal atrial fibrillation. It may be possible to identify patients at risk for paroxysmal atrial fibrillation during sinus rhythm using the preceding two variables, MR_{30} and AR_{50}. When the criterion "$MR_{30} \geq 25$ plus $AR_{50} \geq 40$" was used, the sensitivity, specificity and predictive accuracy were 75%, 56% and 65%, respectively. On the other hand, in time domain analysis (Table 1), the criterion we previously proposed, "the root-mean-square voltage for the last 20 ms of the filtered P wave ≤ 3.5 μV and the total duration of the filtered P wave >120 ms," had a sensitivity of 93%, a specificity of 59% and a predictive accuracy of 75% in this study group. Frequency domain analysis seems to be inferior to time domain analysis of the atrial signal-averaged ECG for detecting patients with paroxysmal atrial fibrillation, but it is possible that differentiation of patients with and without paroxysmal atrial fibrillation by frequency domain analysis can be improved by multiplying analyzed leads (23) and changing analyzed signal duration and phase.

Limitations of this study. Some factors could alter the results of frequency analysis. Kelen et al. (24) reported that the high frequency signal content was found to be dependent on the length and phase of the analyzed segment. The end of the P wave, an important point used to determine the phase of this segment, was visually identified by the use of the computer graphic cursor and standard ECG criteria. The interobserver variation in detecting the end of the P wave was small (2.2 ± 6.7%, n = 14). Thus, the variation of the magnitude ratio at 30 Hz was also subtle (4.4 ± 4.1%, n = 6). Another inherent limitation is frequency resolution, which fundamentally depends on the duration of the signal of interest and is worsened by the window function (9,25,26). Consequently, the frequency resolution in this study might not be strict enough to examine the frequency content of every 10 Hz of the P wave signal. However, it is evident that this study demonstrates the significant difference of the frequency content of the P wave between patients with and without paroxysmal atrial fibrillation despite these limitations.

Conclusions. The 100-ms segment starting 75 ms before the end of the P wave contains more components in the 20- to 50-Hz range, especially at approximately 30 Hz, in patients with than in patients without paroxysmal atrial fibrillation, irrespective of the underlying heart disease. This suggests that frequency domain analysis can characterize the frequency content of the atrial signal-averaged ECG during sinus rhythm in patients at risk for paroxysmal atrial fibrillation.

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