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Signal-Averaged P-Wave Analysis of Normal Controls and Patients with Paroxysmal Atrial Fibrillation: A Study in Gender Differences, Age Dependence, and Reproducibility

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Summary

Background: Atrial fibrillation is often first recognized after a complication such as embolic stroke has occurred. Limited data are available for the prospective identification of patients at risk for developing atrial fibrillation.

Hypothesis: Demonstration of areas of slow conduction in the atrium by means of P-wave signal averaging may identify individuals at risk for atrial fibrillation.

Methods: P-wave signal averaging from the surface electrocardiogram was performed in 199 normal controls and 81 patients with paroxysmal atrial fibrillation using an automated, P-triggered, high-resolution signal for analysis.

Results: Of the variables measured, the filtered P-wave duration and P-wave integral were significantly different between controls and patients (filtered P-wave duration 120 ± 9 vs. 145 ± 21 and P-wave integral 666 ± 208 vs. 868 ± 352), whereas the terminal root-mean-square (RMS) voltages (RMS 20, RMS 30, RMS 40) showed no significant differences between the two groups. Regression analysis of the first and second measurement of the filtered P-wave duration obtained during consecutive tests showed excellent reproducibility (r and r^2 of 0.96 and 0.92). The duration of the filtered P wave showed no age dependence but was shorter in women.

Conclusion: Utilizing the 90th percentile value of the filtered P-wave duration of 133 ms in men and 130 ms in women, the sensitivity was 80 and 81%, the specificity 92 and 90%, the positive predictive value 84 and 73%, and the negative predictive value 90 and 93%, respectively.

Key words: paroxysmal atrial fibrillation, P-wave signal averaging

Introduction

High-resolution P-wave signal averaging from the surface electrocardiogram (ECG) is being increasingly proposed to identify patients prone to atrial arrhythmias, especially atrial fibrillation (AF).[1–7] The utility of this technique rests on the premise that since AF is reentrant tachycardia, areas of slow and fractionated conduction are probably required. Averaging of high-resolution P waves could potentially identify the "atrial late potentials" in a manner akin to ventricular late potentials. However, not only is the methodology of P-wave signal averaging in a state of evolution, but also, in most reported studies, the number of patients with AF has been rather small, typically less than 50. The purpose of this study, therefore, was to establish normal parameters for the high-resolution P-wave signal-averaged electrocardiogram (PWSAECG) in subjects without AF and then to determine its sensitivity by testing patients with paroxysmal AF using a newly developed automated P-wave-triggered algorithm. In addition, this study was also intended to examine the gender-specific differences, age dependence, and reproducibility of the PWSAECG measurements.

Methods

Control and Patient Groups

Subjects from two groups, normal controls and patients with paroxysmal AF, participated in this study. Subjects were considered eligible for participation in the control group if they had no history of AF or other heart disease and had a normal

*A list of the Multicenter PHi-Res Study investigators appears in the Appendix.

Drs. Xue and Reddy are employed by GE Marquette Medical Systems, whose product was used in this study.

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physical examination. Patients with prior AF were chosen on the basis of having documented AF in the past by 12-lead ECG, Holter recording, or event monitoring. To eliminate the confounding variable of the effect of antiarrhythmic medication on the signal-averaged P wave, the test was performed on patients who were on no antiarrhythmic medication other than digitalis or a beta blocker. The study was approved by the Institutional Review Boards of the participating centers and all patients gave informed written or oral consent.

High Resolution P-Wave Signal Averaging Methodology

The P-wave signal-averaging technique used in this study has been previously described[8] and is summarized here. An orthogonal lead arrangement (bipolar X,Y, and Z) is used to record surface ECGs. Initially, QRS complexes are detected and correlated as in standard QRS signal averaging followed by P-wave detection and matching. Before averaging, a P-wave template is generated in the following manner. A seed beat is automatically selected for the initial template and displayed with 9 s of data. After the user confirms the initial selection or selects a different seed beat, template matching is performed with the detected P waves in 9 s data. All P waves that meet the criteria of matching are averaged to form a final template. During averaging, this template is used to match the detected P waves in front of the valid QRS complexes. If a P wave matches, the point at which the highest correlation coefficient is achieved is taken as the alignment reference for averaging. Averaged P-wave signals are filtered using a spectral filter with a bandwidth of 40–250 Hz and are then combined into a vector magnitude [$VM = (x^2 + y^2 + z^2)^{1/2}$]. Noise level is estimated in a 40 ms window in the TP segment of the averaged complex, and P-wave onset and offset (fiducial points) are automatically determined by the system. The measurements computed by the system include the filtered P duration in ms and root-mean-square (RMS) voltage in terminal 20, 30, and 40 ms (RMS20, RMS30, RMS40), expressed in micro-Volts (μV). In addition, the integral of the P wave (area under the VM curve from P-wave onset to offset) is also computed in micro-Volt ms (μV-ms) as previously described.[9]

All the PWSAECG tests were reviewed by an over-reader blinded to the clinical condition or category of the subjects. The over-reader paid particular attention to the accuracy of determination of P-wave onset and offset by the computer and, if necessary, adjusted these fiducial points. The resulting parameters (the computer recalculates all the parameters if the fiducial points are adjusted) were used in this analysis.

Analysis of Reproducibility

Two consecutive records per subject were obtained in a subset of the PWSAECG tests performed in this study. After the first test was completed and the data stored on a permanent magnetic medium, the repeat test was conducted starting with a new template.

Age- and Gender-Matched Analysis

As controls were greater in number and younger than patients with paroxysmal AF, to obtain appropriate age matching, only controls and patients who could be similarly age matched were included for analysis.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation. Differences in the PWSAECG parameters between Group 1 (normal controls) and Group 2 (patients with paroxysmal AF) were examined using the Student's *t*-test. Similarly, the differences between the men and women in both groups were examined using the *t*-test. A p value of ≤ 0.05 was considered statistically significant. Age dependence of the PWSAECG parameters was examined by linear regression analysis of each of these parameters with age. Again, a p value of ≤ 0.05 was considered significant. Reproducibility of PWSAECG parameters was analyzed by performing regression analysis of the parameters obtained during the first and second consecutive tests. From the regression analysis, r value, r^2 value, and the p value were computed.

From the distribution of the parameters in Group 1, the 90th percentile values were determined separately for men, women, and the whole group (all normal controls). Using these 90th percentile values as criteria (cutoff values), sensitivity and specificity of the method for identifying patients with paroxysmal AF were computed. Positive predictive value (PPV) and negative predictive value (NPV) were also computed.

Results

In all, 199 normal controls (Group 1) and 81 patients with paroxysmal AF (Group 2) underwent PWSAECG testing. There were 91 men and 108 women with a mean age of 39 ± 10 years (range 18–78 years) in Group 1, and 45 men and 36 women with a mean age of 63 ± 13 years (range 20–82 years) in Group 2.

P-Wave Signal-Averaged Electrocardiographic Parameters

Intergroup differences: Table I compares the age and PWSAECG parameters of normal controls and patients with paroxysmal AF. Subjects of Group 1 were younger ($p < 0.001$) and had shorter filtered P-wave duration ($p < 0.001$) and smaller P-wave integral values ($p < 0.001$) than patients of Group 2. There were no significant differences in the terminal RMS voltages (RMS20, RMS30, RMS40) between the two groups. Typical examples of VM of filtered P waves from a normal control and a patient with paroxysmal AF are shown in Figure 1A and B, respectively.

Intragroup gender differences: Table II shows the SAECG parameters for male and female normals (Group 1). The filtered P-wave duration in men (122 ± 8 ms) was longer than in

TABLE I P-wave signal averaged electrocardiographic parameters: Comparison of normal controls with patients with paroxysmal atrial fibrillation (PAF)

Parameter	Controls (n = 199)	PAF patients (n = 81)	p Value
Age (years)	39 ± 10	63 ± 13	< 0.001
Filtered P-wave duration (ms)	120 ± 9	145 ± 21	< 0.001
RMS20 (μV)	3.9 ± 2.0	4.1 ± 2.8	NS
RMS30 (μV)	4.7 ± 2.1	5.0 ± 3.1	NS
RMS40 (μV)	5.6 ± 2.2	5.6 ± 3.0	NS
P-wave integral (μV-ms)	666 ± 208	868 ± 352	< 0.001

Abbreviations: RMS = root-mean-square, NS = not significant.

women (118 ± 9 ms, p < 0.003). The terminal RMS voltages RMS20 and RMS30 were not different between men and women in this group. The RMS40 and P-wave integral were different between men and women in this group. Age of men and women in this group did not differ significantly. Table III shows the PWSAECG parameters for patients in Group 2. In contrast with the subjects in Group 1, the filtered P-wave duration in Group 2 patients was not different between men (144 ± 18 ms) and women (147 ± 24 ms, p = 0.60). None of the other parameters differed between men and women in this group (p value 0.33–0.71). The age of men and women in this group did not differ significantly (p = 0.08).

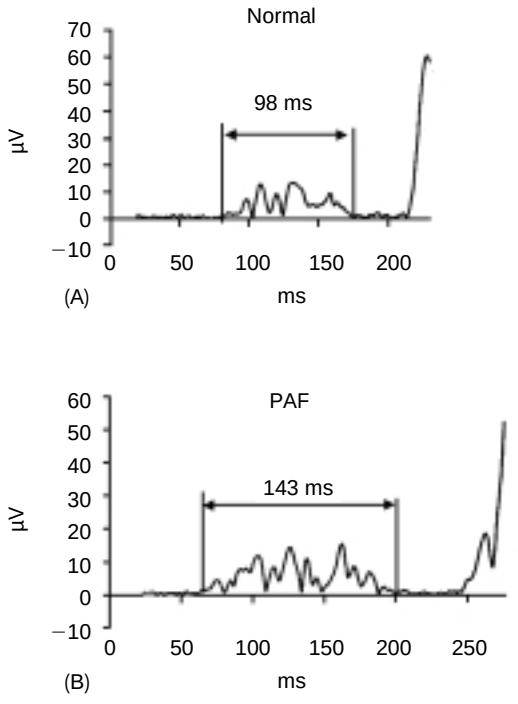

FIG. 1 Examples of vector magnitude (VM) plots of filtered P-wave signals. (A) VM plot from a normal control, (B) from patient with paroxysmal atrial fibrillation (PAF).

TABLE II P-wave signal-averaged electrocardiographic parameters in normal controls by gender

Parameter	Men (n = 91)	Women (n = 108)	p Value
Age (years)	38 ± 10	41 ± 10	NS
Filtered P-wave duration (ms)	122 ± 8	118 ± 9	< 0.003
RMS20 (μV)	4.3 ± 2.1	3.7 ± 2.0	NS
RMS30 (μV)	5.0 ± 2.1	4.5 ± 2.1	NS
RMS40 (μV)	5.8 ± 2.2	5.3 ± 2.2	< 0.023
P-wave integral (μV-ms)	703 ± 223	634 ± 188	< 0.018

Abbreviations as in Table I.

Age and Gender Dependence of P-Wave Signal-Averaged Electrocardiographic Parameters

Analyses of the filtered P-wave duration and P-wave integral in age- and gender-matched controls compared with patients with paroxysmal AF are shown in Table IV. The number of controls and subjects in Table IV is smaller than that in Table I, as only those who could be age- and gender-matched were included in the analyses. In addition, regression analyses of the filtered P-wave duration and P-wave integral with age for subjects of Group 1 were performed and are shown in Figure 2A and B, respectively. Similar analyses for patients of Group 2 are shown in Figure 3A and B. These analyses (and the regression analyses on RMS voltages, not shown here) indicate that the PSAECG parameters did not correlate with age.

Reproducibility of P-Wave Signal-Averaged Electrocardiographic Parameters

The regression analysis of the first and second measurement of the filtered P-wave duration obtained during consecutive tests in 154 normal controls and patients with paroxysmal AF is shown in Figure 4A. The r and r^2 values are very high (0.96 and 0.92, respectively) indicating an excellent reproducibility between the first second measurements of the filtered P-wave duration. Similar analysis for P-wave integral is shown in Figure 4B. The r and r^2 values were very high (0.94 and 0.89, respectively) for this parameter as well.

TABLE III P-wave signal-averaged electrocardiographic parameters in patients with paroxysmal atrial fibrillation by gender

Parameter	Men (n = 45)	Women (n = 36)	p Value NS
Age (years)	65 ± 12	60 ± 14	NS
Filtered P-wave duration (ms)	144 ± 18	147 ± 24	NS
RMS20 (μV)	4.2 ± 3.3	4.0 ± 1.9	NS
RMS30 (μV)	5.1 ± 3.7	4.8 ± 2.3	NS
RMS40 (μV)	5.8 ± 3.5	5.4 ± 2.2	NS
P-wave integral (μV-ms)	832 ± 329	914 ± 379	NS

Abbreviations as in Table I.

TABLE IV Filtered P-wave duration of patients with paroxysmal atrial fibrillation (PAF) and age-matched controls (normals)

	Male		Female	
	Controls (n = 29)	PAF patients (n = 29)	Controls (n = 26)	PAF patients (n = 26)
Age (years)	52 ± 14	52 ± 14	56 ± 10	56 ± 10
Filtered P-wave duration (ms)	127 ± 12	139 ± 16	120 ± 11	140 ± 18
	$p < 0.01$		$p < 0.001$	

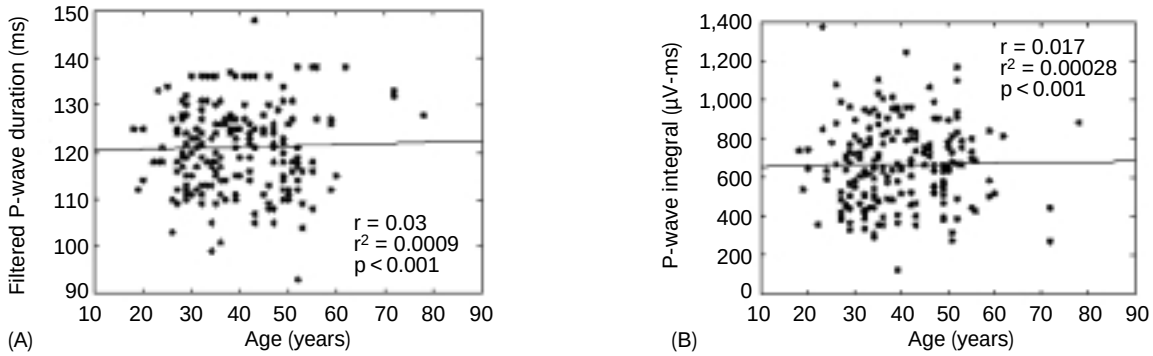

FIG. 2 Regression analysis of two P-wave signal-averaged electrocardiogram (PSAECG) parameters of Group 1 subjects (normal controls) with age. (A) Regression of filtered P-wave duration with age, (B) regression analysis of P-wave integral values with age.

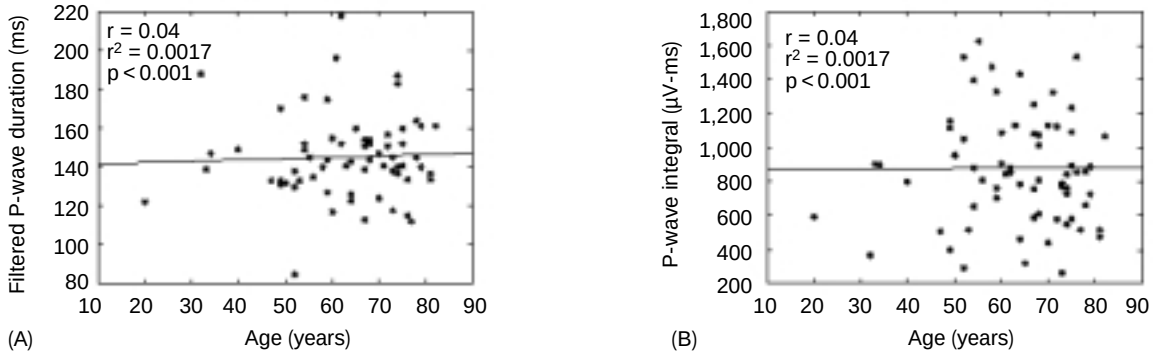

FIG. 3 Regression analysis of two P-wave signal-averaged electrocardiogram (PSAECG) parameters of Group 2 (patients with paroxysmal atrial fibrillation) with age. (A) Regression of filtered P-wave duration with age, (B) regression analysis of P-wave integral values with age.

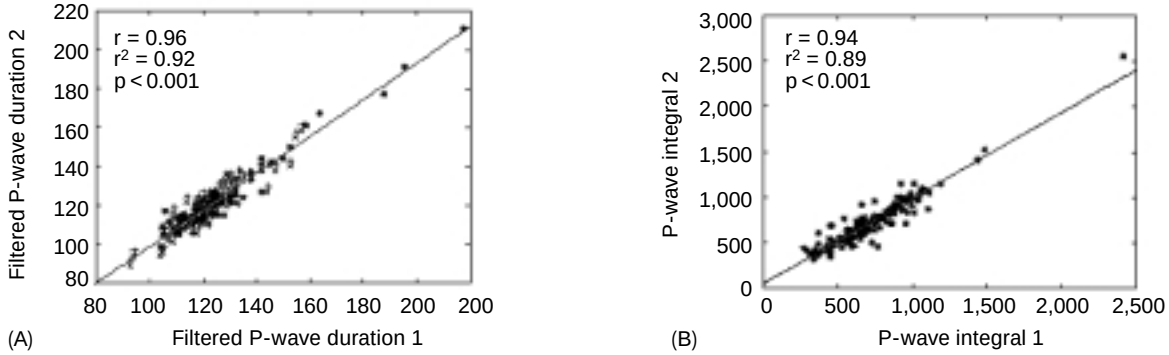

FIG. 4 (A) Regression analysis of two consecutive filtered P-wave durations in 154 subjects (both normal controls and patients with paroxysmal atrial fibrillation) to assess the reproducibility of P-wave signal-averaged electrocardiogram tests. (B) Similar analysis for P-wave integral.

TABLE V Filtered P-wave duration and P-wave integral criteria (cutoff values) based on 90th percentile values of distribution of these parameters in normal controls (Group 1)

	Male criterion (male controls, n = 91)	Female criterion (female controls, n = 108)	Gender-neutral criterion (all controls, n = 199)
Filtered P-wave duration (ms)	133	130	131
P-wave integral (μV-ms)	990	900	950

Separation of Patients with Paroxysmal Atrial Fibrillation from Control

Criteria: The criterion as defined by the upper 90th percentile value of filtered P-wave duration for Group 1 men (n = 91) was 133 ms, while it was 130 ms for women (n = 108; see Table V). The 90th percentile value for all of Group 1 (n = 199) was 131 ms. The 90th percentile value of P-wave integral was 990 μV-ms for men, 900 μV-ms for women, and 950 μV-ms for all.

Identification of patients with paroxysmal atrial fibrillation using filtered P-wave duration: Using the gender-specific criterion for the filtered P-wave duration, the sensitivity for identification of patients with paroxysmal AF was nearly the same for men (80%) and women (81%, see Table VI). Cutoff values for the criterion were chosen at the 90th percentile of the distribution. As expected, the specificity was nearly the same for men (92%) and women (90%). While the positive predictive values (PPVs) were different (84 and 73% for men and women, respectively), the negative predictive values (NPVs) were very similar (90 and 93%, respectively). When the common criterion of 131 ms was used, the overall sensitivity was the same (80%) for men, women, and all patients with paroxysmal AF. However, with this criterion, the specificity, PPV, and NPV were about 5% lower for men (89, 78, and 90%, respectively) than for women (94, 83, and 94%, respectively). In interpreting the values of PPV and NPV (Table VI), it is important to note these values are applicable for the proportion of 2-to-5 of patients with paroxysmal AF to normal controls tested in this study, and these predictive values are expected to be different if this proportion changes.

TABLE VI Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) using different criteria for filtered P-wave duration and P-wave integral

Filtered P-wave duration criterion	Gender	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
133 ms	Men	80	92	84	90
130 ms	Women	81	90	73	93
	Men	80	89	78	90
131 ms	Women	80	94	83	94
	All	80	92	80	92
P-wave integral criterion					
990 μV-ms	Men	27	91	60	72
900 μV-ms	Women	44	91	62	83
950 μV-ms	All	36	90	60	78

Identification of patients with paroxysmal atrial fibrillation using P-wave integral: Using the gender-specific criterion for P-wave integral, the sensitivity and specificity were 27 and 91% for men and 44 and 91% for women. When a gender-neutral criterion was used on all patients with paroxysmal AF and normal controls, the sensitivity and specificity were 36 and 90%, respectively. These accuracy measurements were substantially lower than the corresponding measurements for filtered P-wave duration. The PPV (60 to 62%) and NPV (73 to 83%) were also lower for P-wave integral than for the filtered P-wave duration.

Figure 5 shows the receiver-operator-characteristic curves for filtered P-wave duration and P-wave integral. It is obvious from this figure that filtered P-wave duration provides a better separation between normal controls and patients with paroxysmal AF (area under the curve = 0.9) than the P-wave integral (area under the curve = 0.7).

Discussion

In this study, we found that the automated P-wave-triggered, high-resolution, signal-averaged P wave was abnormally prolonged in patients with paroxysmal AF compared with normal controls. Although these findings replicate several previous reports of a similar nature, the unique features of this study were (1) the large number of normal controls and patients with paroxysmal AF, (2) evaluation of gender-specific differences in PSAECG parameters and the resulting criteria, (3) examination of age dependence of PWSAECG parameters, and (4) analysis of the reproducibility of the PWSAECG parameters. In addition, this is the first study reporting criteria,

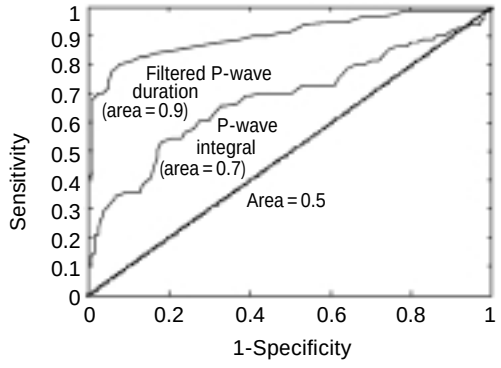

FIG. 5 Receiver-operator-characteristic (ROC) curve for filtered P-wave duration and P-wave integral for detection of paroxysmal atrial fibrillation. Filtered P-wave duration had higher accuracy (area under the curve = 0.9) than the P-wave integral (area under the curve = 0.7).

sensitivity, and specificity for paroxysmal AF using a new signal-averaged P-wave system that uses a P-wave trigger for correlation and spectral filter for high-pass filtering the averaged signals. Each of these features is discussed below.

As the number of normal subjects (n = 199) and patients with paroxysmal AF (n = 81) was large compared with previous studies, we were able to establish normal values for the P-wave signal-averaged ECG and test their accuracy in identifying patients with paroxysmal AF. In normal subjects, women had a shorter duration of the filtered P wave by 3 ms and a lower P-wave integral by 90 μV-ms than did men. These findings could affect interpretation of the P-wave signal-averaged ECG. In the present study, use of the gender-specific criterion for filtered P-wave duration yielded nearly the same sensitivity and specificity for men and women. In contrast, when a gender-neutral criterion was used, the specificity differed by 5% between men and women, while the sensitivity remained the same. Gender differences in the PWSAECG parameters have not been studied adequately;[10] however, differences of 2 to 6 ms in the P-wave duration (measured from conventional 12-lead ECG) between men and women of different age groups have been reported.[11] In the absence of information on atrial size and intra-atrial conduction times, any explanation for difference in P-wave duration in men and women is likely to be speculative.

In the present study, the PWASECG parameters did not correlate with age in either of the two groups. That allows for the criteria developed on younger normal controls (90th percentile values) to be used on generally older patients with paroxysmal AF. The authors are not aware of any studies that have examined the age-dependence of the PWSAECG parameters; however, MacFarlane and Lawrie have reported a small increase in P-wave duration (1 to 5 ms, measured from conventional 12-lead ECG) with increasing age both in men and women, but this is considered to be of "limited practical significance."[11]

The PWSAECG parameters in this study were highly reproducible for filtered P-wave duration and P-wave integral. The regression was better for the filtered P-wave duration than for the P-wave integral. There have been several reproducibility studies on PWASECG parameters.[12–16] Although these studies used different methods of evaluating the reproducibility (regression analysis,[13, 14] coefficient of variation,[12] coefficient of reproducibility,[15] and percent variation[16]), and manual determination of the filtered P-wave onset and offset,[12–14] all of them found that the filtered P-wave duration was highly reproducible, a finding similar to that of the present study. These studies also found that the reproducibility of other PWSAECG parameters such as terminal RMS voltage, spatial velocity, frequency domain measures, were rather poor,[14–16] thus questioning the utility of these parameters for prediction of atrial arrhythmias.[15]

This is the first study reporting criteria, sensitivity, and specificity for identifying patients with paroxysmal AF using a new signal-averaged P-wave system that detects P waves and uses a P-wave template and a P-wave trigger for correlation in signal averaging. This system also uses a spectral filter for high-pass filtering of the averaged signals to delineate P-wave onset and offset. As the PWSAECG parameters are often dependent on features of the system used for signal averaging and analysis, particularly, the filtering method and pass band of the filter,[13, 17, 18] it is imperative to develop and test the criteria that are specific to the system. Earlier studies used systems that were different from the system used in the present study. Accordingly, the criteria for identifying patients prone to paroxysmal AF were also different.

Clinical Significance of Present Findings

This study provides further evidence that the high-resolution, signal-averaged ECG detects changes in patients with paroxysmal AF. It is likely that the prolongation of the filtered P wave reflects conduction abnormalities in the atria that are probably the cause rather than the result of AF. This is supported by the observation that not all patients with paroxysmal AF have abnormal SAECG parameters, and that progression to chronic AF is much more likely in those with the above abnormalities. If this surmise is indeed true, the P-wave SAECG could potentially be used to identify patients at risk for paroxysmal AF. It is well known that patients with paroxysmal and chronic AF are at increased risk for thromboembolic disease and, in fact, the consequences of embolic disease can be the first manifestation of AF. Second, AF begets AF, and intuitively preemptive treatment will likely be more successful. The medical and economic consequences of early detection and prevention are likely to be significant, considering that AF is probably the most common arrhythmia encountered.

The pathogenesis of AF is probably multifactorial. By its ability to identify slow conduction within the atrium, P-wave SAECG may be helpful in differentiating patients with conduction abnormalities from those with predominant functional abnormalities (vagally mediated AF). The therapeutic potential for this differentiation has not been clearly defined at present but is likely to be significant.

Limitations of This Study

Because of the lack of electrophysiologic conduction studies, prolongation of the filtered P wave could not be correlated with atrial conduction abnormalities. However, previous electrophysiologic studies have demonstrated that the filtered P-wave duration can identify intra-atrial conduction delay[19] and latent atrial vulnerability.[20] Second, atrial size was unavailable; however, a previous study has shown that P-wave duration does not correlate with atrial size as assessed by echocardiography.[21] Another study found that the filtered P-wave duration was a better predictor of AF than echocardiographic atrial size.[22] A third limitation of this study was that the control subjects were younger than the patients. We do not think that this has biased our results, as we were unable to demonstrate any correlation between age and filtered P-wave duration in either patients or controls. Also, the criteria developed on control subjects (90th percentile values) were applied to the same group (i.e., training and test sets were the same) to compute specificity. Although a dif-

ferent test group would have been desirable for determining the specificity, the large number of controls in this study (n = 199) suggests that it would be reasonable to expect similar specificity on other controls.

Conclusion

Utilizing high-resolution signal averaging of the P wave, the duration of the filtered P wave is significantly prolonged in patients with paroxysmal AF. While the P-wave integral had lower sensitivity and specificity than the filtered P-wave duration, the RMS voltages in terminal P wave had no discriminating power. In normal subjects, women had shorter filtered P-wave duration than men. These gender differences may represent smaller atrial size in women, differences in the pathogenesis of AF, or other factors. Regardless of the cause of these gender differences, gender-specific values may have a potential for improving the accuracy of identifying patients at risk for atrial fibrillation. In normal controls the filtered P-wave duration and P-wave integral were independent of age, thus facilitating the use of age-independent criteria.

References

1. Fukunami M, Yamada T, Ohmori M, Kumagai K, Umemoto K, Sakai A, Kondoh N, Minamino T, Hoki N: Detection of patients at risk for paroxysmal atrial fibrillation during sinus rhythm by P-wave-triggered signal averaged electrocardiogram. *Circulation* 1991;84:2606–2607
2. Opolski G, Stanislawska J, Stomka K, Kraska T: Value of the atrial signal averaged electrocardiogram in identifying patients with paroxysmal atrial fibrillation. *Int J Cardiol* 1991;30:315–319
3. Stafford PJ, Turner I, Vincent R: Quantitative analysis of signal averaged P waves in idiopathic paroxysmal atrial fibrillation. *Am J Cardiol* 1991;68:751–755
4. Guidera SA, Steinberg JS: The signal averaged P wave duration: A rapid and noninvasive marker of risk of atrial fibrillation. *J Am Coll Cardiol* 1993;21:1645–1651
5. Villani GQ, Piepoli M, Cripps T, Rosi A, Gazzola U: Atrial late potentials in patients with paroxysmal atrial fibrillation detected using a high gain, signal averaged esophageal lead. *PACE* 1994;17: 1118–1123
6. Stafford PJ, Robinson D, Vincent R: Optimal analysis of the signal averaged P wave in patients with paroxysmal atrial fibrillation. *Br Heart J* 1995;74:413–418
7. Gondo N, Kumagai K, Matsuo K, Ogawa M, Annoura M, Moroe K, Arakawa K: The best criterion for discrimination between patients with and without paroxysmal atrial fibrillation on signal averaged electrocardiogram. *Am J Cardiol* 1995;75:93–95
8. Xue Q, Reddy S, Dhala A: High-resolution P wave averaged electrocardiogram for evaluation of patients prone to atrial fibrillation. In *Electrocardiology*, p. 139–142. '96, Proc. XXIII Internatl. Congress Electrocardiol., Singapore: World Scientific Publishers, 1996
9. Chauvin M, Caillard JB, Koenig A, Brechenmacher C: P-wave signal averaged ECG: New algorithms for detecting patients at risk of atrial fibrillation (abstr). *Circulation* 1994;90(Pt 2):I-437
10. Dhala A, Underwood D, Madu E, Angel J, Multicenter P HiRes Study: Gender specific differences in the p wave signal averaged electrocardiogram (abstr). Circulation 1996;94:I-70
11. MacFarlane P, Lawrie TDV: *Comprehensive Electrocardiography—Theory and Practice in Health and Disease*, vol. 1, p. 438. New York: Pergamon Press, 1989
12. Christiansen EH, Frost L, Pilegaard H, Toftegaard-Nielsen T, Pedersen AK: Within- and between-patient variation of the signal averaged P wave in coronary artery disease. *PACE* 1996;19:72–81
13. Hofmann M, Goedel-Meinen L, Beckhoff A, Rehbach K, Schomig A: Analysis of the P wave in the signal averaged electrocardiogram: Normal values and reproducibility. *PACE* 1996;19(Pt. II):1928–1932
14. Ehlert FA, Zaman N, Steinberg JS: Immediate and short-term reproducibility of the P wave signal averaged electrocardiogram. *PACE* 1997;20:1636–1645
15. Stafford PJ, Cooper J, Fothergill J, Schlindwein F, deBono DP, Garratt CJ: Reproducibility of the signal averaged P wave: Time and frequency domain analysis. *Heart* 1997;77:412–416
16. Yamada T, Fukunami M, Shimonagata T, Kumagai K, Kim J, Sanada S, Ogita H, Hoki N: Reproducibility and long-term change of the P wave-triggered signal averaged ECG (abstr). *J Am Coll Cardiol* 1997;29:30A
17. Ehlert FA, Korenstein D, Steinberg JS: Evaluation of P wave signal averaged electrocardiographic filtering and analysis methods. *Am Heart J* 1997;134:985–993
18. Valverde ER, Quinteiro RA, Bertran GC, Arini PD, Glenny P, Biagetti MO: Influence of filtering techniques on the time-domain analysis of signal averaged P wave electrocardiogram. *J Cardiovasc Electrophysiol* 1998;9:253–260
19. Pellerin D, Attuel P, Davy JM, Slama M, Motte G: Evaluation of signal averaged P-wave in patients with and without history of atrial arrhythmias. Comparison with ECG and electrophysiological study. *Eur Heart J* 1991;12(suppl):278
20. Gencel L, Poquet F, Gosse P, Haissaguerre M, Marcus FI, Clementy J: Correlation of signal averaged P wave with electrophysiological testing for atrial vulnerability in strokes of unexplained etiology. *PACE* 1994;17(Part II):2118–2124
21. Zelenkofske SL, Brown E, Mogtader A, Menchavez E, Steinberg JS: Prolonged SAECG P-wave duration is not due to atrial enlargement (abstr). *Circulation* 1993;88:I-311
22. Stafford PJ, Kolvekar S, Cooper J, Fothergill J, Schlindwein F, deBono DP, Spyt TJ, Farratt CJ: Signal averaged P wave compared with standard electrocardiography or echocardiography for prediction of atrial fibrillation after coronary bypass grafting. *Heart* 1997; 77:417–422

Appendix

Multicenter PHi-Res Study Participants

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Clinical Centers

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