The Predictive Value of P-Wave Duration by Signal-Averaged Electrocardiogram in Acute ST Elevation Myocardial Infarction

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ABSTRACT: **Background:** The prognostic value of P-wave duration has been previously evaluated by signal-averaged ECG (SAECG) in patients with various arrhythmias not associated with acute myocardial infarction (AMI).

Objectives: To investigate the clinical correlates and prognostic value of P-wave duration in patients with ST elevation AMI (STEMI).

Methods: The patients (n=89) were evaluated on the first, second and third day after admission, as well as one week and one month post-AMI. Survival was determined 2 years after the index STEMI.

Results: In comparison with the upper normal range of P-wave duration (< 120 msec), the P-wave duration in STEMI patients was significantly increased on the first day (135.31 ± 29.29 msec, $P < 0.001$), up to day 7 (127.17 ± 30.02 msec, $P = 0.0455$). The most prominent differences were observed in patients with left ventricular ejection fraction (LVEF) ≤ 40% (155.47 ± 33.8 msec), compared to LVEF > 40% (128.79 ± 28 msec) ($P = 0.001$). P-wave duration above 120 msec was significantly correlated with increased complication rate; namely, sustained ventricular tachyarrhythmia (36%), congestive heart failure (41%), atrial fibrillation (11%), recurrent angina (14%), and re-infarction (8%) ($P = 0.012$, odds ratio 4.267, 95% confidence interval 1.37–13.32). P-wave duration of 126 msec on the day of admission was found to have the highest predictive value for in-hospital complications including LVEF < 40% (area under the curve 0.741, $P < 0.001$). However, we did not find a significant correlation between P-wave duration and mortality after multivariate analysis.

Conclusions: P-wave duration as evaluated by SAECG correlates negatively with LVEF post-STEMI, and P-wave duration above 126 msec can be utilized as a non-invasive predictor of in-hospital complications and low LVEF following STEMI.

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The surface 12-lead electrocardiogram is a simple non-invasive inexpensive tool for the assessment of cardiac function and hemodynamic status [1-5]. The effect of atrial chamber anatomy and physiology on the P-wave morphology is still controversial. As reported previously [6-11], changes in the P-wave may indicate left or right atrial hypertrophy and/or dilatation, electrical conduction abnormalities, or a combination of these. The P-wave morphology is dynamic in patients with acute myocardial infarction, stable angina and ischemia precipitated by exercise stress test or balloon angioplasty [6-14].

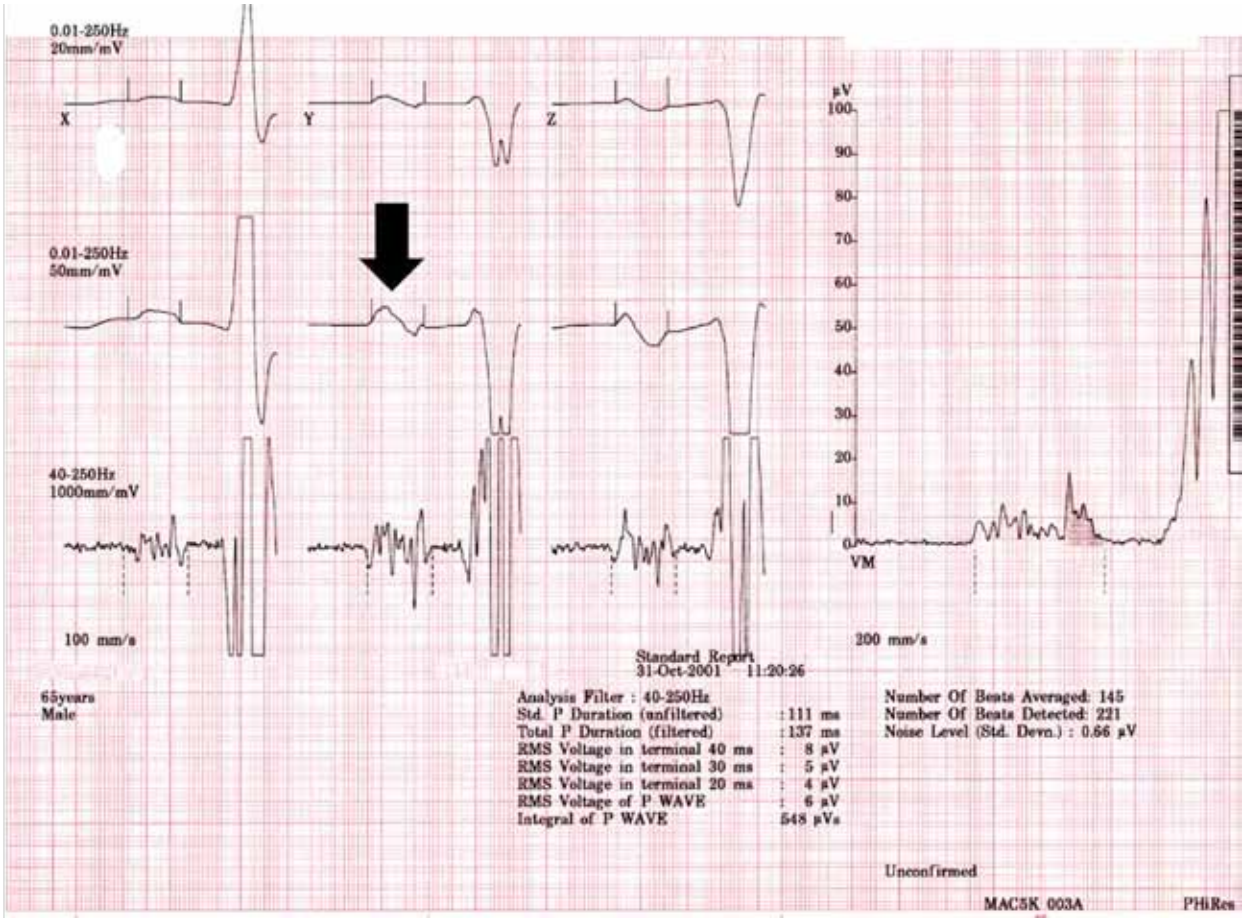
Previously, attention was drawn to the prognostic value of P-wave duration evaluated by signal-averaged ECG in patients with various arrhythmias, not associated with AMI [15]. SAECG P-wave analysis offers precise information on atrial conduction for improved pathophysiological understanding and prognostic determination in cardiac ischemia and failure. Only a few studies have been published on assessment of P-wave duration by SAECG in patients with AMI [7-9]. Moreover, scarce data exist correlating the clinical data obtained from echocardiography and coronary angiography with the P-wave assessment by SAECG. We therefore evaluated the clinical correlates and prognostic value of the P-wave duration in patients with ST elevation AMI.

PATIENTS AND METHODS

This study was approved by the institutional review board. The study population comprised 100 consecutive patients admitted to the intensive cardiac care unit with STEMI. Eleven of the 100 patients were excluded due to chronic atrial fibrillation or flutter, supraventricular arrhythmias during the first 24 hours of their admission, permanent pacemaker implantation, or due to technical reasons. The patients were evaluated on the first, second and third days after admission, as well as one week and one month post-AMI. At each time point, a standard 12-lead ECG was performed, as well as fil-

AMI = acute myocardial infarction
SAECG = signal-averaged electrocardiograph
STEMI = ST elevation AMI

Figure 1. SAECG obtained on the first day after admission of a 65 year old patient with anterolateral STEMI. The P-wave duration (arrow) was 137 msec. The patient had severely decreased LVEF on echocardiography and later developed pulmonary edema, sustained ventricular tachycardia and paroxysmal atrial fibrillation during the in-hospital course



tered and non-filtered signal-averaged P-wave ECG examination with the Marquette Mac 5000™ Resting ECG Analysis System (General Electric, USA) using filtered frequency of 4O–25O Hz. This P-wave signal-averaging system features a templating algorithm that enhances measurement accuracy by maximizing signal fidelity. Multiple subsequent P-wave potentials are acquired to remove interference due to skeletal muscle and to obtain a statistically significant average trace. SAECG recording yields a single, averaged potential, usually printed in a much larger scale than standard ECG, upon which the SAECG software performs calculations to reveal small variations (typically 1–25 mV) in the P-wave [Figure 1]. A pathological P-wave duration was determined as ≥ 120 msec [16]. The examinations were performed in the intensive care unit. Two-dimensional, M-Mode and Doppler echocardiography were performed according to standard methods.

Sixty-three patients underwent coronary angiography before discharge. Significant left ventricular dysfunction was defined as left ventricular ejection fraction < 40%, as assessed on the second day of admission by transthoracic echocardiography with either visual estimation or the Simpson method. The patients were followed periodically in the cardiology outpatient clinic. A telephone call survey was conducted 2 years after the index AMI.

STATISTICAL ANALYSIS

The P-wave duration at various time points and in various groups of patients (as classified according to their clinical status) was documented as an average and median values. The percentage of patients who were within the normal range of P-wave duration (up to 120 msec) was calculated at all time points. The *t*-test for a single sample was used to evaluate whether the P-wave duration on the first day was significantly higher than 120 msec. Differences in P-wave duration were assessed in patients with and without complications and also in patients with normal LV function compared to those with decreased LV function by

LV = left ventricular

means of the unpaired *t*-test or the Wilcoxon rank sum test at all time points. Patients who died were excluded from the temporal analysis. With the aid of statistical tests (Fisher's exact test and chi-square test), the differences between male and female patients with an abnormally prolonged P-wave were calculated. We used multivariate logistic regression analysis to assess the relationship between P-wave prolongation (above 120 msec) and in-hospital complication rate. In this manner, cutoff points were decided by calculating the rate of complications for P-wave duration, after classifying them. Sensitivity and specificity were calculated for these points. Our model included the following parameters that were found to be statistically significant on a univariate analysis: age above 65, diabetes, reduced LV function, female gender and P-wave duration.

RESULTS

We studied 89 patients. Their mean age was 61 ± 14 years, 84% were males, 17% had previous AMI, 47% were hypertensive, 29% were diabetic, 44% had hyperlipidemia, and 57% had a smoking history. Thrombolytic therapy was administered to 60% of the patients, of whom 50% had anterior STEMI, 35% inferior STEMI, and 15% posterior or posterolateral STEMI. Among the patients who underwent coronary angiography, percutaneous coronary intervention was performed in 41, and 7 patients underwent coronary artery bypass surgery. The complications during the first 30 days following the index STEMI were sustained ventricular tachyarrhythmia (36%), congestive heart failure (41%), atrial fibrillation (11%), recurrent angina (14%) and re-infarction (8%). Four patients died in hospital (4.6%).

The mean P-wave duration on the first day was 135.3 ± 29 msec (compared to 120 msec, $P < 0.001$), 126 ± 25 msec on the second day of admission ($P = 0.0075$), 130.3 ± 32 msec on the third day ($P = 0.0015$), 127.2 ± 30 msec on the 7th day ($P = 0.0455$), and 121.9 ± 15 msec ($P = 0.186$) 30 days after the index STEMI. We found a borderline significant trend of reduction in P-wave duration for the first 3 days ($P = 0.068$). Using Wilcoxon signed rank test we found a significant decline from day 1 to day 2 ($P < 0.001$), but not from day 2 to day 3. In addition, a substantial difference in P-wave duration was noted between groups of patients with and without complications during recovery from STEMI [Table 1].

We observed an increase in P-wave duration among patients with overt cardiac failure as well as in patients with cardiac arrhythmias following STEMI. The most prominent differences in P-wave duration were observed between patients with LVEF ≥ 40% and patients with LVEF < 40% as determined by transthoracic echocardiography [Table 2].

In order to assess the utility of P-wave duration as a

Table 1. Signal-averaged P-wave duration in patients with and without post-MI complications

	Without complications				With complications				
	Mean ± SD	Median**	Range	N	Mean ± SD	Median**	Range	N	*P* value*
First day	124.29 ± 21.84	121	90–198	45	146.59 ± 31.79	136.5	100–234	44	< 0.0001
Second day	118.47 ± 19.72	116	82–175	45	135.62 ± 27.99	131	96–230	42	< 0.0001
Third day	120.78 ± 23.85	115	89–179	45	142.47 ± 36.12	130	92–225	38	0.00001
One week	113.77 ± 16.48	116	63–143	26	140.58 ± 34.54	126.5	103–254	26	0.00001
One month	117.32 ± 14.57	120	85–148	28	127.57 ± 14.84	128	97–154	23	0.00001

* Wilcoxon Rank Sum Test
** In order to eliminate the influence of extreme P-wave durations, a median value was used for comparison

Table 2. Correlation of the P-wave duration to cardiac function

	First day	Second day	Third day	One week	One month
LVEF > 40%					
Mean ± SD	128.79 ± 28	120.21 ± 20.4	125.25 ± 26.8	114.05 ± 21.7	118.78 ± 16.5
Median	123	118	116.5	116	119.5
Range	96–234	82–175	89–179	63–168	85–148
N	33	33	32	19	18
LVEF ≤ 40%					
Mean ± SD	155.47 ± 33.8	151.69 ± 33.36	162.85 ± 39.04	151.55 ± 43.83	138.00 ± 6.88
Median	149	154	167	148	140
Range	100–218	101–230	110–225	108–254	133–148
N	17	16	13	11	4
P	0.001	< 0.001	0.002	0.008	0.018

Table 3. Multivariate regression analysis of the correlation of P-wave duration with complication rate following STEMI

	Odds ratio	95% confidence interval	Standard error	*P* value
P-wave	4.27	1.37–13.32	0.58	0.012
Diabetes	0.69	0.22–2.12	0.58	0.532
LVEF < 40%	8.02	2.50–25.72	0.59	0.0001
Age > 65 yrs	3.57	1.13–11.35	0.59	0.029
Female	0.58	0.12–2.89	0.82	0.506

LVEF = left ventricular ejection fraction

clinical tool for prediction of in-hospital complications and LV dysfunction, we performed a receiver operating curve analysis. We found that a P-wave duration of 126 msec had the highest area under the curve, 0.741 ($P < 0.001$), with 79.5% sensitivity and 60% specificity.

Four patients died in hospital during this study. The P-wave duration that was recorded in those patients on the first day was substantially long (157 ± 29 msec), as compared to the average P-wave duration recorded for the whole study population (135 ± 28 msec, $P = 0.041$), and as compared to those who survived (125 ± 29 msec, $P < 0.001$).

CLINICAL FOLLOW-UP

A telephonic follow-up 2 years after admission revealed that 11 patients had died due to cardiac causes during that period, including the 4 patients who died in hospital. A retrospective assessment of P-wave duration on the first day of admission in those patients found a significant P-wave prolongation, in comparison to the rest of the study group (147.1 ± 30.6 vs. 125.44 ± 22.6 msec, $P = 0.006$).

A P-wave duration above 120 msec significantly correlated with the 30 days complication rate, using multivariate logistic regression analysis [Table 3] ($P = 0.012$, odds ratio 4.267, 95% confidence interval 1.37–13.32). We did not find a significant correlation of mortality with P-wave duration by multivariate analysis.

DISCUSSION

Our study is unique in reporting the evolution of P-wave duration over the first month after the acute phase of STEMI and in assessing the long-term (2 year) prognostic power of this non-invasive marker. The study shows a positive correlation of the P-wave prolongation as measured by SAECG with the in-hospital and 30 day complication rate post-STEMI, but not with the 2 year survival rate. Our study also shows a negative correlation with the severity of LV dysfunction in the first days after STEMI.

Filtered SAECG enables signals of low electrical noise to be recorded, thus low level cardiac signals that might be important in several morbid conditions can be identified [17]. It is relatively easy to perform, does not require a high level of expertise, and is not an invasive procedure. Signal averaging followed by augmentation and filtration enables precise measurement of the duration and amplitude of the P-wave. The P-wave represents the electrical atrial depolarization time. It consists of the summation of various electrical vectors recorded along the atrial tissue. In various cardiac diseases, delayed conduction can be caused by prolonged and inconsistent depolarization, in part due to left atrial enlargement [18]. Wave prolongation can reflect increased ventricular end-diastolic pressure and wall stretching, and may occur even prior to other ECG changes in patients with coronary artery disease [19]. Non-homogenous propagation of atrial impulse may be due to microstructural and diverse electrical changes, pressure overload, and increased size of cardiac chambers, wall thickness and volume.

Our study shows that P-wave duration as measured by SAECG correlates with LV systolic function and in-hospital complication rate. P-wave duration of ≥ 126 msec on admission was found to predict a high in-hospital complication rate or decreased LV function. This value can be used as a simple risk marker of patients at risk for arrhythmic complications or post-STEMI heart failure [20]. A similar correlation was also found between clinical convalescence and patients' prognosis (expressed by the increased complication rate) and a prolongation of the P-wave. A clear example of those findings can be seen by focusing on the measurements conducted in the four patients who died in hospital during this study. Moreover, 11 patients died during the 2 year follow-up. The magnitude of their P-wave recording on their admission was significantly higher than the upper limit of normal or of those who survived, again showing the prognostic value of SAECG P-wave duration. However, we did not find a significant correlation with P-wave prolongation by using multivariate analysis, possibly due to the small sample size.

Our study has several limitations. Apart from being relatively small, it was performed under conditions that were not ideal, considering the numerous pieces of electronic instrumentation used in the ICU. Therefore, one cannot exclude the effect of interference from other factors such as electromagnetic field or other mechanical noises on the results of the P-wave duration measurement. Certain information was not taken into consideration, such as blood volume and arterial blood pressure measured when patients suffered pain and the effect of previous medical treatment. It is important to note, however, that during hospitalization all the patients received treatment according to clinical guidelines. This included antihypertensive medications, fluid and electrolyte management, and analgesics. P-wave duration on the first day of STEMI was compared with the upper normal range of P-wave and not with P-wave duration before STEMI onset on an individual basis. Since P-wave duration differs in different subjects, this could mask the real degree of P-wave prolongation on an individual basis. Unfortunately, it is unlikely that this limitation can be overcome in any future study of patients with STEMI.

In conclusion, P-wave duration correlates negatively with left ventricular function post-STEMI. The prolongation of filtered signal-averaged P-wave duration above 126 msec can be utilized as a non-invasive marker and predictor of complications during the in-hospital and short-term period following STEMI.

ICU = intensive care unit

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