Abnormal P-Wave Morphology Is a Predictor of Atrial Fibrillation Development and Cardiac Death in MADIT II Patients

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Background: Several ECG-based approaches have been shown to add value when risk-stratifying patients with congestive heart failure, but little attention has been paid to the prognostic value of abnormal atrial depolarization in this context. The aim of this study was to noninvasively analyze the atrial depolarization phase to identify markers associated with increased risk of mortality, deterioration of heart failure, and development of atrial fibrillation (AF) in a high-risk population with advanced congestive heart failure and a history of acute myocardial infarction.

Methods: Patients included in the Multicenter Automatic Defibrillator Implantation Trial II (MADIT II) with sinus rhythm at baseline were studied (n = 802). Unfiltered and band-pass filtered signal-averaged P waves were analyzed to determine orthogonal P-wave morphology (prespecified types 1, 2, and 3/atypical), P-wave duration, and RMS20. The association between P-wave parameters and data on the clinical course and cardiac events during a mean follow-up of 20 months was analyzed.

Results: P-wave duration was 139 ± 23 ms and the RMS20 was 1.9 ± 1.1 μ V. None of these parameters was significantly associated with poor cardiac outcome or AF development. After adjustment for clinical covariates, abnormal P-wave morphology was found to be independently predictive of nonsudden cardiac death (HR 2.66; 95% CI 1.41–5.04, P = 0.0027) and AF development (HR 1.75; 95% CI 1.10–2.79, P = 0.019).

Conclusion: Abnormalities in P-wave morphology recorded from orthogonal leads in surface ECG are independently predictive of increased risk of nonsudden cardiac death and AF development in MADIT II patients.

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atrial electrophysiology; ischemic heart disease; ICD; atrial fibrillation; ECG

Although risk stratification and prediction of clinical outcome in patients with congestive heart failure (CHF) are traditionally based on a combination of demographical, clinical, electrophysiological, functional, and biochemical factors,¹ the ECG alone may serve as an important source of prognostic information. Several approaches from straightforward QRS width estimation or identification of subjects with cardiac arrhythmias, such as atrial fibrillation (AF) to more sophisticated computer-based analyses, for example, estimations of T-

wave alternans and heart rate variability have been shown to add value when risk stratifying CHF patients.² However, little attention has been paid to the prognostic value of abnormal atrial depolarization in this context. Despite known associations between abnormal P-wave morphologies and left atrial enlargement and overload in patients with CHF, prospective studies evaluating the possible link between P-wave morphologies and the risk of death are lacking. Two reports published in the 1970s demonstrated the prognostic value of

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abnormal left atrial activation with respect to long-term follow-up, in patients surviving acute myocardial infarction.^{3,4}

A noninvasive ECG analysis tool that allows detailed description of P-wave morphology has been developed that includes signal averaging of P waves and automatic classification of P-wave morphology (PSA-ECG).⁵ Using this technique, we have identified P-wave morphologies associated with a history of AF⁶ as well as age-related P-wave changes in healthy individuals.⁷ In a recent study, we demonstrated a significant link between different P-wave morphologies and different patterns of interatrial conduction in patients with paroxysmal AF without structural heart disease.⁸

The objective of this study was to analyze noninvasively the atrial depolarization phase to identify markers associated with increased risk of mortality, deterioration of heart failure, and development of AF in a high-risk population with advanced CHF and a history of acute myocardial infarction who participated in the Multicenter Automatic Defibrillator Implantation Trial II (MADIT II).⁹

METHODS

Study Population and Clinical Characteristics

The design and results of MADIT II have been reported elsewhere.⁹ Briefly, the study included 1232 patients with documented ischemic heart disease (myocardial infarction over 1 month prior to enrolment) and ejection fraction $\leq 30\%$. Patients were randomized to ICD or conventional treatment in a 3:2 fashion. Patients were followed for a mean of 20 months. Exclusion criteria included existing ICD indications, New York Heart Association (NYHA) class IV (within the past 3 months), myocardial infarction within the past month, coronary revascularization within the past 3 months, and other advanced comorbidities. There were no requirements regarding baseline ECG rhythm in MADIT II, but for analyses purposes only patients in sinus rhythm were included in this study. Clinical and demographic data collected at enrolment included information regarding age, gender, race, body mass index, history of myocardial infarction, date of most recent myocardial infarction, hypertension, smoking, diabetes, prior revascularization procedures, and NYHA class. Data regarding medication, ejec-

tion fraction, blood pressure, and blood urea nitrogen (BUN) were also obtained at enrolment.

Study End Points

The primary end point of MADIT II was all-cause mortality.⁹ Secondary end points for this analysis included cardiac death, sudden and nonsudden (categorized as described by Greenberg et al.),¹⁰ hospitalization for CHF, the combined end point of CHF hospitalization and all-cause mortality, ICD efficacy, and finally the probability of AF development. Detection of AF during follow-up was based on clinical evaluation supported by identification of AF on 12-lead ECG.

Data Acquisition and Analysis

A 10-minute high-resolution (1 kHz) bipolar ECG recording (SpaceLab-Burdick 6632 recorder, SpaceLab-Burdick, Milton, WI, USA) was obtained at enrolment of the MADIT II patients. Data analysis was performed using custom-made software running on MATLAB R2007a for Mac OS X (The MathWorks, Inc., Natick, MA, USA). Unfiltered, signal-averaged P waves were analyzed to determine P-wave morphology.^{5,11} Following high-pass (0.5 Hz) and band-stop (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.^{5,11}

Using the previously extracted signal windows of similar morphology, additional band-pass filtered signal-averaged P-wave analysis was performed. The vector magnitude ($\sqrt{X^2 + Y^2 + Z^2}$) was calculated and band-pass filtered using a bidirectional four-pole Butterworth filter with 40 Hz high-pass cutoff. Signal noise was measured as the root mean square (RMS) value of a 40-ms interval in the TP segment of the filtered signal,¹² and P waves were added to the average until a noise level below 0.1 μV was obtained. If the noise level could not be obtained, the recording was discarded from this

analysis. Onset and end of the band-pass filtered vector magnitude was defined as the midpoint of 5-ms segments where the RMS level exceeded the noise level plus three standard deviations.¹² If no point was found that fulfilled this criterion at the P-wave end, the interval with the lowest RMS value in the PQ segment was used as end. P-wave duration and the RMS value of terminal 20 ms of the P wave (RMS20) were analyzed.

Definitions

The P-wave morphology was 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(-/+)) using an automatic algorithm.⁵ P-wave morphologies, compatible with block or delayed conduction in one or more of the interatrial conduction routes (i.e., type 2, type 3 or atypical),⁸ are collectively denoted "abnormal P wave morphology" in the manuscript.

Statistics

Data are expressed as the mean $\pm$ standard deviation. The Mann-Whitney *U* or Kruskal-Wallis test was used to analyze unpaired data. The chi-square test was used when analyzing nominal data. Kaplan-Meier curves with log-rank statistics were used to analyze time to end point events. Cox proportional hazards analyses were used to determine hazard ratios associated with abnormal P-wave morphology. The estimated hazard ratios refer to the increased risk in each P-wave morphology-type step (i.e., from type 1 to 2 and from type 2 to 3/atypical). These analyses were adjusted for relevant baseline risk factors. All tests were two-sided and $P < 0.05$ was considered statistically significant.

Results

Data Availability

At enrolment 912 (74%) of the 1232 patients were found to be in sinus rhythm, excluding patients with pacemaker rhythm and AF. Of the 912 patients in sinus rhythm 802 (88%) were found to have baseline ECG recordings of sufficient quality for further analysis. The results presented are based on this patient subset.

Clinical Characteristics and P-Wave Morphology Distribution at Enrolment

Patient characteristics and P-wave parameters at baseline are summarized in Table 1. Notably, only a small minority of the studied patients was on treatment with antiarrhythmic drugs. The measured P-wave duration was prolonged compared to standard reference values regardless of measurement methodology (145 ± 19 ms and 139 ± 23 ms unfiltered and band-pass filtered duration). Figure 1 illustrates the distribution of P-wave morphology types in the entire population and typical morphological examples. A majority (60%) of the patients were exhibiting type 2 P-wave morphology whereas only a 16% and 2% of the patients exhibited type 1 and type 3, respectively. Twenty-two percent of the studied subjects had an atypical P-wave morphology. Because of the low number of observed type 3 morphologies, these were analyzed together with the atypical P-wave morphology for the subsequent analyses, after making sure that no relevant differences in baseline parameters existed between these groups (data not shown).

Table 1. Clinical Characteristics in Study Population

MADIT II Patients in SR at Baseline (n = 802)

Age	[Years]	63 $\pm$ 10
Male	[%]	82
History of atrial arr	[%]	18
Hypertension	[%]	54
Diabetes	[%]	34
BMI	[kg/m ²]	28 $\pm$ 5
Systolic BP	[mmHg]	122 $\pm$ 18
Diastolic BP	[mmHg]	71 $\pm$ 11
BUN	[mg/dL]	22 $\pm$ 11
NYHA (I/II/III/IV)	[%]	(37/36/24/4)
LVEF	[%]	23 $\pm$ 5
Digitalis	[%]	70
Beta-blocker	[%]	64
CCB	[%]	13
Sotalol	[%]	1
Class I AA	[%]	3
Amiodarone	[%]	6
Heart rate	[bpm]	69 $\pm$ 14
PWD unfiltered	[ms]	145 $\pm$ 19
PWD filtered	[ms]	139 $\pm$ 23
RMS20	[μ V]	1.9 $\pm$ 1.1
Type (1/2/3/atypical)	[%]	(16/60/2/22)

AA = antiarrhythmic; Arr = arrhythmia; BMI = body mass index; BP = blood pressure; BUN = blood urea nitrogen; CCB = calcium channel blockers; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; PWD = P-wave duration; SR = sinus rhythm.

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 (superior-to-inferior-to-superior). The two morphologies within the red rectangle are illustrations of two distinct patterns seen among the atypical P waves. The meaning of these patterns are yet to be elucidated.

Comparison of Baseline Clinical Characteristics and ECG Parameters Based on P-Wave Morphology Classification

Table 2 summarizes the baseline clinical characteristics and ECG parameters based on P-wave morphology classification. Overall, several baseline characteristics show evidence of a progressive worsening or increase from type 1 to type 2 and type 3/atypical (e.g., age, ejection fraction, heart rate, and QT_c). Patients with type 3/atypical P-wave morphology were less likely to be treated with beta-blocking agents than other patients (P < 0.01). Neither P-wave duration nor RMS20 was significantly different among the P-wave morphology classifications.

P-Wave Morphology and Development of AF

Abnormal P-wave morphology was associated with an increased risk of AF development in the univariate model (P = 0.035). Figure 2 shows the Kaplan-Meier analyses for P-wave morphology type as an indicator of AF development risk. Af-

ter adjusting for age, QRS duration, and treatment arm, the hazard ratio was found to be 1.75 [95% CI 1.10–2.79, P = 0.019]. Table 3 shows the factors included in the Cox regression model for prediction of AF development and their corresponding hazard ratios. None of the other P-wave parameters (i.e., P-wave duration, RMS20) was found to be predictive of AF development, neither in univariate nor in multivariate analyses.

Death and Heart Failure in Relation to P-Wave Morphology

Abnormal P-wave morphology was associated with an increased risk of cardiac death (P = 0.04) and nonsudden cardiac death (P = 0.001). The corresponding Kaplan-Meier curves are shown in Figures 3B–C. Borderline significance was observed for increased risk associated with abnormal P-wave morphology of all-cause mortality (P = 0.077, Fig. 3A), CHF hospitalization (P = 0.098, Fig. 3E) and of the combined end point of CHF hospitalization or death (any cause) (P = 0.051, Fig. 3F), while the outcome analysis of sudden

Table 2. Relation between P-Wave Morphology and Clinical Characteristics

		Type 1 (n = 123)	Type 2 (n = 465)	Type 3/Atypical (n = 185)	P =
Age	[Years]	61 ± 11	62 ± 10	64 ± 10	0.01
Male	[%]	84	82	84	0.78
Hx of atrial arr	[%]	13	17	19	0.38
Hypertension	[%]	48	54	55	0.42
Diabetes	[%]	27	36	34	0.19
BMI	[kg/m ²]	28 ± 5	29 ± 5	28 ± 5	0.03
Systolic BP	[mmHg]	119 ± 17	123 ± 19	121 ± 18	0.03
Diastolic BP	[mmHg]	70 ± 10	71 ± 11	72 ± 11	0.37
NYHA (I/II/III/IV)	[%]	(36/41/20/4)	(39/35/21/4)	(33/34/30/3)	0.26
LVEF	[%]	25 ± 5	23 ± 5	22 ± 6	<0.01
Digitalis	[%]	49	56	53	0.36
Beta-blocker	[%]	65	68	52	<0.01
CCB	[%]	10	14	12	0.52
Sotalol	[%]	0	1	1	0.68
Class I AA	[%]	1	3	5	0.11
Amiodarone	[%]	7	5	6	0.84
Heart rate	[bpm]	70 ± 15	71 ± 15	76 ± 16	<0.01
PWD unfiltered	[ms]	145 ± 19	146 ± 16	146 ± 16	0.65
PWD filtered	[ms]	140 ± 19	138 ± 25	142 ± 17	0.42
RMS20	[μV]	1.8 ± 1.2	1.9 ± 1.1	2.0 ± 1.1	0.19
PQ interval	[ms]	192 ± 30	195 ± 37	195 ± 35	0.97
QRS duration	[ms]	114 ± 30	114 ± 28	121 ± 31	0.02
QT interval	[ms]	414 ± 47	417 ± 55	412 ± 57	0.41
QT _c	[ms]	436 ± 43	438 ± 42	441 ± 43	<0.01

The Kruskal-Wallis test was used to analyze unpaired data. The chi-square test was used when analyzing nominal data. Bold P-values indicate $P < 0.05$. AA = antiarrhythmic; Arr = arrhythmia; BMI = body mass index; BP = blood pressure; BUN = blood urea nitrogen; CCB = calcium channel blocker; Hx = history; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; PWD = P-wave duration; SR = sinus rhythm.

Figure 2. The Kaplan-Meier graph for P-wave morphology as a predictor of AF development. As illustrated by the curves there is a progressive and proportional increase in risk of AF development from type 1 to type 2 to type 3/atypical.

Table 3. Cox Regression Analysis (Time to Atrial Fibrillation)

Variables in the Equation	P Value	HR	95% CI for HR	
Age	<0.01	1.74	1.27	2.38
P-wave morphology	0.02	1.75	1.10	2.79
Treatment arm (ICD: conventional)	0.85	0.95	0.53	1.69
QRS > 120 ms	<0.01	2.67	1.44	4.93

The estimated hazard ratios refer to the increased risk of atrial fibrillation with increasing age (measured in 10-year intervals), each P-wave morphology type step (i.e., from type 1 to 2 and from type 2 to 3/atypical) and finally with ICD treatment and QRS duration exceeding 120 ms. CI = confidence interval; HR = hazard ratio.

cardiac death was highly insignificant ($P = 0.469$, Fig. 3D).

After adjustment for relevant covariates (i.e., ICD treatment, NYHA class, age at inclusion, QRS duration, increased BUN, and ejection fraction), abnormal P-wave morphology was shown to be an independent predictor of nonsudden cardiac death (hazard ratio 2.66 [95% CI 1.41–5.04, $P = 0.0027$]). However, only trends were seen regarding the association of P-wave morphology with cardiac death (hazard ratio 1.40 [95% CI 0.996–1.98, $P = 0.052$]), all-cause mortality (hazard ratio 1.29 [95% CI 0.94–1.90, $P = 0.12$]), CHF hospitalization (hazard ratio 1.21 [95% CI 0.92–1.59, $P = 0.18$]), and CHF hospitalization or all-cause mortality (hazard ratio 1.18 [95% CI 0.93–1.48, $P = 0.17$]). Abnormal P-wave morphology was not shown to be predictive of sudden cardiac death in the multivariate regression model (hazard ratio 1.02 [95% CI 0.65–1.61, $P = 0.93$]). No association between P-wave morphology and ICD efficacy was found (interaction P value 0.373 [univariate analysis] and 0.521 [multivariate analysis])

DISCUSSION

Noninvasive ECG analysis using PSA-ECG in the MADIT II population demonstrated additional value of P-wave morphology analysis for risk stratification of high-risk patients with CHF, a history of myocardial infarction, markedly reduced left ventricular ejection fraction, and prolonged P-wave duration. Abnormal P-wave morphology patterns were shown to be independently predictive of risk for nonsudden cardiac death and the development

of AF. Neither P-wave duration nor RMS20 showed any value in the stratification of risk for these parameters in the MADIT II patients.

ECG-Based Risk Stratification in Patients with Ischemic Heart Disease and CHF

Patients with advanced CHF and a history of myocardial infarction represent a high-risk group in regard to the risk of sudden death. In spite of several known risk factors (e.g., AF development, QRS duration exceeding 120 ms, and the presence of frequent ventricular premature beats),^{13–16} further risk stratification of patients with already known high-risk of sudden cardiac death remains a major clinical challenge.

The interest in P-wave morphology in this setting dates back to mid 1960s when Morris et al. introduced the concept of P-wave negative terminal force (PTF) seen as a pronounced, negative deflection in the terminal portion of the P wave in right precordial leads in patients with known mitral or aortic valve disease.¹⁷ In a registry-based analysis of discharge ECGs of 641 patients who survived the acute phase of myocardial infarction, abnormal PTF (PTF > 0.03 mVs), observed in 11% of the patients, was associated with a nearly two-fold increase in 5-year mortality.⁴ In another, smaller study, abnormal PTF was found to be the main predictor of poor prognosis at 4-year follow-up.³ To the best of our knowledge, no other studies have evaluated the impact of P-wave morphology on mortality in any other patient population since.

The PSA-ECG method enables not only analysis of conventional parameters used for characterization of atrial depolarization (e.g., P-wave duration and RMS20) but also automatic classification of P-wave morphology in orthogonal leads that reflects the vector of atrial depolarization.^{8,11} Our finding of an association between types 2 and 3 P-wave morphology and clinical outcome in ischemic patients with CHF is in agreement with the historical data. Abnormal PTF in V1 is likely to represent the same electrocardiographic entity as a biphasic P-wave morphology in lead Z with extreme, positive terminal deflection, that is, a subset of the type 2 P waves. However, there are several important differences; the automatic classification algorithm used in the PSA-ECG analysis calculates the relative size of the positive and negative deflections of P wave and is therefore independent on the absolute values of P-wave amplitude, which are likely

Figure 3. The Kaplan-Meier graphs show the univariate association between the different P-wave morphologies and all-cause mortality (A); cardiac death (B); nonsudden cardiac death (C); sudden cardiac death (D); CHF hospitalization (E); and the combined end point of CHF hospitalization and cardiac death (F). Notably, for all analyzed variables (with sudden cardiac death as the one exception) the increase in risk seems to be highest for the type 3 or atypical P-wave morphologies and lowest for the type 1 P-wave morphology.

to be affected by extracardiac factors. Moreover, the analysis enables characterization of the entire patient cohort, not limiting the applicability of the findings to the small minority of patients with the most prominent P-wave abnormalities.

Substrate of Variable P-Wave Morphology: Structural, Electrical, or Both?

The pathophysiological processes underlying the different P-wave morphologies are still a matter of debate. Abnormal PTF was initially interpreted as a sign of left atrial overload.^{3,4,17} Subsequent studies using echocardiography reported moderate specificity and poor sensitivity of abnormal PTF for detecting left atrial enlargement.^{18–20} In a recent report using cardiovascular magnetic resonance, abnormal PTF was shown to be a highly specific but insensitive ECG sign of left atrial enlargement.²¹ In a pathology study, abnormal PTF was shown to correlate with left atrial hypertrophy but was also observed in 22% subjects without atrial hypertrophy and 12% structurally normal hearts.²²

Interatrial conduction disturbance was suggested as possible cause of abnormal PTF in 1977.²³ This notion was later confirmed using invasive electrophysiological studies in patients with sick sinus syndrome and paroxysmal AF.²⁴ The high prevalence of biphasic P waves in right precordial leads in healthy subjects^{7,25} gives further support to the hypothesis that primary electrical disturbance, at least in part, explains this electrocardiographic phenomenon. Using electroanatomical mapping, our group has reported a significant association between the different P-wave morphologies and the pattern of left atrial activation during sinus rhythm suggesting that variations in anatomical structure or function of interatrial routes may explain differences in P-wave morphologies, at least in patients without structural heart disease.⁸ However, the structural changes in atrial myocardium associated with increasing age or advanced comorbidity, with secondary left atrial overload and dilatation, inevitably deteriorate the atrial conductive properties and may cause abnormal atrial activation reflected in prolonged P waves or changes in P-wave morphology. Although no data on left atrial size were systematically collected in the MADIT II, the markedly reduced left ventricular ejection fraction in this patient cohort suggests that left atrial enlargement is likely to have contributed to the ab-

normal P-wave morphology observed in many of the patients.

P-Wave Morphology Distribution and Clinical Correlates in the MADIT II Population

Patients with CHF and a history of myocardial infarction meeting the MADIT II inclusion criteria comprise a population that has not yet been systematically studied with respect to electrocardiographic signs of abnormal atrial activation. In our earlier studies of P-wave morphology, we have identified positive P waves in leads X and Y, combined with a negative P wave in lead Z (type 1) as a common findings in younger healthy subjects, while biphasic P waves in lead Z (type 2) dominate in elderly, and in patients with a history of AF or structural heart disease, such as hypertrophic cardiomyopathy.^{6,7,26} The high prevalence of type 2 P waves in the MADIT II population is therefore not surprising. On the other hand, the high proportion of patients exhibiting atypical P-wave morphologies in the studied population have not been reported earlier and may be due to advanced underlying cardiac conditions. Interestingly, progressive, though numerically modest, worsening of clinical characteristics (i.e., age, left ventricular ejection fraction, and heart rate) was observed when patients exhibiting type 1 P waves were compared with type 2 and type 3/atypical (Table 2) thus further supporting the theory that type 1 P waves reflect the "healthiest" cardiac substrate while type 2 and type 3/atypical may be seen as markers of more advanced disease and higher risk. Notably, no differences in P-wave duration or RMS20 were identified between the different P-wave morphologies.

P-Wave Morphology and Clinical Outcome in MADIT II

In this study, P-wave morphology was shown to be associated with several measures of clinical outcome, with sudden cardiac death being the major exception. The associations between P-wave morphology and nonsudden cardiac death and P-wave morphology and AF development were present even though the statistical model was adjusted for known outcome predictors (including AF development) and factors not evenly distributed between the different P-wave morphologies.

Abnormal P-wave morphology was found to be an independent predictor of AF development. Atrial conduction disturbances promote reentry, which in turn may facilitate the development of AF.²⁷ The association between the invasive or non-invasive evidence of atrial conduction delay in patients with a history of AF has been reported earlier.^{28,29} However, there is a paucity of human data that would confirm that the conduction disturbance in patients with AF is a cause of AF rather than a consequence of the AF-related electrical remodeling. Our findings of an association between the P-wave morphology at baseline and AF development during follow-up supports the primary role of disturbed atrial conduction for AF initiation. Interestingly, P-wave duration, which in several earlier studies has been shown to be associated with a history of AF^{28,29} was prolonged in all patients regardless of future AF development.

In this study, the value of analyzing the P-wave morphology in patients with previous myocardial infarction and CHF is demonstrated. Certain P-wave morphologies (types 2 and 3/atypical) were shown to be independently predictive of increased risk of nonsudden cardiac death and AF development. Neither P-wave duration nor RMS20 showed any value in the stratification of risk for these parameters in the MADIT II patients.

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