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REVIEW

Analysis of the Surface Electrocardiogram for Monitoring and Predicting Antiarrhythmic Drug Effects in Atrial Fibrillation

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Summary. **Specific antiarrhythmic therapy with class I and III drugs for atrial fibrillation (AF) conversion and prevention of its recurrence is frequently utilized in clinical practice. Besides being only moderate effective, the utilization of antiarrhythmic drugs may be associated with serious side effects. In the clinical setting it is difficult to directly evaluate the effects of antiarrhythmic drugs on the individual patient's atrial electrophysiology, thereby predicting their efficacy in restoring and maintaining sinus rhythm.**

Analysis of the surface electrocardiogram in terms of *P*-wave signal averaged ECG during sinus rhythm and spectral characterization of fibrillatory waves during AF for evaluation of atrial antiarrhythmic drug effects is a new field of investigation. Both techniques provide reproducible parameters for characterizing atrial electrical abnormalities and seem to contain prognostic information regarding antiarrhythmic drug efficacy. Further research is needed which elucidates the most challenging clinical questions in AF management whom to place on antiarrhythmic drug treatment and what antiarrhythmic drug to prescribe. Analysis of the surface ECG might have the potential to answer these questions.

Key Words. **atrial fibrillation, ECG, electrical remodeling, antiarrhythmic drugs, drug monitoring**

Atrial fibrillation (AF) is the most common arrhythmia encountered in clinical practice affecting about 0.5–1% of the general population [1]. AF is not only related with frequent symptoms and reduced quality of life, but also constitutes a major risk factor for stroke [2,3] and for mortality from cardiovascular and all causes [4–6]. AF related symptoms and morbidity are, moreover, responsible for frequent physician visits and hospitalisations leading to substantial and rising cost [7].

Current AF management guidelines [1] suggest that "there are fundamentally two ways to manage the dysrhythmia: to restore and maintain sinus rhythm or to allow AF to continue and ensure that the ventricular rate is controlled". Specific antiarrhythmic therapy with class I and III drugs for AF conversion and prevention of its recurrence is frequently utilized in clinical practice [8–10] (Fig. 1), with 95% of drug initiations occurring after the first AF episode [10]. Oral bolus IC therapy (300 mg flecainide or 600 mg propafenone) has the highest conversion rates in terminating recent-onset AF of <24 to 48 hrs, which can be achieved in 70–80% [11,12]. In contrast, conversion of persistent AF has been observed in about 30% using intravenous ibutilide [13], oral dofetilide [14] or amiodarone [15]. Once sinus rhythm is restored, the major drawback is that AF relapses in about 60–75% within 6 months following AF termination. Administration of cardioselective beta-blockers [16,17], class I agents [18] or sotalol [17] may reduce AF recurrence rates to 40–50%, and amiodarone, being the most potent antiarrhythmic drug, to 20–40% [18,19]. Besides being only moderate effective, the utilization of antiarrhythmic drugs may be associated with serious side effects including life-threatening ventricular arrhythmias and (severe) extracardiac side effects requiring their discontinuation.

In the clinical setting it is difficult to directly evaluate the effects of antiarrhythmic drugs on the individual patient's atrial electrophysiology, thereby predicting their efficacy in restoring and maintaining sinus rhythm. Subsequently, the current AF management guidelines provide no treatment recommendations that "take the various mechanisms and patterns of AF into account" [1]. Thus, it seems desirable to develop and apply non-invasive tests that quantify AF disease state and guide AF management [20].

AF has a complex pathophysiology, with various substrates and mechanisms interacting in a complex fashion. One of its hallmarks is the so-called electrical remodeling which refers to shortened atrial

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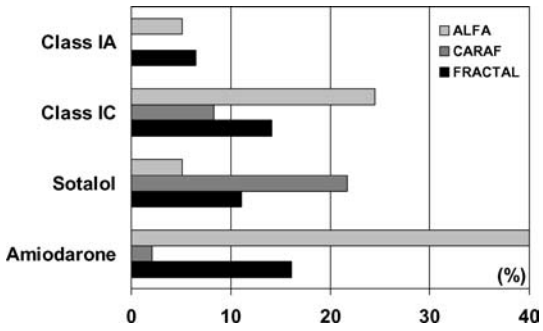

Fig. 1. *Antiarrhythmic drug utilization in new-onset AF. Data are derived from ALFA (Etude en Activé Libérale de la Fibrillation Auriculaire, N = 196) [8], CARAF (Canadian Registry of Atrial Fibrillation, N = 773) [9], and FRACTAL (Fibrillation Registry Assessing Costs, Therapies, Adverse Events and Lifestyle, N = 1005) [10].*

refractoriness, decreased conduction velocity and increased dispersion of both parameters [21,22]. Fibrillatory waves (during AF) or *P* waves (during sinus rhythm) of the surface electrocardiogram (ECG) may be considered as one apparent expression of these electrophysiological changes. The purpose of this review is twofold; (1) to present novel surface ECG analysis techniques for characterizing atrial electrical abnormalities and (2) to evaluate their possible role for monitoring and predicting antiarrhythmic drug effects in AF management.

Termination of Atrial Fibrillation

Class I and III drugs are believed to increase atrial wavelength (refractory period x conduction velocity) in experimental [23,24] and human AF [25] leading to a reduction in the number of re-entry circuits. This concept has recently been challenged by Wijffels et al. [26]. The authors found all cibenzoline, hydroquinidine, flecainide, and *d*-sotalol to be effective in cardioverting chronic AF in a goat model, although these drugs exerted diverse effects on refractoriness, conduction velocity and consequently atrial wavelength; cibenzoline and flecainide even shortening wavelength. The authors suggested that these antiarrhythmic agents rather exert their main antifibrillatory actions during ongoing AF by causing conduction delay at pivot points. This in turn leads to a decrease in fibrillatory rate to a different degree and, because the decrease in fibrillatory rate outweighs refractoriness prolongation, widening of the excitable gap. Subsequently fewer wavelets can exist and the chance for AF termination is increased [26]. Therefore, monitoring antiarrhythmic drug action irrespective of the underlying mechanism may be favourably explored by obtaining fibrillatory rate from the surface ECG.

Frequency analysis of AF

In most studies atrial fibrillatory rate has been obtained by spectral analysis techniques of digital resting ECG recordings such as standard 12-lead [27,28] or (modified) orthogonal recordings [29–31]. The method has, however, also been applied to ambulatory ECG recordings using conventional ambulatory leads [32–34]. Following QRST cancellation, a power spectrum is obtained by using a windowing technique and Fourier analysis to process the remainder ECG (Fig. 2). This as well as the associated windowing technique (window type, length and overlap) determine the appearance of the frequency power spectrum [27]. Variants of Fourier transform based methods including conventional Fourier analysis and spectral averaging techniques based on short overlapping segments have been applied to ECG segments ranging from 10 seconds to 5 min [27,28,35–37]. Recently improved signal processing techniques for cancellation of the ventricular activity (e.g. spatiotemporal beat subtraction [38]) in combination with developments in time-frequency analysis allow moreover to analyze temporal and morphologic AF wave dynamics on a second-to-second basis [39,40]. Typically a distinct spectral peak is obtained which corresponds to the most dominant fibrillatory rate (fibrillatory rate in fibrillations per minute = dominant spectral peak in Hz × 60) [30,41]. Detailed methodological considerations can be found elsewhere [30,42].

A direct comparison between endocardially recorded electrograms and body surface recordings clearly evidences the validity of fibrillatory rate obtained from surface ECG as an index of the average atrial fibrillatory cycle and subsequently atrial refractoriness. Fibrillatory rates calculated from lead V1 substitute the right atrial free wall [27,28] while rates from an esophageal lead reflect atrial septal and left atrial activity [27]. In persistent AF, there is minor short-term rate variability [27,28,35] and considerable diurnal variability [33,34], while repeated daily frequency measurements at identical medication at the same time under similar conditions discloses an insignificant fibrillatory rate variability [43]. In contrast, rate variability in paroxysmal AF seems to be related to its natural course with a rate increase within the first five minutes of an AF episode [32] and a rate decrease prior to termination [32,36].

Monitoring and predicting antiarrhythmic drug action during atrial fibrillation

A substantial reduction in atrial fibrillatory rates following several different intravenously or orally administered class I and III antiarrhythmic drugs [28,29,32,36,37,44,45] as well as following verapamil [43] or magnesium [46] has been reported using serial or continuous frequency analysis of the surface ECG (Table 1). An example of monitoring acute drug effects is presented in Fig. 3 showing the transition from a high

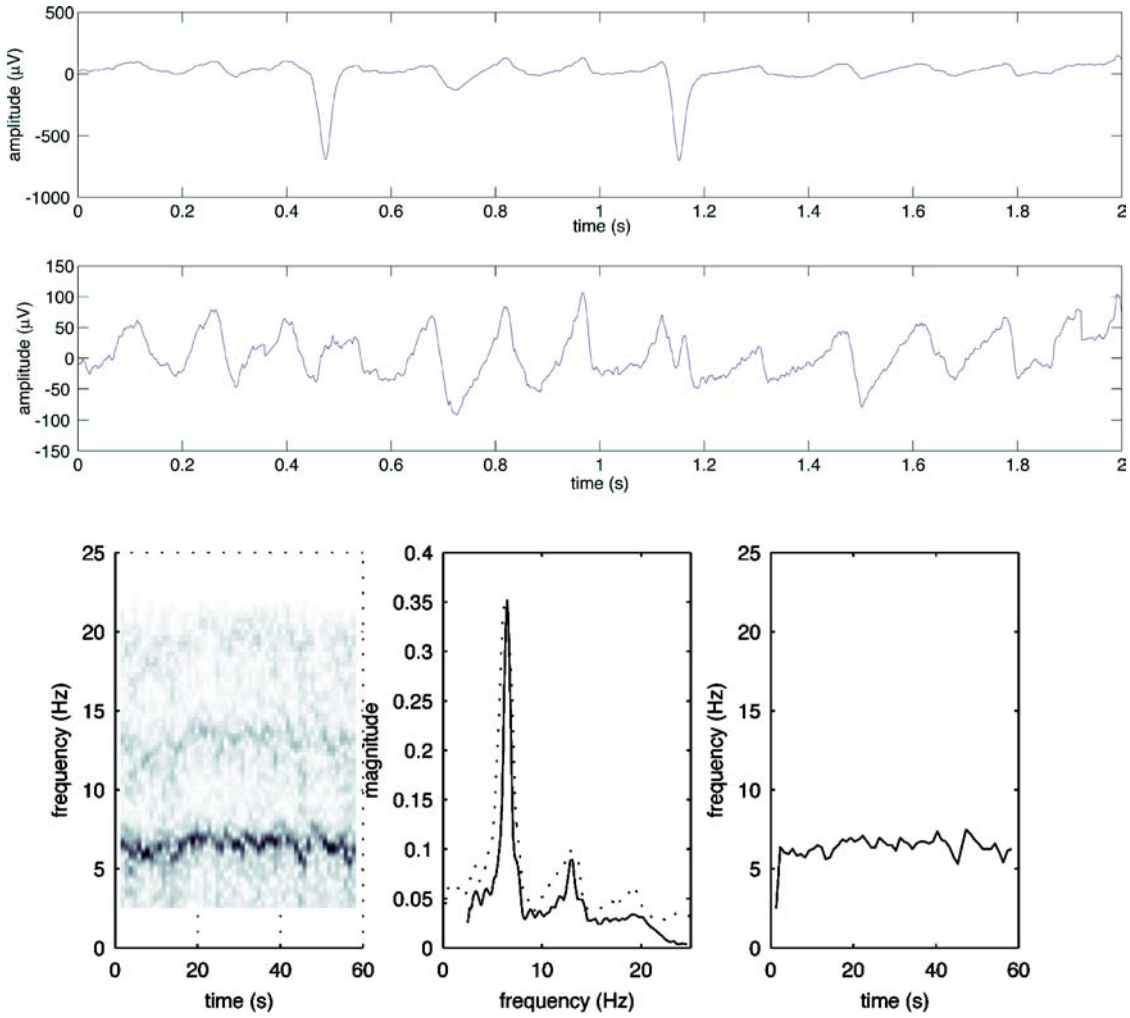

Fig. 2. *Frequency analysis of AF [30]. Two seconds (out of a 60 second recording) of an ECG signal from a patient with AF (upper panel), and the same interval after QRST cancellation (middle panel, amplitude scale is magnified five times). This fibrillatory signal is then subjected to Fourier analysis. Time-frequency distribution (left box), power frequency spectrum clearly showing the dominant fibrillatory rate (middle box), frequency trend over the 60 sceond recording (right box).*

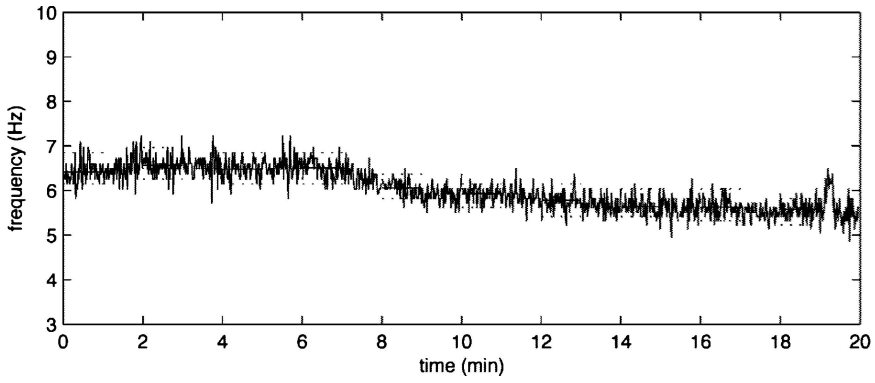

Fig. 3. *Example of antiarrhythmic drug monitoring during AF. Atrial fibrillatory rate obtained from time-frequency-analysis during intravenous infusion of dl-sotalol. The solid black colour indicates the actual fibrillatory rate. Initially, the atrial rate is at the level of 390 fpm (6.5 Hz), but decreases successively to the level of 330 fpm (5.5 Hz) during 20 min.*

Table 1. *Summary of available literature on frequency analysis of AF for monitoring and predicting class I and III antiarrhythmic drug action*

Drug (s)	Dosage	Patients (N)	Drug effect (baseline vs. after drug)	AF termination	Converters vs. non-converters
Flecainide [29]	300 mg bolus + 100–200 mg/day p.o.	18	–108 fpm (6.2 ± 0.5 vs. 4.4 ± 0.4 Hz)	50%	Baseline fibrillatory rate 354 vs. 384 fpm (5.9 ± 0.4 vs. 6.4 ± 0.4 Hz)
Cibenzoline Procainamide [36]	1.4 mg/kg i.v. ($N = 5$) 10 mg/kg i.v. ($N = 3$)	8	–102 fpm (151 ± 17 vs. 203 ± 21 ms)	100%	–
Amiodarone Sotalol Flecainde [32]	600–1200 mg/day p.o. ($N = 5$) 240–480 mg/day p.o. ($N = 3$) 200 mg/day ($N = 1$)	8	–66 fpm (6.9 ± 0.5 vs. 5.8 ± 0.4 Hz)	0%	–
Bepidril [37]	200 mg/day p.o.	32	–	69%	Fibrillatory rate change 31 ± 10 vs. 17 ± 5%
Ibutilide [28]	1 mg (+1 mg if required) i.v.	15	–114 ± 42 fpm	60%	Baseline fibrillatory rate 338 ±55 vs. 436 ± 67 fpm
Ibutilide [45]	1 mg (+1 mg if required) i.v.	19	–82 ± 57 fpm	35%	Fibrillatory rate change 108 ± 60 vs. 68 ± 52 fpm
Sotalol [27]	80 mg i.v.	5	Atrial cycle length increased in all patients	0%	–

Fibrillatory rate (in fibrillations per minute), frequency (in Hz), or cycle length (in ms) have been reported in the original publications. For this review, all variables are expressed as fibrillations per minute with the original values in brackets. Possible issues pertaining to the report of atrial cycle length based on calculations from frequency power spectra can be found elsewhere [30,41]. All reported differences between converters and non-converters are statistically significant ($p < .05$).

rate (less organized) to a low rate (more organized) fibrillation following acute intravenous sotalol infusion.

Besides direct monitoring of antiarrhythmic drug effects, it seems also possible to identify suitable patients for pharmacological cardioversion. A baseline fibrillatory rate of 360 fibrillations per minute was highly sensitive and specific for prediction of AF termination following intravenous ibutilde [28] or oral flecainide [29] (Fig. 4). This finding is in close agreement with a previous study in which a mean right atrial cycle length of 160 ms (375 fibrillations per minute) has been invasively identified as a valuable cutoff-point for conversion to sinus rhythm with ibutilide [47]. No patient with shorter cycle length (higher rate) was converted by ibutilide, whereas conversion occured in 64% of those patients with longer cycle length (lower rate). In contrast, other authors noted no baseline fibrillatory rate difference between patients who converted to sinus rhythm and those who did not following oral bepridil [37] or intravenous ibutilide [45] administration. Instead, larger and more rapid rate decrease were associated with AF termination. This finding is supported by invasive studies showing that AF termination occurred if the atrial

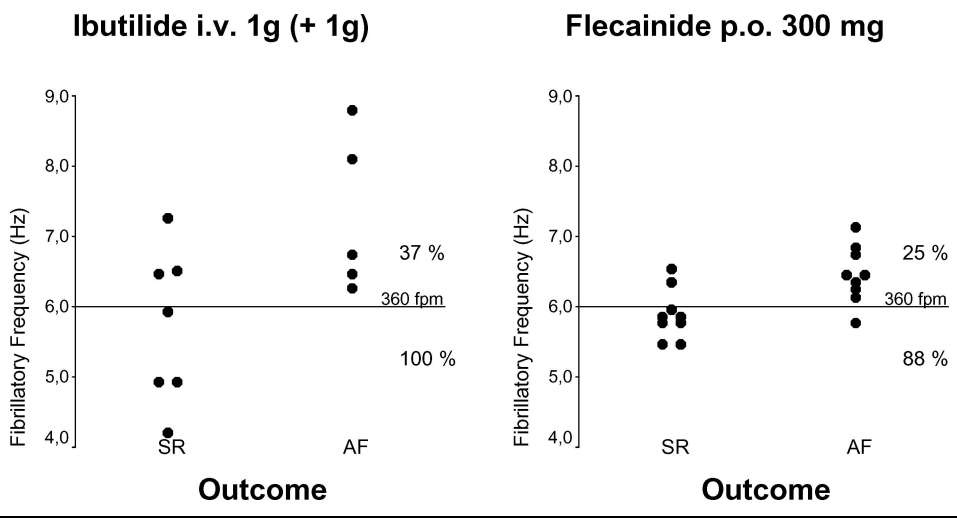

Fig. 4. *Prediction of AF conversion by intravenous ibutilide (left) or oral flecainide (right). AF with slower rates is more likely to respond to antiarrhythmic drug therapy, while faster rates are more often found in drug-refractory AF (modified from [28,29]).*

cycle length had been prolonged to >210 ms (<285 fibrillations per min) after class I drug administration in 88% in contrast to only 10% if the post-drug cycle lengths was shorter [48].

The pathophysiological meaning of those findings can be summarized as follows. Patients with a low fibrillatory rate may have a small number of wavelets, whereas those with higher rates have multiple wavelets [49]. In the former group class I or III antiarrhythmic drugs by decreasing fibrillatory rate may have widened the excitable gap and therefore reduced the number of wavelets that could coexist. This would have increased the statistical likelihood that all wavelets might extinguish simultaneously and terminate the fibrillatory process [23]. In contrast, although fibrillatory rate is substantially reduced in non-converters this reduction is not large enough to reach the critical threshold necessary for AF termination and subsequently AF persisted.

Prevention of Atrial Fibrillation Recurrence

It is a common observation that most AF relapses occur within the first weeks after cardioversion with decreased but constant recurrence rates thereafter [50,51]. Early vulnerability to AF initiation within this time period is related to electrophysiological abnormalities, while structural abnormalities seem to be primarily responsible for later AF recurrences [52]. This time course might be explained by the fact that a reversal of the electrical remodeling process occurs rapidly once sinus rhythm is restored [53–55], while structural changes persist for longer periods [52]. Following restoration of sinus rhythm diverse abnormalities in electrical atrial properties including prolonged intra- and interatrial conduction, shortened atrial effective refractory periods with loss of rate-related adaptation, and increased inhomogeneity of these parameters all favouring re-entry have been described [53–56].

Previous investigations have shown that electrical abnormalities, primarily intra-atrial or interatrial conduction delay or block are reflected by *P*-wave changes on the surface ECG [56–58]. Over the last 10 years numerous investigations have explored the role of *P* wave analysis in order to predict AF from individuals in sinus rhythm reaching sensitivities and specificities of about 80% [59]. Detailed reviews regarding the prediction of paroxysmal or postoperative AF have been provided previously [60,61] while monitoring and predicting antiarrhythmic drug actions has not been reviewed so far.

Antiarrhythmic drugs exhibit multiple, complex atrial effects during sinus rhythm that foster prevention of AF recurrence and include suppressing atrial premature beats which are considered responsible for AF re-initiation, reversing refractoriness dispersion and prolonging refractoriness [62]. It needs to be pointed out that the degree of these effects might be different when comparing AF and sinus rhythm. For instance, owing to reverse use dependency class III drugs exhibit more refractoriness prolongation during sinus rhythm than during AF which might explain why they are much more effective in preventing AF recurrence than terminating it [63], while the opposite seems true for class I agents [64].

P-wave signal averaged ECG

The signal-averaged ECG (SAECG) was initially developed in order to detect low amplitude, high frequency signals in the QRS complex representing areas of slow conduction in the ventricle. The principles for the *P*-wave SAECG (P-SAECG) are the same: P-SAECG recordings are usually obtained from an orthogonal X, Y, and Z lead system. Signal averaging can be triggered on the *R* wave, requiring a stable PR interval, or on the *P* wave, requiring exclusion of premature atrial beats and a good signal-to-noise ratio. Usually 200 to 350 beats are averaged until the noise level is reduced to <1 μV. The signal from each lead is amplified and filtered (bidirectional 40 to 300 Hz filter or others). The filtered X, Y, and Z leads are then combined into a vector magnitude (root mean square, RMS). The total filtered P-wave duration (PWD) and the amplitude (RMS voltage) of the terminal portions of the *P*-wave (e.g. RMS10 for the last 10 ms, RMS20 for the last 20 ms etc.) can be obtained from this vector. Besides this, other indices such as the PWD dispersion ($PWD_{max} - PWD_{min}$) [65] or the *P*-wave dispersion index (PWD standard deviation/PWD mean value × 100) [66] can be calculated from the individual leads. Furthermore, the *P*-wave can be subjected to spectral analysis, where the energy in different frequency bands (20 to 150 Hz) can be analyzed. Over recent years filtered techniques of *P*-wave signal averaging have been most extensively studied. Their combination with unfiltered *P*-wave analysis seems, however, perspective in identifying concealed conduction defects which are of importance for AF inducibility and sustenance [58,67]. Analysis of unfiltered *P*-waves identified two features to be characteristic for lone AF: (1) double-peaked *P*-wave morphology in spatial magnitude and (2) biphasic *P*-waves in the Z-lead [58,67]. Both markers may be considered as indicators of deteriorated interatrial conduction associated with AF development. While the former reflects separation of right and left atrial activation, the latter may be explained by a misbalance between conduction over superior (via Bachmann's bundle) and inferior (via coronary sinus and adjacent myocardial connections) interatrial routes which leads to retrograde activation of the left atrium and explains the positive terminal phase of the *P*-wave in the Z-lead. Figure 5 illustrates general principles for *P*-wave signal averaging, major differences in *P*-wave morphology between patients with paroxysmal AF and healthy subjects using unfiltered *P*-wave analysis as well as the possible superiority of unfiltered over filtered techniques to detect specific conduction abnormalities. A detailed description of technical

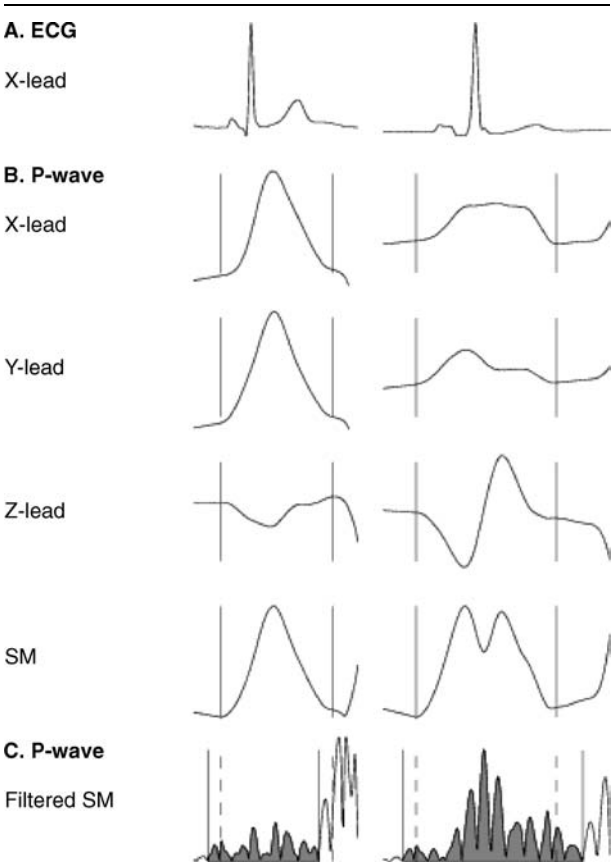

Fig. 5. *Detection of inter-atrial conduction defects from morphology analysis of the unfiltered P-wave SAECG compared to the conventional filtered (40–250 Hz) technique. Registration is shown from a healthy subject (left panel) and a patient with paroxysmal AF (right panel). A: One P-QRS complex from a Frank orthogonal lead X recording. B: Unfiltered signal-averaged P-waves obtained from Frank orthogonal leads X, Y, and Z and their combination into the spatial magnitude ($(X^2 + Y^2 + Z^2)^{1/2}$). The unfiltered signal-averaged P-wave shows a double-peaked morphology in the spatial magnitude and a biphasic signal in the Frank orthogonal lead Z in the AF patient. C: Filtered signal-averaged P-wave. Note the discrepancy between P-wave duration of the filtered P-wave (solid lines) and the unfiltered P-wave (dashed lines), and also the inability to detect morphological differences between normals and patients from the filtered spatial magnitude. (SM = spatial magnitude)*

aspects (e.g. different filtering techniques, frequency domain analysis) can also be found in previous reports [60,68].

Several studies have evaluated the reproducibility of various P-SAECG parameters [69–73]. While the PWD exhibited a good short-, mid- and long-term reproducibility, the RMS voltages and frequency domain parameters were less reproducible. The variability of P-SAECG parameters may stem from physiological modulations such as autonomic tone [74,75] or hemodynamic changes [76]. Furthermore, the applied filtering techniques have a substantial impact on the P-SAECG parameters [71,77]. Finally, inherent difficulties with Fourier-based spectral analysis as applied in transient *P*-waves need to be considered. PWD and RMS reference values were just recently provided for a large cohort of healthy volunteers [78]. These factors have to be taken into account when interpreting the findings of the below presented studies, which have investigated the effects of antiarrhythmic therapy on the P-SAECG and have correlated these effects with drug efficacy (Table 2).

Monitoring and predicting antiarrhythmic drug action during sinus rhythm

Previously, the effects of disopyramide have been studied in 32 patients with paroxysmal AF [79]. The authors determined both the filtered PWD using the conventional P-SAECG and the PWD dispersion using a 16-unipolar P-SAECG mapping system. Three hours after a single oral dose (200 mg) filtered PWD was prolonged and stayed prolonged after a 4-week treatment period (300 mg/day). Both the baseline PWD and the magnitude of *P*-wave prolongation after drug administration were similar in patients with AF recurrence ($n = 15$) compared to patients without AF recurrence ($n = 17$) during a 6 months follow-up. In contrast, the disopyramide loading dose resulted in an increased PWD dispersion ($PWD_{max} - PWD_{min}$) in all patients with AF recurrence, as opposed to a decrease in all patients that remained in sinus rhythm (Fig. 6). While the former was mainly caused by prolongation of maximal filtered PWD, the latter was due to prolongation of minimal PWD.

Similar observations have been made in a different study [65] also measuring dispersion of the signal-averaged PWD on precordial body surface leads in 25 patients with paroxysmal AF. These authors also noted two different PWD dispersion behaviors following a single oral dose of pilsicainide (100 mg), a newly developed, potent class Ic drug. While in 13 patients

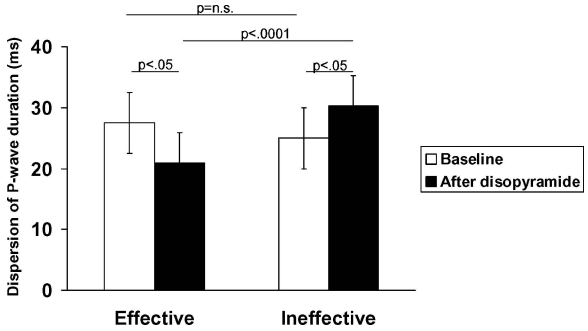

Fig. 6. *Prediction of AF recurrence. The change in filtered P wave duration dispersion after 3 hours of a single dose disopyramide was highly predictive of AF recurrence during follow-up, while baseline dispersion of P-wave duration was not (modified from [79]).*

Table 2. *Summary of available literature on P-wave signal averaging for monitoring and predicting class I and III antiarrhythmic drug action*

Drug	Dosage	Patients (N)	AF recurrence	Follow-up	Drug effect (baseline vs. after drug)
Disopyramide [79]	200 mg bolus +300 mg/day p.o.	32	47%	4 weeks	PWD dispersion non-recurring AF: 27.5 ± 4.9 vs. 20.9 ± 4.6 ms recurring AF: 25.0 ± 5.7 vs. 30.3 ± 6.7 ms
Pilsicainde [65]	100 mg bolus $+120 \pm 32$ mg/day p.o.	25	68%	10 ± 11 months	PWD dispersion non-recurring AF: 23.8 ± 6.1 vs. 18.8 ± 5.5 ms recurring AF: 26.7 ± 7.6 vs. 28.0 ± 8.7 ms
Amiodarone [81]	600 mg/day loading +200 mg/day p.o.	30	23%	8 weeks	PWD non-recurring AF: 129 ± 9 vs. 124 ± 11 ms recurring AF: 127 ± 18 vs. 132 ± 13 ms RMS10 non-recurring AF: 3.9 ± 1.9 vs. 5.1 ± 2.3 μV recurring AF: 4.4 ± 1.6 vs. 5.1 ± 2.7 μV RMS20 non-recurring AF: 5.2 ± 2.3 vs. 6.7 ± 2.3 μV recurring AF: 5.7 ± 2.4 vs. 6.0 ± 2.9 μV
Sotalol [80]	80–240 mg/day p.o.	16	n/a	4–6 weeks	PWD 149 ± 4 vs. 152 ± 3 ms P60 4.3 ± 0.4 vs. 3.3 ± 0.3 μV2.s

All reported differences between non-recurring and recurring AF are statistically significant ($p < .05$).

a decrease was found, PWD dispersion increased in the other 12 patients. In the former group the AF recurrence rate was 46% as opposed to 92% in the latter. While these results are encouraging, it has to be pointed out that in both studies measurements were obtained from a 16-lead P-SAECG mapping system, which currently limits the broad clinical application. Unfortunately, the authors did not provide data on the usefulness of the PWD dispersion obtained from the conventional X, Y, and Z leads.

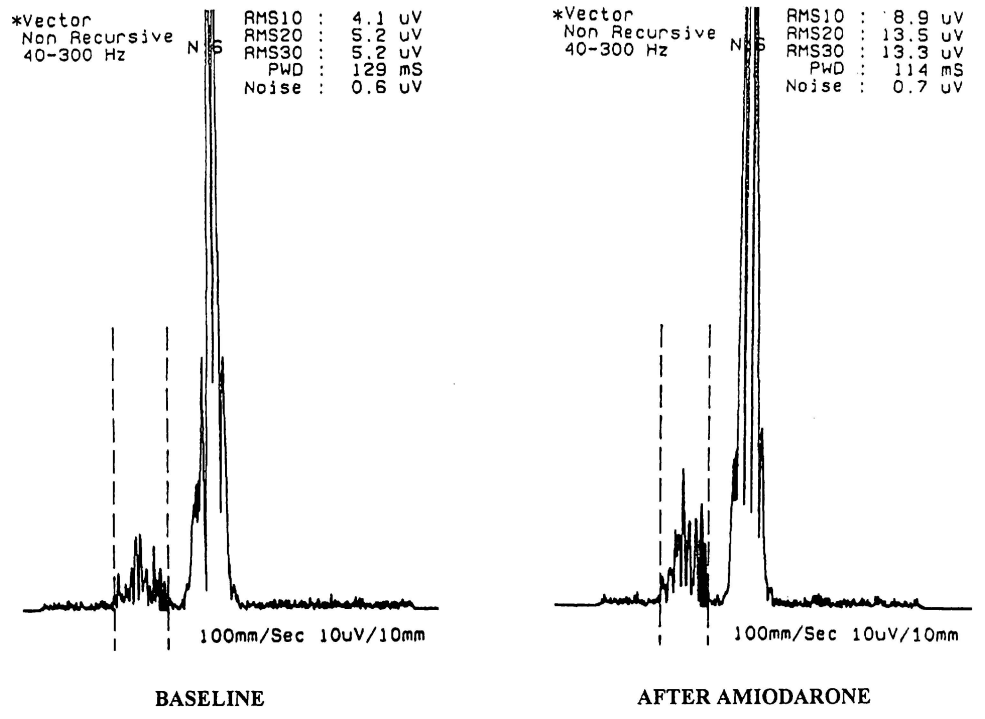

Fig. 7. *Example of antiarrhythmic drug monitoring during sinus rhythm using P-SAECG. Baseline recording (left panel) and after amiodarone therapy (right panel). Please note the favourable increase in RMS values (with permission from [81]).*

Other drugs studied included sotalol [80] and amiodarone [81]. Treatment with low dose sotalol (80–240 mg/day) for 4–6 weeks resulted in a decreased high frequency *P* wave energy with no effect on filtered PWD in 16 patients with paroxysmal AF [80]. No data of the clinical course of those patients were presented, so that no conclusions regarding drug efficacy in preventing further AF episodes can be drawn. The effects of amiodarone on the P-SAECG have been analyzed in 30 patients with paroxysmal AF and coronary artery disease [81]. Filtered PWD and the RMS voltage in the last 10, 20, 30 ms of the filtered *P*-wave at baseline and following 6 weeks of amiodarone treatment (600 mg/day loading dose for 10 days followed by 200 mg/d) were measured. While PWD and RMS30 remained unchanged, RMS10 and RMS20 increased when analyzing the entire study population. During follow-up, AF recurrence was observed in 7 patients. Their baseline P-SAECG parameters did not differ from those 23 patients where AF did not recur. In the former group (AF recurrence), there was no change in any of the P-SAECG parameters, while in the latter group (no AF recurrence) PWD was decreased and RMS10 and RMS20 were increased (Fig. 7).

It needs to be pointed out, that all these studies were carried out in patients with paroxysmal AF with no data available regarding the interval between the last AF episode and the ECG recording. To the best of our knowledge there are no studies that have prospectively assessed this technique for prediction of drug efficacy after cardioversion of persistent AF.

The pathophysiological meaning of those findings can be summarized as follows. Both a decrease in PWD dispersion and an increase in terminal *P*-wave amplitude (RMS10 and RMS20) after antiarrhythmic drug administration is consistent with reversing inhomogeneity of electrical atrial activity. This effect favours prevention of AF recurrence, whereas AF is more likely to occur if inhomogenous conduction persists or even worsens after drug utilization.

Conclusions

Analysis of the surface ECG, namely P-SAECG (in sinus rhythm) and frequency analysis techniques (in AF) for evaluation of atrial antiarrhythmic drug effects is a new field of investigation. Both techniques provide reproducible parameters for characterizing atrial electrical abnormalities and seem to contain prognostic information regarding antiarrhythmic drug efficacy. Further research is needed which elucidates the most challenging clinical questions in AF management whom to place on antiarrhythmic drug treatment and what antiarrhythmic drug to prescribe. Analysis of the surface ECG might have the potential to answer these questions.

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