VIA MEDICA

ORIGINAL ARTICLE

Cardiology Journal
2007, Vol. 14, No. 3, pp. 287–300

ISSN 1897–5593

Analysis of high gain signal-averaged P/A wave time domain parameters recorded from external leads (SA-ECG) and internal electrograms (SA-IEGM) recorded from three right- and left-intraatrial leads

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Abstract

Background: *Time-domain analysis of the P-wave in signal-averaged ECG (SA-ECG) recorded from chest leads is an accepted method for evaluating the inhomogeneity of atrial excitation, predictive for atrial arrhythmias. The aim of the study was to determine the value of the SA-ECG technique for intraatrial signal processing. Additional aims were to evaluate the correlation between SA-ECG parameters (external and intraatrial) and the frequency of atrial fibrillation recurrences, ongoing antiarrhythmic therapy and LA diameter.*

Methods: *Recordings were performed in 24 pts during biatrial pacing system implantation. A surface SA-ECG was obtained from orthogonal leads, and intraatrial signals were recorded and averaged separately from the right and left atrium. We analyzed standard SA-ECG parameters (P/A wave duration, RMS20 and LAS5) and the presence of atrial late potentials (ALP-Pdur > 125 ms and RMS20 < 2.40 μV).*

Results and conclusions: *Intraatrial SA-ECG provides accurate data for ALP analysis, mostly due to its improved signal quality and QRS discrimination. P-duration and RMS20 seem to be parameters with good correlation between external and internal SAECG. Intraatrial SAECG offers a valuable tool to evaluate abnormalities of the final part of atrial excitation. There are no straight associations between SA-ECG parameters and arrhythmic burden, ongoing antiarrhythmic therapy and LA diameter.* (Cardiol J 2007; 14: 287–300)

Key words: signal-averaged ECG, intraatrial signal, P-wave duration, atrial late potentials, atrial fibrillation

Introduction

For the past 15 years, analysis of time- and frequency-domain parameters of signal-averaged P-wave has been applied to estimate electrophysiological properties of the atrial wall, which allow the identification of the group of patients with high risk of paroxysmal/recurrent atrial fibrillation (AF) [1–13]. Impaired conduction in main atrial pathways, as well as the presence of local conduction disturbances in atrial walls, leads to inhomogeneity of atrial activation with increased refractoriness dispersion, creating conditions for re-entrant atrial arrhythmias [14–16]. In the past decade, the recognition of conduction disturbances within the atria have become

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Received: 28.02.2007 Accepted: 3.04.2007

particularly important since the new therapeutic option was introduced — atrial resynchronization therapy (bifocal right atrial pacing, biatrial pacing) [17–19]. Low signal amplitude, notched and relatively sluggish onset of the P-wave recorded from orthogonal Frank's leads, particularly in patients with recurrent atrial arrhythmias, impedes its use as a synchronization trigger in the signal-averaging process. The use of the R-wave, alternatively, for synchronization is limited by the variant P-R segment [1–13].

In patients with interatrial conduction disturbances (mainly within Bachmann bundle), the left atrium is activated with a delay, generating prolongation of the P-wave with its final portion essentially formed by left atrial potential. Therefore, in signal-averaged electrocardiograms (SA-ECG) recorded in such patients, the values of root mean square voltage of the last 20 ms of the P-wave (RMS20) and the duration of low amplitude ($< 5\,\mu V$) signal (LAS5) reveal the micro oscillations occurring in the left atrium. It is well known that local conduction disturbances within the right atrium can have a key role in the pathogenesis of atrial arrhythmias [13–16, 20]. The existence of late potentials (micro oscillations in the final part of atrial activation) in the right atrium and the possibility of reflecting it in classical external Frank's leads are still open questions. According to Keane et al. [21], delayed and fractionated conduction within the right atrium may explain the presence of high-frequency potentials in the final portion of the P-wave after the end of the left atrial activation. Furthermore, there is the question of the existence of micro potentials in the final part of atrial excitation, which are of such small amplitude that they can be omitted in external leads, and the problem of their possible influence on atrial arrhythmia pathogenesis. These doubts raise another question: How long does the activation of the right and left atrium last, and is it possible to assess the final part of atrial depolarization in internal leads? In addition, the final question: Could atrial potentials selected from one out of the three intraatrial leads, having higher amplitude and abrupt acceleration, be appropriate for triggering the synchronization in signal-averaging process, given that the leads will remain in a stable position throughout the recording procedure? All these uncertainties led us to compose the working hypothesis that the potentials acquired from three intraatrial leads, processed with conventional ECG signal-averaging technique, could be helpful in answering all these questions.

The dilatation of atria, influencing re-entrant wavelength, has a considerable role in the perpetuation of arrhythmias; concomitant degenerative lesions additionally give the chance for unidirectional blocks to arise [22, 23]. The atrial dilatation, however, can be a reversible result of tachyarrhythmia [24, 25]. Opinions on associations between echocardiographic patterns of left atrial overload, interatrial conduction disorders, the presence of micro oscillations in the final portion of atrial depolarization and the arrhythmic burden are equivocal [5, 26–28].

Long-lasting or recurrent atrial arrhythmias lead to the remodelling phenomenon, characterized by altered conduction velocity and refractoriness of atrial tissue [29]. It is still unclear, if, and to what extent, recurrent arrhythmias have an influence on local conduction disturbances, by itself most likely contributing to atrial electrical remodelling. The effect of such arrhythmias on high gain signal-averaged ECG and internal electrogram (SA-IEGM) parameters also remains unclear.

Moreover, there is no clear knowledge on the modifying effect of antiarrhythmic therapy on the P-wave time- and frequency-domain analysis of SA-ECG or SA-IEGM. Class I antiarrhythmic drugs, decreasing conduction velocity, and class III drugs increasing action potential duration and atrial refractoriness [30], hypothetically, should influence atrial depolarization homogeneity, particularly in patients with severely impaired conduction within the atria. It could be anticipated that conduction disturbances will be increased by aggressive Ic and/or III class drug therapy, with a shift in depolarization homogeneity (RMS20 values and presence of atrial late potentials — opinions in literature are equivocal [12, 30–33]).

Our study has the following specific aims:

- 1) To attempt to use three low-impedance intraatrial leads to obtain right and left atrial electrograms to be processed with the conventional (body surface) signal-averaging technique.
- 2) The comparison of parameters (atrial potential duration, RMS20 and LAS5, atrial late potentials criteria) yielded by analysis of external (SA-ECG) and intraatrial (SA-IEGM) signals.
- 3) To search for correlations between electrophysiological status of the atria assessed by SA-ECG and SA-IEGM analysis and the essential echocardiographic parameters, indirectly revealing atrial wall strain.
- 4) An estimation of the influence of antiarrhythmic drugs (class Ic and III) on external and intraatrial averaged signal time-domain parameters, and whether ongoing medication should be taken into account during the interpretation of parameters.

The ultimate goal of this study was to evaluate the value of high gain, signal averaged IEGM for the assessment of atrial electrophysiological features of atrial activation.

Methods

Patients

The study was conducted on a group of 24 pts (15 female, 9 male, mean age 68.8 ± 9.97 years) eligible for permanent biatrial pacing due to symptomatic brady-tachycardia syndrome with additional indications for atrial resynchronization therapy: conduction disturbances within the atria (P-wave duration > 125 ms) and recurrent, symptomatic and drug-resistant (≥ 3 drugs, including amiodarone) atrial fibrillation [17]. The underlying condition was arterial hypertension in 13 pts (54%), ischemic heart disease in 5 pts (21%), and valvular disease in 3 pts (12.5%). In the remaining three pts (12.5%), lone atrial fibrillation was diagnosed.

Arrhythmias

In the studied group, we analyzed the frequency of AF recurrences according to the Kingma et al. [35] paradigm. In 7 pts (29.2%) sporadic AF, in 8 pts (33.3%) recurrent AF and in 9 pts (37.5%) frequent AF was identified.

Antiarrhythmic treatment

Due to a high arrhythmia burden the ongoing medication was not modified — discontinuation of treatment could provoke AF episodes thus impeding the measurement of pacing and sensing conditions. During the pacemaker implantation procedures, 5 pts were treated with one drug (amiodarone or propafenone), 8 were on two drugs (propafenone and sotalol/amiodarone) and 11 pts (46%) had no ongoing antiarrhythmic medication.

Procedure

1) Confirmation of arrhythmia type on the basis of medical documentation. 2) Echocardiographic study. 3) 12-lead ECG with 25 mm/s speed and 10 mm/1 mV gain plus leads I–III with 100 mm/s speed 80 mm/1 mV gain. 4) IEGM recording from RAA and CS, simultaneously with ECG lead II. 5) SA-ECG recording from external orthogonal leads. 6) SA-IEGM recording from the right and left atrium separately. Intraatrial signals were obtained with standard bipolar pacing leads introduced during the pacemaker implantation procedure, subsequently employed for permanent pacing.

External SA-ECG recording and processing

Equipment constructed in the National Institute of Cardiology (Warsaw) was applied for signal recording and processing. It consisted of a micropotential amplifier (noise < 1.5 μV in 0.1–300 Hz bandwidth, CMRR > 130 Db), 12-bit A/D converter, 486 CPU PC and software designed for signal-averaging processes and subsequent analysis of data. Standard Ag/AgCl electrodes were applied on carefully cleansed chest skin. The P-wave was derived from three bipolar orthogonal (Frank) leads. Signals (from each lead) were amplified (× 1000), passed through a band-pass filter (cut-off frequency 0.1–300 Hz) and digitized by the A/D converter with a 12-beat accuracy. The signal-averaging process was synchronized by the R-wave trigger. Ectopic beats, if present, were identified and rejected. Approximately 50 beats were averaged and stored on PC HD. The process was described before [11].

High-gain SA-ECG P-wave parameter time-domain analysis

The first stage was to combine filtered (Butterworth bidirectional filter) and averaged signals from three leads X, Y and Z to a spatial vector magnitude $(X^2 = Y^2 + Z^2)^{1/2}$. The onset and offset of P-wave were defined as the points at which the atrial signal exceeded and returned to the 1.5 μV level, respectively. The following parameters were measured and calculated automatically: 1) filtered P-wave duration (Pdur), 2) root mean square voltage of the final 20 ms of filtered P-wave (RMS20), 3) duration of low amplitude signal < 5 μV (LAS5). Atrial late potentials (ALP) were considered positive with Pdur > 125 ms and RMS20 < 2.4 μV [11].

Intracardiac SA-IEGM recording and processing

Three bipolar pacing leads were used: a standard "J" shaped lead implanted into the right atrial appendage (RAA) and the second lead was introduced into the coronary sinus (CS). The third lead (for permanent ventricular pacing) was temporarily placed in the LRA position. The same equipment (as described above) was employed for signal recording and processing. To obtain right- and left-atrial signals, intracardiac leads were attached to the micro-potential amplifier via sterile connectors according to scheme in Figure 1. The right atrial electrogram was recorded from three combined intraatrial leads X' Y' Z', and left atrial electrogram from X'' Y'' Z'' leads. The signal from each lead was augmented and filtered in the same mode as during external signal recording. The averaging process was synchronized by the A wave trigger. The employed technique was described before [36, 37].

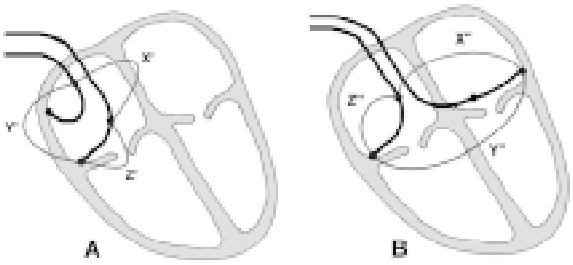


Figure 1. Scheme presenting the connections of intracardiac leads to obtain right atrial (X′ Y′ Z′) (**A**) and left atrial (X″ Y″ Z″) (**B**) signals.

High-gain SA-IEGM A wave parameter time-domain analysis

Intracardiac signals were processed and obtained parameters analyzed in the same way as the external SA-ECG.

Interatrial conduction evaluation with IEGM recordings

The internal electrogram (IEGM) was recorded from the RAA and CS leads connected to a dual-chamber pacemaker via telemetry (Fig. 2), simultaneously with lead II ECG. The following timing parameters were determined: 1) P-wave duration in lead II or III in standard ECG (25 mm/s speed, 10 mm/mV scale), 2) P-wave duration in lead II or III in high resolution ECG (100 mm/s speed, 20 mm/mV × 4 scale), 3) interatrial conduction time (IACT) measured from the onset of A wave in RAA signal to the onset of A wave in CS signal, 4) total atrial activation time (TAAT) measured from the onset of P-wave in lead II ECG to the end of atrial activation in the CS signal (Fig. 3).

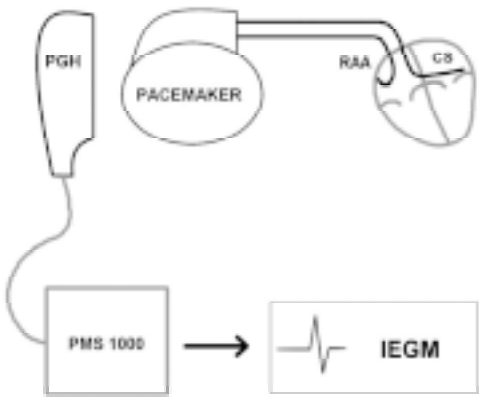


Figure 2. Internal electrogram (IEGM) recorded from the RAA and CS leads connected to a dual-chamber pacemaker via telemetry.

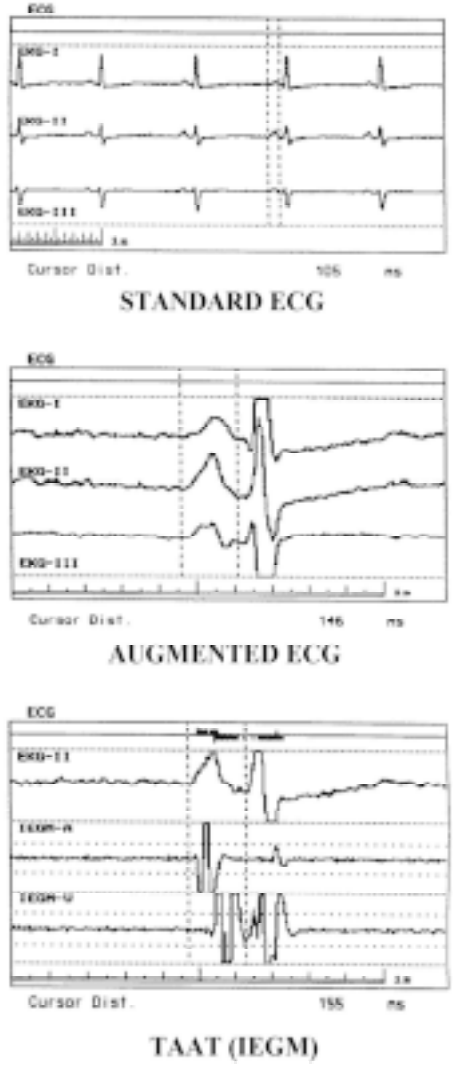


Figure 3. Values of P-wave duration in standard and augmented ECG compared to total atrial activation time (TAAT) in the same patient.

Echocardiographic examination

Echocardiographic examination was performed with Hewlett Packard SONOS 100 equipment with a 2.5 MHz transducer. The anteroposterior dimension of the left atrium and left ventricle was measured in the long axis parasternal view. The left ventricular ejection fraction (LVEF) was calculated from data acquired in the apical four-chamber view according to Simpson's method.

Statistical analysis

The results are presented as the mean ± standard deviation. The statistical significance of the

Table 1. General results. Values of ECG, IEGM and SA ECG/IEGM examined parameters.

Parameters	No.	Aver.	Median	Min.	Max.	SD
ECG						
Pdur — standard ECG	24	128.5	128.0	105.0	152.0	14.5
Pdur — high resolution ECG	24	157.7	159.0	125.0	199.0	16.0
IEGM						
IACT	24	103.7	99.0	55.0	148.0	22.6
TAAT	24	181.5	182.0	144.0	225.0	22.4
High gain SA ECG — external (Frank's) leads						
Ext. Pdur	24	156.2	155.4	119.3	186.8	16.8
Ext. RMS20	20	2.17	1.96	1.09	3.69	0.76
Ext. LAS5	24	6.68	5.50	0.00	26.70	7.48
High gain SA IEGM — right atrium (RA)						
Int. RA Adur	24	174.8	168.8	144.4	224.5	24.1
Int. RA RMS20	23	1.77	1.69	0.75	3.46	0.72
Int. RA LAS5	23	12.91	11.00	0.00	33.00	7.92
High gain SA IEGM — left atrium (LA)						
Int. LA Adur	23	175.3	169.6	138.2	237.1	26.7
Int. LA RMS20	15	2.33	1.78	0.98	4.81	1.19
Int. LA LAS5	15	9.01	9.40	0.00	18.80	6.17

differences between the groups was evaluated using the Student's t-test and χ^2 test. Correlation was estimated using Pearson's r-test for parametric values and Spearman's rank R-test for nonparametric values. A p level of < 0.05 was accepted as statistically significant.

Results

The results are presented in Table 1. The average P-wave duration in standard ECG was 129 ms; the same parameter derived from augmented ECG was 30 ms higher (158 ms). Thus, in the subsequent analysis, the latter method was applied. Prolonged averaged values of Pdur (158 ms), IACT (140 ms) and TAAT (181 ms) confirm the predominance of atrial conduction disturbances in the examined group of patients. The duration of the A wave in the right atrial SA-IEGM was more prolonged (175 *vs*. 156 ms); the RMS20 lower (1.8 *vs*. 2.2 μV) and the low amplitude signal almost twofold (12.9 *vs*. 6.7 ms) in comparison to the external SA-ECG. Moreover, we observed that the duration of the right atrial A wave in SA-IEGM was 20 ms longer in comparison to the P-wave duration in external SA-ECG. The duration of the left (basal right+left) atrial A wave in SA-IEGM was also noticeably prolonged and virtually equal to the right-atrial (175 ms); the RMS20 was slightly higher (2.3 μV) compared to RA and equal to the external Frank's leads values. The low amplitude signal was distinctly longer (9.0 *vs*. 6.7 ms) in comparison to the external SA-ECG.

The significance of the differences (analysis of variance and LSD test) in atrial potential duration and its RMS20 and LAS5 values in SA ECG/ /IEGM recordings is presented in Table 2. The duration of A wave measured in the SA-IEGM from RA and LA did not differ, but it must be recognized that different timings were measured — the onset and the ending of LA A wave was recorded distinctly later in comparison to the RA A wave timing. There were no significant differences between the RMS20 of the external P-wave and the RA A wave, yet the LA A wave RMS20 was significantly higher in comparison to RA. This finding may suggest that the LA activation terminates in a more uniform (homogenous) way than in the right atrium. Correspondingly, the LAS5 values were significantly higher in the RA than in the LA SA-IEGM and the external SA-ECG, which can reflect less homogenous termination of RA potential.

Examinations of mutual correlation (r Pearson's) between atrial potential duration, its RMS20 and LAS5 values derived from external and intraatrial signal-averaged signals are presented in Table 3. There was a strong correlation between the duration of SA-ECG P-wave and SA-IEGM A waves in both right and left atria; however, the external P-wave duration was, on average,

Table 2. Comparison of atrial potential duration and its RMS20 and LAS5 in recordings obtained from external (Frank's) and intraatrial leads.

Examined parameters	N	Leads	Average	SE	Analysis of variance	LSD test				
						Groups	Comparison	Aver. diff.	SD of diff.	P
S.A. ECG/IEGM	23	Extern.	155.9	3.57	F = 1411.6	1	1 *vs*. 2	–18.7	3.1	0.000
P&A wave	23	Int. RA	174.6	5.13	p = 0.000	2	1 *vs*. 3	–19.4	3.1	0.000
duration	23	Int. LA	175.3	5.56		3	2 *vs*. 3	–0.70	3.1	0.821
S.A. ECG/IEGM	12	Extern.	1.94	0.20	F = 118.6	1	1 *vs*. 2	0.32	0.30	0.308
P&A RMS20	12	Int. RA	1.62	0.17	p = 0.000	2	1 *vs*. 3	–0.60	0.30	0.059
	12	Int. LA	2.54	0.36		3	2 *vs*. 3	–0.92	0.30	0.006
S.A. ECG/IEGM	15	Extern.	8.38	3.59	F = 98.5	1	1 *vs*. 2	–6.18	2.54	0.022
P&A LAS5	15	Int. RA	14.56	11.24	t = 0.000	2	1 *vs*. 3	–0.62	2.54	0.807
	15	Int. LA	9.01	5.59		3	2 *vs*. 3	5.55	2.54	0.037

Table 3. Examinations of mutual correlation (*r* Pearson's) between atrial potential duration, its RMS20 and LAS5 examined in external and intraatrial recordings.

Parameters	Leads	No.	Average	SD	r(X,Y)	t	p
P&A wave duration in external and internal leads	External Int. RA	23	155.9 174.6	17.1 24.6	0.73	4.965	0.000
	External Internal LA	23	155.9 175.3	17.1 26.7	0.77	5.559	0.000
	Internal RA Internal LA	23	174.6 175.3	24.6 26.7	0.94	12.229	0.000
RMS20 of P&A wave in external and internal leads	External Int. RA	12	1.94 1.62	0.67 0.58	0.61	2.437	0.035
	External Internal LA	12	1.94 2.54	0.67 1.25	0.53	1.984	0.075
	Internal RA Internal LA	12	1.62 2.54	0.58 1.25	0.03	0.107	0.916
LAS5 of P&A wave in external and internal leads	External Int. RA	23	6.970 12.91	7.51 7.92	0.16	0.728	0.475
	External Internal LA	15	8.38 9.01	8.65 6.17	–0.12	–0.446	0.663
	Internal RA Internal LA	15	14.56 9.01	5.99 6.17	–0.24	–0.878	0.396

20 ms shorter than in internal recordings. The difference of mean values indicates that, in spite of strong correlation (r = 0.7), referred parameters are not entirely compatible.

The most significant correlation was attained between the left and right atrial A wave durations (in IEGM records). There was a significant correlation (r = 0.5) between RMS20 values derived from external SA-ECG and the right atrial SA-IEGM; there was no significant correlation between RMS20 values derived from the external SA-ECG and left atrial SA-IEGM. There were no associations between the RMS20 and LAS5 values derived from the right and left atrial SA-IEGM, which proves there is no connection between atrial potential termination patterns in the right and left atria.

Thereafter, we analyzed the relationship between atrial potential duration and two basic atrial conduction indicators — IACT and TAAT (Table 4). There was a significant correlation between IACT (r = 0.6) along with TAAT (r = 0.8) and external P-wave duration as well as intraatrial SA-IEGM A wave duration. Since all the above parameters reflect the conduction time within the atria, such an outcome was anticipated. However, we noticed that the external SAECG P-wave duration does not reveal atrial activation entirely, since it is 15 ms shorter than the total atrial activation

Table 4. Examination of mutual correlation (*r* Pearson's) between IACT/TAAT and S.A. P/A duration recorded from external and intraatrial leads.

Pairs of variables		No.	Average	SD	*r*(X,Y)	t	p
Correlations with IACT	IACT Ext. Pdur	24	103.7 156.2	22.6 16.8	0.52	2.839	0.009
	IACT Int. RA Adur	24	103.7 174.8	22.6 24.1	0.53	2.910	0.008
	IACT Int. LA Adur	23	103.9 175.3	23.1 26.7	0.63	3.754	0.001
Correlations with TAAT	TAAT Ext. Pdur	24	181.5 156.2	22.4 16.8	0.76	5.471	0.000
	TAAT Int. RA Adur	24	181.5 174.77	22.4 24.10	0.83	7.096	0.000
	TAAT Int. LA Adur	23	181.1 175.3	22.9 26.7	0.89	9.131	0.000

time (TAAT). The duration of atrial potential in SA-IEGM recorded from right and left atria is virtually equal, although it starts earlier in the right atrium, which indicates that in the two recordings, the activation of diverse atrial regions is evaluated.

Occurrence of atrial late potential criteria in external SA-ECG and intraatrial SA-IEGM. ALP criteria were positive in 79% of pts in external SA-ECG (Fig. 4), in 96% of pts in the right atrial and in 86% of pts in the left atrial SA-IEGM (Table 5).

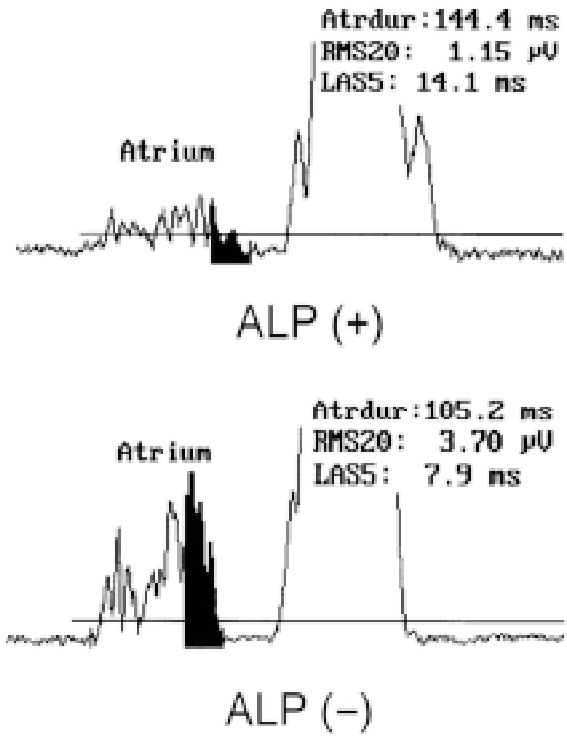


Figure 4. Example of positive and negative atrial late potentials (ALP).

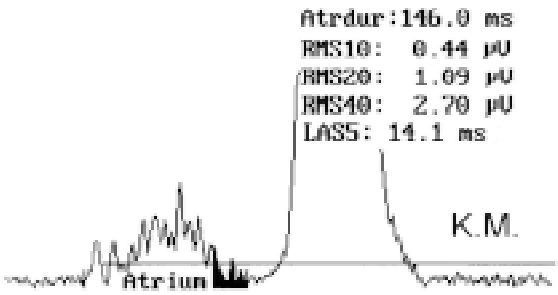
Both methods were consistent in 83% of pts; the presence of ALP in external SA-ECG was always confirmed by the right atrial SA-IEGM — in 17% of pts, the opposite phenomenon was observed. It may be a sign of greater sensitivity of intraatrial SA-IEGM, or the necessity of different ALP evaluation criteria. In only in 1 out of 24 pts (4%), was the ALP in external SA-ECG not confirmed by the left atrial SA-IEGM; in 9% of pts, an opposite phenomenon was observed. There was 91% compatibility in the right and left atrial ALP occurrence, only in 2/24 pts (9%) was ALP presence in the right atrial SA-IEGM not confirmed by the left atrial SA-IEGM; the opposite phenomenon — ALP presence in the left but not in the right atrium — was not observed. These records may suggest the leading role of right atrial conduction disturbances as a background of atrial arrhythmias (Fig. 5).

Correlations between dimensions of the left atrium, left ventricle, LVEF and basic atrial activation parameters (P/A wave duration, RMS20, LAS5) revealed by SA-ECG/IEGM are presented in Table 6. There was no significant correlation between LA dimension and SA-ECG/IEGM derived atrial activation parameters. There were minor correlations between LVDd and P-wave duration (r = 0.53) and RMS20 (r = –0.53); also between LVEF and P-wave duration (r = –0.47) and right atrial A wave duration (r = –0.50). These results suggest that there is neither an association between LA enlargement nor LV contractility, and inhomogeneity of atrial activation revealed by the existence of micro oscillations in its final part.

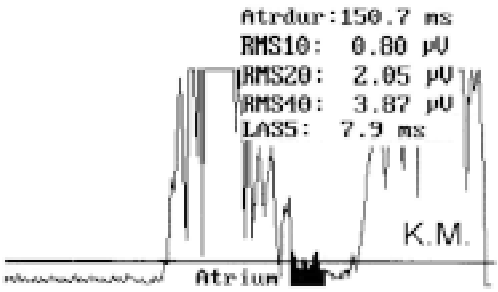
Correlations between the frequency of arrhythmia recurrences and basic atrial activation parameters (P/A wave duration, RMS20, LAS5) revealed by SA-ECG/IEGM are presented in Table 7.

Table 5. Presence of positive atrial late potentials (ALP) criteria in SA-ECG/IEGM recorded from conventional and intraatrial leads.

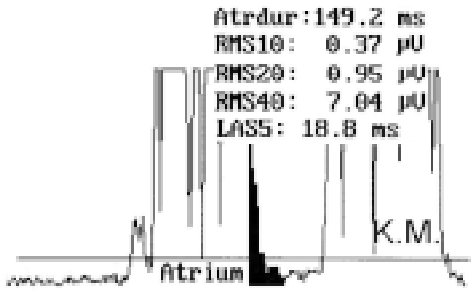
Leads	Ext. lead	Int. RA lead	Int. LA lead
ALP Yes	19 (79.2%)	23 (95.8)	19 (86.4%)
ALP No	5 (20.8%)	1 (4.2%)	3 (13.6%)
Lack (not available)	0	0	2
All examined	24 (100%)	24 (100%)	22 (100%)
Examination of accordance of ALP appearance in external and intraatrial leads			
ALP in ext. leads *vs.* ALP in Int RA leads		$\chi^2 = 3.965$; p = 0.046	
ALP in ext. leads *vs.* ALP in int. LA leads		$\chi^2 = 3{,}818$; p = 0.0500	
ALP in Int RA leads *vs.* ALP in int. LA leads		$\chi^2 = 6.634$; p = 0.010	



External SA-ECG



Internal RA SA-ECG



Internal LA SA-ECG

Figure 5. Signal-averaged electrogram obtained from external and intraatrial leads in the same patient.

Mean values of the P/A wave duration increased along with the arrhythmic burden but did not differ significantly. The opposite tendency was observed in the RMS20 values, lower (but not significant) in pts with a high frequency of arrhythmic episodes. There was no correlation between the arrhythmic burden and inhomogeneity of atrial activation revealed by the existence of micro oscillations in its final part.

Correlation between the frequency of arrhythmia recurrences and ALP occurrence in the external and intraatrial SA-ECG/IEGM is presented in Table 8. There was a minor positive correlation between arrhythmic burden and ALP occurrence in external SA-ECG but not in intraatrial SA-IEGM. These results confirm that there is no general association between inhomogeneity of atrial activation and severity of arrhythmia.

Correlations between ongoing antiarrhythmic therapy and basic atrial activation parameters (P/A wave duration, RMS20) revealed by the SA-ECG/IEGM are presented in Table 9. In the subgroups of pts non-treated and those treated with one and two antiarrhythmic drugs, the values of P/A waves increased ambiguously with no significant change in RMS20 values, suggesting no straight association between antiarrhythmic therapy and conduction disturbances or activation inhomogeneity within the atria.

Correlation between ongoing antiarrhythmic therapy and ALP occurrence in external and intraatrial SA-ECG/IEGM is presented in Table 10. Atrial late potential criteria in the external SA-ECG were positive in 54% of the non-treated pts and in all (100%) pts treated with one or two antiarrhythmic drugs — the differences were significant with positive correlation. Atrial late potentials in intraatrial SA-IEGM were present in virtually all pts in subgroups with no statistical differences, which suggests no clear association between

Table 6. Examination of mutual correlation between values of LA diameter, LVd diameter and LVEF and S.A. P-wave time domain parameters in records obtained from conventional and intraatrial leads.

LA diameter and parameter of S.A. ECG/IEGM	No.	Aver.	r(X,Y) p	LVd diameter and parameter of S.A. ECG/IEGM	No.	Aver.	r(X,Y) p	LVEF and parameter of S.A. ECG/IEGM	No.	Aver.	r(X,Y) p
LA diam.	24	44.30	0.34	LVd diam.	24	53.4	0.53	LVEF (%)	24	55.2	–0.47
Ext. Pdur		156.2	0.099	External Pdur		156.2	0.008	Ext. Pdur		156.2	0.019
LA diam.	20	44.4	0.17	LVd diam.	20	53.3	–0.36	LVEF (%)	20	54.5	0.33
Ext. RMS20		2.17	0.462	Ext. RMS20		2.17	0.122	Ext. RMS20		2.17	0.147
LA diam.	24	44.29	–0.13	LVd diam.	24	53.4	0.02	LVEF (%)	24	55.2	–0.38
Ext. LAS5		6.68	0.528	Ext. LAS5		6.68	0.938	Ext. LAS5		6.68	0.063
LA diam.	24	44.29	0.30	LVd diam.	24	53.4	0.29	LVEF (%)	24	55.2	–0.50
Int. RA Adur		174.8	0.160	Int. RA Adur		174.8	0.170	Int. RA Adur		174.8	0.012
LA diam.	23	43.9	0.12	LVd diam.	23	53.2	–0.53	LVEF (%)	23	54.7	0.11
Int. RA RMS20		1.77	0.590	Int. RA RMS20		1.77	0.009	Int. RA RMS20		1.77	0.614
LA diam.	23	43.9	–0.15	LVd diam.	23	53.2	0.32	LVEF (%)	23	54.7	–0.08
Int. RA LAS5		12.91	0.482	Int. RA LAS5		12.91	0.137	Int. RA LAS5		12.91	0.711
LA diam.	23	44.0	0.33	LVd diam.	23	53.4	0.29	LVEF (%)	23	55.3	–0.38
Int. LA Adur		175.3	0.128	Int. LA Adur		175.3	0.178	Int. LA Adur		175.3	0.072
LA diam.	15	43.5	–0.23	LVd diam.	15	54.3	–0.19	LVEF (%)	15	51.9	0.16
Int. LA RMS20		2.33	0.411	Int. LA RMS20		2.33	0.502	Int. LA RMS20		2.33	0.571
LA diam.	15	43.5	0.27	LVd diam.	15	54.3	0.21	LVEF (%)	15	51.9	–0.34
Int. LA LAS5		9.01	0.331	Int. LA LAS		9.01	0.452	Int. LA LAS5		9.00	0.209

antiarrhythmic therapy and atrial activation inhomogeneity.

Discussion

Recognition of atrial conduction disturbances, an essential substrate of atrial arrhythmias have become particularly important since the launch of the new therapeutic option — atrial resynchronization therapy [17–19]. The most comprehensive data is revealed by electrophysiological study (EPS), but this invasive and expensive procedure is neither suitable for a preliminary selection for atrial resynchronization therapy nor to evaluate its electrophysiological effects. Analysis of time- and frequency-domain parameters of signal-averaged high-gain P-wave introduced 15 years ago brought great hope, although low signal amplitude and a relatively sluggish onset of the P-wave recorded from orthogonal Frank's leads complicate the synchronization process [1–13]. The application of oesophageal leads to the signal-averaging technique considerably improved signal quality (mostly its amplitude), leading to enhanced detection of atrial refractoriness inhomogeneity (sluggish termination and micro-oscillations in the final portion of atrial potential). This provides a more reliable recognition of the arrhythmia recurrence hazard; however, the procedure is far less comfortable [3]. The described oesophageal signal averaging technique was also applied by the authors [39], though it gave no prospect to answer the questions put in the introduction (concerning the right atrial potential termination) since the terminal part of the oesophageal signal originates from the left atrium.

The presented results demonstrated the technical possibility of using three low-impedance intraatrial leads to obtain right and left atrial electrograms to be processed with the conventional signal-averaging technique. Intraatrial SA-IEGM provided registration of an additional 20 ms of atrial activation omitted in external recordings. The extinction of atrial activation in pts with severe atrial arrhythmias was less homogenous in the right than in the left atrium. Moreover, the right atrial SA-IEGM allows for more frequent identification of atrial late potentials in comparison to the external SA-ECG, if the same criteria are applied.

Although atrial dimensions have an important role in arrhythmia perpetuation [37–40], far less is known about their influence on atrial conduction disturbances, particularly on the presence of microoscillations in the final part of atrial activation. Fukunami demonstrated that the P-wave duration in SA-ECG

Table 7. P duration and its RMSA20 and AF severity.

AF severity (freq. of recurr.) — Leads	No.	Average (SD)					
		P duration			RMS20		
		Extern.	Int. RA	Int. LA	Extern.	Int. RA	Int. LA
Sporadic (S) (monthly)	7	148.9 (18.2)	164.8 (12.1)	164.8 (14.7)	2.50 (0.82)	1.88 (0.73)	2.31 (1.37)
Recurrent (R) (weekly)	8	154.4 (18.2)	168.4 (18.4)	172.7 (30.9)	2.26 (0.69)	1.86 (0.73)	2.67 (1.57)
Frequent (F) (daily)	9	163.4 (13.2)	188.2 (30.5)	185.5 (29.2)	1.91 (0.82)	1.60 (0.75)	2.17 (1.08)
Analysis of variance	F	1.587	2.611	1.265	0.884	0.353	0.202
	p	0.229	0.097	0.304	0.431	0.707	0.819
LSD test	S *vs.* R	0.526	0.758	0.582	0.618	0.967	0.718
	S *vs.* F	0.096	0.051	0.134	0.226	0.489	0.876
	R *vs.* F	0.276	0.084	0.346	0.372	0.480	0.537

Table 8. Severity of AF and presence of ALP in external and intraatrial RA and LA recordings of SA ECG/IEGM during the study.

AF severity (freq. of recurr.)	Leads		
	Extern.	Int. RA	Int. LA
Sporadic (monthly)	4/7 (57.1%)	7/7 (100%)	6/6 (100.0%)
Recurrent (weekly)	6/8 (75.0%)	7/8 (87.5%)	5/7 (71.4%)
Frequent (daily)	9/9 (100%)	9/9 (100%)	8/9 (88.9%)
All	19/24 (79.2%)	23/42 (95.8%)	19/22 (86.4%)
χ^2	4.511	2.087	2.322
p	0.104	0.352	0.313

Table 10. Number of utilized antiarrhythmic drugs and presence of ALP in external and internal leads.

Parameters	Presence of ALP		
	Exten. lead	Int. RA lead	Int. LA lead
0	6/11 (54.6%)	10/11 (90.9%)	9/11 (81.8%)
1	5/5 (100.0%)	5/5 (100.0%)	4/4 (100.0%)
2	8/8 (100.0%)	8/8 (100.0%)	6/7 (85.7%)
χ^2	7.464	1.233	0.827
p	0.0239	0.539	0.661

was significantly increased in pts with recurrent atrial fibrillation in comparison to healthy subjects, regardless of the similar left atrial dimensions in both groups [2]. According to Stafford, atrial dilatation has an influence on the frequency-domain rather than time-domain SA-ECG parameters [26]; several other authors share this view [24, 28]. Provost emphasizes that the P-wave duration in SA-ECG and the atrial size have no relation and correspond to independent (electrophysiological and

Table 9. Number of utilized antiarrhythmic drugs and P/A wave duration and RMS20 in external and intraatrial leads.

Leads	No.	Average (SD)					
		P/A wave duration			RMS20		
		Extern.	Int RA	Int. LA	Extern.	Int RA	Int. LA
0	11	149.6 (19.3)	168.3 (24.6)	171.6 (39.9)	2.39 (0.84)	1.81 (0.72)	2.06 (1.56)
1	5	163.2 (15.3)	187.0 (24.4)	184.4 (22.0)	2.33 (0.97)	2.09 (0.87)	2.29 (1.13)
2	8	160.9 (11.7)	176.0 (23.0)	174.6 (24.4)	1.87 (0.51)	1.51 (0.61)	2.54 (1.07)
Analysis of variance	F	1.701	1.065	0.380	1.015	1.018	0.213
	p	0.206	0.362	0.688	0.383	0.379	0.811
ASD test comparison	0 *vs*. 1	0.135	0.162	0.395	0.884	0.479	0.802
of three groups	0 *vs*. 2	0.150	0.493	0.824	0.204	0.400	0.527
	2 *vs*. 3	0.805	0.430	0.546	0.309	0.174	0.783

anatomical) substrates [27]. Buncova explains increased LA dimension and SA-ECG P-wave duration in pts after long-lasting atrial fibrillation with the remodelling phenomenon [28], which corresponds with further observations. The prolonged P-wave and slight atrial dilatation are consequences of arrhythmia rather than the cause of it. With this knowledge, the interpretation of the findings in pts shortly after the termination of the long-lasting atrial arrhythmia must be carried out cautiously. In our study we demonstrated that although there is a weak correlation between echocardiographical indices of LV function and SA-ECG/IEGM parameters reflecting atrial conduction disorders (P/A wave duration), there is no correlation between the left atrium size and homogeneity of atrial potential termination (RMS20 and LAS5 parameters). We can ascertain that the left atrium size has a negligible influence on atrial conduction disturbances, and our results confirm the hypothesis that conduction disorders within the atria are independent of the left atrial dimensions [2, 5, 27, 28].

Prolonged or recurrent atrial fibrillation leads to the remodelling phenomenon (a shift in conduction velocity and refractoriness of atrial tissue), thus fibrillation itself becomes the cause of arrhythmia and this explains the conversion from paroxysmal to chronic AF [29]. There are a few articles analyzing the relationship between the arrhythmic burden and time-domain parameters of SA-ECG P-wave. Michelicci demonstrated that there is no difference in the P-wave triggered SAECG time- and frequency-domain parameters between the groups of pts with frequent ($\geq$ 2 episodes per year) and non-frequent ($<$ 2 episodes per year) lone paroxysmal atrial fibrillation [5]. Opolski et al. [6] and Raitt et al. [12] observed prolonged SA-ECG P-wave duration in pts with early AF recurrence after DC cardioversion. Kurogouchi demonstrated significantly increased P-wave duration and decreased RMS20 values in pts directly after arrhythmia termination and an improvement or normalization of analyzed parameters in the 3 months follow up, not followed by normalization in left atrium size [43]. Thereafter, time-domain parameters of the P-wave in SA-ECG appear to disclose not only the substrate of arrhythmia but also its (possibly reversible) consequences. The presented results demonstrated that even though there is a weak correlation between the arrhythmic burden (evaluated by rate of recurrence) and SA-ECG/IEGM parameters reflecting the degree of interatrial conduction disturbances (P/A wave duration), there is still no general association between severity of arrhythmia and inhomogeneity of atrial activation (reflected by micro-oscillations in the terminal part of atrial activation) in the group of pts selected for atrial resynchronization therapy. We must remember, on the other hand, that in some pts, drug-resistant arrhythmia may result from an existing focal trigger — frequently localized in pulmonary vein ostia [40].

When analyzing time- and frequency-domain parameters of signal-averaged P-wave in pts after the termination of atrial fibrillation, we must consider ongoing antiarrhythmic therapy, since there are numerous studies revealing the effect of AA drugs on the SA-ECG P-wave [30–33]. Ic class AA drugs, slowing down conduction within the atria, and III class, prolonging action potential and refractory period [30], should, hypothetically, have an influence on the homogeneity of atrial potential termination, particularly in pts with atrial conduction disorders. Stafford confirmed that III class AA drugs do not prolong the P-wave duration, but only increase the atrial refractory period, which is not reflected in SA-ECG P-wave parameters [31]. Haberl et al. [32] demonstrated that sotalol decreased the P-wave amplitude with an ambiguous influence upon its duration. Igarhasi et al. [33] demonstrated that flecainide prolongs P-wave duration, with no significant influence on RMS20 and LAS5 values. Procainamide had no apparent influence on SA-ECG P-wave parameters — the author assumes that the analysis of P-wave duration can be applied to assess the risk of AF recurrence regardless ongoing antiarrhythmic therapy. A contradictory opinion was presented by Raitt et al. [12], who believes that the P-wave duration can be a predictor of arrhythmic hazard only in pts without antiarrhythmic therapy since it reflects mostly atrial dilatation and conduction velocity but not atrial refractoriness. Its prolongation (a typical effect of class III antiarrhythmic drugs) significantly reduces the incidence of arrhythmia, regardless of abnormal SA-ECG P-wave parameters. Redfearn demonstrated that flecainide slows down conduction velocity, the adaptation of the refractory period to the heart rate, prolongs the P-wave duration and reduces its spectral energy [34].

Analysis of the presented data confirmed no straight association between antiarrhythmic therapy and conduction disturbances (P/A wave duration) or activation inhomogeneity (RMS20 and LAS5) within the atria assessed by SA-ECG/IEGM parameters. Some weak associations revealed in the study, in our opinion, are determined by the electrophysiological background and secondary arrhythmia escalation rather than the antiarrhythmic treatment.

The presented literature and our results suggest that analysis of the time- and frequency-domain

P-wave parameters in high gain, signal-averaged electrograms in pts with recurrent atrial arrhythmia reveal not only morphological changes in the atria with consequent local conduction disorders, but also the haemodynamic status (atrial wall strain) and the effects of prolonged arrhythmia (atrial remodelling) and ongoing antiarrhythmic medication.

Limitations of the study

The signal-averaging process was triggered by the R-wave, since P-wave synchronization was inadequate in pts with fragmented, low-amplitude P-wave, frequent in the studied group. The echocardiographic examination was restricted merely to essential parameters. The applied "left atrial" lead system is not purely left atrial — the introduction of a multipolar catheter to the left atrium via transseptal approach and selection of three bipolar leads would be a better option. It is a routine procedure in pulmonary vein ectopy mapping and ablation but not during pacemaker implantation. In the study group there were no indications for left heart catheterization; therefore, we applied a pacing electrode introduced to the coronary sinus connected to the tip and ring of the electrode placed in the low right atrium. Consequently, in the "left atrial" leads, the activation of the lower part of the right atrium was additionally recorded. Since the final part of the left atrial excitation has superior importance, we consider this solution satisfactory.

At the start of the study, there was some doubt whether the fragmented termination of the potential recorded from the right atrium truly reflects right atrial activation or just a far field sensing from the left atrium. However, parallel recordings performed during left atrial and biatrial pacing confirmed the existence of what were clearly right atrial late potentials, since the left atrium was activated earlier during pacing [41, 42]. The study was performed in the selected group of patients with recurrent atrial arrhythmia and considerable conduction disturbances within the atria, thus our conclusions must not be applied to the general population of patients with paroxysmal atrial fibrillation.

Conclusions

1. There is a technical possibility to obtain averaged signals from the right and left atria separately by means of the conventional technique designed for external high-gain signal-averaged ECG recording. By this means, an additional 20 ms of atrial potential is registered, suggesting superior scientific and diagnostic potential.
2. The right atrial SA-IEGM allows for more frequent ALP recognition in comparison to external SA-ECG, with the same criteria applied.
3. The termination of right atrial activation in patients with interatrial conduction disturbances and recurrent atrial fibrillation is less homogenous compared to the left atrium.
4. Although there is a weak correlation between echocardiographic indices of LV function and SA-ECG/IEGM parameters reflecting atrial conduction disorders (P/A wave duration), there is no correlation between LV function indices and the homogeneity of atrial potential termination.
5. Although there is a weak correlation between the arrhythmic burden (evaluated by rate of recurrence) and SA-ECG/IEGM parameters reflecting the degree of interatrial conduction disturbances (P/A wave duration), there is no clear association between the severity of arrhythmia and inhomogeneity of atrial potential termination
6. There is no direct association between antiarrhythmic therapy and conduction disturbances (P/A wave duration) or activation inhomogeneity (RMS20 and LAS5) within the atria assessed by SA-ECG/IEGM parameters.
7. The differences in P/A wave duration in SA-ECG and intraatrial SA-IEGM with diverse homogeneity of atrial potential termination in right and left atria, as well as limitations of external Frank leads SA-ECG, indicate that the investigation of intraatrial three-lead SA-IEGM may be a valuable diagnostic tool e.g. for comparative analysis of different atrial pacing modes.

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