

Atrial Fibrillation Recurrence Predictors after Conversion to Sinus Rhythm

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ABSTRACT: Purpose: We aimed to identify predictors of atrial fibrillation recurrence after conversion to sinus rhythm. Material/Methods: We included 100 patients with a history of documented atrial fibrillation in the last 12 months that were assessed by transthoracic echocardiography, 12-lead electrocardiogram and signal averaged electrocardiogram of the P wave. Follow-up was 7.3 ± 2.2 months. Results: Atrial fibrillation recurrence was documented in 27 patients. It was more frequent in patients with longer duration of previous atrial fibrillation episode, with increased left atrium size and left ventricular mass, and it was correlated with the filtered P wave duration and Integral of the P wave. Conclusions: Signal averaged ECG of the P wave, left atrium size and left ventricular mass determined by echocardiography could be helpful in predicting the risk of atrial fibrillation recurrence after conversion.

KEYWORDS: atrial fibrillation, signal-averaged ECG, P wave

Introduction

Atrial fibrillation (AF) is the most frequent cardiac arrhythmia and is associated with increased risk of death, stroke and other thromboembolic events, heart failure and hospitalizations, left ventricular dysfunction, decreased quality of life and work incapacity.

Atrial fibrillation it is seen in 1% of patients over 60 years and over 5% of those over 69 years. Atrial fibrillation is more common in men than in women - about 1.5 times as in Framingham study [1, 2]. In the first two decades of life, atrial fibrillation is relatively rare, as associated with congenital heart disease or the presence of accessory pathways. Whereas until a few decades ago, valvular diseases were the most common causes of atrial fibrillation, the most common diseases today associated with atrial fibrillation (AF) are hypertension and coronary disease.

Extrapolating data from health surveys we can assert that in our country atrial fibrillation is under-diagnosed and under-treated - about 1% of Romania's population is affected by atrial fibrillation; only 50% of this population is diagnosed, and only 65% are treated. Among those treated only 45% have a good control of their treatment [3].

In practical terms there are defined three categories of classification of AF [4]:

Paroxysmal AF - is an arrhythmic episode that started less than 48 hours (< 7 days), documented or symptomatic, is converted spontaneously to sinus rhythm (SR) in 60% of cases within 48 hours of evolution, does not necessarily require anticoagulation (< 48 hours).

Persistent AF - arrhythmic episode lasting more than 7 days (may be older than one year) in which it was not indicated or tried the cardioversion or AF with unspecified debut. It rarely spontaneously converts to SR. It can be a culmination of recurring PxAF or it may be recurring itself.

Permanent AF - includes persistent AF > 1 year or PsAF that could not be converted to SR or SR could not be maintained, and AF associated with a severe disease, which is not suitable conversion.

Prediction of recurrence of AF after conversion to sinus rhythm is an important issue because by identification of patients at high risk of recurrence they may benefit from closer monitoring and more aggressive antiarrhythmic therapy [5]. Among the parameters that have been studied, high resolution electrocardiography (SAECG) has been shown to have the highest predictive value; the parameters of SAECG can identify patients at risk of developing atrial fibrillation (useful in primary prevention), or patients at risk of fibrillation recurrence after conversion to sinus rhythm (useful in secondary prevention).

Material and methods

This study was part of a research start-up grant that targeted patients with atrial fibrillation. The method we proposed for the management of patients with AF consisted of:

-an active local community screening to identify patients with atrial fibrillation.

-implementation of current European guidelines for diagnosis and treatment of atrial fibrillation.

-guiding treatment by high resolution electrocardiography result.

-educational measures of the target population to raise awareness of atrial fibrillation and risk of stroke, which is relatively unknown Romanian population.

Patient population

This prospective study enrolled 100 patients (55 men, mean age 68.21 ± 9.26 years) with a history of documented atrial fibrillation in the last 12 months, and that were currently in sinus rhythm. Patients were on standard medical treatment – as considered by the curing physician. Patients with NYHA II-IV chronic heart failure were not included.

Written informed consent was obtained from each patient at the screening visit.

Patient assessment

Echocardiography

Standard transthoracic echocardiography (Philips CX50) with simultaneous ECG monitoring was performed in all patients measuring: Left atrium diameter and volume, Left ventricular (LV) diameters, LV wall thickness, LV ejection fraction (LVEF - by modified Simpson rule), LV mass (Devereux).

P-wave signal-averaged electrocardiogram (P-SAECG)

Signal-averaged ECGs were recorded using General Electric MAC 5500; target noise level was $< 1 \mu\text{V}$. The following parameters of the P-wave SAECG were analyzed:

filtered P wave duration (fPWD);

the root mean square in the last 40, 30 and 20 ms (RMS40, RMS30, RMS20);

integral of the voltages in the entire P wave (INTP).

Follow-up

All patients were followed for an average of 7.3 ± 2.2 months. A phone contact was made every month in order to adjust the oral anticoagulant dosage and to obtain relevant information about patient status. Clinical follow-up was done at six months for the evaluation of atrial fibrillation recurrence (only documented – ECG or Holter – episodes were considered) and of adverse events.

Statistical analysis

Statistical analyses were performed by using SPSS 15.0 for Windows. Student's t test was used to analyze differences between mean values. A probability value of 0.05 or less was considered significant. To verify the normality of data repartition we used Kolmogorov-Smirnov and Shapiro-Wilk tests. All results are expressed as mean \pm standard deviation.

Table 1. Clinical, ECG and echocardiographic parameters.

	Min	1st Qu	Median	Mean	3rd Qu	Max	St dev
Age (years)	33	63	67	68.21	63	93	9.26
BMI (kg/m ²)	17.3	24.2	26.1	27.11	24.2	36.3	5.15
AF duration (months)	0.25	8	48	45.25	8	120	35.52
HR (/min)	46	62	74	75.19	62	151	17.78
PWD (ms)	56	83.5	104	98.9	83.5	124	20.86
QRS duration (ms)	66	80.5	88	92.27	80.5	140	17.62
LA diameter (mm)	31	40	44	44.76	40	65	7.05
LA volume (ml)	31	64.9	80	83.21	64.9	176	32.24
LA area (cm ²)	13.7	21.97	25	28.13	21.97	132.8	16.24
IVST (mm)	9	12	13	13.03	12	43	3.29
PWT (mm)	9	12	12.5	12.79	12	43	3.24
LVM (g)	131	180	203	209.95	180	332	45.88
LVESD (mm)	23	30.5	33	33.71	30.5	53	5.38
LVEDD (mm)	37	45	48	48.90	45	63	5.08
LVEF (%)	36	50	55	53.65	50	60	7.11

BMI-body mass index; AF-atrial fibrillation; HR-heart rate; PWD-P wave duration; QRS duration; LA-left atrium; IVST-interventricular septum thickness; PWT-posterior wall thickness; LVM-left ventricular mass; LVESD-left ventricular endsystolic diameter; LVEDD-left ventricular enddiastolic diameter; LVEF-left ventricular ejection fraction.

Results

Table 1 summarizes the patient characteristics. Mean age was 68.21 ± 9.26

years. Mean P wave duration measured on the standard ECG was 92.27 ± 20.86 ms.

Table 2 presents the measured values for P wave SAECG in all patients.

Table 2. P wave SAECG parameters.

	Min	1st Qu	Median	Mean	3rd Qu	Max	St dev
fPWD (ms)	124	133	138.5	151.25	133	202	26.34
RMS20 (μ V)	1	3	3	4.08	3	10	2.42
RMS30 (μ V)	1	3	4.5	4.66	3	12	2.99
RMS40 (μ V)	1	3.75	5	5.16	3.75	11	2.62
INTP (μ Vs)	304	394.5	742	648.33	394.5	1010	248.59

During follow-up atrial fibrillation recurrence was documented in 27 patients. Data comparing these patients with those in which AF did not reappear is presented in table 3. Patients with AF recurrence had longer duration of the previous episode, left atrium dilatation, and left ventricular hypertrophy (by LV mass). There was no correlation with left ventricular ejection

fraction. Regarding signal averaged ECG parameters only filtered P wave duration (162.15 ± 29.21 ms vs. 148.78 ± 18.93 ms, $p = 0.004$) and Integral of the P wave (628.63 ± 265.57 μ Vs vs. 724.11 ± 238.34 μ Vs, $p = 0.02$) showed significant differences.

Table 3. Predictors of atrial fibrillation recurrence.

	Recurrent AF	Non-recurrent AF	p
Age (years)	67.12 ± 11.12	69.05 ± 9.19	ns
BMI (kg/m ²)	27.32 ± 6.22	27.02 ± 5.10	ns
AF duration (months)	49.12 ± 38.34	42.12 ± 34.76	0.04
HR (/min)	71.32 ± 21.32	76.25 ± 15.66	ns
PWD (ms)	108.23 ± 25.42	94.32 ± 19.56	ns
QRSD (ms)	96.2 ± 14.83	90.17 ± 18.16	ns
LA diameter (mm)	49.45 ± 9.14	42.54 ± 6.93	0.008
LA volume (ml)	88.53 ± 34.74	80.13 ± 30.12	0.03
LA area (cm ²)	32.16 ± 12.8	27.11 ± 18.11	0.05
IVST (mm)	12.81 ± 3.4	13.43 ± 3.12	ns
PWT (mm)	13.21 ± 3.45	12.46 ± 3.21	ns
LVM (g)	214.34 ± 57.12	206.12 ± 38.42	0.05
LVESD (mm)	35.34 ± 12.11	31.89 ± 4.12	ns
LVEDD (mm)	52.12 ± 7.83	46.70 ± 4.88	ns
LVEF (%)	49.64 ± 11.23	55.87 ± 6.02	ns
fPWD (ms)	162.15 ± 29.21	148.78 ± 18.93	0.004
RMS20 (μ V)	3.78 ± 1.87	5.13 ± 2.12	ns
RMS30 (μ V)	4.12 ± 2.05	5.23 ± 2.34	ns
RMS40 (μ V)	4.86 ± 2.22	5.78 ± 2.18	ns
INTP (μ Vs)	628.63 ± 265.57	724.11 ± 238.34	0.02

BMI-body mass index; AF-atrial fibrillation; HR-heart rate; PWD-P wave duration; QRSD-QRS duration; LA-left atrium; IVST-interventricular septum thickness; PWT-posterior wall thickness; LVM-left ventricular mass; LVESD-left ventricular endsystolic diameter; LVEDD-left ventricular enddiastolic diameter; LVEF-left ventricular ejection fraction.

Discussions

There are three main therapeutic targets for patients with AF: to restore and maintain SR, to control the ventricular rate, and prevention of systemic and pulmonary thromboembolism.

The decision to restore the sinus rhythm or to control ventricular rate must be individualized for each patient, assessing the risk - benefit ratio. Benefits of SR include improved symptoms, preventing the transition to permanent AF and probably reduced embolic accidents. In patients with persistent atrial fibrillation, recurrences are common even after successful conversion to sinus rhythm. Most recurrences appear to be related to the age of atrial fibrillation, left atrial size and other predisposing factors (such as hyperthyroidism or postoperative status).

Our study demonstrates that atrial fibrillation recurrence after conversion to sinus rhythm is related to the duration of the AF episode, left atrial size (diameter, area, and volume), left ventricular mass and P wave SAECG parameters.

Left atrial size has long been recognized as an important factor in the development of atrial fibrillation and in its recurrence [6]. However, it was recently shown [7] that left atrium dysfunction could be present even in patients with normal LA size, carrying a risk of AF. Considering that the evaluation of left atrium function is not accessible to the practicing physician, other markers could be helpful. In our group left atrium dimensions were significantly greater in patients with atrial fibrillation recurrence (LA diameter: 49.45 ± 9.14 mm vs. $42.54 \text{ mm} \pm 6.93$ mm, $p = 0.008$; LA volume: 88.53 ± 34.74 ml vs. 80.13 ± 30.12 ml, $p = 0.03$; LA area 32.16 ± 12.8 cm² vs. 27.11 ± 18.11 cm², $p = 0.05$).

Other possible predictors of AF are indices of the P wave on standard ECG and signal averaged electrocardiogram, based on the hypothesis that prolongation of intra- and interatrial conduction and inhomogeneous impulse propagation are electrophysiological condition for AF. These conditions are reflected on the surface ECG by P wave duration and dispersion (defined as the difference between the maximum and minimum P wave durations) [8]. We did not find a correlation between P wave duration and AF. In the study of Magnani et al. [9] which followed 1.550 subjects from the Framingham Heart cohort (median follow-up was 15.8 years) the upper 5% of maximum P wave duration was associated with an HR of

2.51 (95% CI 1.13 to 5.57, $p = 0.024$) for AF, heart failure, or all-cause mortality in multivariable analysis.

Left ventricular systolic dysfunction and heart failure are related to AF [10]. In our study there was no relation to left ventricular ejection fraction, but we did not include patients with heart failure, and LVEF was above 50% in the majority of them.

Changes in SAECG parameters were seen in the setting of different cardiac conditions, and were associated with the risk of atrial fibrillation [5, 11].

Limitations of our study derive from the small number of patients and the relatively short follow-up.

Conclusion

Signal averaged ECG of the P wave, left atrium size and left ventricular mass determined by echocardiography could be helpful in predicting the risk of atrial fibrillation recurrence after conversion.

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References

1. Benjamin EJ, Levy D, Vaziri SM, et al. Independent risk factors for atrial fibrillation in a population-based cohort: the Framingham heart study. *JAMA*. 1994; 271: 840-844.
2. Kannel WB, Benjamin EJ. Current perceptions of the epidemiology of atrial fibrillation. *Cardiol Clin*. 2009; 27(1): 13-24.
3. Popescu R, Dan GA, Buzea A. Characteristics of patients with atrial fibrillation and history of stroke or transient ischemic attack – some results from the FACTS database. *Romanian Journal of Neurology*. 2013; 12(2): 53-57.
4. Camm AJ, Kirchhof P, Lip GY, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Eur Heart J*. 2010; 31(19): 2369-429.
5. Militaru C, Donoiu I, Ionescu DD. P wave signal-averaged ECG in normal population and in patients with converted atrial fibrillation. *Ann Noninvasive Electrocardiol*. 2011; 16(4): 351-6.
6. Henry WL, Morganroth J, Pearlman AS, et al. Relation between echocardiographically determined left atrial size and atrial fibrillation. *Circulation*. 1976; 53(2): 273-9.
7. Gupta DK, Shah AM, Giugliano RP, et al. Left atrial structure and function in atrial fibrillation: ENGAGE AF-TIMI 48. *Eur Heart J*. 2013 Dec 2. [Epub ahead of print]
8. Magnani JW, Williamson MA, Ellinor PT, et al. P wave indices: current status and future directions in epidemiology, clinical, and research applications. *Circ Arrhythm Electrophysiol*. 2009; 2(1): 72-9.

9. Magnani JW, Johnson VM, Sullivan LM, et al. P wave duration and risk of longitudinal atrial fibrillation in persons ≥ 60 years old (from the Framingham Heart Study). *Am J Cardiol.* 2011; 107(6): 917-921.
10. Sanders P, Morton JB, Davidson NC, et al. Electrical remodeling of the atria in congestive heart failure: electrophysiological and electroanatomic mapping in humans. *Circulation.* 2003; 108(12): 1461-8.
11. Darbar D, Jahangir A, Hammill SC, et al. P wave signal-averaged electrocardiography to identify risk for atrial fibrillation. *Pacing Clin Electrophysiol.* 2002; 25(10): 1447-53.

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