Review Article

Atrial fibrillation risk assessment in patients with metabolic syndrome with atrial premature complexes: A prospective study

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Abstract

Background

The prognostic significance of atrial premature complexes (APC) in patients with metabolic syndrome (MS) is not fully elucidated. We aimed to determine the risk of atrial fibrillation (AF) in patients with MS, by using the integrated analysis of this type of arrhythmia predictors and analysis of APC in prospective study.

Material and methods

We observed 1427 patients with MS aged 45–75 years mean age, 66.3±2.7years with registered APC from 1998 to 2012. In addition to general clinical examination parameters of hemodynamics, P wave signal-averaged electrocardiogram (ECG) and P wave dispersion (Pd) were evaluated in all patients. The character of APC with the calculation of the risk index for AF (IRAF) was also determined. After inclusion into the study, patients were followed up for 1 up to 5 years. The primary outcome of the study was the existence or absence of AF development.

Results

In prospective observation, paroxysmal or persistent AF developed in 156 (10.93%) patients within 4–5 years. The long-term risk of developing AF was identified in patients with MS aged over 55 years and with a body mass index $\geq$30 kg/m^2 when detecting atrial dilatation and/or abnormal values of P wave signal-averaged ECG, Pd. The short-term (for 1–2 years after the first examination) risk of AF in patients with MS was evaluated by observing patients in the dynamics. Compared with the baseline values, decrease of IRAF values by 35% or more for every 3–4 months of observation indicates AF development in patients with MS within 1–2 years. If IRAF values are $\leq$0.5 units at the subsequent decrease of this parameter by 70% or more within 1–3 months of observation, it indicates AF development within 6 months after the observation.

Conclusions

Comprehensive survey of patients with MS with APC, including the detection of predictors of AF development and IRAF, allows determination of both long-term and short-term risks of developing AF.

Keywords

- Metabolic syndrome
- Atrial fibrillation risk assessment

Introduction

Any structural heart disease can cause slow, but progressing ventricular and atrial structural remodeling,

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particularly resulting in local heterogeneity of atrial conductivity; thus, this promotes development and maintenance of atrial fibrillation (AF).[1,2] The European and American AF guidelines have specified that metabolic syndrome (MS) is one of the most common causes of arrhythmia.[1,2] In recent years, various predictors of AF development have been observed and include[1–4]

- Left atrial dilatation
- Mitral valve calcification
- Decreased left ventricular ejection fraction (LVEF)
- Diminished spectral transmitral flow
- Presence of pathological values of parameters P wave signal-averaged electrocardiogram (ECG)
- Atrial premature complexes (APC)
- Increase in P wave dispersion (Pd)

Despite the progress in identification of predictors of this arrhythmia, the current recommendation for timely detection of AF includes a screening by palpation of the pulse for all patients over 65 years of age and ECG registration in case of an irregular pulse.[1,2] ECG monitoring is indicated if the patient experiences rapid heartbeat and shortness of breath; implantable loop recorders may be used if necessary.[1,2] However, the integrated use of AF predictors in patients with MS and APC character analysis, for diagnosing patients with the potential risk of AF in the prospective study, was not found in the literature available.

Aim

To determine the risk of AF in patients with MS, using the integrated analysis of arrhythmia predictors and analysis of APC, in the prospective study.

Materials and methods

We observed 1427 patients with MS from 1998 to 2012, aged 45–75 years mean age, 66.3±2.7 years). MS diagnosis was based on the standard criteria.[5] Inclusion criteria were the presence of sinus rhythm, APC, chronic heart failure in NYHA class I or II, the absence of AF registration, including 2–3 procedures of 1–3 day (24–72 hours) ECG monitoring. Patients were informed and consent was obtained for investigation and treatment.

Patients with acute coronary syndrome, Wolff–Parkinson–White syndrome, sick sinus syndrome, atrioventricular block, implanted artificial pacemaker, ventricular tachycardia and extrasystole (II–V class due to Rayn classification), ischemic heart diseases, cardiomyopathies, thyroid gland dysfunction, uncontrollable arterial hypertension, severe somatopathies, which could affect the results of the study, and patients with LVEF < 45%, left ventricle aneurism, chronic heart failure in NYHA class III-IV were not included in the study. Essential hypertension was present in 1133 (79.40%) patients, 914 (64.05%) patients had diabetes mellitus, and 216 (15.14%) patients had chronic obstructive pulmonary disease.

Besides general clinical examination (clinical and biochemical blood tests, ECG registration, etc.), all patients underwent the central hemodynamic investigation using Hitachi EUB-5500 Diagnostic Ultrasound Scanner with Doppler transthoracical echocardiography; Holter ECG monitoring was performed using 12-leads with the device "Kardiotekhnika-4000" (firm «Incart», Russia) following the standard techniques.[6,7] Using the modified biplane Simpson's rule, such hemodynamic parameters as LVEF, we also calculated left atrial end-diastolic index (LAEDI), left ventricular myocardial mass index (LVMMI), and detected maximum rates of transmitral blood flow in the early (E), late (A) phase of diastolic filling, and E/A ratio.[6] Data analysis was conducted according to the standards prescribed by ACC/AHA.[7] According to the recorded ECG monitoring results of the total number of APC per day and per hour, pre-ectopic interval APC (from P wave sinus complexes to P' wave APC in milliseconds) and post-ectopic interval (from P' wave APC to P wave sinus complexes in milliseconds) were determined. All indicators of APC (pre- and post-ectopic interval APC) were corrected to heart rate (these were divided into $\surd$ R-R interval of sinus rhythm).

We detected P wave signal-averaged ECG signal in the frequency band from 40 Hz to 250 Hz with registration bipolar leads X, Y, Z and averaging by Frank 400 complexes wave «P» with commercially available device (MAC 5000, Marquette Hellige, Germany) and "Poly-Spectrum-signal-averaged ECG" (firm "Neurosoft", Ivanovo, Russia) with automatic exclusion from the research of extrasystoles.[8] The following time values (in milliseconds) were determined: difference between the duration of the filtered and unfiltered wave «P» (FiP-P and Un-FiP), duration of the "P" signals at the end of the wave below 5 mV (D5) and amplitude parameters (in microvolts)—amplitude of the last 20 ms of P wave (RMS-20). Pathological values of P wave signal-averaged ECG parameters were considered as FiP-P > 120 ms, D5 > 25 ms, and RMS-20 < 3.5 microvolt.[8] The presence of positive P wave signal-averaged ECG was determined if at least these two criteria were fulfilled: FiP-P > 120 ms and RMS-20 < 3.5 microvolt.[8] Pd was determined with the help of a computer complex "Poly-Spectrum-ECG" (firm "Neurosoft", Ivanovo, Russia) automatic method by calculating the maximum difference of at least 10 complexes P-QRST between the duration of maximum

and minimum "P"; the average values for each patient Pd were considered.[8] Pathological values of Pd were considered as more than 40 ms.[9] Furthermore, calculated ratio FiP-P to Pd was expressed in units.[10]

All patients underwent basic hypotensive therapy by the inhibitors of angiotensin converting enzyme (enalapril, ramipril, etc.), saluretics [indapamid (arifon), etc.], and blood glucose and lipid content correction by diet, hypoglycemic and hypolipidemic drugs, statins in particular.[11,12] Antiarrhythmic drugs for treatment of APC were not used. Risk index for atrial fibrillation (IRAF) was calculated by the formula:

$$IRAF = (FiP\text{-}P \div Pd) \times (A \div B)$$

where IRAF is risk index for atrial fibrillation; FiP-P is filtered P wave duration signal-averaged ECG (in ms); Pd is P wave dispersion (in ms) determined as a difference between the maximum and minimum values of P wave duration in 12-leads standard ECG recorded; A is linear deviation of the corrected pre-ectopic interval APC not less than in 50 atrial extrasystoles; B is the number of APC used for the study, expressed in a number of extrasystoles for an hour.[10]

Detection of corrected pre-ectopic interval APC not less than 50 extrasystoles excludes false positive data in the assessment of this indicator.[10] It should be noted that at frequent APC, for more accurate visualization of P wave, especially when it was poorly visualized or superimposed with T wave, the transesophageal ECG leads recording was performed.

After inclusion into the study, patients were followed up for 1 up to 5 years till the existence or absence of AF development. All studies, including daily ECG monitoring, were conducted at least once every 3–4 months and monitoring of patients and ECG recording was conducted once a month. Patients performed regular monitoring of blood pressure and heart rate independently.

Statistical analysis of the results was conducted using a Student's t-test, x^2, the odds ratio (OR), confidence interval (CI) of the mean values and OR, and standard software packages of "Statistics", version 11.0. A p value of < 0.05 was considered statistically significant.

Results

After inclusion into the study, 156 (10.93%) of 1427 patients showed paroxysmal or persistent AF within 1–5 years after initial examination. All patients were divided into two groups. Group I consisted of 1271 (89.07%) patients without AF development and group II consisted of remaining patients with the development of this arrhythmia during prospective observation. Eight (5.13%) patients of group II were studied within 3–6 months, 15 (9.62%) patients were studied within 6–12 months, 35 (22.44%) patients were studied within 1–2 years, and the remaining patients were studied within 2–5 years before AF development. Gender and rate of hypertension, diabetes mellitus, and chronic obstructive pulmonary disease were not significantly different in patients of groups I and II.

Clinical and laboratory parameters of patients in groups I and II are presented in Table 1. The table shows that patients of group II belonged to the elderly category, and had statistically significant increased body mass index (BMI), waist circumference, triglycerides, low-density lipoprotein cholesterol, the number of APC (per hour) in comparison with group I, whereas significant differences in other studied parameters in patients of these groups was not registered. Changes in hemodynamic parameters, P wave signal-averaged ECG, and IRAF in patients of group II are presented in table 2. The table shows that examination of patients of group II 4–5 years prior to AF development revealed statistically significant increase of LAEDI, LVMMI, FiP-P, D_s, Pd and statistically significant decrease of FiP-P/Pd, E/A ratio, RMS-20, IRAF values in comparison with patients of group I. There were no significant differences in other parameters studied. In groups I [386 (30.36%)] and II [94 (60.26%)], P wave signal-averaged ECG sensitivity, specificity, and predictive values were 60%, 95% and 19%, respectively ($p < 0.05$). In groups I [254 (19.99%)] and II [105 (67.31%)], Pd sensitivity, specificity, and predictive values were 67%, 96% and 29%, respectively ($p < 0.05$). In groups I [273 (21.48%)] and II [118 (75.64%)], atrial dilatation sensitivity, specificity, and the predictive values were 76%, 97%, and 30%, respectively ($p < 0.05$). Beginning from the 3rd year of observation of AF development in patients of group II, significant increase in LAEDI, FiP-P, D_s, Pd, LVMMI and significant decrease of RMS-20, FiP-P/Pd ratios, E/A ratio in comparison with the same parameters of these patients for 4–5 years prior the development of this arrhythmia were noted. Beginning from the 2nd year and at follow-up observation, IRAF values considerably decreased (an average 95% and more) in comparison with the results obtained 3 years prior AF detection (Table 2). AF development correlated ($p > 0.7$) with age 60 years and above, BMI > 30 kg/m^2, RMS-20 < 3.1 microvolts, E/A ratio <0.95, LAEDI >30 ml/m^2, Pd >55 ms, FiP-P > 135 ms, FiP-P/Pd <2.5 units, IRAF <0.5 units, and AE determination $\geq$

1200 APC in a day of observation (Table 3). Determination of FiP-P/Pd values of ≤2.5 units together with FiP-P ≥ 135 ms and/or LAEDI ≥ 30 ml/m^2 and in combination with the decrease of IRAF values by 35% and more within each 3–4 months of observation in comparison with the initial values correlated with AF development within 1–2 years (p = 0.93, OR = 16.2, C ore for 1–3 months of observation; this further correlated with AF development within half a year after examination(p = 0.95, OR = 17.6, CI OR = 16.7–18.4).

Table 1: Clinical features and laboratory parameters of patients in groups I and II (M ± m)

Groups of patients	Group I	Group II
	n=1271	n=156
Parameters/features	M ± m	M ± m
Age, years	53.7 ± 3.2	65.9 ± 0.5*
BMI, kg/m^2	29.4 ± 0.2	33.9 ± 0.5*
Waist circumference, cm	101.2 ± 5.1	125.2 ± 1.5*
Blood glucose, mmol/l	6.4 ± 0.2	6.8 ± 0.5
Total cholesterol, mmol/l	6.3 ± 0.2	6.9 ± 0.3
Low density lipoprotein cholesterol, mmol/l	3.2 ± 0.2	4.3 ± 0.5*
High-density lipoprotein cholesterol, mmol/l	0.8 ± 0.2	0.9 ± 0.2
A number of APC, per hour	24 ± 1	34 ± 2*

Note: ,*significant difference compared to group I (p < 0.05).

Table 2: Hemodynamic parameters, P wave signal-averaged ECG, IRAF in patients of group II in the dynamics in a prospective study (M±m and 95% CI for the mean)

Groups of patients	Group I‡ n = 1271	Group II n = 156 Examination before the development of AF (years)				
Parameters/ features		4–5 years‡	3 year‡	2 year‡	1 year‡	>0,5 year‡
LVEF, %	58.43 ± 0.23 49–71	57.83 ± 0.76 48–69	56.84 ± 0.77 47–66	56.64 ± 0.76 47–68	57.89 ± 0.85 48–69	58.87 ± 0.97 49–71
E/A, un.	1.14 ± 0.02 0.96–1.32	1.01 ± 0.02* 0.72–1.29	0.95 ± 0.02*† 0.71–1.23	0.91 ± 0.02*† 0.66–1.15	0.86 ± 0.02*† 0.61–1.11	0.85 ± 0.02*† 0,61–1,09
LAEDI, ml/m^2	25.37 ± 0.44 18–33	30.06 ± 0.52* 24–38	31.56 ± 0.53*† 25–39	32.96 ± 0.51*† 25–41	34.79 ± 0.64*† 28–43	35.93 ± 0.52*† 29–45
LVMMI, g/m^2	128 ± 0.3 115–143	132± 0.3* 122–143	134 ± 0.3*† 123–145	135±0.3*† 127–148	136±0.3*† 128–150	138 ± 0.3*† 128–152
Un-FiP, ms	108 ± 0.5 90–126	129 ± 1* 119–141	131 ± 1*† 121–143	132 ± 1*† 122–144	133 ± 1*† 123–144	133 ± 1*† 123–144
FiP-P, ms	116 ± 0.5 93–134	138 ± 1* 125–151	141 ± 1*† 126–154	142 ± 1*† 129–155	143 ± 1*† 130–155	144 ± 1*† 132–155
D5, ms	25 ± 0.1 10–30	26 ± 0.5* 20–32	27 ± 0.4*† 23–33	31 ± 0.5*† 26–36	34 ± 0.3*† 30–38	37 ± 0.3*† 33–41
RMS-20, microvolt	4.2 ± 0.04 2.3–5.2	3.3 ± 0.07* 2.2–4.3	2.9 ± 0.07*† 2.0–3.7	2.7 ± 0.07*† 1.7–3.5	2.6 ± 0.07*† 1.6–3.3	2.4 ± 0.07*† 1.4–3.2
Pd, ms	31 ± 1 17–52	42 ± 1* 35–59	52 ± 1*† 39–63	57 ± 1*† 51–65	65 ± 1*† 58–78	67 ± 0.6*† 59–79
FiP-P/Pd, un	3.74 ± 0.05 5.39–2.41	3.29 ± 0.03* 3.67–2.53	2.71 ± 0.01*† 3.23–2.34	2.49 ± 0.02*† 2.59–2.31	2.20 ± 0.02*† 2.51–2.02	2.15 ± 0.02*† 2.33–2.01
IRAF, un	24.18 ± 2.34 2.31–54.17	10.25 ± 1.8* 1.93–28.57	8.57 ± 1.15* 1.28–19.44	0.43 ± 0.09*† 0.12–1.34	0.29 ± 0.04*† 0.05–0.7	0.12 ± 0.02*† 0. 01–0.5

Note: 1, at the top M ± m, at the bottom – 95% confidence interval (CI) for the mean; ‡, average data for the period of observation; *, significant difference of parameters compared to group I, †, data of patients for 4–5 years prior the AF development ($p < 0.05$); ECG, an electrocardiogram; IRAF, risk index for atrial fibrillation; LVEF, left ventricular ejection fraction; E and A, maximum rates of transmitral blood flow in the early and late phase of diastolic filling; LVMMI, left ventricular myocardial mass index; LAEDI, left atrial end-diastolic index; Un-Fip and FiP-P, unfiltered and filtered P wave duration; Pd, P wave dispersion; D_s, duration of signal at the end of the P wave under 5 microvolts; RMS-20, the root mean square amplitude of the last 20 ms of P wave.

Table 2: The correlation (value $r > 0.7$) and OR of clinical and instrumental features of AF development in patients with MS

Parameters/features	R	OR	CI OR
Age over 60	0.72	2.8	2.0–3.5
BMI > 30 kg/m^2	0.83	3.4	2.4–3.9
RMS-20 < 3.1 microvolt	0.75	6.3	5.6–6.8
E/A < 0.95	0.77	3.3	2.6–3.8
LAEDI > 30 ml/m^2	0.79	6.2	5.1–6.8
Pd > 55 ms	0.87	8.4	7.9–8.9
FiP-P > 135 ms	0.91	7.6	6.8–8.1
FiP-P/Pd < 2.5 un.	0.90	11.3	10.4–11.9
IRAF < 0.5 un.	0.93	14.8	12.3–15.8
≥1200 APC per day of observation	0.86	6.5	5.6–7.1

Note: AF, atrial fibrillation; MS, metabolic syndrome; APC, atrial premature complexes; OR, odds ratio; CI, confidence interval; IRAF, risk index for atrial fibrillation; E/A ratio, the ratio of the early (E) to late (A) ventricular filling velocities at atrial contraction; LAEDI, left atrial end-diastolic index; FiP-P, filtered P wave duration; Pd, P wave dispersion, RMS-20, the root mean square amplitude of the last 20 ms of P wave.

Discussion

The incidence of AF in the total population is approximately 2% and the risk of developing arrhythmia at the age of 40 years and above is approximately 25%.[1,2] Any diseases of cardiovascular system can cause the progressive "structural and/or electric remodeling" of the atrial myocardium, contributing to the emergence, since multiple waves reenter the atria and result in AF development.[1,2,13,14] The existence of frequent APC and/or short asymptomatic AF episodes increase the risk of stroke and other complications.[1,2,15] Therefore, detection of patients with the potential risk of AF development (recommended along with pulse screening) thorough examination and observation for early diagnostics of the pathology, and determination of the principles of primary prevention of this arrhythmia are actual problems in modern cardiology.

This prospective study included 1427 patients with MS with the registered APC, aged 45–75 years. Each patient was observed for 1–5 years—the endpoint of the study was the presence or absence of AF. In 10.93% of the examined patients, prospective observation within 4–5 years showed paroxysmal or persistent AF.

The results of the study indicated that AF development in patients with MS was significantly more often recorded at the age over 60 with the BMI 30 kg/m^2, increased triglycerides, low density lipoprotein cholesterol, left ventricular volume increase, presence of abnormal values of P wave signal-averaged ECG, and Pd. Our findings are consistent with the results of previous studies.[1,2,8,9,12,14]

In recent years, it was established that abnormal values of P wave signal-averaged ECG and Pd identify delayed, fragmented conduction of excitement, which represents the anatomic substrate predisposing to the formation of the re-entry loop and AF, especially in the development of atrial dilatation.[3,7,8,12,13] Meanwhile, despite rather high sensitivity and specificity of these parameters, according to the results of the present study, their predictive value with regard to the AF development (new-onset AF) in patients with MS did not exceed 30%. Similar data were obtained by other researchers in previous studies.[16]

According to the Framingham Risk Score of AF development,[17] in all examined patients, the ten-year risk of developing AF was 25–30% (or 12%–15% within 4–5 years). In the present study, we found a significantly lower percentage of AF development in patients with MS, which may be due to the exclusion of patients with LVEF < 45%, left ventricular aneurysm, valvular heart diseases, and chronic heart failure in NYHA class III-IV from the study.

Development of APC may be due to various cellular mechanisms such as the presence of trigger activity (early or delayed afterdepolarizations, re-entry, etc.).[18] For example, the ectopy caused by the delayed afterdepolarization is usually associated with hyperpolarization of the cellular membrane in cardiomyocyte within 60–70 mV. This indirectly reflects the reversible nature of myocardiocytes function, and its induction can be the result of stress, vegetative or electrolytic imbalance, myocardium ischemia, etc., and after removing the cause, as a rule, it is relieved.[18]

Meanwhile, in progressive hyperpolarization of the cellular membrane in cardiomyocyte, for example, from 50 to 60 mV, local delay of excitation spread with the formation of unidirectional conduction block, leading to the development of re-entry in the area was noted. In most cases, this occurrence of arrhythmia mechanism was associated with more severe metabolic disturbances, and/or as a result, with an organic lesion of cardiomyocytes, which can form an anatomic substrate in atria, predisposing it to AF development.[17] In addition, an ectopic pacemaker or ectopic focus in the atrial myocardium or within pulmonary veins can be the source of APC.[18] It can be assumed that the frequent, prolonged, or recurrent APC, due to these mechanisms can contribute to the deterioration of the initially disturbed inhomogeneous excitation of the atria, increasing the potential risk of AF development, which is indirectly confirmed by the results of the present study—detection ≥ 1200 APC per day of observation, combined with the presence of predictors of AF highly correlated to development of this arrhythmia ($r = 0.86$, OR = 8.5,

CI OR = 7.8–9.1). In this study, the nature of APC was evaluated by determining IRAF, including a comprehensive assessment of both linear deviation of the corrected pre-ectopic interval of APC and parameters of P wave signal-averaged ECG, particularly FiP-P and Pd.[10] The previous clinical and experimental studies showed that the revealed linear deviation of the corrected pre-ectopic interval of APC indicators, for example, ≤10 ms, indirectly confirm re-entry mechanisms and/or formation of abnormal ectopic foci, and a large variability of this indicator is the presence of the trigger mechanisms.[19]

This study revealed a wide variability of IRAF values (from 0.01 to 54 units) both in patients with and without AF development, which indirectly indicates the presence of a variety of AF induction mechanisms in the examined patients.[10,19] According to the data obtained, for 2 years prior and during the follow-up observation up to AF development, significant decrease of IRAF values (an average by 95% and more) was noted in comparison with both the results of the survey of the same patients for 3–4 years prior to the formation of this arrhythmia, and with patients without the development of AF. It should be stressed that there was a progressive decrease in IRAF values (an average of 35% and more for every 3–4 months compared to the baseline values) in all patients within 2 years of observation before AF development that may reflect the base of AF development.[9,18] The IRAF values decrease within the period of observation is highly correlated with the increase in FiP-P ⩾ 135 ms, FiP-P/Pd ratio ⩽ 2.5 units, and also LAEDI ⩾ 30 ml/m^2 and AF development (r = 0.93, OR = 16.2, CI OR = 14.7–17.9).

Based on the data obtained, we can conclude that the detection of atrial dilatation and/ or abnormal parameters of the P wave signal-averaged ECG, Pd, APC in patients with MS after a single examination determines the long-term or indefinite duration risk of the possible development of AF, for example, for 5–10 year and more. Expediency of use of the category of long-term risk of AF developing in patients with MS is largely due to a large number of patients, who are usually in "low" and "medium" risk groups, which according to the results, comprise approximately 90%. According to different authors, in order to prevent AF development in patients with MS, the correction of potentially modifiable factors, such as body weight, arterial hypertension, normalization of blood glucose, and lipids content is recommended.[5,12,16] Therefore, the correction of the modifiable factors as primary AF prevention should be used for all patients with MS, which ultimately in the long-term leads to a decrease in the number of patients with so-called "high risk".[5,12,16]

The specific time interval designated as the short-term risk, for which AF is most likely to develop in patients with MS with APC, is detected only by observing patients in dynamics with a multiplicity of examinations at least once every 3–4 months. The decrease of IRAF values by 35% and more for every 3–4 months of observation in comparison with the baseline values in combination with FiP-P ≥ 135 ms and/or LAEDI ≥ 30 ml/m^2, FiP-P/Pd of ≤ 2.5 units correlates with AF development within 1–2 years (r = 0.93, OR = 16.2, CI OR = 14.7–17.9), and in detecting IRAF values ≤0.5 units at the subsequent decrease of this parameter by 70% and more for 1–3 months of observation it correlates with AF development for 6 months after the observation (r = 0.95, OR = 17.6, CI OR = 16.7–18.4). For the early diagnosis of AF in patients with MS, in detecting a short-term risk of its development, one of the chosen methods apart from the pulse control is ECG monitoring (24–72 hours or more) or the use of the implantable loop recorders. Detection of ≥1200 APC per day of observation and/or short-term risk of AF development are recommended for the primary prevention of its arrhythmia in this category of patients in whom the use of antiarrhythmic drugs is indicated. For example, starting with class II drugs, and if they are ineffective, recommending class III (I) drugs or other treatments.[20,21]

Conclusion

1. Patients with MS over 60 years of age, with a BMI ≥ 30 kg/m^2 and increased triglycerides and low density lipoprotein cholesterol are at risk of developing AF.

2. Detection of atrial dilatation and/ or abnormal parameters of Pd, the P wave signal-averaged ECG, and APC in patients with MS after a single examination characterizes the presence of the long-term risk of AF development, for example, for 5–10 year period or more, but it does not mean that it will be eventually realized.

3. The specific time interval designated as the short-term risk, for which AF is most likely to develop in patients with MS with APC is detected only by identifying IRAF in the dynamics of observation with a multiplicity of at least once every 3–4 months.

4. Compared with the baseline values, decrease of IRAF values by 35% or more for every 3–4 months (OR > 16) of observation indicates AF development in patients with MS within 1–2 years. If IRAF values are ≤ 0.5 units at the subsequent decrease of this parameter by 70% or more within 1–3 months (OR=17) of observation, it indicates AF development within 6 months after the observation.

5. For the early diagnosis of AF in patients with MS, while detecting the short-term risk of its development, one of the chosen methods apart from the pulse control is ECG monitoring (1–3 days) or the use of the implantable loop recorders.

6. For all patients with MS with detected long-term risk of AF development, correction of potentially modifiable factors, such as body weight, arterial hypertension, normalization of blood glucose and lipids content is recommended as primary prevention of this arrhythmia.

7. Detection ≥ 1200 APC per day of observation and/or short-term risk of AF development in patients with MS besides correction of the modifiable factors, the use of antiarrhythmic drugs is indicated, for example, starting with a class II, and in case of their inefficiency, proceeding to drugs of class III (I) are recommended for the primary prevention of its arrhythmia.

Study Limitations

This study had some limitations. The present study was conducted from 1998 to 2012. In our study, we did not include the last criteria for diagnosis of the left ventricle diastolic dysfunction and MS, which have been used in recent years.[21–23] Therefore, future investigation will clarify the diagnostic criteria patients with MS and with short-term risk of AF development, taking into account the latest recommendations. Furthermore, in further prospective investigation in these patients, different methods should be used for AF primary prevention, including using of lifestyle modification, correction of potentially modifiable factors, exercise and/or increase physical activity, and antiarrhythmic drug and/or ablation of arrhythmogenic focus APC.

References

1. Camm AJ, Lip GY, De Caterina R, et al. ESC Committee for practice Guidelines (CPG). 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation. Developed with the special contribution of the European Heart Rhythm Association. Europace. 2012;14(10):1385–413.

2. January CT, Wann LS, Alpert JS, et al. ACC/AHA Task Force Members. 2014 AHA/ACC/HRS guideline for the management with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. Circulation. 2014;130:e199–e267.

3. Perez MV, Dewey FE, Marcus R, et al. Electrocardiographic predictors of atrial fibrillation. Am Heart J. 2009;158(4):622–8.

4. Dewland TA, Vittinghoff E, Mandyam MC, et al. Atrial Ectopy as a Predictor of Incident Atrial Fibrillation A Cohort Study. Ann Intern Med. 2013;159(11):721–8.

5. Grundy SM, Brewer HB, Cleeman JI, et al. American Heart Association; National Heart, Lung, and Blood Institute. Definition of Metabolic Syndrome. Report of the National Heart, Lung and Blood Institute/American Heart Association conference on scientific issues related to definition. Circulation.2004;109:433–8.

6. Galito L, Badano L, Fox K, et al. The European Association of Echocardiography (EAE) Textbook of Echocardiography. Oxford Academ; 2011.

7. Kadish AH, Buxton AE, Kennedy HL, et al. ACC/AHA clinical competence statement on electrocardiography and ambulatory electrocardiography: a report of the ACC/AHA/ACP-ASIM task force on clinical competence (ACC/AHA committee to develop a clinical competence statement on electrocardiography and ambulatory electrocardiography) endorsed by the International Society for Holter and noninvasive electrocardiology. Circulation. 2001;104:3169–78.

8. 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.

9. Dilaveris PE, Gialafos EJ, Sideris SK, et al. Simple electrocardiographic markers for the prediction of paroxysmal idiopathic atrial fibrillation. Am Heart J. 1998;135(5 Pt 1):733–8.

10. Olesin AI, Konstantinova IV, Litvinenko VA, et al: [Method for determine risk development of atrial fibrillation in patients with atrial exstrasystoles]. Patent RU № 2556602, 2015. (In Russ.). (http://www.findpatent.ru/patent/255/2556602.html).

11. Le Heuzey JY, Marijon E, Chachoua K, et al. Pathophysiology of atrial fibrillation: insights into the renin-angiotensin system. Arch Cardiovasc Dis. 2008;101(11–12):787–91.

12. Watanabe H, Tanabe N, Watanabe T, et al. Metabolic Syndrome and Risk of Development of Atrial Fibrillation. The Niigata Preventive Medicine Study. Circulation. 2008;117(5): I255–60.

13. Kourliouros A, Savelieva I, Kiotsekoglou A, et al. Current concepts in the pathogenesis of atrial fibrillation. Am Heart J. 2009;157(2):243–52.

14. Sanoski CA. Prevalence, pathogenesis, and impact of atrial fibrillation. Am J Health Syst Pharm. 2010;67(9)(Suppl 5):S11–6.

15. Wallmann D, Tüller D, Kucher N, et al. Frequent atrial premature contractions as a surrogate marker for paroxysmal atrial fibrillation in patients with acute ischemic stroke. Heart. 2003;89(10):1247–8.

16. Olesin AI, Litvinenko VA, Al-Barbari AV, et al. Atrial fibrillation onset risk in patient with metabolic syndrome: prospective study. Russian J Cardiol. 2014;12(116):25–30. (In Russ.) DOI:10.15829/1560-4071-2014-12-25-30.

17. Schnabel RB, Sullivan LM, Levy D, et al. Development of a risk score for atrial fibrillation (Framingham Heart Study): a community-based cohort study. Lancet. 2009;373:739–45.

18. Antzelevitch C, Burashnikov A. Overview of Basic Mechanisms of Cardiac Arrhythmia. Card Electrophysiol Clin. 2011;3(1):23–45.

19. Olesin AI, Litvinenko VA, Al-Barbari AV, et al. [Ventricular extrasystoly with high risk of life-treatment arrhythmias development in acute coronary syndrome without ST elevation: evalution of revascularization effectiveness.] Russian J Cardiol. 2014;(11):38–43. (In Russ.) DOI:10.15829/1560-4071-2014-11-38-43.

20. Lee SH, Tai CT, Hsieh MH, et al. Predictors of non-pulmonary vein ectopic beats initiating paroxysmal atrial fibrillation: implication for catheter ablation. J Am Coll Cardiol. 2005;46(6):1054–9.

21. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2016;37(27):2129–2200.

22. Garvey WT, Mechanick JI, Brett EM, et al. American association of clinical endocrinologist and American college of endocrinology of comprehensive clinical practice guidelines for medical care of patients with obesity. Endocr Pract. 2016;22 Suppl 3:1–203.

23. Srikanthan K, Feyh A, Visweshwar H, et al. Systematic Review of Metabolic Syndrome Biomarkers: A Panel for Early Detection, Management, and Risk Stratification in the West Virginian Population. Int J Med Sci. 2016;13(1):25–38.

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Prevent: A poem by Dr. Tiny Nair

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Kaplan Meir curves diverge early
Applause erupts in dark halls, claps everyone
We owe all the credit, disclosures none.

Do we ever go back and think?
Preventive medicine needs uplink
Sugar, pressure, lipids and smoke
Plaque build up, coronary choke.
Exercise, diet and strictly no smoke
Can easily avoid an MI or stroke
Miss the applause, the claps and the thrill?
Gratitude of health for sure, duly fulfill.