

Short Report

Detected Atrial Arrhythmias with the 12-lead Holter System in Patients Complaining of Palpitations with Normal 12-lead ECGs – Gender and Age Differences

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Abstract

Objective. Hypoestrogenemia in postmenopausal female has important effects on the heart with possible arrhythmic consequences. We studied the prevalence of atrial arrhythmias in 12-lead Holter in patients with normal baseline ECGs. We used morphologic ECG data to define the origin of the arrhythmias.

Methods. Twelve lead Holter recordings in 172 consecutive patients in the community were analyzed. The prevalence of ectopic and reentry nonsustained atrial tachycardia (NSAT), atrial fibrillation, atrial flutter, and right and left premature atrial complexes, was studied in men and women. Patients aged ≥ 50 years and < 50 years were analyzed separately.

Results. Premature atrial complexes were frequent in all the four groups. In women aged ≥ 50 years, the prevalence of ectopic NSAT was 57%. Women aged ≥ 50 years, who showed episodes of atrial fibrillation or flutter, had a prevalence of concomitant ectopic NSAT of 67%. All the NSAT episodes were repetitive (≥ 10 episodes/24h). There was a striking gender difference, as the corresponding number for men in the same age group was only 17%.

Conclusions. Ectopic NSAT is frequently associated with atrial fibrillation or flutter in women aged ≥ 50 years. We propose a hypothesis related to hormone metabolism and collagen expression in the heart to explain this phenomenon.

Keyword: Holter, Atrial arrhythmia, atrial fibrillation, estrogen, postmenopausal

Introduction

In patients with recurrent symptoms suggestive of arrhythmia, it is essential to confirm the presence of arrhythmia and delineate its possible mechanism. A 12-lead ECG demonstrates the vector of an ectopic atrial or ventricular beat, but only for a short period at rest. Documentation of a sustained or nonsustained arrhythmia requires that the patient has the clinical arrhythmia at the time of ECG recording. Serial Holter recordings and implanted loop recorders may enable arrhythmia diagnosis, but do not provide detailed information concerning the location of the arrhythmogenic focus. An ambulatory 12-lead Holter recording system combines the advantages of both standard 12-lead ECG and Holter.¹

Palpitations in combination with a normal 12-lead ECG is frequently encountered in patients in the community. The symptom may be caused by atrial or ventricular rhythm disturbances. Modern ECG interpretation enables determination of the myocardial status with high sensitivity and specificity.² Molecular biology and electrophysiology

observations from the experimental laboratories help the clinician to understand the background of cardiac disorders.³

The aim of our study was to explore the prevalence of atrial arrhythmias in patients with normal resting ECGs complaining of palpitations with special reference to age and gender. We used morphologic data from the 12-lead Holter to indicate the origin and mechanisms of the arrhythmias.

Materials and Methods

We retrospectively collected 1203 consecutive 12-lead Holter recordings performed in the Maccabi Health Organization in Israel from March 1999 to March 2000 from patients aged ≥ 18 years with cardiac symptoms with the intention to find patients evaluated for palpitations. The Mortara system (Mortara Instruments, Inc, Milwaukee, Wis) was used for the 24h Holter recordings. We excluded patients not primarily evaluated for palpitations, and those with pathologic standard 12-lead ECGs, like atrial or ventricular conduction delay, asymmetric physiologic remodeling, asymmetric congenital

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or induced hypertrophy, and inverted T waves in leads I, II, V3-V6. Also patients on anti-arrhythmic, antihypertensive or antidiabetic medication were excluded. A total of 172/1203 (14%) patients with palpitations and normal resting 12-lead ECG were included in the final study group.

We divided the patients into four groups based on age and gender: 1) female aged <50 years (F50-), 2) male aged <50 years (M50-), 3) female aged ≥50 years (F50+), and 4) male aged ≥50 years (M50+).

For standard ECG normality, the P wave had to be positive in leads I, II, V4-V6 and negative in aVR. The T wave had to be positive in leads I, II and V4-V6. R and S wave criteria are presented in Table-1.⁴

Arrhythmia classification

Non sustained atrial tachycardia (NSAT) was defined as 3 – 60 consecutive premature atrial complexes (PAC). We divided the NSAT cases into two groups. In the ectopic NSAT (Fig. 1): a) the morphology of the PAC is very similar to the sinus P wave suggesting its origin from the upper part of the right atrium; b) the R'-R' intervals are irregular; c) the P'-R' intervals are irregular and d) the T wave morphology varies due to overlapping P' waves. The reentry NSAT (Fig. 2A) is

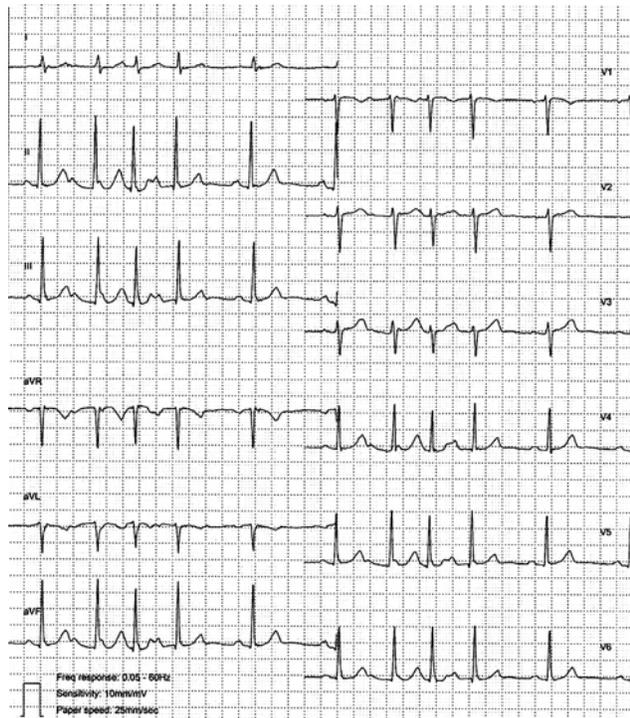


Fig. -1: A normal sinus beat is followed by three consecutive beats, representing ectopic NSAT. The P' waves have similar vector orientations as the sinus P; the P' wave is positive in lead LII and V5 and inverted in lead aVR. The P'-P' and R'-R' intervals are irregular and there is no fixed P'-R' interval. The morphology of the T' waves changes from beat to beat.

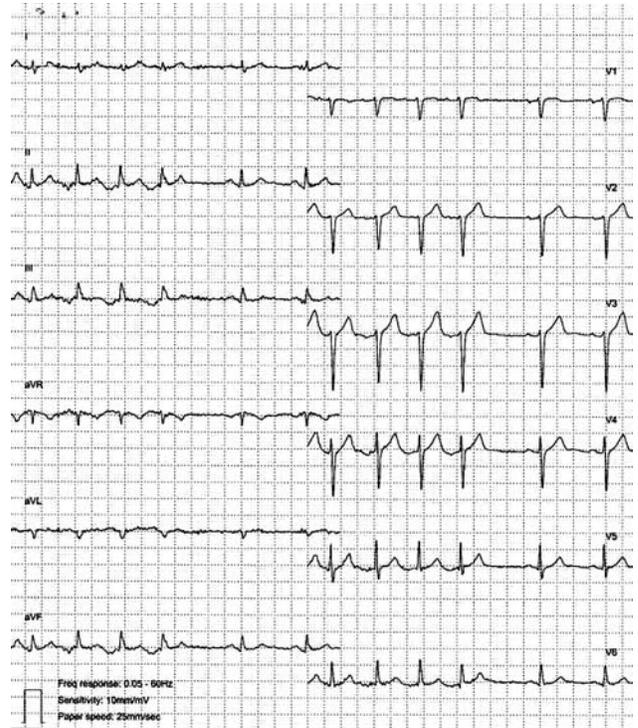


Fig. 2A: An example of NSAT of the reentry type: the P' morphology differs from that of the sinus P, the P'-P' intervals are regular, the P'-R' interval is fixed, and there is no deformation of the T' waves.

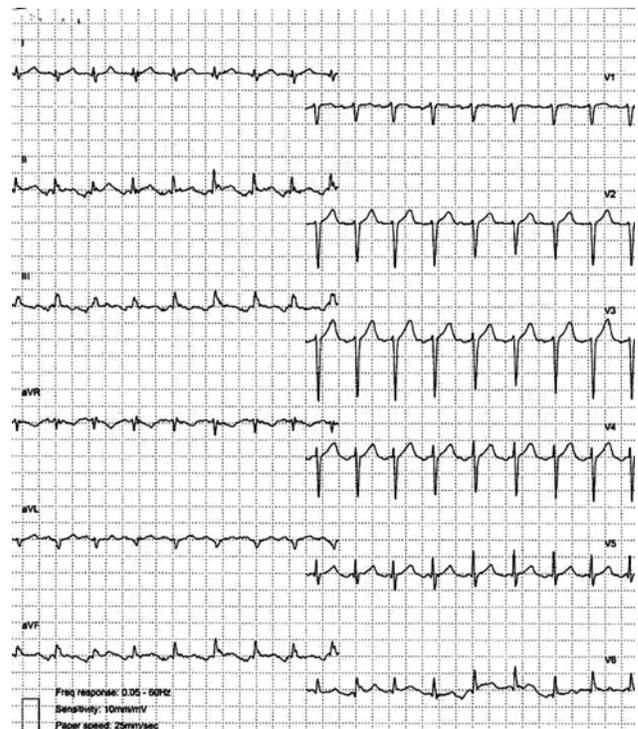


Fig. 2B: The reentry NSAT evolves to sustained atrial tachycardia.

characterized by the following: a) the P' morphology is different from the sinus P wave;⁵ b) the R'-R' interval is regular; and c) the P'-R' segment is constant. We arbitrarily divided the NSAT categories into: 1) ≥ 10 episodes (repetitive) and 2) <10 episodes (non-repetitive) during 24 h recording.

We defined a PAC originating in a right atrial focus as showing a positive P' wave in lead LI, LII, V5 and V6, while in case of a left atrial focus the P' wave in lead V1 is positive (Fig. 3).



Fig.-3: PACs not originating in the parasinus area: the P' wave is inverted in leads LII, LIII, V4-V6 and positive in aVR, the P'-R' interval is fixed and the T wave morphology does not change.

Statistical methods

Categorical variables were expressed as numbers of patients or %. Proportions were compared with the χ^2 test or Fisher's exact test. A probability value of < 0.05 was considered statistically significant.

Results

The prevalence of arrhythmias according to age and gender is presented in Table 2. Ectopic NSAT occurred in more than 50 % of F50+, while the reentry type was observed most frequently in F50- (25%). PACs, both with a morphology indicating right and left atrial origin, were frequent in all age

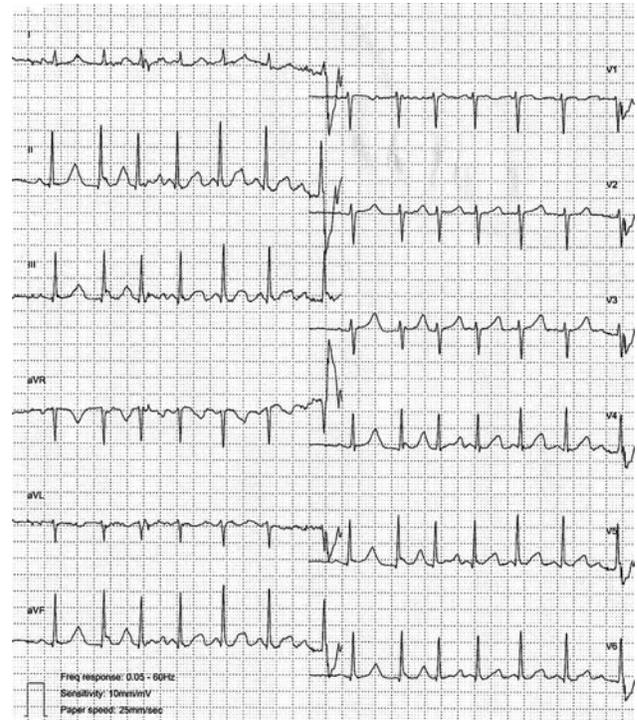


Fig.-4: A sinus beat is followed a short burst of ectopic NSAT consisting of three beats. The NSAT is immediately followed by atrial fibrillation.

groups. Episodes with atrial fibrillation and flutter showed a clear preponderance for 50+ patients. In F50+ with atrial fibrillation or flutter, the prevalence of concomitant ectopic NSAT during the 24h recording was 67%. They all represented repetitive NSAT (≥10 episodes/24h). In M50+ the corresponding number was 17%. Also, in M50- there was a frequent combination (67 %) of these arrhythmias, but the total number of patients with atrial fibrillation or flutter was small (Table-II). For the whole study population, concomitant ectopic NSAT and atrial fibrillation or flutter was observed in 32 % of the cases. For reentry NSAT, the corresponding number was 5%.

Table-I

Upper limits of normal for R and S wave amplitudes (mm) for females and males.

	Female	Male
R wave in the limb leads	10	10
S wave in the limb leads	10	10
S wave in leads V2 and V3	15	20
R wave in leads V4 and V5	15	20

Table-II
Arrhythmia prevalence during 12-lead Holter recording according to age and gender.

	< 50 years		≥ 50 years		p-value
	Female n=28%	Male n=43%	Female n=79%	Male n=22	
Ectopic atrial tachy ≥10*	7	2	32	18	<0.001
Ectopic atrial tachy <10*	10	5	27	9	0.008
Reentry atrial tachy ≥10*	0	2	5	0	0.415
Reentry atrial tachy <10*	25	7	0	18	<0.001
PAC right	68	30	49	41	0.017
PAC left	39	44	24	41	0.098
Atrial fibrillation	0	5	22	14	0.004
Atrial flutter	0	2	8	23	0.013

*Number of episodes/24h

Tachy=tachycardia; PAC=premature atrial complex

Discussion

In the present study, we introduced ECG morphology parameters to study the origin of atrial arrhythmias in 12-lead Holter analyses in individuals with normal standard 12-lead ECG. We found age and gender differences in the prevalence of the arrhythmias. Palpitations are very frequent both in healthy persons and in patients with cardiac diseases. The cause of palpitations ranges from benign isolated premature beats to life threatening arrhythmias, like sustained ventricular tachycardia. Even ventricular fibrillation can occur in individuals without structural heart disease.⁶ It is well recognized that advanced age is an important factor for changes in the structure of the myocardium, thereby generating substrates for serious arrhythmias.⁷

Patients with ectopic NSAT typically have no evidence of underlying heart disease. Chou and Ceaser found one or more transient episode of ectopic NSAT in 582 (21.6 %) of 2670 consecutive adults in 12- to 24-hour Holter recordings.⁸ In our experience, healthy postmenopausal female represent the majority of patients complaining of palpitations due to NSAT and ventricular arrhythmias. In our material, 59 % of F50+ showed ectopic NSAT, defined as a P' wave morphology similar to that of the sinus P wave, with irregular P'-P' intervals. In this type of arrhythmia, the P' waves coincides with the T wave, changing the morphology of the T waves form beat to beat (Fig. 1). Interestingly, when arbitrarily separating the ectopic NSAT patients into two groups, we found a frequency of 67 % of recordings with repetitive (>10 episodes/24 h) ectopic NSAT in patients, who showed concomitant atrial fibrillation or atrial flutter (Fig. 4). Based on the morphologic criteria - a positive P' wave in leads

LI, LII, V4-V6 and a negative P' wave in aVR - it is probable that this arrhythmia originates from the upper part of the right atrium (the parasinus area). Accordingly, we propose as a hypothesis that the origin of paroxysmal atrial fibrillation in female with normal standard 12-lead ECG is in the upper right atrium, that is close to the entrance of the superior vena cava. This finding may have important therapeutic implications. Authors have stated that the right atrium regulates the entrance of blood flow during pregnancy to increase cardiac stroke volume and cardiac output by about one third without increasing oxygen demand.⁹ We speculate that the increase in collagen I in the interstitial space of the right atrium in postmenopausal female generate a substrate for developing complicated arrhythmias.¹⁰ The increase in collagen I in elderly female is due to reduced estrogen and relaxin levels.^{11,12} These hormones have important regulatory effects on collagen. During pregnancy, relaxin is secreted from the ovarium and placenta and its main biological function is to regulate the levels of collagen I.¹³ The hormone also has important effects on cardiac metabolism. Estrogen has a regulatory effect on the fibroblasts, maintaining the collagen I/III ratio.^{9,10} Normally, in the heart the ratio is 70/30, but to improve cardiac function during pregnancy, the ratio is reduced in favour of collagen III (soft collagen). In our group 3, F50+, we assume that due to low levels of estrogen and relaxin, the relative distribution of collagen is in favour of collagen I (steel collagen).¹²

We found concomitant reentry NSAT and atrial fibrillation or flutter in only 5 % of the study population. The prevalence of the arrhythmia did not differ between the groups. In this type of arrhythmia, contrary to the ectopic NSAT, the P'

wave is inverted in leads LI, LII, V4-V6 and positive in aVR. Accordingly, the origin of the reentry NSAT is not in the upper right atrium but in the left atrium or in the lower part of the right atrium. The reentry NSAT, which may evolve to sustained atrial tachycardia (Fig. 2B), has different pathophysiology and hence is different from the therapeutic point.

Conclusions

Based on the ECG morphology in 12-lead Holter, we found age and gender differences in the prevalence of atrial arrhythmias. We found a frequent association between ectopic NSAT and atrial fibrillation or flutter in F50+. We propose a hypothesis related to hormone metabolism and collagen expression in the heart to explain this phenomenon.

Limitations

This study has a number of limitations. It was a retrospective study and the number of patients was rather small. However, we included consecutive patients in the community, who thus should not represent a selected cohort. We do not have follow-up data for outcome analyses for the patients. Also there is lack of information regarding baseline characteristics, except for those mentioned in the Methods section. However, patients with anti-hypertensive or anti-diabetic medication, and also those with ECG signs of remodeling, were excluded. Our results should be looked upon as hypothesis-generating, and need to be confirmed in future prospective studies.

Conflict of Interest: None

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