

A.V. Ivankova, N.V. Kuzminova, S.E. Lozinsky, A.O. Havryliuk, I.I. Knyazkova¹, E.I. Ivanova
National Pirogov Memorial Medical University, Vinnytsya
¹National Medical University, Kharkiv

PECULIARITIES OF DAILY ECG CHANGES IN PATIENTS WITH ESSENTIAL HYPERTENSION OF THE SECOND STAGE

e-mail: ivanovanasty92@gmail.com

The total of 156 patients (65 men and 91 women) with stage II hypertension were examined. The main clinical group included 124 persons with the evidence of frequent supraventricular or ventricular extrasystole according to the daily Holter ECG monitoring data. Patients with stage II hypertension but without cardiac arrhythmias (32 persons) were the comparison group. It was established that the persistent pattern of the supraventricular extrasystole, which occurred in 36.5 % of patients with essential hypertension, was more common than the persistent pattern of ventricular extrasystole (6 %, $p < 0.001$). In contrast, the ventricular extrasystole pattern of sporadic occurrence compared to supraventricular extrasystole during the active time of day was significantly more common (36.0 % vs. 18.9 %, respectively, $p < 0.03$). Patients with both arrhythmias (supraventricular and ventricular) had borderline circadian index (1.18 and 1.21, respectively). Besides that, short asymptomatic episodes of supraventricular tachycardia and atrial fibrillation have been reported in patients with essential hypertension and supraventricular extrasystole.

Key words: essential hypertension, extrasystole, daily ECG monitoring, circadian index, atrial fibrillation, supraventricular tachycardia.

А.В. Іванкова, Н.В. Кузьміна, С.Е. Лозинський, А.О. Гаврилюк, І.І. Князькова, Є.І. Іванова ОСОБЛИВОСТІ ЗМІН ПОКАЗНИКІВ ХОЛТЕРІВСЬКОГО МОНІТОРУВАННЯ ЕЛЕКТРОКАРДІОГРАМИ У ХВОРИХ НА ГІПЕРТОНІЧНУ ХВОРОБУ II СТАДІЇ

Обстежено 65 чоловіків і 91 жінку (156 пацієнтів) із гіпертонічною хворобою II стадії. До основного клінічного масиву включені 124 з них, які за даними холтерівського моніторингу електрокардіограми мали часту суправентрикулярну або шлуночкову екстрасистолію. Хворі на гіпертонічну хворобу II стадії без порушень серцевого ритму (32 особи) склали групу порівняння. Встановлено, що суправентрикулярна екстрасистолія у хворих на гіпертонічну хворобу II стадії частіше ніж шлуночкова екстрасистолія носить постійний характер: 36,5 % проти 6 %, відповідно, $p < 0.0001$. У пацієнтів із шлуночковою екстрасистолією, порівняно з суправентрикулярним варіантом, аритмія достовірно частіше виникає епізодично в активний час доби (36,0 % проти 18,9 % відповідно, $p < 0.03$). Пацієнти з екстрасистоліями (суправентрикулярними та шлуночковими) мали межові значення циркадного індексу (1.18 та 1.21 ум.од., відповідно). У хворих на гіпертонічну хворобу II стадії та суправентрикулярну екстрасистолію зафіксовані короткі асимптомні епізоди суправентрикулярної тахікардії та фібриляції передсердь.

Ключові слова: гіпертонічна хвороба, екстрасистолія, холтерівське моніторування електрокардіограми, циркадний індекс, фібриляція передсердь, суправентрикулярна тахікардія.

The work is a fragment of the research project "Metabolic risk factors, cardiovascular remodeling and functional status of the kidneys in patients with cardiovascular pathology. Possibilities of pharmacological correction", state registration No. 0119U101849.

Essential hypertension (EH) is an urgent problem of our time as the overall prevalence of hypertension in adults makes about 30 % – 45 %. It is the same worldwide, regardless of the income status [6].

In recent years, the role of EH in the development of cardiac arrhythmias has been intensively debated. The pre-conditions for the cardiac arrhythmias may occur in patients with essential hypertension along with the disease progression at any stage of the cardiovascular disease course [4]. In contrast with atrial fibrillation (AF), which is the most common and well-known, cardiac arrhythmia in patients with EH, the reasons and mechanisms of extrasystolic arrhythmia progression remain insufficiently studied [1, 11].

Today we have irrefutable evidence of an association between the left ventricle (LV) diastolic dysfunction and supraventricular arrhythmia in EH [3]. Some researchers have observed SVE in patients with high systemic blood pressure (BP) regardless of the LV hypertrophy presence [14]. The signal mean characteristics of the P wave, along with the presence of concentric LV hypertrophy were of some importance as the precursory symptoms of SVE [12].

The first reports of VE in hypertension and left ventricular hypertrophy were performed a long time ago by Messerli et al. (1984). It was found that in patients with hypertension and ECG signs of left ventricular hypertrophy the number of VE was greater than in those without hypertrophy and hypertension. Moreover, the incidence of VE increased with LV myocardial mass increasing. These data were confirmed

by several later studies [8, 13, 15]. The combination of VE, ECG signs of LV hypertrophy, and ST-segment depression are referred to the extremely dangerous symptoms due to a significant increase of the fatal arrhythmias likelihood and sudden arrhythmic death [9]. Simultaneously, the question remains: do we consider the extrasystole to be the specific marker of future malignant arrhythmias or to the marker of the EH severity?

The purpose of the study was to assess the pattern of cardiac arrhythmias in patients with stage II hypertension and frequent extrasystoles.

Materials and methods. The study was preceded by a screening and thorough collection of complaints and medical history. Signing of informed consent to participate in the study was done in compliance with the ethical rules of the Helsinki Declaration.

The total of 156 patients with stage II EH was included in the study. 124 of them, aged 27 – 75 (mean age 58.2 ± 0.9) years were referred to the EH II with frequent extrasystole. They formed the main group of the clinical study. Besides, 32 patients with stage II EH without any cardiac arrhythmias aged 32 – 72 (mean age 55.9 ± 1.7) years, were included in the comparison group. In the main group, 50 (40.3 %) patients were male and 74 (59.6 %) were female. The comparison group consisted of 15 (46.9 %) men and 17 (53.1 %) women. There were no statistically significant differences between the main and the comparison groups by age and gender ($p > 0.05$), which indicated the age and gender homogeneity of the participants [10].

Totally 124 patients with EH and concomitant extrasystoles were involved in the study. SVE was registered in 74 (59.7 %) cases and VE – in 50 cases (40.3 %). History of arrhythmia ranged from 1 to 27 years and the mean age was 8.06 ± 0.42 years.

All patients were assessed according to the guidelines of the Ukrainian Arrhythmologists Association and the working group of rhythm disorders of the Association of Cardiologists of Ukraine (2015).

All patients were examined and treated in the cardiology department of the Vinnytsia Pirogov Memorial Regional Clinical Hospital, in the clinical and diagnostic department or the department of heart rhythm disorders of communal non-commercial enterprise “Vinnytsia Regional Clinical Center of Cardiovascular Pathology” during 2017-2020.

All patients were examined by a complete clinical, laboratory, and instrumental methods as follows: 1) general clinical assessment, measurement of blood pressure; 2) 12-lead standard ECG; 3) daily ECG monitoring.

The general clinical examination included identifying indications and contraindications to the inclusion of patients in the study, establishment of the underlying diagnosis and comorbidity, and assessment of the history. It was followed by the formation of clinical groups in the study. Blood pressure was measured in compliance with the Guidelines of the Ukrainian Society of Cardiology (2013) using a sphygmomanometer (Microlife, Switzerland) [5, 10].

The 12-lead electrocardiography was performed using the “UKARD” (Hungary) equipment according to the standard rules.

Daily ECG monitoring (DM ECG) was performed using the “DiaCard” (JSC “Solvaig”, Ukraine) hardware and software according to the standard protocol [7]. The following parameters were determined to assess the pattern of arrhythmia: the daily number of SVE and VE; maximal frequency of SVE and VE per 1 hour (SVE1 and VE1, respectively); the number of patients with paired and group VE and their number per 24 hours. [2, 11]. Besides, we analyzed the number and pattern of episodes (arrhythmia duration up to 30 s) of supraventricular tachycardia (SVT) and AF, which were recorded during the day.

Statistical processing of the study results was performed using the “Statistica” v. 12.0 software produced by “StatSoft” company according to the guidelines for biomedical data processing. The results were presented as the mean (M) and the error of the mean (m) for quantitative values and as a percentage (%) for relative values. Comparisons of relative values (%) were performed using the Mann-Whitney U test (for 2 samples) and the Kruskal-Wallis ANOVA test & Median test (in 3 independent samples) [10, 11].

Results of the study and their discussion. The study, as it was noted earlier, included patients with frequent symptomatic extrasystole (> 30 episodes of extrasystole per 1 h by DM ECG data). Two different topical types were identified according to DM ECG: supraventricular and ventricular extrasystole. SVE was established in 74 (59.7 %) cases of the patients with essential hypertension and concomitant arrhythmia and VE – in 50 (40.3 %; $p < 0.05$).

In the main group of patients, 30 (24.2 %) experienced arrhythmia constantly during the last year (tab. 1), as the variety of subjective symptoms. The most common was the feeling of heartbeat failure or

pauses in the heart rhythm. The vast majority (94 (75.8 %) patients) experienced arrhythmia sporadically in the form of intermittent episodes. In 32 of them (25.8 %) arrhythmia occurred in the active time of day (within 6⁰⁰ and 21⁰⁰). It was related to the physical, psychoemotional load, or stress. In 14 (11.3 %) patients arrhythmia occurred during the inactive time of day (within 21⁰⁰ and 6⁰⁰), at rest, in the absence of physical and psycho-emotional stress, in the sleeping settings, or when lying in bed. It was noted that in 38.7 % of patients arrhythmias were observed at any time of the day regardless of the type of daily activity (tab. 1).

Table 1

Clinical characteristics of patients with extrasystole

Characteristics of arrhythmia	Main clinical group (n=124)
Permanent arrhythmia	30 (24.2 %)
Episodic (intermittent) arrhythmia	94 (75.8 %)
Episodic arrhythmia predominantly during the active time of day	32 (27.4 %)
Episodic arrhythmia predominantly during the inactive time of day (night time / quiet state)	14 (11.3 %)
Episodic arrhythmia independently of the daytime period	48 (38.7 %)

After analyzing the complaints of patients depending on the topical extrasystole type it has been noted that in 36.5 % of patients with SVE arrhythmias were experienced constantly all day long. In contrast, only 6.0 % of the patients with VE noted the permanent pattern of arrhythmia. It was significantly ($p=0.0001$) different from patients with SVE (tab. 2). At the same time, 36.0 % of patients with VE noted that their extrasystole occurred mainly during the active time of day, while the number of such persons was significantly less (18.9 %, $p=0.03$) among patients with SVE. In both types of the patients, with SVE and VE, the fewer number experienced (10.8 % and 12.0 % respectively) premature beats at rest and at night time, while more than a third of the patients (33.8 % of persons with SVE and 46.0 % with VE, $p>0.05$) reported that arrhythmia occurred sporadically, at any time of day.

Table 2

Clinical characteristics of extrasystole depending on its topical variant

Clinical characteristics	SVE (n=74)	VE (n=50)	P
Arrhythmia is permanently experienced throughout the day	27 (36.5 %)	3 (6.0 %)	0.0001
Arrhythmia is experienced as episodic, predominantly during the active time of day	14 (18.9 %)	18 (36.0 %)	0.03
Arrhythmia is experienced as episodic, predominantly during the night time of day / in a calm state	8 (10.8 %)	6 (12.0 %)	0.84
Arrhythmia is experienced as episodic at any time of day	25 (33.8 %)	23 (46.0 %)	0.17

Note. The intergroup percentage difference is calculated by the mx^2 criterion

Analysis of the heart rate daily pattern in patients of the main clinical group evidenced that the mean heart rate per day (AHR) was 72-73 strokes per minute, while the mean heart rate during day and night (DHR and NHR) ranged 79 – 80 and 67 – 68 beats per minute, respectively (tab. 3). The mean value of the circadian index (CI) was 1.18 in patients with SVE and 1.21 in patients with VE. There was no significant difference between the groups ($p>0.05$).

Table 3

Daily heart rate pattern in patients of the main group depending on the extrasystole type

Parameters of heart rate	SVE (n = 74)	VE(n = 50)	P
AHR	72 (66; 81)	73 (70; 80)	0.90
DHR	80 (70; 87)	79 (75; 87)	0.91
NHR	67 (60; 76)	68 (61; 72)	0.62
CI	1.18 (1.10; 1.25)	1.21 (1.10; 1.27)	0.41

Notes: 1. SVE – supraventricular and VE – ventricular extrasystole; 2. AHR – mean heart rate during the whole day; DHR – mean heart rate during daytime; NHR – mean heart rate during nighttime; CI – circadian index; 3. The intergroup significance of the difference was calculated by Kruskal-Wallis ANOVA test and Median test (3 groups were compared: to groups with SVE and VE and to the group without extrasystole).

The result of the analysis of the structure and frequency of different types of extrasystole was predictable and was only performed in clinical groups (the comparison group included patients without any cardiac arrhythmia). It should be noted that we allowed the patients with a certain number of different

extrasystoles (except for paired extrasystoles) to be involved in the comparison group. Their number did not exceed 10 episodes per day and exactly met modern physiological standards, even for healthy persons [2].

The results showed that in patients with SVE, in contrast with patients with VE, a naturally higher number of SVE, both per day (SVE_D, $p < 0.0001$) and per hour (SVE₁, $p < 0.0001$) were recorded (tab. 4).

In its turn, the number of VE was naturally higher in patients with VE, both per day (VE_D, $p < 0.0001$) and per hour (VE₁, $p < 0.0001$). The number of VE did not exceed 50 per day and 2 per hour.

Paired and polytopic extrasystoles were registered in patients with VE in 56.8 % and 28.4 %, respectively, while in patients with SVE they were absent at all. Thus, the results of the analysis showed the expected distribution of extrasystoles in different clinical groups.

Table 4

Distribution of cardiac arrhythmia in patients of the main group depending on the extrasystole type

DM ECG parameters	SVE (n = 74)	VE (n = 50)	P
SVE per whole day	n = 74 [458-11287] 764 (547; 933)	n = 37 [1-58] 4 (4; 17)	<0.0001
SVE ₁ , number per 1 hour	[19-470] 32 (23; 39)	[0-2] 0 (0; 2)	<0.0001
Persons with at least 1 episode of SVT per day, number of patients (%)	11 (14.9 %)	-	-
SVT, number per day	[1-5] 2 (1; 4)	-	-
Duration of SVT episodes, sec.	[4-27] 20 (12; 24)	-	-
Presence of at least 1 episode of AF per day, number of patients (%)	19 (25.7 %)	-	-
Number of AF episodes, per day	[1-5] 1 (1; 2)	-	-
Duration of AF episodes, sec.	[4-140] 18 (14; 20)	-	-
VE number per day	n = 63 [4-118] 24 (12; 48)	n = 50 [564-4271] 1278 (854; 1682)	<0.0001
VE ₁ , VE number per 1 hour	[0-5] 1 (0; 2)	[24-178] 53 (36; 70)	<0.0001
The number of persons with paired VE (%)	-	42 (56.8 %)	-
Number of paired VE per day	-	[2-32] 8 (4; 12)	-
The number of persons with VE (%)	-	21 (28.4 %)	-

Notes: 1. n – absolute number of patients with the above heart rhythm disorders; 2. minimum and maximum values of the parameter are given in square brackets; 3. significance of differences between the mean values is calculated by Mann-Whitney U Test.

The daily pattern of SVT and AF including frequency and the duration (up to 30 sec) of episodes was analyzed in addition to the patterns of different extrasystole types. It should be noted that patients with a duration of SVT and AF of more than 30 sec were not included in the study. The control group patients were excluded from the analysis due to the complete absence of the above rhythm disorders. We analyzed the number of patients (%) with at least one episode of SVT (more than three narrow (<0.12 sec) QRS complexes with the same distance between the complexes and heart rate >140 per 1 min) or AF (more than three QRS complexes with the presence of alternating QRS amplitude and distances between the complexes) during daily ECG monitoring, and the daily number and maximum duration (in sec) of these episodes. Verification of the supraventricular arrhythmia type was performed according to the present Guidelines for the DM ECG assessment [2, 7].

It was established, that SVT was recorded in 14.9 % of patients. We observed in them from 1 to 4 episodes with the duration not exceeding 24 sec (tab. 4). Episodes of AF were registered in 27.5 % of patients (from 1 to 2 episodes lasting up to 20 sec). The described episodes of SVT and AF were asymptomatic, were not followed by the changes of ST-segment and hemodynamic disorders.

The mean value of the circadian index (CI) was 1.18 in patients with SVE and 1.21 in patients with VE (tab. 3). There was no significant difference between the groups ($p > 0.05$). These values may be referred to as the borderline values because according to the literature, the value of CI less than 1.2 may indicate autonomic “denervation” of the heart and is associated with a poor prognosis and a high risk of sudden

death [2, 3, 7]. The described episodes of SVT and AF were asymptomatic, were not followed by the changes of ST-segment and hemodynamic disorders. Therefore, the results of our study confirmed the well-known opinion that frequent SVE is an electrophysiological marker of a possible development of SVT and AF. It should be noted that we did not register any episodes of ventricular tachycardia in our patients. It coincides with the results of other researchers, who only observed episodes of ventricular tachycardia in case of the underlying morphological substrate such as severe structural myocardial hypersensitivity, myocardial infarction, or severe cardiac failure [8, 9]. Instead, the clinical array of this study was dramatically different.

Conclusions

1. Supraventricular type of extrasystole was recorded more frequently than ventricular one in patients with stage II EH.

2. Extrasystole in patients with stage II EH and SVE is more likely to be permanent than in patients with VE (36.5 % vs. 6 %, respectively, $p < 0.0001$). Whereas in patients with VE, compared to patients with EH and SVE, the sporadic pattern of arrhythmia during the active time of day occurs significantly more frequently (36.0 % vs. 18.9 %, respectively, $p < 0.03$).

3. The patients with extrasystoles have borderline values of CI (1.18 in SVE and 1.21 in VE, $p > 0.05$) according to the results of the daily heart rate pattern. It may be considered as an additional risk factor of fatal arrhythmia and sudden cardiac death in these patients.

4. Short asymptomatic episodes of SVT (up to 20 sec) and short AF episodes (up to 18 sec) may be registered in 14.9 % and 25.7 %, respectively, of patients with stage II EH and frequent SVE but without the history of persistent tachyarrhythmia.

5. Paired VEs are registered in 56.8 %, and polytopic VEs – in 28.4 % of patients with EH and frequent SVE, which raises the degree of VE complexity gradation.

References

- Zharinov OI, Talaieva TV, Lishchysyna OM, Bozhko LI, Hetman TV, Zalevskiy VP. [ta in.] Adaptovana klinichna nastanova, zasnovana na dokazakh. Fibryliatsiia peredserd. Rekomendatsii Robochoi hrupy z porushen rytmu sertsia Asotsiatsii kardiologiv Ukrainy. 2016; 11–7. [in Ukrainian]
- Makarov LM. Kholterovskoe monitoryrovanye. Moskva: Medpraktika-M. 2017; 502. [in Russian]
- Nedostup AV, Blahova OV. Kak lechit aritmii. Narusheniya ritma i provodymosti v klinicheskoy praktike. Moskva: MEDpress-inform. 2014; 365. [in Russian]
- Nykyforov VS, Marsalskaia OA, Metso KV, Palahutyn MA. Arterialnaya gipertenziya i narusheniya ritma serdtsa. Zdorovye – osnova chelovecheskogo potentsiala: problemy i puti ikh resheniya. 2016. 2; 594–96. [in Russian]
- Sirenko JuM. Hipertonichna khvoroba: dovidkove vydannia. Kyiv: Zdorovya. 2013; 240. [In Ukrainian]
- Sirenko JuM. Rekomendatsii ESC I ESH z likuvannia arterialnoyi hipertenzii. Kyiv: Zaslavskiy OJu. 2019; 22–23. [In Ukrainian]
- Sychov OS, Lutai MI, Romanova OM. Ambulatorne EKH-monitoruvannia. Rekomendatsiyi Asotsiatsiyi kardiologiv Ukrainy. 2010; 44. [in Ukrainian]
- Agarwal S, Heiss G, Rautaharju P, Shahar E, Massing M, Simpson R. Premature ventricular complexes and the risk of incident stroke: the Atherosclerosis Risk in Communities (ARIC) study. Stroke; 2010; 143 (3). 535–40.
- Hoogendijk MG, Geczy T, Yap S, Szili-Torok T. Pathophysiological mechanism of premature ventricular complexes. Front Physiol. 2020; 11: 406. <https://doi.org/10.3389/fphys.2020.00406>.
- Kuzminova NV, Ivankova AV, Ivanov VP, Lozinsky SE, Knyazkova II, Gavruluk AO. Daily blood pressure pattern disorders in patients with stage II essential hypertension and frequent premature beats. World of medicine and biology. 2020; 1(71): 72–77. <https://doi.org/10.26724/2079-8334-2020-1-71-72-77>.
- Kuzminova NV, Ivankova AV, Ivanov VP, Lozinsky SE, Knyazkova II, Gavruluk AO. Structural and functional changes of the heart in patients with essential hypertension and concomitant frequent extrasystoles. World of medicine and biology. 2020; 2(72): 79–85. <https://doi.org/10.26724/2079-8334-2020-2-72-79-85>.
- Lip G, Coca A, Kahan T, Boriani G, Manolis AS, Olsen MH. [et al.] Hypertension and cardiac arrhythmias: a consensus document from the EHRA and ESC Council on Hypertension, endorsed by the HRS, Asia-Pacific Heart Rhythm Society APHRS and SOLEACE. Europace. 2017; 19 (6): 891–911. <https://doi.org/doi:10.1093/europace/eux091>.
- Pannikath R, Reiner K, Uy-Evanado A, Teodorescu C, Gunson K, Jui J, Chung S. Electrocardiographic predictors of sudden cardiac death in patients with left ventricular hypertrophy. Annals of Noninvasive Electrocardiology. 2013.18(3); 225–29.
- Purmah Y, Proietti M, Laroche C, Mazurek M, Tahmatzidis D, Novo S. Rate vs. rhythm control and adverse outcomes among European patients with atrial fibrillation. Europace. 2017; 19 (3): 241–50. PMID: 28160483. <https://doi.org/doi:10.1093/europace/euw421>.
- Zeng Z, Zhou R, Liang O. Comparison of arrhythmias different left ventricular geometric patterns in essential hypertension. J. Tongji. Med. Univ. 2011; 21 (2): 93–6.

Стаття надійшла 28.03.2020 р.