



Evaluation of Main Parameters of Holter ECG Monitoring in Patients with Combined Rheumatoid Arthritis and Ischemic Heart Disease

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Abstract

Introduction: In recent years, the method of daily ECG monitoring, which plays an important role in the presence of painless myocardial ischemia in patients with RA, has been widely used to detect patients with rheumatoid arthritis (RA) in a timely manner.

Method and Materials: A system of three modified leads was used for daily (Holter) ECG monitoring (HM ECG). ECG monitoring was performed for 24 hours, the dynamics of heart rate (HR), the number of episodes of pain (AMI) and painless ischemia (BMI), their duration, changes in ectopic activity were assessed. An episode of ischemia was considered to be ST depression in the horizontal and oblique type $ST \geq 1$ mm, which was determined at a distance of 0.06 s from the J point and lasted more than 60 s.

Results: In patients with RA and ischemic heart disease (IHD), 24-hour ECG monitoring, compared with patients with IHD alone, revealed more serious changes, such as sinus tachycardia, extrasystole, paroxysmal tachycardia, ischemic changes in the ST segment and T wave. The most pronounced ECG changes during daily monitoring, it was noted in RA III degree of activity. According to 24-hour ECG monitoring, rhythm disturbances (sinus tachycardia, extrasystole, paroxysmal tachycardia) are more often diagnosed in patients with RA for more than 5 years. Changes in the T wave and ST segment are more characteristic of RA patients with a disease duration of more than 10 years.

Conclusion: Thus, HM ECG revealed a significant association between an increase in cardiac arrhythmias and an increase in RA activity.

Keywords: Cardiac Rhythm; Holter Monitoring; Ischemic Heart Disease; Variability Of Cardiac Rhythm; Rheumatoid Arthritis

Abbreviations: RA: Rheumatoid Arthritis; HR: Heart Rate; IHD: Ischemic Heart Disease; RF: Rheumatoid Factor.

Introduction

One of the difficult issues of modern medicine is the issue of integrated assessment of the patient's health, providing medical care to patients with concomitant and combined pathology, prescribing treatment based on drug interactions, providing recommendations on the mode and duration of their reception. There is a tangible and justified active interest of researchers in the last decade in polymorbidity in RA, but the concept of management of such patients is not yet fully integrated into clinical practice [1].

Recent studies have shown that the risk of cardiovascular complications in RA patients is significantly higher than in the general patient population and does not differ from the risk of cardiovascular complications in patients with proven high cardiovascular risk (type 2 diabetes mellitus, hypertension, hypertension) [2]. It was found that an increased risk of mortality from cardiovascular disease is observed in the onset of RA and is associated with seropositivity with rheumatoid factor (RF), rather than with classical risk factors [3].

The most common form of polymorbid condition for RA is coronary heart disease, angina pectoris. Activation of the immune system is considered a major risk factor for the progression of cardiovascular disease. Recently, there have been many publications in the scientific literature on the importance of inflammatory mediators not only in the development of RA symptoms, but also in the occurrence of vascular wall inflammation with the subsequent development of generalized atherosclerosis, including coronary [4]. In addition to nonspecific inflammatory processes in some cases, patients develop RA accompanied by specific heart disease, which is histologically manifested by the formation of rheumatoid granulomas, which can develop in any part of the heart and its membranes. Polymorphism of histological changes leads to the peculiarities of cardiovascular pathology in RA: multiple lesions of the coronary arteries, high frequency of "painless" myocardial ischemia and "silent" myocardial infarction, asymptomatic chronic heart failure, atypical manifestations of debut of cardiovascular pathology [5]. All this largely determines the low level of medical treatment, and leads to late diagnosis and untimely initiation of therapy, which further increases the risk of adverse effects in RA. The medical and social significance of this problem is also determined by its high prevalence, steadily progressive course, unsatisfactory long-term prognosis and lack of positive dynamics of cardiovascular morbidity and mortality in RA in recent decades, despite a significant decrease in the general population [6]. Thus, untimely diagnosis of cardiovascular manifestations in RA patients determines unfavorable epidemiological trends.

Materials and Methods

121 patients with RA and IHD were examined. The diagnosis of stable IHD was established in accordance with the Order of the Ministry of Health of Ukraine № 152 of 02.03.2016 [1], the diagnosis of RA was established in accordance with the requirements of the Order of the Ministry of Health of Ukraine № 263 of 11.04.2014 [2]. The criterion for inclusion in the study was the presence of the target disease (isolated coronary heart disease, RA alone or in combination with coronary heart disease) in patients of both sexes aged 35-85 years, subject to informed consent. Exclusion criteria were: duration of the disease less than 6 months; IVPA functional class; modification of the means or dosage of basic RA therapy during the last 3 months; patients taking oral glucocorticoids at a dose higher than 10 mg / day (prednisolone) or at a dose that has changed over the past 4 weeks; patients who have been forced to take NSAIDs in unstable dosages during the last month; treatment with biologically active drugs or intra-articular injections for the last 2 months; the presence of any other connective tissue diseases; the presence of sub- and uncompensated heart failure; active pathology of the liver, manifested by an increase in ALT or ACT levels by more than 2 times the upper limit of normal, or bilirubin, which would be 1.5 times higher than normal; history of diabetes mellitus or newly diagnosed with HbA1c > 7.1%; treatment-resistant hypertension with CAT \geq 200 mm Hg or DBP \geq 100 mm Hg (despite therapy); planned coronary revascularization or other major surgery during the follow-up period; AIDS (HIV-positive) patients or hepatitis B, C-positive patients; history of chronic renal failure; drug or alcohol dependence (> 2 units / day for the last six months); mental or psychiatric disorders that make it difficult to communicate and assess the patient's condition.

The electrical activity of the heart in the selected contingent of patients was studied using a combined cardiomonitor "Cardiotechnika-4000" ("Inkart", Russia). ECG was recorded on 3 channels. Ischemic episodes were recorded under conditions of oblique ascending or horizontal depression of the ST segment or its elevation of 1 mm or more, lasting at least 60 s. An episode of ischemia was considered to be an episode with the above changes, which occurred not earlier than 1 minute from the previous one. All patients kept diaries that indicated periods of sleep, physical activity and rest, food and medication, and subjective pain during the day. The obtained results of HM ECG made it possible to assess the dynamics of heart rate, the number of episodes of BIM and BBIM, their duration, changes in ectopic activity on the background of therapy.

HM ECG was performed with the study of heart rate variability (HRV). The following time parameters were analyzed: SDNN - standard deviation of normal NN intervals

within 24 h; SDANN - standard deviation of the average values of the NN intervals for every 5 minutes of continuous ECG recording; rMSSD - standard deviation of the difference of successive intervals NN; pNN50 - the percentage of consecutive NN intervals, the difference between which exceeds 50 ms. Spectral analysis was performed using the following indicators: HF - high-frequency component of the spectrum (0.15-0.4 Hz), LF - low-frequency component of the spectrum (0.04-0.15 Hz), LF / HF - sympathetic-parasympathetic balance coefficient, TP - total spectrum power.

STATISTICA 6.0 software package using standard information processing methods was used in statistical data analysis. The mean values (M), their errors (m), correlation coefficient (r), reliability of statistical indicators (p) were evaluated. To compare the averages of the two groups with a normal distribution used the calculation of the Student's t test.

Results

Heart rate and heart rate variability at the initial examination of patients were analyzed. As can be seen from (Table 1), in patients with PA + IHD compared with patients in group IXC, there were significantly ($p < 0.05$) higher heart rate, so heart rate was higher by 3.1%, heart rate - by 12.73 %, Heart rate max - by 11.6%, respectively. Increased sympathoadrenal effects are confirmed by analysis of heart rate variability. Comparison of HRV spectral analysis in the selected contingent indicates a more pronounced decrease in total spectral power (34.82%, $p < 0.001$), high-frequency component of the spectrum (15.94%, $p < 0.05$) in patients with RA + IHD compared with patients with coronary heart disease. These differences in autonomic regulatory tone also applied to temporal indicators. Thus, SDNN in the group of patients with RA with combined pathology of IHD was significantly lower compared to the same indicator in the group of patients with isolated IHD (11.56%, $p < 0.05$).

Indicator	IHD, n = 61	RA + IHD, n = 60	p
Heart rate min, beats / min	54,2±3,5	56,4±4,2	p<0,05
Heart rate, beats / min	76,1±4,7	87,2±6,3	p<0,001
Heart ratemax, beats / min	121,5±5,6	135,6±7,1	p<0,05
HF, mc	345±63	290±54	p<0,05
LF, mc	806±46	993±29	p<0,05
TP, mc	1838±116	1198±193	p<0,001
SDNN, mc	49,3±5,1	43,6±4,9	p<0,05
RMSSD, mc	23,2±1,43	21,9±0,79	p<0,05
pNN50%	8,37±1,12	5,31±0,83	p<0,05

Table 1: Heart rate and HRV in patients with CHD and RA + CHD.

Note: n is the number of patients.

P is the probability of the difference between the groups of IHD and RA + IHD.

It is known from scientific sources that the prognosis is unfavorable for the quality of health is determined by the decrease in this time indicator. The positive correlation between the degree of decrease in HRV and the severity of the pathological process reflects the opinion of many authors the participation of autonomic imbalance in the clinical manifestations of the disease and is a quantitative measure of damage depth and prognosis.

The detected decrease in the tone of the parasympathetic nervous system and violation of the physiological mechanisms of daily control of heart rate variability correlated with indicators of activity and duration of RA (Table 2). Thus, the HF index (%) was 29.7 ± 2.3 in patients

with grade I activity, 26.9 ± 1.7 in the case of grade II activity and 25.4 ± 2.5 - grade III activity; the TR index was 1821 ± 131 , 1583 ± 242 and 1219 ± 210 in the case of activity of I, II and III degree, respectively. There was a significant difference between these indicators in patients with I and III degree of activity with $p < 0,05$. Analysis of the data indicated the greatest difference in each of the groups in patients with extra-articular manifestations of RA. Analysis of heart rate variability in patients with RA duration < 5 years and > 10 years indicated the most pronounced decrease in variability indicators with increasing RA duration. Thus, HF decreased by 17.55% ($p < 0.05$), TP by 27.39% ($p < 0.05$) and SDNN by 7.52% ($p < 0.05$), respectively.

	HF,%	TP, ms	SDNN, ms
RA activity I			
II	29,2±2,3	1821±131	89,7±8,2
III	26,9±1,7	1583±242	86,9±6,7
	25,4±2,5*	1219±210*	85,4±9,8
Duration of RA			
<5 years	30,2±1,7	1789±152	45,2±2,8
5-10 years	25,6±2,4	1634±247	44,5±3,7
> 10 years	24,9±1,8**	1299±193**	41,8±2,9

Table 2: Dynamics of heart rate variability indicators in the group of patients with RA + IHD, n= 60.

Note: * -significant differences in relation to one indicator in the group of subjects with I and III degree of RA activity ($p < 0,05$); ** - significant differences in relation to one indicator in the group of subjects with a duration of RA <5 years and > 10 years ($p < 0,05$).

The analysis of arrhythmias in the selected contingent of patients attracts attention. Supraventricular arrhythmias predominated among arrhythmias in the number of cases (Table 3). Atrial fibrillation was most often observed in the

group of patients with a combination of RA and coronary heart disease, although the differences compared with the group of patients with IHD were not significant.

Indexes	IHD, n= 61	RA + IHD, n= 60
Frequency of supraventricular extrasystoles	13 (21,31%)	15 (25,00%)
Frequency of ventricular arrhythmias	6 (9,84%)	7 (11,67%)
Atrial fibrillation	2 (3,28%)	3 (5,00%)
Violation of conductivity (NBPNPG)	8 (13,11%)	7 (11,67%)
Violation of conductivity (NBLNPG)	9 (14,75%)	11 (18,33%)

Table 3: Violation of automatism and conductivity in patients in IHD and RA + IHD, n (%).

Note. n is the number of patients

According to HM ECG, we analyzed ischemic changes in the selected group of patients. As can be seen from the above data (Table 4), in patients with combined pathology of RA and coronary heart disease, significantly ($p < 0,05$) were more frequent episodes of both pain (23.21%) and painless (36.62%). The ratio of episodes of IBD to AMI in patients with

RA + IHD was higher (1.6) than in the group of patients with IHD. The same applies to the duration of episodes of BIM and BBIM, it was significantly longer in patients with combined RA and chronic coronary heart disease. It should also be noted that the overall incidence of cardiac arrhythmias and conduction was associated with the incidence of BPD.

Indexes	IHD, n= 61	RA + IHD, n= 60
Episodes of painful myocardial ischemia, n	6,42±0,93	8,36±0,97*
Duration of episodes of painful myocardial ischemia, min / day	7,36±1,07	9,51±1,34
Episodes of painless myocardial ischemia, n	8,36±0,87	13,19±1,48*
Duration of episodes of painless myocardial ischemia, min / day	9,22±2,19	12,71±2,24*
Depression of the ST segment, μV	211±39	209±19
Inversion of the tooth T, n (%)	11 (18,03%)	18 (30,00%)*

Table 4: HM ECG parameters in patients with IHD and RA + IHD.

Note: * -significant differences in one indicator between groups of patients with IHD and RA + IHD ($p < 0,05$).

Discussion

The parameters of the HRS spectral analysis (VLF, LF, HF) are significantly lower in patients with RA and coronary artery disease than in patients with IHD only ($p < 0.05$) (Table 1). HRS parameters, which characterize the parasympathetic part of the autonomic nervous system (ANS), are significantly reduced in patients with RA, which indicates a weakening of the activity of the parasympathetic part of the ANS and a decrease in the "protection" of the heart against the occurrence of life-threatening arrhythmias [7].

The analysis of HRS in patients with RA according to the degree of activity shows that as the degree of disease activity increases, the sympathetic activity of the ANS increases: at the 1st degree it is minimal, at the 3rd degree it is maximal [8].

24-hour Holter ECG monitoring of the RA group showed ST depression of 1 mm in at least two consecutive leads was observed more often, and occurred statistically more often for the highest stage of RA, respectively. Also, no differences were found in the frequency of rhythm disturbances between the RA group and the group with IHD. However, silent episodes of myocardial ischemia occurred more often in the RA group [9].

According to some authors, the identified relationship of indicators indicates the potentiation of the course of these nosologies. It is known that RA creates conditions for overproduction of inflammatory mediators (acute inflammatory proteins, cytokines, immune complexes) and reduced vascular NO. As a result, endothelial dysfunction, vasoconstriction, lipid peroxidation, hypercoagulation, which activates the sympathetic nervous system and suppresses vagus exposure, which in turn leads to chronic inflammation. Thus, simultaneous assessment of inflammatory activity of RA and variability of heart rate may be an additional method of identifying patients at high risk of cardiovascular events.

Conclusion

In patients with RA and CHD, 24-hour ECG monitoring, compared with patients with IHD alone, revealed more serious changes, such as sinus tachycardia, extrasystole, paroxysmal tachycardia, ischemic changes in the ST segment and T wave. The most pronounced ECG changes during daily monitoring were noted in RA III degree of activity. According to the data of daily ECG monitoring, rhythm disturbances (sinus tachycardia, extrasystole, paroxysmal tachycardia) are more often diagnosed in patients with RA over 5 years old. Changes in the T wave and ST segment are more characteristic of RA patients with a disease duration of more than 10 years.

Conflicts of Interest Disclosure

The authors declare that there are no conflicts of interest with regard to this study.

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