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COMPARISON OF VARIABILITY INDICATORS HEART RHYTHM IN WOMEN RHEUMATOID ARTHRITIS AND WOMEN WITHOUT RHEUMATIC DISEASES

Abstract :Goal. Compare daily heart rate variability (HRV), normalized by age and average heart rate during the day (HRV)
in women with rheumatoid arthritis (RA) and women in the control group.
Materials and methods. 97 patients with a reliable diagnosis of RA aged from 20 to 60 years were examined. The control group included 25 women without rheumatic diseases. In addition to the clinical manifestations, the degree of activity and severity of RA, the presence of the main traditional risk factors for cardiovascular diseases was assessed, Holter ECG monitoring (XM-ECG) was performed with automatic calculation of the frequency characteristics of the sinus rhythm of the heart, temporal and spectral parameters of HRV. In order to offset the influence of age and heart rate on HRV indicators, the initial HRV parameters were converted into their logarithms, the standardization of logarithms by age and HRV, and the calculation of the exponent from the standardized logarithm.
Results. The temporal and frequency indices of HRV, normalized by age and HRSS (HRSs), were significantly lower in women with RA than in the control group. A decrease in HRSp is observed in 14-24% of women with RA, while the greatest decrease was noted among the parameters characterizing the tone of the parasympathetic division of the autonomic nervous system (RMSSDn, pNN50n, HFn).
Conclusion. Young and middle-aged female RA patients differ from women in the control group by a significant decrease in temporal and spectral HRV indicators, normalized by age and heart rate.
Key words: rheumatoid arthritis, heart rate variability

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune disease with a proven high
cardiovascular risk. A meta-analysis of 17 prospective studies indicates a 60% increase in cardiovascular mortality in RA compared with the general population. The main causes of high mortality from cardiovascular complications (CVD) are accelerated progression of atherosclerosis, development of chronic heart failure (CHF) and sudden cardiac death. The risk of coronary heart disease (CHD) and myocardial infarction in RA is increased by 2 times, cerebral stroke — by 1.9 times, CHF — by 1.8 times compared with the general population. Disorders of the neurohumoral regulation of blood circulation play an important role in the development and progression of cardiovascular diseases in the general population and in patients with RA. Chronic hypersympathicotonia contributes to the development and maintenance of arterial hypertension (AH), myocardial ischemia, cardiac arrhythmias, accelerates the processes of vascular remodeling and hypertrophy of the left ventricular myocardium and can lead to sudden cardiac death. The determination of HRV indicators is recognized as the most informative and accessible method for assessing the autonomic regulation of heart rhythm. A decrease in HRV is associated with an increased risk of CVD in patients who have had a

myocardial infarction, suffering from CHF of any etiology, diabetes mellitus, hypertension, metabolic syndrome, and in people without obvious signs of CVD.

Currently, it has been proven that the value of HRV depends on many factors, the main of which are gender, age, and heart rate. In the absence of adjustments to the values of HRV indicators for these factors , incorrect interpretation of the data obtained is possible. For example, if the pathological process is characterized by an increase in heart rate, there is a risk of overestimating the value of reduced HRV indices, since an increase in heart rate reduces the parasympathetic parameters of HRV due to the ratio of frequency and HRV indicators, phase shifts of vagal impulses with changes in the duration of the cardiac cycle and the modulating effect sympathetic activity on the manifestations of respiratory arrhythmia. Previously, only isolated studies on small samples demonstrated a decrease in HRV values obtained by analyzing short (5-minute) and daily ECG recordings in RA patients compared with individuals without rheumatic diseases.

The aim of the study was to compare HRV indicators, normalized by age and HRSS (HRSs), in women with RA and the control group.

MATERIALS AND METHODS OF RESEARCH

The study included 122 people, including 97 patients with a reliable diagnosis of RA. The control group consisted of 25 women without rheumatic diseases who did not meet the exclusion criteria. All subjects signed an informed consent. The study did not include people over 60 years of age, with coronary heart disease (angina pectoris, myocardial infarction), with clinical manifestations of CHF II–IV FC, stroke survivors, patients with diabetes mellitus, valvular heart disease, grade 3–

4 obesity, peptic ulcer of the stomach and duodenum, cancer, clinically significant thyroid diseases. During the study, patients and subjects in the control group did not take beta-blockers, angiotensin converting enzyme inhibitors, statins and sedatives. Daily ECG monitoring was performed using a 3-channel monitor. ECG monitoring was started in the morning before 12 o'clock. Recordings with the number of artifacts exceeding 5% of the total number of detected signals, as well as recordings with a duration of less than, were not accepted for analysis. For 20 hours, the recordings were processed semi-automatically with manual processing of the results of the morphological classification of QRS complexes and artifacts, and manual adjustment of the prematurity criteria for supraventricular ectopic contractions. A daily HRV analysis was performed. The following indicators were determined in the time domain: NNpc — the average value of the RR intervals of sinus origin (NN) for the entire study period; SDNN — the standard deviation of the NN intervals; SDANN — standard deviation of NN averages in 5-minute intervals; SDNNindex is the 24—hour average value of NN standard deviations in 5-minute intervals; RMSSD is the square root of the sum of the squares of the differences of adjacent NN intervals over a 24-hour period; pNN50 is the number of NN intervals that differ from the previous ones modulo more than 50 ms, expressed as a percentage of the total number of NN intervals. The spectral analysis of HRV conducted in a 24-hour period included the construction of a trend of NN intervals, reflecting the dependence of the interval values NN from time to time. At the same time, the discreteness of The time (t) was 0.5 s. In the presence of artifacts or extrasystolic complexes, the preceding and subsequent RR intervals were excluded from consideration, and the current value of the NN interval was calculated using linear interpolation. The total power of the spectrum (1.15x10-5–0.40 Hz) — TotP, the oscillation power NN in the range of ultra-low frequencies

(1.15x10–5—0.0033 Hz) – ULFP, the oscillation power NN in the range of very low frequencies (0.0033-0.04 Hz) were determined — VLFP, NN oscillation power in the low frequency range (0.04–0.15 Hz) — LFP, NN oscillation power in the high frequency range (0.15–0.40 Hz) —

HFP. To describe the distribution of the analyzed indicators, frequencies for discrete variables or parameters for continuous ones were calculated using the standard representation M±m or percentiles. The reliability of quantitative differences between the groups was assessed using Student's t-criteria. To verify the correctness of the use of parametric statistics methods, the forms of the distribution of variables were analyzed.By When comparing frequencies between groups, the $\chi 2$ "chi-square" criterion was used (for 2x2 tables, in the exact Fischer solution). In the case when it was necessary to analyze the real significance of a risk factor in relation to a certain clinical manifestation, the probability of which significantly depended on age or other factors, partial correlation coefficients were calculated and analyzed under the control of age or another factor. Differences in indicators were considered significant at $p<0.05$.

THE RESULTS AND THEIR DISCUSSION

Nonsteroidal anti-inflammatory drugs (NSAIDs) were taken by 94% of RA patients, glucocorticoids (GCs) by 52%. Baseline anti-inflammatory drugs (BIDs) were taken by 78% of women, including methotrexate by 59%. women, of which methotrexate - 59%, leflunomide - 21%, and plaquenil - 21%. 21%, plaquenil - 7%, sulfasalazine - 7%, and other anti-inflammatory drugs (cyclophosphate - 7%).

DMARDs (cyclophosphan, azathioprine, gold, cyclosporine A, chlorbutin) - 6%.

Women with RA compared to controls were older in age, the former more often had AH, postmenopause, hypodynamia, hypertriglyceridemia, hypoalphalipoproteinemia, increased values of atherogenicity index and body mass index. In women with RA, the values of HRcr were higher compared to those in the control group. When adjusting for age, women with RA and controls retained differences in the frequency of hypertriglyceridemia, hypoalphaliphaliporoproteinemia, AH, Age-adjusted frequency of hypercholesterolemia in RA was significantly lower than in controls. was significantly lower than in controls. Women with RA differed from the control group by the lower values of temporal and frequency parameters of HRV normalized for age and HRcr (BPCn), except for the LFn/HFn index. In the study of partial correlations, no significant contribution of other traditional correlations was no significant contribution of other traditional other traditional CVD risk factors (AH, dyslipidemia, increased weight loss, physical inactivity, physical inactivity, physical inactivity, and weight loss. weight loss, physical inactivity, menopause) in reducing BPCn in RA patients compared to controls ($p>0.05$). As conditional criteria of normal values, BPCn indicators calculated in the control group of The women differed from the control group with lower values of time and frequency indicators of HRV, normalized by age and heart rate. (HRSp), with the exception of the LFn/HFn index. The study of partial correlations did not reveal a significant contribution of other traditional CVD risk factors (hypertension, dyslipidemia, overweight, physical inactivity, menopause) to the reduction of Hrv in RA patients compared with controls ($p>0.05$). Hrv indicators calculated in the control group of individuals (less than 5 percentile for all studied parameters, above 95 percentile for the LF/HF index) were used as conditional criteria for normal values. Among women with RA, there is a decrease SDNNn<112 ms was present in 40 (14%) patients, SDANNn<103 ms — 50 (17%), TRp<13975 ms2 – 54(19%), ULFPn<11685 ms2 — 55(19%), SDNNin<43 ms — 42 (15%), VLFPn<1091 ms2 — 53 (18%), LFPn<510 ms2 — 50 (17%), RMSSDn<22 ms — 70 (24%), pNN50%n<2,9% — 66 (23%), HFPn<126 ms2 — 64(22%), LFn/HFn>6 — 52 (18%). This study included the study of HRV in a fairly large group of young and middle-aged female RA patients in conditions of withdrawal of previous therapy with cardiopreparations, which makes it possible

to identify the relationship between HRV features and the specifics of the disease. For the first time, we have identified a significant decrease in all time and frequency indicators of HRV,

normalized by age and heart rate, in women with RA compared to the control group. The results obtained reflect a violation of the neuro-autonomic autonomous control of cardiac activity (increased influence of the sympathetic and/or decreased influence of the parasympathetic parts of the autonomic nervous system on cardiac activity) in RA. A particularly pronounced decrease in HRV was observed in the group of parameters characterizing the tone of the parasympathetic division of the autonomic nervous system. (RMSSDn, pNN50n, HFn) — from 22% to 24%. Such shifts in the neuro-autonomic regulation of cardiac activity are prognostically unfavorable, as They are closely associated with the development of life-threatening arrhythmias and an increased risk of sudden cardiac death. The results of most previous studies on the study of the autonomous regulation of cardiac activity in RA patients also indicate the development of hypersympathicotonia in this disease.

CONCLUSIONS

Thus, in young and middle-aged female patients with RA, there is a significant decrease in the time and frequency indices of HRV, normalized by age and heart rate. A particularly pronounced decrease in HRV is observed among the parameters characterizing the tone of the parasympathetic division of the autonomic nervous system (RMSSDn, pNN50n, HFn). The clinical application of the data obtained will be possible after identifying the factors leading to a decrease in HRV in women with RA, and it is also necessary to conduct prospective studies with an assessment of "solid" endpoints to determine the role of reduced HRV as a risk factor for the development of CVD in RA and the expediency of developing preventive measures aimed at increasing HRV in order to prevent CVD.

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