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Cardiac Autonomic Dysfunction in Patients with Systemic Lupus, Rheumatoid Arthritis and Sudden Death Risk

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SUMMARY

Introduction The manifestations of autonomic nervous system (ANS) dysfunction in autoimmune diseases have been the subject of many studies. However, the published results pertaining to such research are controversial. Sudden cardiac death due to fatal arrhythmias is frequent in patients with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA).

Objective To analyse risk predictors of sudden cardiac death related to the degree of autonomic dysfunction.

Methods We performed cardiovascular ANS assessment in 90 patients in this case-controlled study, including 52 (6 male, 46 female) patients with SLE, 38 (6 male, 32 female) with RA and 41 (23 male, 17 female) healthy subjects. The methodology included a comprehensive ECG analysis (with Schiller software AT-10) of QTc interval, late potentials, short-term heart rate variability (HRV) and nonlinear HRV (Poincare plot) analysis; 24-hour Holter ECG monitoring with ECG QTc interval analysis, HRV analysis; 24-hour blood pressure monitoring with systolic and diastolic blood pressure variability; cardiovascular autonomic reflex tests (according to Ewing). Vagal dysfunction was established by performing 3 tests: Valsalva maneuver, deep breathing test and heart rate response to standing test. Dysfunction of the sympathetic nervous system was examined by applying 2 tests: blood pressure response to standing and handgrip test.

Results In all cardiovascular reflex tests, the frequencies of abnormal results were significantly higher among the patients than among the healthy subjects. Severe autonomic dysfunction was more common in RA. QTc interval was more prolonged in patients with SLE. Both diseases were associated with depressed heart rate variability compared to controls, the reduction being greater in RA patients. In the patients with SLE, autonomic dysfunction is predominantly with higher sympathetic activity while in RA vagal predominance is evident.

Conclusion SLE and RA are associated with severe autonomic dysfunction and the presence of significant risk predictors related to the onset of sudden cardiac death.

Keywords: autonomic dysfunction; systemic lupus erythematosus; rheumatoid arthritis; sudden cardiac death

INTRODUCTION

Numerous epidemiological studies have shown higher cardiovascular mortality in patients with rheumatoid arthritis (RA) [1]. According to some data, positive late potentials and severe ventricular arrhythmias are more frequent in patients with systemic lupus erythematosus (SLE) [2]. The higher mortality rate in such patients is mainly the result of myocardial infarction and serious arrhythmias due to autonomic nervous system (ANS) dysfunction [2].

Although the relationship between autoimmune diseases and ANS dysfunction has been the subject of many studies, there are still controversies concerning the role of ANS dysfunction in autoimmune diseases. Also, there is still no data detailing the role of ANS dysfunction in the pathogenesis of sudden cardiac death in patients with autoimmune diseases [3, 4].

Lack of relevant data from previous studies is related to the methodology applied in ANS function assessment and sudden cardiac death risk factor evaluation.

OBJECTIVE

Having the above-mentioned in mind, the aim of this study was to evaluate the presence and level of ANS dysfunction in patients with SLE and (RA) and to identify cardiovascular risk factors associated with sudden cardiac death.

METHODS

Study patients

The study group consisted of 52 (46 female, 6 male, mean age 43.3±22.8) patients with SLE, 38 (32 female, 6male, mean age 56.3±13.1) patients with RA and 41 (23 male, 17 female, mean age 37.4±14.6) healthy subjects.

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The diagnosis of SLE and RA was established using the criteria developed by the American College of Rheumatology. All patients with autoimmune rheumatic diseases were in stable condition. SLE activity was determined according to the SLEDAI score. RA activity was determined by the Ritchie articular index and erythrocyte sedimentation rates (ESR).

Control subjects were selected from a population of healthy individuals without signs of ANS dysfunction (ANSD) and they were not taking any medications. The control group was formed to approximately match the mean age of the SLE and RA patient groups; the controls also did not differ significantly by gender from the patients with autoimmune diseases.

Patients were excluded from the study if they had any of the following conditions: pregnancy, renal or liver insufficiency, cardiac or respiratory failure, severe cardiac arrhythmias, acute thrombosis, or other severe organic or functional manifestations.

Majority of the patients did not show high activity of their primary disease. Thus, only 12% of SLE patients had the SLEDAI score higher than 25.4 (7.4%) and were seronegative, while 25 (46.3%) had antiphospholipid antibodies (LA, aCL or b_2BGPI). Twenty-five (64.1%) RA patients had positive RF >1:80. The mean ESR in all RA patients was 14.3±12.25. The mean number of swollen joints and the Ritchie articular index was low in most of these patients.

Testing of patients was approved by the Scientific Ethical Committee of the Clinical Hospital Centre, Bezanijska Kosa. Written informed consent was obtained from all subjects.

Methodology

All patients were tested in the Neurocardiology Laboratory using the original protocol for the assessment of ANS function and identification of those at risk of cardiac death. The protocol included complete testing of the ANS, 24-hour Holter ECG and ambulatory blood pressure monitoring. Complete testing first included cardiovascular reflex tests, followed by short time heart rate variability (HRV) spectral analysis (10 minutes) using the commercial software Schiller AT-10. ECG recording included spectral and nonlinear analysis (Poincare plot) of heart rate variability, as well as analysis of late potentials. Patients were tested under uniform conditions which included testing at room temperature (23°C), after restraining from alcohol, nicotine, or food intake.

Clinical Autonomic Function Tests

Cardiovascular reflex tests according to Ewing's battery were the first step in our assessment of autonomic function [18]. Participants rested in the supine position for 10 minutes before starting the tests and also rested for 2 minutes between each test.

Results of all four tests were expressed as normal, borderline or abnormal, according to cut-off values given by Ewing. Based on the results of the cardiovascular reflex tests, a scoring system was applied and autonomic dysfunction in each patient was qualified as: vagal denervation, vagal and sympathetic damage or severe autonomic neuropathy [4].

Parasympathetic tests

Valsalva maneuver

The patient rested before commencement of the test. While lying recumbent, the patient was asked to maintain a column of mercury at 40 mm Hg for 15 seconds by blowing into a modified sphygmomanometer, with simultaneous ECG recording. The result, expressed as a Valsalva ratio (VR), was taken as the maximum ECG RR interval obtained during 15 seconds following expiration divided by the minimum RR interval during the same maneuver.

Heart rate response to deep breathing test

Respiratory sinus arrhythmia was assessed by the performance of 6 deep breaths at 0.1 Hz frequency. Patients were given adequate rehearsal to achieve the required frequency and counted through 6 breaths. The response was taken as the mean of the differences between the maximum and minimum instantaneous heart rate for each cycle.

Heart rate response to standing test (30:15 ratio)

Heart rate response after standing was expressed as a ratio between the longest RR interval corresponding to the 30th heart beat after starting and the shortest RR interval corresponding to the15th beat. The ratio was measured using a ruler from an electrocardiograph trace which was recorded continuously.

Sympathetic tests

Blood pressure response to standing test

Orthostatic blood pressure change was calculated as the difference between the systolic blood pressure 180 seconds after standing and the systolic blood pressure prior to standing.

Short-term ECG and short-term HRV analysis

Analysis of standard 12-lead ECG recordings using the commercially available software (Schiller AT-10, Suisse) included ECG wave and interval analysis: duration of P wave, PQ interval, QRS complex, QT and QTc intervals. QT parameters were measured automatically from the 12-lead ECG recording (ECG recorder model AT-10; Schiller, Austria) at a paper speed of 50 mm/s (gain, 10 mm/mill volt). The QT interval was measured from the

onset of QRS complex to the end of T wave. Each QT interval was corrected for patient heart rate according to Bassett's formula [18]: QTc=QT/√ (RR interval), where QT and RR intervals are expressed in seconds. Short-term HRV analysis was done from 512 consecutive RR intervals using the commercial software (Schiller AT –10, Austria) according to the previously published guidelines [19]. Short -term HRV analysis includes: time domain analysis, frequency domain analysis and nonlinear HRV analysis (Poincare space plot). The following time domain variables from dRR tachogram were computed for each subject: average dRR, standard deviation of dRR (SD), mean deviation of dRR (MD), square root of the mean of squared differences of two consecutive RR intervals (r-MSSD) and percentage of adjacent RR intervals differing >50 ms (pNN50). The following short-term frequency domain indices were determined using Hanning window type signal limitation before Fourier transformation: very low frequency (VLF: 0.016-0.05 Hz), low-frequency power (LF: 0.05-0.15 Hz), high-frequency power (HF: 0.15-0.35 Hz), and LF/HF ratio.

Nonlinear analysis (Poincare space plot)

Results of nonlinear Poincare space plot analysis were divided based on visual form (cigarette, cluster, comet or spot), and based on the distribution of these forms in space (space segment of bradycardia, tachycardia and normal rhythm).

Rhythm analysis and long-term HRV analysis

Twenty-four-hour ambulatory ECG recordings were acquired by a 3-lead electrocardiogram, with a sampling rate of 1000 Hz per each lead (Biosensor, USA) and analysed by an experienced analyst. Cardiac rhythms were screened for ventricular premature beats (VPB) and supraventricular premature beats (SVPB). The recordings were reviewed, and the beat classifications were manually checked, corrected, and prepared for further analysis. After all of the artifacts and misclassified beats were corrected, time and frequency domain HRV analysis, QT and QTc interval analysis and T wave morphology analysis were carried out using the software package present in the system. The Fast Fourier transformation (FFT) and Hanning window were used for analysis of the frequency (spectral) domain parameters. In rhythm analysis, the total number of VPBs and SVBPs for the whole recording period was determined and the number of VPB per hour calculated. Also, the degree of arrhythmias was quantified according to Lown classification. From time domain HRV analysis following time domain variables, the following were computed: mean RR interval for 24 h (mean NN), standard deviation of normal RR intervals (SDNN), standard deviation of all 5-min mean normal RR intervals (SDANN), square root of the mean of the sum of the squares of differences between adjacent RR intervals (r-MSSD), and percentage of adjacent RR intervals differing >50 ms (pNN50). From frequency domain HRV analysis following 24-h Holter-ECG, the following frequency domain indices were determined: total power (TP: 0-0.4 Hz), high-frequency power (HF: 0.15-0.4 Hz), low-frequency power (LF: 0.04-0.15 Hz), and the LF/HF ratio. Heart rate was measured in milliseconds (ms); variance, which is referred to as the power in a portion of the total spectrum of frequencies, was measured in squared milliseconds (ms^2).

24-hour ambulatory blood pressure monitoring

Evaluation of 24-hour blood pressure (BP) profile was done using a recorder and the commercial software for analysis (Mobil-O-graph). Monitoring began at approximately 11 a.m. and BP measurements were performed by the oscillometric method every 15 minutes during the 24-hour period. From these data, the following variables were calculated for each patient: average total (24 hour), daytime (from 9 a.m. till 9 p.m.) and nighttime (from 0 a.m. till 6 a.m.) systolic BP, diastolic BP and pulse pressure; systolic and diastolic blood pressure variability during day and during night expressed as the standard deviation of all systolic and all diastolic BP measurements during daytime and during night (automatically calculated using the same software).

Statistics

All data were analysed using the computer software package SPSS 11.05. Nominal values were presented as mean with standard deviation (X±SD). Parametric data were analysed using independent ANOVA to show differences between groups, while nonparametric data were analysed using the Kruscal–Wallis test. Results were deemed as statistically significant for p values less than 0.05.

RESULTS

Cardiovascular autonomic reflex tests

Sympathetic dysfunction, manifested as orthostatic hypotension, was present in 8 (15.7%) patients with SLE and 8 (22.3%) with RA. Vagal denervation was diagnosed in 18 (34.6%) with SLE versus 12 (34.3%) with RA. Complete vagal and sympathetic dysfunction was registered in 17 (32.7%) SLE patients and 10 (29.4%) with RA. Severe autonomic dysfunction was more common in the patients with RA 11 (31.4%), the SLE patients versus 12 (23.1%) the RA patients. Deep breathing test was also more often positive in the RA patient group. Heart rate response to the standing test was positive in about two thirds of patients in both groups. Patients were considered as having autonomic neuropathy if two or more positive tests were obtained. This was registered in 43 (82.7%) and 30 (85.7%) the patients with SLE and RA respectively (Table 1).

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Table 1. Cardiovascular reflex tests

Cardiovascular reflex tests	n/N (%)			p
	SLE	RA	Control group	
Orthostatic hypotension	8/51 (15.7)	8/35 (22.8)	2/39 (5.1)	<0.001
Valsalva maneuver	13/52 (25.0)	10/36 (27.8)	4/39 (10.3)	0.057
Deep breathing test	14 /52 (26.9)	14/34 (41.2)	2/39 (5.1)	0.003
HR response to standing (30:15 ratio)	39/51 (76.5)	25/35 (71.4)	16/38 (42.1)	<0.001
Vagal dysfunction	18/52 (34.6)	12/35 (34.3)	3/39 (7.7)	0.004
Vagal and sympathetic dysfunction	17/52 (32.7)	10/34 (29.4)	3/39 (7.7)	0.016
Severe autonomic neuropathy	12 /52 (23.1)	11/35 (31.4)	0/39 (0)	<0.001
Autonomic neuropathy	43 /52 (82.7)	30/35 (85.7)	17/39 (43.6)	<0.001

n – number of study patients with positive test; N – whole number of study patients; SLE – systemic lupus erythematosus; RA – rheumatoid arthritis

Table 2. QT, QTc, PQ interval, QRS and P wave duration (ms)

Parameters	SLE	RA	Control group	p
QTc	442.4±28.6	434.4±22.9	412.2±5.1	<0.001
QT	385.4±29.2	387.1±33.8	386.9±27.3	0.965
PQ	152.4±28.5	152.7±27.0	158.4±21.3	0.570
QRS	90.7±13.6	85.5±7.3	94.2±24.7	0.137
P wave	108.3±13.2	101.7±18.7	102.0±18.1	<0.001

QT interval

Analysis of the QTc interval showed that it was of significantly longer duration in patients with SLE, compared to patients with RA and healthy individuals. No significant difference was found between groups concerning duration of non-corrected QT intervals, PQ intervals or QRS complexes. P waves were also prolonged in the patients with SLE compared to the patients with RA and healthy subjects (Table 2).

Short time heart rate variability analysis

It was observed that the overall heart rate variability was diminished in the patients with SLE and RA compared to controls. Time domain variable PNN50 which depicts vagal activity was the lowest in the patients with RA. Spectral parameters VLF, LF and HF were also lower in comparison to the control group. The patients with SLE had higher values of LF expressed as normalized and absolute values in comparison to the RA and control groups. The patients with RA had higher VLF and lower values of HF compared to the SLE and control groups (Table 3).

Table 3. Short time heart rate variability analysis

Parameters	SLE	RA	Control group	p
Mean d RR	13.3±8.4	12.7±6.8	33.9±18.3	0.159
SDNN	11.1±7.3	11.2±5.4	28.7± 14.5	<0.001
MD	8.3 ±5.3	7.8±4.0	21.6±11.6	<0.001
P NN 50%	2.2± 4.7	1.5±2.8	13.4±11.2	<0.001
RMSSD	17.5±11.5	17.2±8.3	44.2±23.7	<0.001
VLF	78.3±90.4	108.8±105.3	255.7± 240.7	<0.001
LF	94.7±107.7	84.3±111.9	332.1±325.0	<0.001
HF	49.7 ±80.6	36.3±39.7	213.1±264.7	<0.001
LF/HF	4.4±5.1	2.9±2.2	2.8±2.9	0.228
VLF (nu)	29.1±14.4	35.1±12.2	33.2±45.4	0.041
LF (nu)	33.4± 14.6	22.3±11.2	31.5±12.6	0.003
HF (nu)	14.7±9.9	12.6±8.8	23.9±26.4	0.020
LF/HF (nu)	1.4±0.7	1.3±0.7	1.3±0.7	0.898

Mean d RR – mean average d RR interval; SDNN – standard deviation of RR intervals; MD – mean deviation of d RR interval; RMSSD – square root of the mean of squared differences of two consecutive RR intervals; pNN50 – percent of beats with consecutive RR interval difference of more than 50 ms; VLF – very low frequency interval (0.016-0.05 Hz); HF – high frequency interval (0.15-0.35 Hz); LF – low frequency interval (0.05-0.15 Hz); LF/HF – low and high frequency ratio; nu – normal unit

Long-term heart rate variability analysis and arrhythmias

The association of ventricular arrhythmias with both autoimmune diseases did not reach statistical significance, however, supraventricular arrhythmias were more common in patients with RA. Time domain and spectral parameters were lower in patients with autoimmune diseases compared to healthy subjects. The value of time domain parameter SDANN which depicts global autonomic function was the lowest in the patients with RA, but RMSSD, a marker of vagal activity, was high. The patients with RA had lower values of spectral parameter LF. The patients with SLE had

Table 4. Long time heart rate variability analysis, ventricular and supraventricular premature beats

Parameters	SLE	RA	Control group	p
VPB	59.4±192.6	370.4±1077.0	12.6±45.6	0.054
SPB	28.6±86.0	286.8±801.1	5.5± 15.6	0.024
Mean RR	752.4 ±86.1	754.7±77.1	796.0±69.2	0. 056
SDNN	130.2±32.7	135.9±37.8	310.2±774.8	0.108
SDANN	132.7±58.9	126.0±59.0	173.6±70.8	0. 007
RMSSD	45.9±26.6	71.7±96.3	67.5±28.7	0.023
TRI INDEX	42.5±12.4	46.6±14.9	55.4±10.3	<0. 001
LF/HF	4.1 ±1.8	3.3±1.6	3.6±1.6	0. 074
LF	2383.1±3750.0	2315.2±3218.1	5759.2±8853.7	0. 018
HF	818.7±1702.2	36608.7±216477.3	1771.5±2292.0	0. 364

VPB – total number of ventricular premature beats during ECG monitoring; SPB – total number of supraventricular premature beats during ECG monitoring; SDNN – standard deviation of all the RR intervals; SDANN – standard deviation of all 5-min mean normal RR intervals; RMSSD – square root of the mean of squared differences of two consecutive RR intervals; TRI INDEX – triangular index; LF – low frequency interval; HF – high frequency interval; LF/HF – low and high frequency ratio

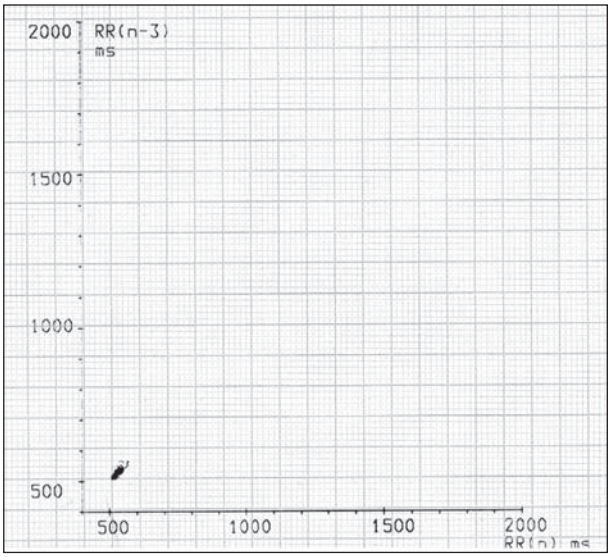

Figure 1. Characteristic form of nonlinear parameter Poincare plot as a point or cigarette

Table 5. Nonlinear analysis – Poincare plot

Shape of Poincare plot	Number of patients (%)			p
	SLE	RA	Control group	
Dot form	10 (24.4)	7 (25.9)	1 (2.9)	0.019
Comete form	26 (63.4)	18 (66.7)	13 (38.2)	0.035
Cluster form	5 (12.2)	2 (7.4)	20 (58.8)	<0.001

lower values of Triangular index, a parameter of cardiovascular risk, corresponding to higher sympathetic activity and risk of cardiac death (Table 4).

Nonlinear analysis (Poincare plot)

Poincare point-like shape was significantly prevalent in patients with immunologic diseases compared to controls (Figure 1). Appearance of Poincare comete shape was more frequent in SLE and RA patient groups, whereas a cluster Poincare shape was predominant in healthy controls (Table 5).

Ambulatory blood presure monitoring

Total mean systolic blood pressure during 24 hours was 121.6±14.0 in the patients with SLE, 125.5±15.4 in the RA group and 112.7±8.8 in control subjects (p=0.007). Total mean diastolic blood presure during 24 hours was 76.4±8,4 in SLE patients, 77.9±10.7 in the RA patient group and 73±5.5 in controls, however, these differences did not reach statistical significance (p=0.239). Also, no statistical significance was detected related to the same parameters measured during night and day and parameters of blood pressure variability.

DISCUSSION

In this study, we performed non-invasive cardiovascular reflex tests, short and long-term heart rate variability and nonlinear (Poincare plot) analysis to evaluate the functional status of the ANS and its effects on cardiac function. We investigated the prevalence, severity and cardiovascular risk factors related to the onset of sudden cardiac death.

Previous studies dealing with the relationship between ANS function and autoimmune diseases found signs of parasympathetic and sympathetic dysfunction in rather variable proportions in patients with autoimmune diseases (between 24 and 100% in various tests), depending on the methodology used. Cardiovascular reflex tests, although rather simplified, are quite accurate, and thereby useful in classifying patients depending on the presence of autonomic neuropathy and its severity, compared to new methods such as heart rate variability [4].

As the initial diagnostic step in evaluation of autonomic dysfunction in patients with immunologic disorders, we performed a cardiovascular reflex test examination established by Ewing. In order to obtain more sensitive results, borderline values of test results (tests) were considered negative [4].

Nevertheless, in spite of lower sensitivity of cardiovascular reflex tests vs. classic RR variability, over 80 % patients in both groups had autonomic neuropathy accompanied with two or more positive CV reflex tests. Orthostatic intolerance as a cardinal sign of sympathetic dysfunction was found in 20% of patients, whereas vagal dysfunction was noticed in 30% of patients. Autonomic neuropathy and severe autonomic dysfunction were more frequent in the patients with RA than in the SLE group.

Louthrenoo et al reported that only the deep breathing test was positive in both groups [5]. However, Gledhill and Liote demonstrated that over 80% patients with SLE had autonomic neuropathy, a finding similar to our results. Besides this, almost identical results were obtained in the group of patients with RA [6, 7].

However, contrasting data were also published. Omdal et al. did not find the existence of autonomic dysfunction in the patients with SLE [8].

Current data regarding autonomic dysfunction in the patients with RA are also inconsistent. Edmonds showed parasympathetic dysfunction in 30 % patients with RA which coincides with our findings [9]. However, Bekkelund et al. did not find autonomic dysfunction in 43 patients with RA [10].

Summarising the published data regarding autonomic nervous system activity in patients with immunologic disorders, great discrepancies in results and subsequent conclusions exist. The spectre of published results varies from normal findings of ANS activity to exaggarated ANS dysfunction, as was the case in our study [11].

In contrast to the majority of previous studies that lack diagnostic sensitivity and specifity, this is one the most comprehensive studies examining ANS activity in patients with immunologic disorders. Unlike less sensitive cardiovascular refelex tests which were used most frequently in previous studies, we performed complete and expanded ANS function testing including short- and long-time HRV with nonlinear analysis (Poincare plot) as well as analysis of QT interval for assessment of cardiovascular risk.The QT

interval reflects changes in repolarization and can point out the heterogeneity of this process and a substrate for ventricular arrhythmias. Prolonged QT interval is associated with increased cardiac mortality and high risk for the onset of sudden cardiac death [12, 13, 14].

There are many problems regarding standardization of measurements. QT interval dispersion and several heart rate correction formulas have been reported [15-18]. We measured QT interval duration using the commercial software (Schiller, Suisse) during 5 minutes under the resting conditions and found that QT c interval was of longer duration in the patients with SLE compared to the patients with RA and controls. However, these differences did reach statistical significance. On performing short-term analyses of time domain and spectral variables of heart rate variability, a significant reduction in HRV in patients with autoimmune diseases compared to controls was demonstrated. Analysing the LF component expressed in normal units, higher values were noticed in the patients with SLE, implicating sympathetic predominance in those patients.

Long-term analyses showed lower values of SDANN in the group of patients with RA accompanied with higher values of RMSSD in the same group. With great certainty, we can conclude that, compared with controls, the patients with SLE and RA have marked autonomic dysfunction with sympathetic predominance in the patients with SLE and parasympatehtic predominance in the patients with RA. Supaventricular arrhythmias were more frequent in the patients with RA. Other authors also pointed out decreased heart rate variability including time domain and spectral parameters in patients with autoimmune diseases using the long-term analysis of autonomic dysfunction [19-22].

In comparison with standard battery of cardiovascular reflex tests according to Ewing, the analysis of HRV is a more sensitive method, which can discover subclinical forms of autonomic dysfunction [23, 24]. Our results related to autonomic dysfunction in RA are very simillar to the results of other authors, especially regarding the lower values of time domain and spectral paremeters related to the general status of sympatho-vagal function [25]. Evrengul and co-workers also found higher values of pNN50% and RMSSD time domain parameters which correlated with higher vagal activity in RA [26]. The stage of autonomic dysfunction depends on the speed of disease progression during many years of patient follow-up [27].

Nonlinear visual analysis of the spatial form of Poincare plot showed a statistically significant difference pertaining to the shape of the plot corresponding to the expressed autonomic dysfunction. To the best of our knowledge, there are no published data related to the form of Poincare plot in autoimmune diseases. In the majority of patients we found a typical dot shape of Poincare plot associated with severe autonomic dysfunction and poor prognosis with statistical significance in comparison with controls. Analysis of risk predictors for sudden cardiac death related to autonomic dysfunction, revealed statistically significant reduction in HRV, depressed triangular index, presence of supraventricular arrhythmias, prolonged QTc interval and Poincare plot in the shape of a dot.

CONCLUSION

The results of this study pointed out that the increased risk for sudden cardiac death in SLE and RA is most probably related to severe autonomic dysfunction with sympathetic predominance and hyperactivity, leading to the onset of fatal arrhythmias.

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Предиктори изненадне срчане смрти и дисфункција аутономног нервног система код болесника са системским еритемским лупусом и реуматоидним артритисом

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КРАТАК САДРЖАЈ

Увод Манифестације поремећаја функције аутономног нервног система код аутоимуних обољења предмет су многих истраживања. Међутим, објављени резултати ових испитивања и даље су контроверзни. Изненадна срчана смрт услед тешке аритмије честа је код особа оболелих од системског еритемског лупуса (СЕЛ) и реуматоидног артритиса (РА).

Циљ рада Анализа предсказатеља ризика изненадне срчане смрти повезаних са степеном поремећаја аутономне функције.

Методе рада Примењујући контролисани избор случајева, испитана је кардиоваскуларна аутономна функција 90 болесника, међу којима су била 52 испитаника (46 жена и шест мушкараца) са СЕЛ и 38 испитаника (32 жене и шест мушкараца) са РА. Контролну групу је чинила 41 здрава особа (23 мушкарца и 17 жена). Урађени су: свеобухватна анализа ЕКГ налаза (*Schiller, AT-10*), анализа *QTc* интервала, касних потенцијала, краткорочне варијабилности срчане фреквенције (ВСФ) и анализа нелинеарне ВСФ (*Poincaré plot*), 24-часовно праћење холтер ЕКГ налаза и ЕКГ анализе *QTc* интервала, ВСФ анализе, 24-часовно мерење крвног притиска и варијабилности систолног и дијастолног крвног притиска и кардиоваскуларни рефлекс-тестови према Јуингу (*Ewing*). Утврђен је поремећај функције нерва вагуса помоћу Валсалва маневра, теста дубоког удаха и теста одговора срчане фреквенције у мирном стајаћем положају. Поремећај симпатичке функције испитиван је помоћу одговора крвног притиска у мирном стајаћем положају и теста снаге стиска шаке.

Резултати У свим испитивањима кардиоваскуларног рефлекса резултати који су указивали на поремећај фреквенције били су знатно чешћи код болесника него код здравих особа. Тежак поремећај аутономне функције био је чешћи код болесника с РА. *QTc* интервал је био дужи код болесника са СЕЛ. У поређењу с контролном групом, оба обољења била су удружена са депримованом ВСФ, с тим да је снижење било изразитије код болесника с РА. Код болесника са СЕЛ поремећајем аутономне функције предоминира повишена активност симпатикуса, док код болесника с РА очигледно преовлађује вагус.

Закључак СЕЛ и РА су праћени тешким поремећајем аутономне функције и значајним присуством предиктора ризика од изненадне срчане смрти.

Кључне речи: поремећај аутономне функције; системски еритемски лупус; реуматоидни артритис; изненадна срчана смрт

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