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Echocardiographic Findings, 24-hour Electrocardiographic Holter Monitoring in Patients with Rheumatoid Arthritis According to Steinbrocker's Criteria, Functional Index, Value of Waaler–Rose Titre and Duration of Disease

M. Wisłowska[1], S. Sypuła[2] and I. Kowalik[3]

[1]Outpatients Department of Rheumatology and [2]Cardiology Department, Central Clinical Hospital, and [3]Coronary Disease Department, Institute of Cardiology, Warsaw, Poland

Abstract: Electrocardiographic (ECG) and echocardiographic examinations and 24-h ECG Holter monitoring were carried out in 100 patients (age <65 years) with rheumatoid arthritis (RA) of stages II–IV according to Steinbrocker's criteria. One hundred patients with osteoarthrosis, spondyloarthrosis and painful shoulder matched for age, sex and body surface area constituted the control group. All patients with myocardial infarction, hypertension, rheumatic fever or a history of diabetes were excluded. Cardiac involvement, evaluated by echo-Doppler cardiography, 24-h ECG Holter monitoring and an ECG at rest, occurred in 52 (52%) patients with RA and in 23 (23%) control group patients ($p<0.0005$). In the RA group ECG examination, 1 mm ST depression in at least two consecutive leads was observed more frequently, and occurred statistically more frequently for the highest stage of RA according to Steinbrocker's criteria, highest level of functional index and longer duration of disease. The 24-h Holter ECG monitoring did not show any differences in frequency of rhythm disorders between the RA group and the control group. However, silent myocardial ischaemia episodes appeared more often in the RA group. An ECG examination revealed more cases of valvular heart disease, especially mitral insufficiency, in RA patients than in the control group. A mitral valve prolapse was noted in 6% of patients and a pericardial effusion in 4% of patients. Patients with RA were noted to have a larger diastolic left ventricular diameter and aortic root diameter, and smaller ejection fraction, mean velocity of circumferential fibre shortening and fractional shortening. The results of the examinations show that RA is associated with cardiac involvement in a significant proportion of cases.

Keywords: Echo-Doppler cardiography; Rheumatoid arthritis; Silent myocardial ischaemia; Valvular heart disease; Ventricular function

Correspondence and offprint requests to: M. Wisłowska, Outpatients Department of Rheumatology, Central Clinical Hospital, Woloska 137, 02-507 Warsaw, Poland.

Introduction

One of the current issues in rheumatology is the type and extent of pathological changes in the heart in the course of rheumatoid arthritis (RA). However, there is more anatomopathological research than clinical research. A great divergence is noted between the frequency of anatomopathological changes in the myocardium of patients with RA and the clinical picture. At least twice as many changes in the heart are noted after death than are recognised during the patient's life-time. The problems with diagnosis are due to a very limited number of clinical symptoms showing that cardiac muscle is affected by a disease process and that symptoms do not always appear. Commonly used methods of clinical examination also fail, there are no characteristic auscultatory symptoms, the complaints of

patients are not typical, non-specific changes are seen on an electrocardiographic (ECG) examination and the chest radiograph is usually normal.

The aim of this study was to search for cardiac abnormalities in patients with RA by means of ECG and echocardiographic examinations and 24-h ECG Holter monitoring and to correlate cardiac abnormalities with the stage of RA according to Steinbrocker's criteria, functional index, value of the Waaler–Rose titre and duration of disease.

Material and Methods

Patients

A total of 100 consecutive outpatients aged 22–65 years (average age 49.9 ± 11.3 years) with definite or classic RA (ARA criteria) [1] attending the Rheumatologic Outpatient Department of the Central Clinical Hospital in Warsaw were included in the study. In the RA group there were 82 women (average age 49.0 ± 10 years) and 18 men (average age 54.4 ± 12 years). Body surface area (BSA) was 1.72 ± 0.7 m^2. According to Steinbrocker's criteria [2], 16 patients were in stage II, 73 in stage III and 11 in stage IV of the disease. The first level of the functional index was seen in 33 patients, the second level in 45, the third level in 20 and the fourth level in two. All the patients were shown radiologically to have geodes and erosions on the joint surfaces and on bones close to the joints. The presence of subcutaneous nodules was observed in 26 patients. The duration of disease ranged from 2 to 38 years (mean 9.4 ± 6.7 years). The disease duration was less than 5 years in 39 patients, between 5 and 10 years in 29 and more than 10 years in 32 patients.

A Waaler–Rose titre below 1:20 was confirmed in 22 patients (seronegative patients). In the remaining 78 seropositive patients the following Waaler–Rose test scores were noted: 1:160 in 33 patients, 1:320 in 24, 1:640 in 14, 1:1280 in six and 1:2560 in one.

Virtually all the RA patients were taking non-steroidal anti-inflammatory drugs (NSAIDs), 29 were taking gold salt, 33 antimalarials, 25 sulphasalazine, three D-penicillamine, and four methotrexate, three azathioprine and one cyclophoshamide. Thirty-six patients were treated with low-dose prednisolone, of whom two were treated only with low-dose prednisolone because of an allergy to other drugs.

Each RA patient was matched with a control for sex, age (± 1 years) and BSA (± 0.17 m^2). The control group comprised 100 patients aged 22–65 years (average age 49.8 ± 11.1 years), there were 82 women (average age 49.0 ± 10.8 years) and 18 men (average age 54.4 ± 12.9 years) who attended the clinic at the same time with osteoarthrosis and spondyloarthrosis (92 patients) or painful shoulder (eight patients).

Patients with a history of myocardial infarction, arterial hypertension, rheumatic fever, type I or II diabetes or general amyloidosis were excluded from the study. All patients agreed to participate in the research and consent was obtained from the deontologic commission.

On the basis of clinical examinations and chest radiographs (postero-anterior and lateral), which were reported by a cardiologist and a radiologist (without clinical data), pulmonary diseases were also excluded.

Stenocardial Pains and ECG Examination

In both groups, attention was paid to the occurrence of substernal pain, the criterion being paroxysmal pain which is at the same time substernal, radiating to the left shoulder and down the inside of the left arm, even to the fingers. It may radiate straight through to the back, into the throat, jaws, teeth and, occasionally, even down the right arm, appearing on physical activity and disappearing after 3 min in approximately 97% of cases after the activity has stopped or 0.5–3 min after nitroglycerine has been taken.

In a standard 12-lead electrocardiogram, attention was paid to the appearance of the following changes: characteristic features of myocardial ischaemia, non-specific ECG changes in an ST segment, sinus pauses, supraventricular premature beats, ventricular premature beats, atrial fibrillation, atrioventricular block (degrees I, II or III). His right bundle branch block (RBBB), His left bundle branch block (LBBB), left anterior hemiblock (LAH), left posterior hemiblock (LPH) and PQ and QT intervals.

The accepted criterion for ischaemia is an ST segment depression of at least 1 mm horizontally or downsloping, measured 80 ms from point J in at least in two consecutive leads. In laboratory examinations, disturbances of ion balance were excluded.

The accepted criterion for non-specific ECG changes in an ST segment is an upsloping or depression of this segment that does not exceed 1 mm and/or a change of T wave, i.e. flattening or a change in its shape (symmetrical inversion excluded).

24-h ECG Holter Monitoring

The 24-h ECG Holter monitoring was undertaken with a Hewlett Packard Vectra 386/25 apparatus. During these examinations the patients followed their usual daily routines and activities. The following aspects were analysed: average heart frequency, highest and lowest heart frequency, appearance of supraventricular and ventricular premature beats, presence of bigeminia, trigeminia, runs and episodes of sinus pauses.

According to the Bjerregaard criteria [3], greater than 100 instances of supraventricular premature beats per 24 h in patients aged up to 60 years and greater than 1000 per 24 h in patients over 60 years are accepted as pathological. The pathological number for ventricular

premature beats was assumed to be above 100 per 24 h for patients up to 50 years old and above 200 per 24 h for patients more than 50 years old.

The course of an ST segment was analysed within 24 h as well as ST depression of >2 mm lasting >1 min. The measuring point was 80 ms from point J.

Echocardiographic Examinations

Echocardiographic examinations (M-mode, D-dimensional and enriched with colour-Doppler technology) were performed in a standard manner with an Acuson 128 XP/10 echocardiographic apparatus, using a 3.5 or 2.5 MHz phased-array transducer. All examinations were recorded and stored on videotape. These examinations were carried out by the same cardiologist, who did not know the clinical diagnosis or condition of the patients. M-mode echocardiographic measurements were made according to the recommendations of the American Society of Echocardiography. The following structures and factors were assessed during the echocardiographic examination: left atrial end-systolic diameter (LA), left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic thickness (LVEST), right ventricular end-diastolic diameter (RVEDD), interventricular septum end-diastolic thickness (IVSEDT), left ventricular posterior wall end-diastolic thickness (LVPWEDT), aortic root diameter (AO), ejection fraction (EF), mean velocity of circumferential fibre shortening (mVcF) and fractional shortening (FS).

In a M-mode technology, the end-systolic antero-posterior diameter in the parasternal projection of the left side of a patient is accepted as the size of the left atrium (LA).

The end-diastolic antero-posterior diameter in the parasternal projection of the left side of a patient is accepted as the size of the left ventricle (LV), right ventricle (RV), thickness of an interventricular septum (IVS), left ventricle posterior wall (LVPW) and aortic root diameter (AO).

The ejection fraction was calculated as follows:

LV diastolic volume – LV systolic volume / LV diastolic volume $\times$ 100 [4].

The shortening fraction (left ventricular end-diastolic - end-systolic distance / end-diastolic $\times$ 100) and mean velocity of circumferential fibre shortening (mVcF = shortening fraction / ejection time) were calculated [4].

The Penn convention formula [5,6] was used to calculate the left ventricular mass:

$$\text{LV mass} = 1.04\,[(\text{IVSEDT} + \text{LVEDD} + \text{LVPWEDT})^3 - (\text{LVEDD})^3] - 13.6\text{g}$$

where LV = left ventricle, IVSEDT = interventricular septum end-diastolic thickness, LVEDD = LV internal end-diastolic diameter and LVPWEDT = LV posterior wall end-diastolic thickness.

Measurements of the left ventricular mass were divided by BSA to obtain the left ventricular mass index.

Pericardial effusion was measured as the largest distance between the parietal and visceral pericardium at peak systole behind the left ventricular posterior wall.

In order to assess a mitral insufficiency a semi-quantitative method was used that is based on the assessment of a revolving wave extension which penetrates inside an atrium or a ventricle [7]. A four-grade scale was used. When a revolving wave registered during the whole period of systole whose width was greater than 2 mm reached up to one-quarter of the atrium, then a mitral insufficiency of degree I was noted. When the revolving wave registered in a left atrium whose width was approximately 5 mm reached up to one-third of the atrium, then a mitral insufficiency of degree II was noted. When a revolving wave reached up to one-half of the atrium and it was wider than 5 mm, a mitral insufficiency of degree III was noted. Finally a mitral insufficiency of degree IV was noted when a revolving wave took up more than 50% of the atrium.

The insufficiency of aortic valve cusps was also assessed using a four-degree scale: degree I, a revolving wave under a valve; degree II, a revolving wave registered during the left ventricle reflux at the level of an anterior mitral cusp; degree III, a revolving wave reaches the level of the papillary muscles; degree IV, a revolving wave takes in a horizontal cross-section of at least 50% of a ventricle surface at the level of the papillary muscles.

A trace of mitral, aortal and trigeminal insufficiency was recognised when a thin revolving wave appeared just under a valve during a short period of time, i.e. for less than 100 ms. As these types of changes are often seen in healthy people, patients with such a complication were excluded from the statistical analysis.

Finally, a comparative analysis of recognised changes in the heart between both groups was undertaken.

Exercise testing was not performed because of movement restrictions of the majority of RA patients.

Laboratory Tests

Blood was collected after 4 h fasting for analysis of erythrocyte sedimentation rate (ESR) (Westergren, mm/h), morphology, C-reactive protein (CRP) (mg/l), cholesterol (mmol/l), HDL cholesterol (mmol/l), LDL cholesterol (mmol/l), triglycerides (mmol/l), glycaemia (mmol/l) and urid acid (μmol/l), and for a Waaler–Rose test, within the Department of Clinical Chemistry.

Statistics

The following tests were applied:

1. Relations between qualitative variables were compared with a χ^2 Pearson test with continuity correction. However, for small numbers, i.e. if

under the null hypothesis one expected all sizes to be smaller than 5, Fisher's exact test was used instead of the χ^2 test [6].
2. A value for an average quantitative variable was assessed on the basis of a Student's *t*-test. The comparison of echocardiographic measurements was made by a paired *t*-test [8].

The overall significance level for statistical analysis was 5% (two-sided) [8].

Results

Stenocardial Pain and ECG Assessment

Stenocardial pain, 1 mm ST depression in at least two consecutive leads and non-specific ECG changes of an ST segment in the course of an ECG at rest appeared more frequently in the RA patients (Table 1).

In the ECG at rest, sinus pauses occurred in one patient with RA, atrio-ventricular blocks were not recognised in any patients, LBBB was seen in three patients with RA, RBBB in two patients with RA and in one patient from the control group, and LAH in one patient with RA and in two patients from the control group.

Stenocardial pain and 1 mm ST depression in at least two consecutive leads in the ECG at rest were clearly more frequent for higher RA stage according to Steinbrocker's criteria, higher levels of functional index and longer duration of disease in RA patients (Table 2).

PQ and QT intervals were analysed for the ECG at rest. In RA patients the average PQ interval was 0.152 ± 0.021 s and the average QT interval 0.378 ± 0.032 s; in the control group these were, respectively, PQ 0.151 ± 0.026 s and QT 0.376 ± 0.030 s; no statistical differences were found.

24-h ECG Holter Monitoring

In the RA patients the average heart beat frequency was 81 ± 9 per minute, while in the control group it was 79 ± 9 per minute (NS). The minimal level observed was 61 ± 10 per minute and in the control group it was 56 ± 9 ($p. < 0.001$); the maximal level was 127 ± 20 per minute and in the control group 131 ± 24 (NS).

Among 100 RA patients, seven (7%) had a pathological number of supraventricular premature beats (mean ± SEM: 468 ± 237), seven (7%) had a pathological number of ventricular premature beats (mean ± SEM: 1986 ± 1030), four (4%) had bigeminia and trigeminia, two (2%) had runs and one (1%) had episodes of sinus pauses.

Table 1. Comparison of stenocardial pain, 1 mm ST depression, non-specific changes in ST segment and PQ and QT intervals on an ECG between the RA group and control group patients

	Stenocardial pain	1 mm ST depression on ECG	Non-specific changes in ST segment on ECG	PQ interval (s) on ECG	QT interval (s) on ECG
RA group (n = 100)	**44** (44%)	**18** (18%)	**60** (60%)	0.152 ± 0.021	0.378 ± 0.032
Control group (n = 100)	**17** (17%)	**4** (4%)	**44** (44%)	0.151 ± 0.026	0.376 ± 0.030
p	<0.0001	<0.005	<0.005	NS	NS

Table 2. Comparison of RA stage according to Steinbrocker's criteria, level of functional index, seropositivity and seronegativity and duration of disease with stenocardial pain, 1 mm ST depression and non-specific changes in the ST segment on ECG in RA patients

	Stages of RA			Level of functional index				Waaler–Rose titre		Duration of disease (years)		
	II	III	IV	1	2	3	4	≤20	>20	<5	5–10	>10
Stenocardial pains	4	30	10	8	19	15	2	6	38	15	10	19
%	25	41.1	90.9	24.2	42.2	75	100	27.3	48.7	38.5	34.5	59.4
p		<0.005			<0.005				NS		NS	
1 mm ST	0	12	6	0	6	11	1	2	16	3	5	10
Depression %		16.4	54.5		13.3	55	50	9.1	20.5	7.7	17.2	31.3
p		<0.005			<0.00001				NS		<0.05	
No-spectfic changes in ST segment	12	43	5	22	29	8	1	12	48	27	19	14
%	75	58.9	45.5	66.7	64.4	40	50	54.5	61.5	69.2	65.5	43.8
p		NS				NS			NS		NS	

NS, not significant.

Table 3. Episodes of myocardial ischaemia and silent myocardial ischaemia in 24-h ECG Holter monitoring in RA patients and in control group patients

	Examined groups	Number of patients with episodes of ST-T segment depression	Mean number of episodes of ST-T segment depression (± SEM)	Length of ST-T segment depression (± SEM)	Max. time of duration of ST-T segment depression (± SEM)
All ST-T segment depression episodes	RA group (n=100)	23/100 (23%)	4.7 ± 0.4	33.6 ± 2.5	13.3 ± 0.9
	Control group (n=100)	10/100 (10%)	4.4 ± 0.9	18.7 ± 3.5	7.8 ± 1.5
	p	<0.05	NS	<0.01	<0.005
Silent ST-T segment depression episodes	RA group (n=100)	18/23 (78%)	3.7 ± 0.4	17.7 ± 1.8	7.2 ± 0.7
	Control group (n=100)	4/10 (40%)	4.8 ± 0.9	15.7 ± 2.8	5.3 ± 0.7
	p	<0.05	NS	<0.01	NS

NS, not significant.

Among 100 control group patients, five (5%) had a pathological number of supraventricular premature beats (mean ± SEM:198 ± 68), one (1%) had a pathological number of ventricular premature beats (n = 269), one (1%) had runs and two (2%) had episodes of sinus pauses.

A comparison of the pathological number of ventricular and supraventricular premature beats per 24 h recorded on 24 h ECG Holter monitoring with the stage of RA according to Steinbrocker, level of functional index, seropositivity or seronegativity and duration of disease did not reveal any statistical significance.

Episodes of myocardial ischaemia and silent ischaemia on 24 h ECG Holter monitoring in RA patients and in control patients are presented in Table 3.

A comparison of episodes of myocardial ischaemia and silent ischaemia on 24 h ECG Holter monitoring in RA patients with the stage of RA according to Steinbrocker, level of functional index, seropositivity or seronegativity and duration of disease did not reveal any statistical significance.

Table 4. Echocardiographic measurements in 100 RA patients and 100 control group patients

	RA	Control group	p
LA-ESD (cm)	3.67 ± 0.45	3.61 ± 0.39	NS
RV-EDD (cm)	2.26 ± 0.30	2.18 ± 0.32	NS
IVS-EDT (cm)	0.83 ± 0.16	0.82 ± 0.09	NS
LVPW-EDT (cm)	0.84 ± 0.14	0.83 ± 0.08	NS
LV mass index ($g\,m^{-2}$)	96.1 ± 31.4	88.1 ± 17.2	NS
LV-EDD (cm)	4.91 ± 0.42	4.81 ± 0.41	<0.05
LV-EST (cm)	2.80 ± 0.33	2.76 ± 032	NS
AO (cm)	3.06 ± 0.40	2.68 ± 0.38	<0.001
EF (%)	67.4 ± 7.3	71.8 ± 7.6	<0.05
mVcF (cir. s^{-1})	1.25 ± 0.20	1.41 ± 0.23	<0.01
FS (%)	37.4 ± 5.2	41.6 ± 6.3	<0.05

AO, aortic root diameter; LA, left atrium; RV, right ventricle; LV, left ventricle; IVS, interventricular septum; LVPW, left ventricular posterior wall; EF, ejection fraction; FS, fractional shortening; mVcF, mean velocity of circumferential fibre shortening; EDD, end-diastolic diameter; ESD, end-systolic diameter; EDT, end-diastolic thickness; EST, end-systolic thickness; LV mass index, left ventricular mass index; NS, not significant.

Echocardiographic Examination

A comparison of the average values of echocardiographic measurements was made between the RA group and control group (Table 4).

Left ventricular end-diastolic diameter in the RA group was significantly greater than in the control group (4.91 ± 0.42 vs 4.81 ± 0.41 cm) as was the aortic root diameter (3.06 ± 0.40 vs 2.68 ± 0.38 cm).

The ejection fraction in the RA group was significantly lower than in the control group (67.4 ± 7.3 vs 71.8 ± 7.6 %) as well as the mean rate of circumferential shortening (1.25 ± 0.20 vs 1.41 ± 0.23 circ. s^{-1}) and fractional shortening (37.4 ± 5.2 vs 41.6 ± 6.3%).

A comparison of the echocardiographic measurements with the stage of RA according to Steinbrocker, level of functional index, seropositivity or seronegativity and duration of disease did not reveal any statistical significance.

In 39 (39%) RA patients and 19 (19%) control patients, valvular heart diseases were discovered as a result of the echocardiographic examination ($p<0.05$) (Table 5). These were: mitral insufficiency of degrees I and II in 29 (29%) RA patients and 10 (10%) control patients ($p<0.005$), aortic insufficiency of degrees I and II in eight RA patients and four control patient (NS), tricuspid insufficiency in three RA patient and two control patients (NS), mitral stenosis in one RA patient, and mitral valve prolapse in six RA patients and three control patients (NS). In total, valvular heart disease was seen in 47 RA patients (including mitral valve prolapse) and 19 control patients.

Table 5. Echo-Doppler echocardiographic findings in 100 RA patients and 100 control group patients

	RA patients (n=100)	Control group (n=100)	p
Pericarditis effusion	4 (4%)	0	NS
Hypokinesis	0	0	
Normal valves	61 (61%)	81 (81%)	<0.05
Aortic cup sclerosis (including slight)	2 (2%)	0	NS
Aortic insufficiency grade I	7 (7%)	3 (3%)	NS
Aortic insufficiency grade II	1 (1%)	1 (1%)	NS
Mitral valve thickening	7 (7%)	4 (4%)	NS
Mitral insufficiency grade I	23 (23%)	10 (10%)	<0.005
Mitral insufficiency grade II	6 (6%)	0	
Mitral stenosis	1 (1%)	0	NS
PAP >35 mmHg	0	0	
Mitral valve prolapse	6 (6%)	3 (3%)	NS

PAP, pulmonary artery pressure.

A comparison of the presence of valvular heart diseases with the stage of RA according to Steinbrocker, level of functional index, seropositivity or seronegativity and duration of disease did not reveal any statistical significance.

Pericardial effusion was found behind the left ventricular posterior wall in only four RA patients (4%) and in none of the control group; in all four cases it was small (less then 300 ml). Pericardial effusion was not found in the course of a clinical examination.

Laboratory Tests

Results of laboratory tests in both the RA and control group patients showed no statistically significant differences (Table 6).

Cardiac involvement, evaluated by echo-Doppler cardiography, 24-h ECG Holter monitoring and an ECG at rest, occurred in 52 (52%) patients with RA and 23 (23%) control group patients ($p<0.0005$). Among the cardiac abnormalities in RA patients, 48 (48%) patients had one, 14 (14%) two and four (4%) three abnormalities.

Table 6. Laboratory parameters in RA patients and control group patients

Parameters	RA patients	Control group patients	p
Cholesterol	5.41 ± 1.1	5.77 ± 1.3	NS
LDL-cholesterol	3.9 ± 0.9	3.7 ± 0.8	NS
HDL-cholesterol	1.5 ± 0.4	1.4 ± 0.4	NS
Triglycerides	1.3 ± 0.54	1.21 ± 0.45	NS
Glycaemia	4.55 ± 0.56	4.5 ± 0.44	NS
Urid acid	262 ± 83	250 ± 89	NS

Data expressed as mean ± SEM.

Discussion

Rheumatoid arthritis is a connective tissue disease that affects many organs. The main clinical symptoms are swollen and painful joints and functional disability in the advanced stage of the disease. Changes in other organs are neglected or often not noticed and are sometimes treated as additional diseases, not related to RA. However, the changes in other organs may constitute an integral part of the rheumatoid process in many RA patients. Changes in the cardiovascular system seem to be especially important.

Some RA patients complain of chest pain, particularly stenocardial pain, or fatigue. However, most RA patients are not energetic and avoid moving too much. Because of this they either disregard or pay no attention to these types of symptoms. Moreover, they associate chest pain with rheumatoid changes rather than cardiac changes.

Having looked through the literature we found only a few reports of the frequency of ECG features of myocardial ischaemia in RA patients. However, there are many studies on post-mortem assessment of atheromatous process intensification in coronary vessels among these patients. Bonfiglio and Atwater [9] found that atherosclerosis (smooth or ulcerated yellow or white plaques on the intimal surface of the aorta and coronary arteries) was significantly less common among RA patients. Davis and Engleman [10] in their study at autopsy showed significantly lower morbidity and mortality from myocardial infarction in RA patients than in 62 matched control patients. However, Cathcart and Spodick [11] studied 254 RA patients with age- and sex-matched controls and found that there was an increased prevalence of coronary artery disease.

In a clinical examination MacDonald et al. [12] found that 11 (21.5%) RA patients had ischaemic heart disease, but Mody et al. [13] found it only in three RA patients (3.9%). Our 24-h ECG Holter monitoring revealed a higher frequency of silent myocardial ischaemia in RA patients compared with the control group (1.9). Silent myocardial ischaemia is one of the significant symptoms of ischaemic heart disease. We can therefore indirectly conclude that myocardial ischaemia in RA patients appears more frequently than in the control group. A standard electrocardiogram at rest revealed more frequent repolarisation changes in RA patients than in the control group patients. There was also a statistically significant relation between stage of RA according to Steinbrocker's criteria, level of functional index and duration of disease in RA patients and the frequency of 1 mm ST depression. ECG repolarisation changes might be related to myocardial ischaemia, but in some of our patients it might be also related to pericardial involvement, myocarditis, myocardial fibrosis or non-ischaemic cardiomyopathy.

We agree with Rosenberg (quoted in [14]) that lying patients are less prone to have a myocardial infarction. However, it should be emphasised that a myocardial infarction in RA patients may be caused by other vessel changes, not by the atheromatosis, mainly due to

necrotic inflammation of the coronary vessels wall and thromboses in the lumen. A specific RA complication is vasculitis and there is some evidence that it may cause a myocardial infarction in the course of RA [15–17]. Scott et al. [18] diagnosed a myocardial infarction in five out of 90 RA patients. Cruikshank [19] observed inflammation of the coronary vessels in 20 out of 100 autopsies and Lebowitz [20] found this in 12 out of 62 autopsies.

Swezey [15] and Levin et al. [14] suggest that myocardial infarction occurs in RA as a result of inflammation of the coronary vessels. This theory is opposed by Karten [16] who states that myocardial infarction is mainly due to atheromatosis. Among 102 patients in his study, only six had diffuse vasculitis. Two of these six patients also sustained myocardial infarction.

However, independently of the primary reason for changes in the coronary vessels, the differences in frequency of their appearance in different studies is explained by regular use of aspirin and its antiaggregating activity towards thrombocytes. Aspirin was taken periodically by all of the RA patients in our study. This may have influenced the development of the atheromatous process in vessels but it did not have an effect on the development of vasculitis. The examinations do not indicate the type of changes. The essence of the disease suggests, however, that at least partially these changes in the coronary vessels are of a vasculitic type. Post-mortem examinations suggest the presence of vasculitis in the small coronary vessels in more than 20% of RA patients [11]. Bonfiglio and Atwater [9] stated that RA patients with clinically observed symptoms of coronary heart disease, when examined post-mortem, revealed the predominance of inflammatory and granulomatic changes over atheromatous changes.

24-h ECG Holter monitoring showed no significant differences in the frequency of rhythm disorders between the RA and control patients. In addition, changes in cardiac conduction were noted only in 6% of RA patients. A small number of cases of rhythm and conduction disorders is not surprising. Among the RA patients, those with a history of myocardial infarction or arterial hypertension had been excluded, and changes in the heart in the course of RA are usually discounted and rarely lead to changes in the heart conduction system.

Heart valvular diseases were revealed on echocardiographic examination in 39% of RA patients, including 6% with mitral valve prolapse. In total, in RA patients 47 cases of heart valvular disease were diagnosed, compared with 19 cases in the control group. Insufficiency of the mitral valve was included and accounted for 29 cases in the RA patients compared with 10 in the control group. These differences were statistically significant. The frequency of other heart disorders, e.g. tricuspid insufficiency, aortic insufficiency, was higher in the RA group than in the control group, but this was not statistically significant.

Similar observations have been made by other authors. In 1973 Bacon and Gibson [21] for the first time examined with echocardiography 22 nodular and 22 non-nodular RA patients. They found changes in the mitral valve in three patients (6.9%) and they concluded that these changes were a rheumatoid arthritis systemic manifestation. Also in 1973, using one-dimensional echocardiography, Prakash et al. [22] examined 16 RA patients aged from 30 to 64 years. The patients did not report any heart diseases. In this small group there were four cases (25%) of mitral valve abnormalities. Nomeir et al. [23,24] were also interested in this issue and in 1973 they examined 30 RA patients aged from 25 to 75 years, also with the use of one-dimensional echocardiography, and found mitral valve abnormalities in nine patients (30%).

In 1977 MacDonald et al. [12] examined 51 RA outpatients aged from 25 to 86 years and mitral valve abnormalities were found in five patients (10%). A later study by Mody et al. [13] used two-dimensional echocardiography to examine 84 RA patients. Mitral valve abnormalities were found in 10 patients (13%), aortic insufficiency in one and mitral valve prolapse in three.

Other studies were carried out on larger numbers of patients and these also indicated a greater frequency of heart disorders. In 1988 Nagyhegyi et al. [25] carried out echocardiographic examinations on 100 RA patients. In 24% of patients, valve abnormalities were shown. In 1990 Alusik and Skalicka [26] found 22 cases of mitral valve prolapse in a group of 104 RA patients aged from 24 to 71 years, seven patients showed symptoms of valve insufficiency and 15 did not. Mitral insufficiency was proved in 10 patients, mitral stenosis in 10 patients (of whom five showed symptoms of insufficiency), aortic stenosis in 14 patients and aortic insufficiency in four patients.

Toumanidis et al. [27] stated that in their study mitral and aortic cusps without granuloma formation were visualised as thickened and sclerotic in most RA patients.

The problem of frequency of mitral valve prolapse in the general population and in RA patients is controversial. In recent studies the frequency of this disorder has been estimated to be 3–8% and even estimated as high as 18% [28,29]. It is not a characteristic of RA because its frequency is comparable to other groups of patients [25,30].

In our RA group only 4% proved to have pericardial effusion yet this abnormality is treated as the most common heart complication in RA patients. Although this disorder is found in about 30% of RA patients by pathologists, its clinical manifestation is rare. According to Cathcart and Spodick [11], in a group of 254 RA patients only six had clinical manifestation of pericarditis. Mody et al. [13], in echocardiographic examinations, found the presence of pericardial effusion in 6% of their patients.

Tamponade and constrictive pericarditis in RA occurs very rarely. Constrictive pericarditis is a little more frequent than tamponade but its occurrence is also sporadic [31–35] and does not exceed 0.5%. Unfortunately, its prognosis is very poor.

In our study, as a result of the echocardiographic examination, RA patients were found to have larger left ventricles and aortic root diameters than the control group patients. According to Bacon [36], in systemic diseases of connective tissue the aortic valve is affected most often. The pathological process occurring in this area is characteristic also for RA. According to Goehrs et al. [37], non-specific aortitis in RA patients is detected on post-mortem examination in 20%. We may suppose that it is related to damage of the valve apparatus by the rheumatoid process.

It seems that echocardiographic evaluation of left ventricle measurements is extremely important. Ejection fraction, mean velocity of circumferential fibre shortening and fractional shortening were significantly smaller in RA patients than in control group patients. All the parameters mentioned above prove a myocardial disorder and functional defects in RA patients.

Nagyhegyi et al. [25] and Villecco et al. [38] showed thickening of the interventricular septum and of the left ventricular posterior wall as well as abnormalities in kinetics of the left ventricle walls and interventricular septum. According to these authors these features may be present in 10–25% of RA patients. Hernandez-Lopez et al. [39] found in a small percentage of RA patients a reduction in the mean velocity of circumferential fibre shortening, which probably indicates a symptomless dysfunction of the left ventricle.

Nagyhegyi et al. [25] and Villecco et al. [38] noticed reduced dynamics of systole in the left ventricle in 3–40% of RA patients on policardiographic examination. In the course of a policardiographic examination in a group of young women with RA, Krauze [40] found latent disorders of contractility, and Villecco et al. [37] found an increase in the contractility index (PEP/LVET) in 3% of RA patients. Nagyhegyi et al. [25] described a high contractility coefficient (PEP/LVET) of above 0.40 in 11 (14.4%) out of 76 RA patients.

In our study it was observed that the minimum heart frequency was higher in RA patients than in control group patients, which reflected the changes in cardiac sufficiency in RA patients. Volpio-Pulkki et al. [41] found in 182 RA patients a mild, resting tachycardia and a reduction of systolic and diastolic arterial pressure at rest. Men with seropositive RA were noted to have an increased mass of the left ventricle. Maione et al. [42] observed left ventricular abnormalities, probably secondary to myocardial fibrosis, in 26% of RA patients. Toumanidis et al. [27] stated that their RA patients had a thicker ventricular posterior wall and the regional ejection fraction of the apical region had a higher contractility.

The results of the studies quoted and the changes in kinetics of the left ventricle observed in our work indicate that contractility of the left ventricle has been damaged in RA patients.

Pincus et al. [43] studied mortality in RA patients for over 9 years. They stated that in the absence of consensus regarding criteria to determine whether an individual RA patient's clinical status was better or worse, changes in the status of patients were depicted using widely different criteria. In their study significant differences between patients who survived or died over the next 9 years were seen for eight variables, one of which is the presence of concurrent heart disease.

Wallberg-Jonsson et al. [44] in their study established that the overall mortality and death due to cardiovascular disease and ischaemic heart disease were in both sexes increased in seropositive RA. Male sex and high age at disease onset predicted death and cardiovascular events.

The conclusion of our study is that the presence of heart disease in RA patients is not only dependent on concurrent heart disease but is also caused by RA disease.

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