Original article

Relationship between inflammatory markers and clinical patterns of atrial fibrillation in patients with congestive heart failure

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Abstract

Background: Occurence of atrial fibrillation (AF) adversely affects left atrial size and cardiac function. This arrhythmia is also associated with an increase of plasma CRP and fibrinogen concentration. It is not clear whether elevated levels of inflammatory markers in patients with congestive heart failure (CHF) are associated with AF, clinical symptoms or adverse cardiac remodelling.

Aim: To investigate the association between levels of inflammatory markers and selected clinical and echocardiographic parameters as well as used treatment in the population of CHF patients with various forms of AF.

Methods: The cross-sectional study included 99 patients with CHF divided into 3 groups. Group I included patients with sinus rhythm. Group II consisted of patients admitted to hospital with AF and discharged with sinus rhythm (the category of paroxysmal and persistent AF). Group III comprised patients with permanent AF. In all patients plasma CRP and fibrinogen concentrations were measured and echocardiographic examination was carried out. Left atrial dimension (LA), ejection fraction (LVEF) and right ventricular systolic pressure (RVSP) were assessed.

Results: Mean CRP concentration in group III (5.83±5.36 mg/l) was significantly higher than in group I (p=0.001) and group II (p=0.033). In the group with permanent AF mean fibrinogen concentration was elevated to a higher level (391.0±77.3 mg/dl) than in group II (p=0.007) and group I (p=0.099). Mean LA and RV dimensions and RVSP in group III were significantly higher than in group I and group II. Multivariable analysis revealed that plasma CRP concentration was significantly associated with the presence of arterial hypertension (p <0.001) and LA enlargement (p=0.007). A significant association between fibrinogen level and CRP level (p=0.038), presence of permanent AF (p=0.045) and metabolic syndrome (p <0.05) was found. Values of ln CRP were significantly correlated with LA diameter (r=0.24; p=0.015).

Conclusions: Increased plasma CRP level in patients with CHF were significantly associated with arterial hypertension and LA enlargement. Permanent form of AF and CRP level have been shown to be significantly associated with increased plasma fibrinogen concentration in the course of CHF.

Key words: congestive heart failure, atrial fibrillation, CRP, fibrinogen, echocardiography

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Introduction

Atrial fibrillation (AF), congestive heart failure (CHF) and metabolic syndrome with diabetes mellitus type II are three of the most common conditions with epidemically growing incidence over recent years [1]. It is estimated that AF affects 0.4-1.0% of the general population [2].

Numerous reports indicate that there is a relationship between AF and markers of systemic inflammation such as C-reactive protein (CRP), fibrinogen, tumour necrosis factor alpha (TNF-α), plasma amyloid-A, interleukin-1, and interleukin-6 [3-7]. The greatest importance is assigned to measurement of CRP concentration. Elevation of its serum levels is a recognised predictor of cardiovascular events, such as sudden cardiac death [8], myocardial infarction (MI) [9] and stroke [10].

It is commonly known that increased levels of inflammatory markers are present also in chronic CHF [4, 11]. A relationship between increasing CRP level and left ventricular end-diastolic pressure (LVEDP) was documented [11]. Hower, there are no reports concerning the relationship between concentrations of inflammatory markers and clinical presentation of AF (paroxysmal, persistent or permanent) in patients with CHF.

The study aimed to investigate the association between levels of inflammatory markers and selected clinical and

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echocardiographic parameters as well as treatment used in the population of CHF patients with various clinical forms of AF.

Methods

Patients

The approval of the Ethical Committee was obtained for the study. The study enrolled 99 consecutive in-hospital patients (65 males and 34 females at mean age of 69.63±9.12 years) diagnosed with CHF, based on the Framingham criteria [12]. Patients were excluded if they had acute or chronic infections at baseline. They were divided into 3 groups. Group I (n=30, mean age of 68.7±8.2 years) included patients with sinus rhythm. Group II (n=26, mean age of 70.3±9.5 years) consisted of patients admitted with AF and discharged with sinus rhythm (patients with paroxysmal or persistent AF). In this group patients with paroxysmal AF made up 92%, while subjects with persistent AF made up 8% of the group; mean duration of AF was 2.6 days. Group III (n=43, mean age of 69.9±9.6 years) comprised patients with permanent AF. The above AF classification was implemented based on recent ESC guidelines [2].

Laboratory tests

Blood was collected up to 24 hours after admission. CRP levels were measured using an immunoturbidimetric method involving CRP agglutination with latex beads coated with anti-human CRP monoclonal antibodies [13]. Measurements were performed with a COBAS INTEGRA 400 analyzer. Plasma fibrinogen levels were determined using Clauss' coagulometric method [14]. Measurements were carried out with an STA Compact analyzer.

Echocardiography

All patients underwent echocardiography using GE Vingmed System FIVE and a 2.5-5.0 MHz standard probe. The following echocardiographic parameters were assessed: left atrial diameter (LA), right ventricle diameter (RV), right ventricular systolic pressure (RVSP) and left ventricular ejection fraction (LVEF). LA diameter was measured by M-mode in the long axis of the parasternal view. The largest atrial diameter was measured during maximum anterior movement of the posterior aortic wall. RVSP was measured with the simplified Bernoulli method with right atrial pressure approximation to 5 mmHg in all patients regardless of inferior vena cava width and its reaction to respiration [15]. Left ventricular ejection fraction was calculated with the modified Simpson method.

Statistical analysis

The results are shown as means ± standard deviation or numbers and percentages. Differences between the analysed variables were compared with χ^2 test for qualitative parameters and Student's t-test or Cochran-Cox test for quantitative parameters.

The influence of chosen factors on the variability of the analysed parameter (CRP or fibrinogen) was investigated using univariate analysis of variance. As CRP levels did not meet normal distribution criteria, ln CRP (CRP natural logarithm) was used for analyses.

The overall influence of selected factors on the analysed parameters was assessed using multivariate analysis of variance. The test results are presented as F and p values for main factors without interaction. The relationship between variables was evaluated by calculation of significance of Pearson's linear correlation factor (r) and its presentation in a diagram.

Test hypotheses were verified with critical significance level of p=0.05. Statistical analysis was performed with STATISTICA 6.0 PL software.

Results

Demographic and clinical data are presented in Table I. There were no gender differences between the study groups. The most fragmently diagnosed of CHF in all groups was arterial hypertension followed by MI. The prevalence of past MI was significantly lower in Group III than in both remaining ones (III vs. II: p=0.005, III vs. I: p=0.056).

Laboratory and echocardiographic parameters are summarised in Table II. Mean CRP level in Group III was significantly higher than in Groups I and II (p=0.001 and p=0.033, respectively). No significant differences were found regarding mean CRP levels between Groups I and II. In Group III patients mean fibrinogen concentration was elevated to the highest level and differed significantly as compared to Group II (p=0.007). Mean LA, RV and RVSP values in Group III were considerably higher than in the remaining groups.

Mean CRP levels in the classes of analysed parameters are presented in Table III, which also shows evaluation of the differences between classes. Analysis of variance of lnCRP values showed that CRP was significantly dependent on BMI classes, presence of arterial hypertension, permanent AF, past deep vein thrombosis and increased serum fibrinogen. Of the analysed echocardiographic parameters, significantly higher CRP levels were found with mean LA above 5.0 cm.

Multivariate analysis (Table IV) which included all significantly different parameters – as shown by the univariate analysis – revealed a considerable relationship between serum CRP concentration and arterial hypertension as well as LA enlargement. The trend to reach statistical significance was confirmed for past deep vein thrombosis and increased fibrinogen level.

The ln CRP values significantly correlated with LA diameter (r=0.24, p=0.015) (Figure 1).

Univariate analyses for fibrinogen levels (Table V) revealed a significant increase in patients with permanent

Table I. Demographic data, heart failure causes, and current treatment

Variable	Group I No AF	Group II Paroxysmal and persistent AF	Group III Permanent AF	p		
				I-II	I-III	II-III
Number	30 (100.0%)	26 (100.0%)	43 (100.0%)			
Gender (% of males)	21 (70.0%)	17 (65.4%)	27 (62.8%)	–	–	–
Age [years]	68.7±8.2	70.3±9.5	69.9±9.6	–	–	–
BMI	29.2±5.2	29.2±5.0	30.2±0.9	–	–	–
Abdominal circumference [cm]	103.1±12.5	100.6±10.3	103.4±16.2	–	–	–
Systolic blood pressure [mmHg]	138.5±17.9	130.6±14.2	130.1±18.8	–	–	–
Diastolic blood pressure [mmHg]	81.4±10.4	76.7±8.4	78.5±10.5	–	–	–
CHF type (% of systolic)	17 (56.7%)	19 (73.1%)	30 (69.8%)	–	–	–
NYHA (% of class III)	5 (16.7%)	10 (38.5%)	24 (55.8%)	0.082	0.001	–
Metabolic syndrome	13 (43.3%)	9 (34.6%)	13 (30.2%)	0.001	–	–
Peripheral oedema	9 (30.0%)	13 (50.0%)	24 (55.8%)	–	0.031	–
Diabetes mellitus	13 (43.3%)	12 (46.2%)	10 (23.3%)	–	0.074	0.051
DVT	4 (13.3%)	2 (7.7%)	4 (9.3%)	–	–	–
Smoking	4 (13.3%)	3 (11.5%)	4 (9.3%)	–	–	–
ACE-I	28 (93.3%)	26 (100.0%)	38 (88.4%)	–	–	0.071
Beta-blocker	27 (90.0%)	21 (80.8%)	38 (88.4%)	–	–	–
Statin	27 (90.0%)	22 (84.6%)	22 (51.2%)	–	0.001	0.006
Spironolactone	20 (66.7%)	18 (69.2%)	35 (81.4%)	–	–	–
Diuretics	21 (70.0%)	17 (65.4%)	37 (86.1%)	–	0.101	0.045
ASA	25 (83.3%)	22 (84.6%)	21 (48.8%)	–	0.004	0.004
Acenocumarol	3 (10.0%)	10 (38.5%)	33 (76.7%)	0.016	<0.001	0.002
Previous myocardial infarction	18 (60.0%)	19 (73.1%)	16 (37.2%)	–	0.056	0.005
PTCA	3 (10.0%)	2 (7.7%)	3 (7.0%)	–	–	–
CABG	7 (23.3%)	5 (19.2%)	4 (9.3%)	–	0.101	–
Arterial hypertension	21 (70.0%)	18 (69.2%)	32 (74.4%)	–	–	–
Dilated cardiomyopathy	4 (13.3%)	3 (11.5%)	8 (18.6%)	–	–	–
Valvular disease	2 (6.7%)	2 (7.7%)	12 (27.9%)	–	0.029	0.050
Bradycardia	4 (13.3%)	1 (3.9%)	7 (16.3%)	–	–	–
Atrioventricular block	3 (10.0%)	3 (11.5%)	2 (4.7%)	–	–	–
Bundle branch block	10 (33.3%)	4 (15.4%)	11 (25.6%)	–	–	–
Pacemaker	2 (6.7%)	0	8 (18.6%)	–	–	0.021

Abbreviations: AF – atrial fibrillation, BMI – body mass index, NYHA – New York Heart Classification, ACE-I – angiotensin II converting enzyme inhibitor, ASA – acetylsalicylic acid, PTCA – previous percutaneous coronary transluminal coronary angioplasty, CABG – previous coronary artery by-pass grafting, DVT – history of deep vein thrombosis

AF (p=0.014) and with elevated CRP (p=0.022). In addition to permanent AF and CRP, parameters reaching trends towards statistical significance were selected for evaluation of overall influence on the fibrinogen levels: enlargement of the LA, heart failure severity according to NYHA classification, and presence of metabolic syndrome (Table VI). It was shown that the extent of fibrinogen elevation was significantly affected by CRP, permanent AF and presence of metabolic syndrome.

Discussion

The analysis performed revealed that rise in CRP levels in CHF patients was highly significantly correlated with presence of hypertension and LA enlargement. A similar relationship regarding hypertension was reported in the observational study by Sesso et al. [16], who analysed the influence of interleukin-6 and CRP on the presence of hypertension and showed that only a gradual increase of CRP levels was significantly correlated with development

Table II. Comparison of biochemical and echocardiographic parameters between the study groups

Variable	Group I No AF	Group II Paroxysmal and persistent AF	Group III Permanent AF	p		
				I-II	I-III	II-III
hs-CRP [mg/l]	2.69±2.62	3.44±3.73	5.83±5.36	–	0.001	0.033
ln hs-CRP	0.51±1.10	0.70±1.14	1.26±1.14	–	0.007	0.054
Creatinine [mg/dl]	1.02±0.46	1.14±0.73	1.09±0.31	–	–	–
Fibrinogen [mg/dl]	360.1±76.6	339.8±67.1	391.0±77.3	–	0.099	0.007
RVSP [mmHg]	23.7±16.9	24.2±13.9	38.7±15.6	–	0.001	0.033
LVEF [%]	47.7±15.6	40.9±10.7	43.1±15.0	0.060	–	–
LA [cm]	4.51±0.71	4.55±1.00	5.31±0.85	–	0.002	0.006
LV [cm]	5.83±0.88	5.88±1.07	6.01±1.06	–	–	–
RV [cm]	2.61±0.38	2.51±0.57	2.91±0.71	–	0.024	0.012
Mean heart rate [beats/min]	65.9±8.3	65.8±9.5	76.6±13.0	–	<0.001	<0.001

Abbreviations: RVSP – right ventricular systolic pressure, LVEF – left ventricular ejection fraction, LA – left atrium, LV – left ventricle, RV – right ventricle, AF – atrial fibrillations

Table III. hs-CRP concentration [mg/l] in the studied parameters ranges (unifactorial analysis of variance)

Variables	Categories of evaluated variables			Differences between categories (p-value)
	1	2	3	
NYHA	Class I 2.02±1.11	Class II 3.72±4.28	Class III 5.49±4.90	1-3 (p=0.099) 2-3 (p=0.057)
BMI	≤25 4.11±5.65	26-30 3.44±3.99	>30 5.74±4.32	1-3 (p=0.040) 2-3 (p=0.004)
Hypertension	NO 2.04±1.97	YES 5.12±4.86	–	1-2 (p <0.001)
Permanent atrial fibrillation	NO 3.03±3.17	YES 5.82±5.36	–	1-2 (p=0.005)
DVT	NO 3.94±4.39	YES 6.99±4.33	–	1-2 (p=0.019)
Fibrinogen [mg/dl]	≤400 3.57±4.19	>400 5.81±4.74	–	1-2 (p=0.005)
RVSP [mmHg]	≤30 3.15±3.03	>30 4.96±5.08	–	NS
LVEF [%]	≥45 4.94±5.43	<45 3.73±3.54	–	NS
LA [cm]	≤4 3.18±4.68	4-5 3.28±3.32	>5 5.91±5.11	1-3 (p=0.004) 2-3 (p=0.009)

Abbreviations: see Tables I and II

of hypertension. Univariate analysis showed significantly higher CRP levels in patients with permanent AF than in the ones free of this arrhythmia; however, the most severe form of arrhythmia failed to influence CRP when evaluated together with LA diameter. Chung et al. observed a similar phenomenon of increasing CRP levels depending on the severity of atrial arrhythmia, including AF in a population without CHF; however, they did not assess the relationship between LA diameter and CRP levels [5].

Of the analysed patients with CHF, no significant differences were found regarding CRP levels between the sinus rhythm group and the other one comprising both patients with paroxysmal and persistent AF. Patients with paroxysmal AF analysed by Chung et al. had significantly

Table IV. Influence of analysed parameters on CRP levels (multifactor analysis of variance)

Factors	Evaluation of factor impact F test	
	F	p-value
BMI	2.087	0.13
Hypertension	13.124	<0.001
Permanent AF	1.024	0.314
DVT	3.742	0.056
Fibrinogen	3.247	0.075
LA	5.227	0.007

Abbreviations: see Tables I and II

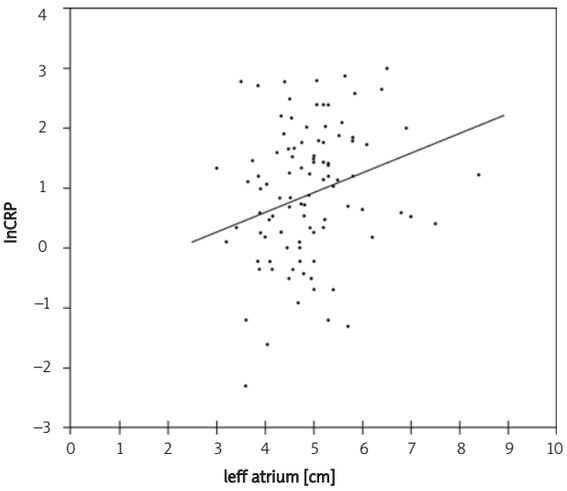

Figure 1. Distribution plot of ln CRP and left atrium diameter (r=0.24, p=0.015)

lower CRP levels than patients with persistent form defined as arrhythmia lasting over 30 days [5]. Also Watanabe et al. noted the relationship between AF duration and elevation of CRP levels, which was significantly higher when arrhythmia duration was more than 30 days [7]. The shorter time frames based on recent ESC guidelines [2] that were adopted in our study for permanent AF, and predominance of paroxysmal forms of AF (92%) in the second group, could both result in lack of differences in CRP levels compared to subjects with sinus rhythm.

Maintenance of increased levels of inflammatory markers, including CRP, 2 weeks after successful cardioversion, as pointed out by Sata et al., suggests that inflammation plays an important role in AF development [17]. The long-term observational study of Aviles et al. showed that increased CRP levels predict higher risk of AF [3]. Dernellis and Panaretou documented that steroid therapy prevented recurrences of persistent AF by reducing the range of inflammation and CRP levels [18]. These

Table V. Fibrinogen levels in the studied parameters ranges (unifactorial analysis of variance)

Variables	Categories of evaluated variables			Differences between categories (p-value)
	1	2	3	
NYHA	Class I 355.1±65.2	Class II 353.1±60.3	Class III 391.0±93.1	2-3 (p=0.074)
BMI	≤25 350.6±65.6	26-30 358.5±77.6	>30 394.9±76.5	NS
Metabolic syndrome	(-) 357.5±70.2	(+) 387.9±85.3	–	0.097
Hypertension	(-) 346.5±64.6	(+) 376.8±79.9	–	NS
Permanent AF	(-) 350.8±72.5	(+) 391.0±77.3	–	0.014
DVT	(-) 368.1±77.8	(+) 370.2±71.1	–	NS
CRP [mg/dl]	≤1 327.7±56.2	>1 379.8±78.3	–	0.022
RVSP [mmHg]	≤30 362.2±82.3	>30 372.2±73.6	–	NS
LVEF [%]	≥45 373.5±70.2	<45 364.4±81.8	–	NS
LA [cm]	≤4 374.9±92.5	4-5 348.4±68.0	>5 388.7±74.7	2-3 (p=0.061)

Abbreviations: see Tables I and II

Table VI. Influence of selected parameters on fibrinogen levels (multifactor analysis)

Factors	Evaluation of factor impact F test	
	F	p-value
NYHA	0.720	0.489
Metabolic syndrome	3.977	0.049
Permanent AF	4.154	0.044
CRP	4.415	0.038
LA	1.976	0.144

Abbreviations: see Tables I and II

papers suggest that systemic inflammation may be an abnormality underlying AF. It was observed [19] that increased inflammatory marker levels in patients with AF are accompanied by LA enlargement; however, the mechanisms linking those relationships remain unknown. The significant correlation between CRP and LA diameter found in our study population suggests that a similar process is true also for patients with CHF.

In our study mean LA diameter in patients with paroxysmal and persistent AF did not differ significantly compared to patients with sinus rhythm. A statistically significant increase of LA size was observed in the group with permanent AF as compared with other groups.

The relationship between duration of AF and increasing size of LA was presented in the RACE trial and a prospective, 4-year Canadian study [20, 21]. On the one hand significant enlargement of the LA in patients from Group III may be linked to long-term persistent arrhythmia, but on the other hand the influence of haemodynamic factors cannot be excluded. Wozakowska-Kaplon pointed out that after cardioversion, in addition to maintenance of sinus rhythm, good control of hypertension [22] also had a beneficial influence on LA diameter. One may speculate that the favourable effects of such treatment on LA size resulted from the reduction of LV diastolic dysfunction. Shah et al. [11] reported that LV end-diastolic pressure is higly correlated with serum CRP level. LVEDP has a known impact on LA size, and is undoubtedly associated with hypertension. The relationship between hypertension, LA enlargement and increasing CRP levels showed in our study, suggest that inflammation is important in both of these conditions in the course of CHF. The analysis performed in our study showed that permanent AF in the CHF population is a heterogeneous disorder gradually losing connection with increased CRP level, when taking into consideration LA size in the multivariate analysis. It seems that only prospective studies will allow us to determine which of the two factors – inflammation or LA enlargement (which may result from other causes) – is more important in the CHF population for the occurrence and maintenance of AF.

In our study significantly higher RVSP was found in the permanent AF group. No significant differences regarding LVEF in individual groups implies that maintenance of AF is a potential cause of the observed differences. There are no reports concering the relationship between permanent AF in CHF patients and increase of pulmonary pressure. It seems that increase of RVSP in subjects with CHF, in whom permanent AF occurred, may be associated with LA remodelling, which leads to increase of pulmonary venous pressure, but an additive role of increased LVEDP cannot be ruled out.

In our multivariate analysis permanent AF was shown to be significantly correlated with increased serum fibrinogen levels. Similar results were obtained by Li-Saw-Hee et al., who evaluated patients with paroxysmal, persistent, and permanent AF and found that increase of fibrinogen levels is associated with the presence of a permanent form of this arrhythmia in petiens without CHF [6]. Higher fibrinogen values associated with permanent AF in the study population confirm this regularity also with coexisting CHF.

It is known that in the case of deficiency of natural anticoagulants, increase of fibrinogen levels may intensify blood clotting [23]. In the available literature the possible influence of increased fibrinogen level on coagulation profile in patients with CHF has not been studied. Comparing a small group of patients with CHF, secondary pulmonary hypertension and AF to a similar group of patients with sinus rhythm, a significant reduction of 12-month mortality rate was observed with implementation of anticoagulation therapy in the former one [24]. In a comparable group of patients without signs of pulmonary embolism and other apparent signs of thrombosis, more than 6-fold increase of serum D-dimer levels was found, indicating activation of coagulation and fibrinolysis in CHF [25]. The above observations suggest that the coagulation system plays a features role in this condition, in particular when associated with permanent AF and pulmonary hypertension. The presented mechanism requires further patho-physiological research. It cannot however be excluded that sustaining AF through increase of pulmonary artery pressure plays an important role for subsequent RV deterioration and further unfavourable course of heart failure.

Conclusions

1. Increased CRP levels in patients with CHF are significantly associated with presence of hypertension and LA enlargement.
2. Increase of fibrinogen levels in patients with CHF depends on rise of CRP levels and presence of permanent AF.

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Związek między markerami zapalenia a postaciami klinicznymi migotania przedsionków u chorych z przewlekłą zastoinową niewydolnością serca

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Streszczenie

Wstęp: Wystąpienie migotania przedsionków (AF) niekorzystnie zmienia wielkość jam serca i jego funkcję. Arytmia ta łączy się także ze zwiększeniem stężenia białka C-reaktywnego (CRP) i fibrynogenu w surowicy krwi. Nie jest jasne, czy opisywany wzrost markerów zapalenia u chorych z niewydolnością serca (CHF) ma związek z towarzyszącą arytmią, objawami klinicznymi czy niekorzystnym remodelingiem jam serca.

Cel: Ocena zależności między poziomami markerów stanu zapalnego a wybranymi parametrami klinicznymi i echokardiograficznymi oraz stosowanym leczeniem w populacji chorych z CHF i różnymi postaciami AF.

Metodyka: Do badania włączono 99 chorych z CHF, których podzielono na 3 grupy. Grupę I stanowili chorzy z rytmem zatokowym. Do grupy II zaliczono chorych przyjętych z AF, a wypisanych z rytmem zatokowym (chorzy z napadowym i przetrwałym AF). Do grupy III włączono chorych z utrwalonym AF. U wszystkich chorych oznaczono stężenie CRP i fibrynogenu oraz wykonano badanie echokardiograficzne. Oceniano następujące parametry: wymiar lewego przedsionka (LA), frakcję wyrzutową lewej komory (LVEF) oraz ciśnienie skurczowe w prawej komorze (RVSP).

Wyniki: Średnie stężenie CRP w grupie III (5,83±5,36 mg/l) było istotnie statystycznie wyższe niż w grupie I (p=0,001) i II (p=0,033). W grupie chorych z utrwalonym AF średnie stężenie fibrynogenu było najwyższe (391,0±77,3 mg/dl) i różniło się w porównaniu z grupą II (p=0,007) i I (p=0,099). Średni wymiar LA, prawej komory (RV) oraz RVSP w grupie III były istotnie większe niż w pozostałych badanych grupach. W analizie wieloczynnikowej istotny związek ze stężeniem CRP w surowicy wykazano dla obecności nadciśnienia tętniczego (p <0,001) i powiększenia LA (p=0,007). Wykazano znamienny związek pomiędzy stężeniem fibrynogenu a stężeniem CRP (p=0,038), obecnością utrwalonego AF (p=0,045) oraz zespołu metabolicznego (p <0,05). Wartości ln CRP znamiennie korelowały z wielkością LA (r=0,24, p=0,015).

Wnioski: Zwiększone stężenie CRP u chorych z CHF jest istotnie związane z wystąpieniem nadciśnienia tętniczego i powiększeniem LA. Zwiększenie stężenia fibrynogenu w przebiegu CHF zależy od zwiększenia stężenia CRP i obecności utrwalonego AF.

Słowa kluczowe: zastoinowa niewydolność serca, migotanie przedsionków, CRP, fibrynogen, echokardiografia

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