Long-term prognosis and risk factors for cardiac adverse events in patients with chronic systolic heart failure due to hypertension

Bożena Szyguła-Jurkiewicz[1], Aleksander Owczarek[2], Agata Duszańska[3], Jacek Sikora[1], Andrzej Lekston[1], Robert Pudlo[4], Romuald Wojnicz[5], Lech Poloński[1]

[1] III Department of Cardiology in Zabrze, Medical University of Silesia, Katowice, Poland
[2] Department of Applied Informatics, Łódź, Poland
[3] I Department of Cardiology in Zabrze, Medical University of Silesia, Katowice, Poland
[4] Department of Psychiatry in Tarnowskie Góry, Medical University of Silesia, Katowice, Poland
[5] Department of Histology and Embryology in Zabrze, Medical University of Silesia, Katowice, Poland

Abstract: Objectives. The long-term prognosis and predictors of adverse cardiac events in hypertension-related chronic systolic heart failure (CHF) remain uncertain. Therefore, we sought to determine the major adverse cardiac events (MACE) in this group of patients. **Patients and methods.** One hundred and thirty two patients (83% males, age 48.6 ±8.2 years) in NYHA class II and III with hypertension-related chronic CHF were prospectively evaluated for three years. Hypertension was defined as blood pressure ≥140/90 mmHg documented clinically twice for at least 5 years before the onset of CHF symptoms. All patients underwent coronary angiography to exclude coronary artery disease as a cause of CHF. Analysis of predictors of MACE (death, urgent heart transplantation and re-admission to the hospital due to CHF progression) during the 3 years of follow up was performed. **Results.** After follow up the frequency of MACE was 41.7%. The independent predictors of MACE occurrence were as follows: the symptoms of depression [hazard ratio (HR) 2.58 (95% CI 1.44–4.63, p <0.01)], end-diastolic diameter of the right ventricular (EDDRV) [HR 1.07 (95% CI 1.02–1.12, p <0.01)] and D-dimers [HR 2.24 (95% CI 1.08–4.67, p <0.05)]. To define optimal prognostic accuracy of EDDRV and D-dimers the receiver operating characteristics curve analysis was performed. The cut-off for EDDRV was 28 mm (sensitivity 50%, specificity 67.6%, area under curve [AUC] 0.64, p <0.01) and for D-dimers 0.23 μg/ml, (sensitivity 58%, specificity 64.2%, AUC 0.62, p <0.05). **Conclusions.** In analysed group the symptoms of depression, higher baseline right ventricular diastolic diameter and higher baseline D-dimers level were independent predictors of MACE.

Key words: arterial hypertension, chronic systolic heart failure, outcomes

INTRODUCTION

Chronic heart failure (CHF) despite developments in pharmacological treatment is still associated with high mortality and morbidity. It affects 1% of the general population and morbidity tends to increase in developed countries [1,2]. It is essential to identify risk factors for cardiac adverse events in this inhomogeneous group of patients in order to select subjects who should benefit from this thorough clinical observation, intensive educational programs and alternative methods of treatment, i.e. resynchronization therapy and heart transplantation. Several risk factors for cardiac adverse events have been already identified: elevated creatinine plasma level, age, female gender, NYHA class, left (LV) and right (RV) ventricular function, the peak exercise oxygen reuptake test (VO_2) and brain natriuretic peptide (BNP) plasma level [3-6]. Despite established prognostic value of combined measurements of BNP and VO_2, those tests are not commonly used in general practice as they are time-consuming and expensive.

The aim of the study was to define risk factors for major adverse cardiac events (MACE) in patients with chronic systolic heart failure due to hypertension in the 3-year follow-up.

PATIENTS AND METHODS

One hundred and thirty two consecutive patients with chronic systolic heart failure (NYHA II: 77.2%, NYHA III:

Correspondence to:
Bożena Szyguła-Jurkiewicz, MD, PhD, III Katedra i Oddział Kliniczny Kardiologii, Śląski Unwiersytet Medyczny, ul. Szpitalna 2, 41-800 Zabrze, Poland, phone: +48-32-271-52-61, fax: +48-32-234-64-46, email: b.szygula@sccs.pl
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22.8%) were included in the prospective study between January 2003 and October 2004. According to the European Guidelines for heart failure management, all patients were treated with angiotensine converting enzyme inhibitor (ACEI) or angiotensine receptor antagonist (ARA), β-blocker (metoprolol CR or carvedilol) in maximal tolerated doses, spironolactone 25 mg/d, furosemide 40g–80 mg/d [7]. Digoxine was administered in 64.9% of patients. Before admission into hospital all the patients had been treated with constant doses of medications for at least 4 weeks.

Inclusion criteria:
- symptoms of systolic heart failure for at least 2 years
- increased LV end-diastolic diameter (LVEDD >57mm) and reduced LV ejection fraction (LVEF <45%) shown by the ECG
- 5-year or longer history of hypertension before the onset of heart failure symptoms (documented at least 2 episodes of systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg)
- lack of significant (>30%) narrowing in coronary arteries indicated by the coronary angiogram.

Exclusion criteria:
- confirmed coronary artery disease and/or history of myocardial infarction
- acquired or congenital valve disease leading to impairment of myocardial function excluding functional mitral and/or tricuspid regurgitation
- connective tissue disease and/or neoplasm
- infection
- endocrine diseases, i.e. diabetes mellitus, hyper- or hypothyroidism, Cushing disease
- advanced liver or kidney disease
- no signed consent form for the inclusion in the study.

In all the patients thorough history and physical examinations were followed by blood tests, echocardiography, resting ECG, the 6-minute walk test, coronary angiogram, right heart catheterization and diagnostic tests for depression. The blood tests included: full blood count, electrolytes, creatinine, bilirubin, high-sensitivity C-reactive protein (hsCRP), N-terminal pro brain natiuretic peptide (NT-proBNP), cholesterol and triglycerides, glucose, coagulation and liver function tests. In patients with elevated fasting glucose, glucose tolerance tests were performed.

The evaluation of hsCRP was performed using the immunoturbidimetric method with a wave length of 552nm and augmentation of latex particles (Cobas Integra 800, Roche). Plasma level of NT-pro-BNP was measured by the Elecsys 2010 (Roche), and D-dimers were assessed by the STA – Compact (Roche).

The echocardiography (M-mode, 2-D and Doppler) was performed with the Vingmed VIVID-5 (General Electrics). The fraction of LV ejection (EF = [LVEDV – LVESV] × 100% /LVEDD [LVEDV – left ventricular end-diastolic volume, LVESV – left ventricular end-systolic volume]) was measured from the biplane apical 4-chamber and 2-chamber view by the Simpson method [8]. The diastolic function of LV was evaluated according to the following mitral flow parameters: ratio of early (E) mitral flow velocity to atrial (A) mitral flow velocity (E/A), isovolumetric relaxation time (IVRT), deceleration time (E-DT) of E wave.

All echocardiograms were assessed by 2 independent echocardiographers off-line using the ComPACS software (Medimatic).

Coronary angiograms were performed from femoral access. The 6 Fr sheath was advanced over the 0.035–0.038 guide-wire for diagnostic imaging. Different Judkins coronary catheters were used for left and right coronary cannulations. Non-iod contrast was used in all the patients. Right heart catheterization was performed in patients in the supine position by placing a triple lumen, balloon-tipped thermodilution catheter introduced into the right internal jugular or right femoral vein over the 0.035–0.038 guide-wire through the haemostatic sheath 6F. Pressure measurements in the pulmonary artery, right ventricle and right atrium were made during mild apnea in order to exclude the influence of the respiratory phase on the results.

The presence of depression was diagnosed according to a patient's history, clinical observation, the Beck Depression Inventory [9] and the Hamilton rating scale for depression [10]. Psychopathological symptoms and signs of depression were assessed in the course of structural inquiries about hallucinations, disillusions, psychomotor inhibition, stupor, depersonalization, derealization, imperatives, phobias and insomnia.

If depression was suspected further psychiatric and psychological tests were performed.

The clinical observation of patients began on admission to hospital and lasted for 3 years. Follow-up data were achieved during control visits, through questionnaires including questions about cardiac adverse events, and through telephone contact with patients. Sudden death and a combined end-point including death, the necessity for urgent heart transplantation and hospitalization due to exacerbation of CHF (MACE) during the 3-year observation as well as risk factors for MACE were analyzed. The study protocol was accepted by the Bioethical Committee of Silesian Medical University in Katowice.

Statistical analysis

Data in the tables were presented as the mean ± standard deviation (SD) with the 95% CI for variables with normal distribution or the median with lower and upper quartiles for variables without normal distribution. Descriptive variables were presented as the mean ±SD. Variables distribution was evaluated by the Shapiro-Wilk test. Variation homogeneity was assessed by the Levene test. Study hypotheses were verified by: χ^2 or χ^2 with the Yates correction test for discreet variables, the t-Student test for unpaired variables with normal distribution or the U Mann-Whitney test for unpaired variables without normal distribution.

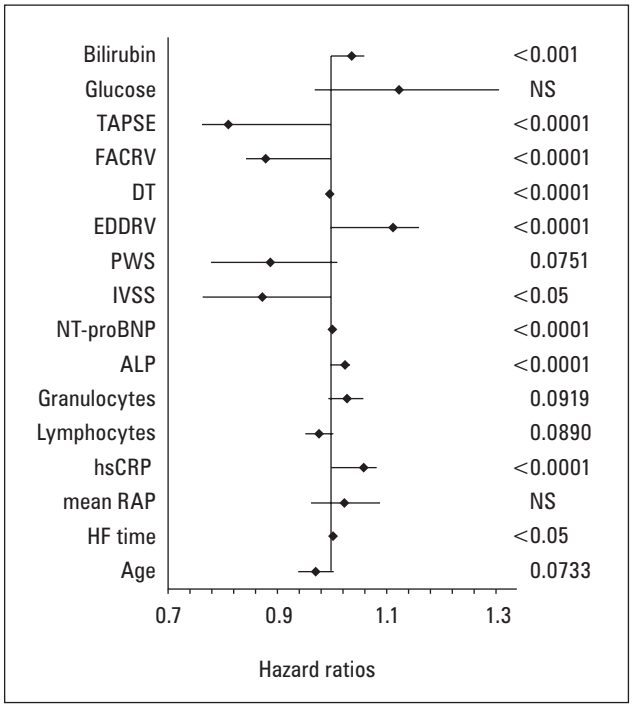

Fig. 1. Hazard ratios (HRs) for major adverse cardiac events outcome. Squares denote HRs, horizontal lines represent 95% CI. The p values are derived from univariate analyses of Cox proportional hazard. The picture does not contain: D-dimers (hazard ratio [HR] 2.32, 95% CI 1.23–4.40), E/A (HR 1.76, 95% CI 1.38–2.25) and depressive syndromes (HR 2.96, 95% CI 1.69–5.17). Abbreviations: ALP – alcalic phosphatase, DT – deceleration time, EDDRV – end-diastolic diameter of the right ventricle, FACRV – fractional area change of right ventricle, HF – heart failure, hsCRP – high-sensivity C-reactive protein, IVSS – systolic intraventricular septum thickness, NS – not significant, NT-proBNP – N-terminal pro brain natiuretic peptide, PWS – posterior wall thickness of the left ventricle, mean RAP – right atrial pressure, TAPSE – tricuspid annular plane systolic excurision

Cut-off values for bilirubin, D-dimers, hsCRP and end-diastolic diameter of the right ventricular (EDDRV) were achieved from receiver operating characteristics curves (ROC). The results included the area under the curve (AUC), sensitivity, specificity, the 95% CI and the significance level.

The univariate Cox proportional hazard analysis defined MACE hazard ratios in the 3-year follow-up. All variables found statistically significant in the univariate analysis ($p < 0.05$) were included in the multivariate backward analysis. The results of multivariate analysis were presented as hazard ratios with the 95% CI and the significance level. The survival analysis was shown with the Kaplan-Meier curve.

All calculations were performed using the commercially available statistical package STATISTICA 7.0, Medcalc and Excel package MS Office.

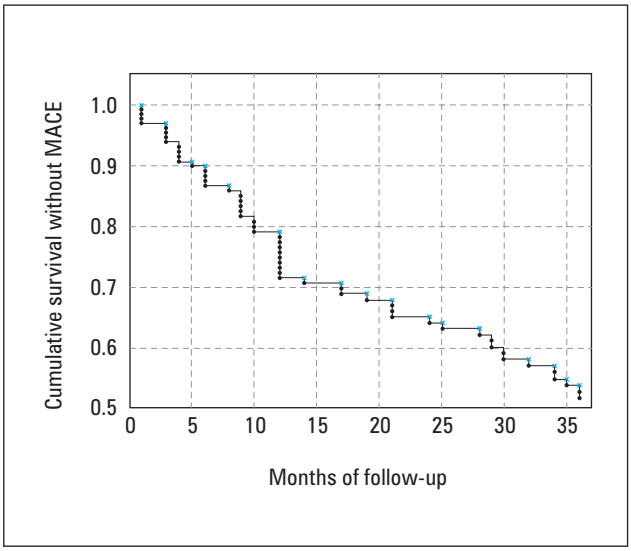

Fig. 2. Kaplan-Meier estimates of the percentage of patients remaining free of major adverse cardiac events (MACE); lower quartile: 12 months

RESULTS

A hundred and thirty two subjects (mean age 48.6 ±8.2) were enrolled in the study. Patients with combined end-points (MACE) formed group B (n = 55 [41.7%]), the other patients were included in group A (n = 77 [58.3%]). Twenty-four (18.2%) patients died, 2 patients (1.5%) were qualified for an urgent heart transplantation, 30 patients (22.7%) were re-admitted into hospital due to deterioration of heart failure symptoms.

Table 1 and 2 present study group characteristics and Table 3 presents baseline blood test results.

Figure 1 shows MACE risk factors identified by the univariate Cox proportional hazard analysis. Figure 2 presents the Kaplan-Meier curve of survival without MACE. Table 4 shows combined end-point risk factors defined by the multivariate Cox analysis.

High-sensitivity CRP, D-dimers and EDDRV were identified as risk factors for MACE, while bilirubin showed just a tendency towards statistical significance (Tab. 5). Plasma level of hsCRP and D-dimers were found highly sensitive and specific for MACE. Right ventricular end-diastolic diameter and bilirubin presented low sensitivity, but high specificity.

DISCUSSION

Hypertension and coronary artery disease have been identified as the most common causes of systolic heart failure in developed countries. However, it is not possible to establish real participation of those morbidities in development of heart failure as they often coexist with each other [11].

Table 1. Study group characteristics in groups A and B

	Total	Group A	Group B	p
	132	77 (58.3%)	55 (41.7%)	
Age (years)	48.6 ±8.2 (47.2–50.0)	49.8 ±7.3 (48.2–51.5)	46.96 ±9.1 (44.5–49.4)	<0.05
Men	109 (82.6%)	67 (87%)	42 (76.4%)	NS
CHF duration (months)	13.0 7.0/45.0	12.0 6.3/24.5	24.0 8.0/60.0	<0.05
BMI (kg/m^2)	28.6 ±4.6 (27.8–29.4)	28.8 ±4.6 (27.8–29.9)	28.4 ±4.6 (27.2–29.7)	NS
6-minute walk (m)	370.3 ±65.4 (359.1–381.6)	390.9 ±55.5 (378.3–403.5)	341.5 ±67.7 (323.2–359.8)	<0.001
Chronic atrial fibrillation	13.9%	11.8%	16.7%	NS
HR (1/min)	77 67.0/90.0	75 65.0/90.0	82 70.5/90	0.0783
LBBB	21.2%	29.7%	20.9%	NS
QTc (ms)	441.3 ±39.4 (434.0–448.8)	437.6 ±38.9 (428.0–447.1)	446.1 ±39.5 (434.9–457.4)	NS
Depressive symptoms	45.5%	31.2%	65.5%	<0.001
ACEI	98.5%	97.4%	100%	NS
Digoxine	64.9%	63.3%	66.7%	NS
Loop diuretics	87.8%	88.3%	87.0%	NS

ACEI – angiotensine converting enzyme inhibitors, BMI – body mass index, CHF – chronic heart failure, HR –heart rate, LBBB – left bundle branch block, NS – not significant, QTc – corrected QT

We would like to emphasize that our study group included selected subjects with systolic heart failure due to hypertension in whom coronary artery disease had been excluded by the coronary angiogram. In the 3-year follow-up we found relatively low incidence of MACE in this group of patients: death in 18.2%, urgent heart transplantation in 1.5%, exacerbation of heart failure symptoms requiring hospitalization in 22.7% of patients.

A similar population was analyzed by Frimm et al. [12]. The incidence of death in their study group including 90 patients with systolic heart failure due to hypertension was 26% in the 5-year follow-up.

Felker et al. [13] analyzed patients with cardiomyopathies of different etiology. They found that prognosis in patients with hypertensive cardiomyopathy was much better compared to systolic heart failure patients due to other reasons. According to All et al. [14], one-year incidence of death in systolic heart failure patients due to coronary artery disease was 42.2% and 30.9% in primary cardiomyopathy. Hypertension affected 40% of subjects and was considered as one of additional risk factors for heart failure development. In the study by Likoff et al. [15] death affected 42% of patients during the 2-year follow-up. Although the percentage of death cases was much higher in their study population compared to our group, 75% of their patients presented NYHA class III and IV, whereas the majority of our subjects were in NYHA class II and III. The time of observation was also longer than in our study.

In our report the following risk factors for MACE were identified: symptoms of depression, EDDRV enlargement and elevated D-dimers. High-sensitivity CRP and bilirubin plasma level showed just a tendency towards statistical significance. Despite that fact both hsCRP and bilirubin were included in the discussion as borderline statistical significance does not exclude clinical significance [16-19] and both those factors affect prognosis in patients with heart failure [20-23].

Symptoms of depression were found the most important independent factor affecting long-time prognosis. The presence of depressive symptoms increased the risk of MACE two-fold. Our results were in concordance with other studies defining depressive symptoms as an independent risk factor for hospitalization and death in patients with chronic heart failure despite etiology [13,24,25]. Therefore effective treatment of depression in patients with chronic heart failure may improve their long-time prognosis. It is a common clinical problem – in our study population depressive symptoms were present in 45% of subjects. In other studies depression was found in 11–25% of out-patients and 35–70% of in-patients [26-28]. There is

Table 2. Baseline echocardiographic and right heart catheterization parameters in groups A and B

	Total	Group A	Group B	p
	132	77 (58.3%)	55 (41.7%)	
MnPAP (mmHg)	22.4 ±9.2 (20.6–24.1)	22.2 ±8.1 (20.1–24.2)	22.7 ±10.4 (19.6–25.7)	NS
MnRAP (mmHg)	6.9 ±4.3 (6.0–7.7)	6.4 ±4.4 (5.3–7.5)	7.5 ±4.3 (6.2–8.8)	<0.05
LVEF (%)	30.70 ±7.2 (29.4–31.9)	31.2 ±7.3 (29.6–32.9)	30.0 ±7.6 (27.9–32.1)	NS
FS (%)	22.9 ±7.3 (21.7–24.2)	22.9 ±7.1 (21.4–24.6)	22.9±7.5 (20.8–24.9)	NS
LV mass index (g/m^2)	177.6 ±41.7 (169.8–185.4)	175.8 ±40.8 (165.9–185.8)	180.2 ±43.5 (167.1–193.2)	NS
EDDRV (mm)	26.9 ±7.3 (25.6–28.2)	25.2 ±6.3 (23.7–26.6)	29.4 ±6.1 (42.3–45.6)	<0.001
FACRV	33.5 ±7,0 (32.3–34.8)	36.8 ±4.6 (35.8–37.9)	28.8 ±7.2 (26.8–30.8)	<0.001
TAPSE	20.4 ±4.6 (19.6–21.2)	22.5±2.7 (21.8–23.1)	17.5 ±5.1 (16.0–18.9)	<0.001
E/A	1.424 ±1.457 (1.057–1.791)	0.633 ±0.780 (0.361–0.905)	2.351 ±1.528 (1.770–2.932)	<0.001
DT (ms)	269.4 ±152.3 (230.9–307.7)	346.9 ±103.9 (310.6–383.2)	178.4 ±150.8 (121.1–235.8)	<0.001
Restrictive mitral inflow	36.5%	8.8%	68.9%	<0.001

DT – deceleration time, E/A – early to atrial mitral inflow velocities ratio, EDDRV – end-diastolic diameter of the right ventricular, FACRV – fractional area change of the right ventricle, FS – fractional shortening, LVEF – left ventricular ejection fraction, MnPAP – mean pulmonary artery pressure, MnRAP – mean right atrial pressure, TAPSE – tricuspid annular plane systolic excursion

a discrepancy of depression incidence in several studies which can be explained by study population characteristics and different diagnostics tools used in depression assessment [28-30].

Therefore it seems important to perform screening tests for depression in all patients with heart failure, and further psychiatric tests if depression is suspected.

Increased EDDRV, tricuspid annular plane systolic excursion (TAPSE) and right ventricular fractional area change (FACRV) were identified as risk factors for MACE. Enlarged EDDRV was found an independent risk factor for MACE. According to ROC curve EDDRV 28 mm was associated with 50.0% sensitivity and 67.6% specificity in prediction of a combined end-point. The greater the TAPSE, reflecting RV systolic function and correlating with RV ejection fraction measured by nuclear methods [31], and FACRV, the lower the risk of MACE [32]. Other findings included increased RV diameter and the mean right atrial pressure while right heart catheterization in group B compared to group A.

Similar results were found in other studies. Spinarova et al. [33] reported increased RV diameter and pressure in the right heart in patients with impaired LV ejection fraction and RV systolic function in comparison with patients with normal RV systolic function. Di Salvo et al. [34] defined RV systolic dysfunction as an independent prognostic factor in patients with advanced heart failure. Having analyzed patients with moderate heart failure Groote et al. [35] drew similar conclusions.

In our study D-dimers, reflecting the activation of coagulation system, were also identified as an independent prognostic factor. In the multivariate analysis hsCRP presented a trend and in the ROC curve analysis it reached statistical significance ($p < 0.05$) in prediction of MACE.

According to ROC curve cut-off point for D-dimers 0.23 µg/ml presented 58.0% and 64.2% sensitivity. Cut-off value for hsCRP 1.85 [mg/l] showed 65.4% specificity and 58.2% specificity in prediction of MACE.

Both our and other studies [20,36-39] suggest that chronic inflammation and increased pro-coagulation activity are associated with development and progression of heart failure. Human and animal experimental studies report increased indexes of inflammation and coagulation system activation in chronic heart failure [39,41]. In our study, like in the studies of Alehagen et al. [20] and Marcucci et al. [39], D-dimers level was defined as an independent risk factor for adverse events in patients with heart failure.

Table 3. Baseline blood test results

	Total	Group A	Group B	p
hsCRP (mg/dl)	3.9 ±5.5 (2.9–4.9)	2.8 ±3.1 (2.0–3.5)	5.5 ±7.3 (3.4–7.5)	<0.05
Fibrynogen (mg/dl)	380.5 ±84.3 (365.4–395.6)	367.8 ±73.9 (350.2–385.4)	397.6 ±94.6 (371.2– 423.9)	0.0775
D-dimers (μg/ml)	0.37 ±0.31 (0.31–0.42)	0.31 ±0.19 (0.26–0.36)	0.44 ±0.40 (0.33–0.55)	<0.05
Na (mmol/l)	138.3 ±3.9 (137.6–138.9)	138.6 ±3.9 (137.7–139.5)	137.8 ±3.8 (136.8–138.8)	NS
Creatinine (μmol/l)	86.7 ±17.4 (83.7–89.7)	85.5 ±16.1 (81.86–89.2)	88.4 ±19.1 (83.2–93.5)	NS
eGFR (ml/min/1.73m^2)	85.6 ±18.9 (82.3–88.9)	87.3 ±18 (83.2–91.5)	83.1 ±20.1 (77.6–88.6)	NS
Triglicerydes (mmol/l)	1.9 ±1 (1.8–2.1)	2.0 ±0.8 (1.8–2.1)	1.8 ±1.2 (1.6–2.1)	<0.05
Total cholesterol (mmol/l)	5.3 ±1.2 (5.1–5.5)	5.3 ±1,2 (5.1–5.6)	5.34 ±1.23 (5.0–5.7)	NS
Glucose (mmol/l)	5.8 ±1.4 (5.6–5.9)	5.6 ±1.1 (5.4–5.8)	5.9 ±1.7 (5.6–6.3)	NS
Glucose >5.8 (mmol/l)	64 (32.0%)	32 (27.6%)	32 (38.1%)	NS
NT-proBNP (pg/ml)	1405.5 ±1598.5 (1103.4–1707.6)	885.9 ±1002.5 (633.4–1138.4)	2101.9 ±1958.2 (1527.1–2676.9)	<0.01
Alcalic phosphatase (U/l)	73.4 ±28.2 (68.2–78.7)	66.2 ±18.2 (61.7–70.7)	83.5 ±35.8 (72.9–93.9)	<0.05
AST (U/l)	27.7 ±11.9 (25.6–29.7)	26.8 ±11.6 (24.1–29.4)	28.8 ±12.5 (25.5–32.2)	NS
ALT (U/l)	34.8 ±19.6 (31.4–38.2)	33.6 ±19.5 (31.09–40.05)	33.8 ±19.9 (28.5–39.2)	NS
Bilirubin (μmol/l)	20.4 ±11.7 (18.4–22.4)	18.3 ±9.1 (16.3–20.4)	23.3 ±14.1 (19.5–27.1)	0.0795

ALT – alanine transferase, AST – asparagine transferase, eGFR – estimated glomerular filtration rate, hsCRP – high-sensivity C-reactive protein, NT-proBNP – N-terminal pro brain natiuretic peptide

Prognostic value of CRP has been already demonstrated [21,38]. In the population analyzed by Alonso-Matinez et al. [22], like in our study, elevated CRP was associated with increased risk of hospitalization in long-term observation. However, in contrary to our study they evaluated patients with heart failure despite etiology. Kaneko et al. and Maeda et al. also observed negative influence of elevated hsCRP on prognosis in heart failure patients [21,40].

Prognostic value of liver function tests was also demonstrated in our study. Elevated plasma bilirubin indicated by the univariate analysis was found a marker for cardiac adverse events. The multivariate analysis demonstrated that it showed a trend towards statistical significance. Cut-off bilirubin 16 [μmol/l] in the ROC curve analysis showed 58.2% sensitivity and 52.6% specificity in prediction of MACE. We also observed elevated plasma level of alcalic phosphatase and bilirubin in group B compared to group A. According to Lau et al. [23], liver dysfunction in heart failure patients manifested as increased cholestasis markers is potentially reversible, particularly in the presence of normal liver ultrasound. The results of our study were in concordance with other reports and showed the importance of evaluation of liver function in heart failure patients. Routine measurements of liver function parameters enable the assessment of prognosis and modification of treatment in order to reduce the risk of death and heart failure deterioration.

Conclusions from this strudy are as follows:

– depressive symptoms are independent risk factors for cardiac adverse events in patients with chronic systolic heart failure

Table 4. Multivariate analysis-Cox proportional hazard and prognostic values of risk factors for cardiac adverse events

Parameter	HR	±95% CI	Wald statistic	P
Symptoms of depression	2.5864	1.4444–4.6314	10.22	<0.01
EDDRV	1.0704	1.0224–1.1206	8.44	<0.01
D-dimers	2.2498	1.0836–4.6715	4.73	<0.05
hsCRP	1.0392	0.9980–1.0821	3.47	0.0622
Bilirubin	1.0197	0.9976–1.0423	3.05	0.0806

HR – hazard ratio, other – see Table 2 and 3

Table 5. ROC curve analysis for hsCRP, D-dimers, EDDRV and bilirubin

	p	AUC	±95% CI	Cut-off	Sens.	±95% CI	Specifity	±95% CI
EDDRV	<0.01	0.639	0.549	>28	50.0	35.8	67.6	55.7
			0.723			64.2		78.0
D-dimer	<0.05	0.620	0.525	>0.23	58.0	43.2	64.2	51.5
			0.708			71.8		75.5
hsCRP	<0.05	0.609	0.515	>1.85	65.4	50.9	58.2	45.5
			0.697			78.0		70.1
Bilirubin	0.0764	0.590	0.501	>16	58.2	44.1	52.6	40.8
			0.675			71.3		64.2

AUC – area under curve, ROC – receiver operating characteristics curves, other – see Table 2 and 3

– markers of right ventricular dysfunction and D-dimers were found predictors of long-time prognosis, whereas bilirubin and hsCRP showed a trend towards statistical significance.

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