Impact of depressive disorders on clinical outcomes in patients with chronic heart failure

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Abstract

Introduction: To date, there are no literature reports of research investigating the relationship between depression and chronic heart failure (CHF) in relation to selected nutritional, cardiac and laboratory parameters.

Aim: To compare CHF parameters in relation to nutritional and laboratory parameters between depressed and non-depressed patients.

Material and methods: We enrolled 94 CHF individuals from Lubelskie Voivodeship to assess depression prevalence and to compare values of cardiac, laboratory and nutritional parameters between depressed and non-depressed patients.

Results: Depression was diagnosed in 66 (70.2%) individuals. We noted significantly lower ejection fraction (EF) (EF%) in the group of depressive patients compared to disease-free individuals (mean EF%: 42 ±12 and 49 ±9; p = 0.030) and worse outcomes in NYHA examination (p < 0.001). Depressed patients had lower body weight (p = 0.023), body mass index (BMI) (p = 0.044), serum albumin concentration (p = 0.015), and hemoglobin concentration (p = 0.042) and an elevated level of C-reactive protein (CRP) (p = 0.025) in comparison to the non-depressed group. The moderate or severely depressed group had a lower level of EF% (p = 0.019) and higher left anterior descending artery (LAD) (p = 0.040) compared with the group suffering from mild depression. We observed greater susceptibility to develop cachexia in patients diagnosed as moderately or severely depressed (p = 0.030). Moreover, in the mentioned group of patients, lower values of body weight (p = 0.037), fat-free mass (FFM) (p = 0.022) and hemoglobin concentration (p = 0.007) were found. Moreover, an inverse correlation between Beck Depression Inventory (BDI) score and EF% (r = –0.371; p = 0.017) was recorded.

Conclusions: Depression in CHF patients is associated with worse cardiac, laboratory and nutritional outcomes. Unfavorable clinical characteristics of CHF patients are related to depression severity.

Key words: chronic heart failure, cachexia, depression, inflammation, nutrition.

Summary

Physiological and behavioral changes observed in depression may affect nutritional status, clinical exponents of the cardiovascular system condition, and laboratory test results in patients with chronic heart failure. The results obtained in our study seem to support the hypothesis that depression may be significantly associated with the clinical picture of chronic heart failure.

Introduction

Depression is one of the most frequently diagnosed psychiatric ailments. Its occurrence is related both to a considerable decrease in the patients’ quality of life and to substantial utilization of resources [1]. Depression is defined as the presence of either decreased mood or loss of interest along with a lack of pleasure accompanied by at least four additional symptoms. They include the following symptoms: alterations in appetite/weight, decreased energy, altered psychomotor activity and recurrent thoughts of death, suicidal ideation or attempts [2]. Prevalence of depression is generally higher in women (20.2%) than in men (13.2%) [3]. The coexistence of depression with chronic diseases is a well-known issue related to medication nonadherence and more frequent

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hospitalizations. It consequently leads to additional complications in the management of those conditions [4]. Depression is associated with an increasing risk of occurrence of several cardiovascular disorders (myocardial infarction, stable or unstable angina, transient ischemic attack, stroke, peripheral arterial disease as well as abdominal aortic aneurysm) [5]. Heart failure (HF) patients are susceptible to develop depression even as much as 3-fold more often than the general population. Its prevalence in this group of patients is estimated at around 24–42%. Moreover, younger HF patients (aged below 60 years) seem to be more susceptible to depressive disorders [6–8]. According to recent findings, in the Caucasian population depression affects 25.3% of HF patients [9].

Current knowledge on the etiopathogenesis of HF indicates that pro-inflammatory cytokines (e.g. interleukin 1β (IL-1β), interleukin 6 (IL-6), tumor necrosis factor α (TNF-α)) probably have a pivotal role in the remodeling of the myocardium by affecting the physiology of myocytes, surrounding tissues, and extracellular matrix. Aforementioned conditions eventually participate in the substantial progression of the HF course [10, 11]. In HF patients, high serum concentration of IL-6 and TNF-α were correlated with numerous adverse outcomes [12]. High concentrations of the mentioned pro-inflammatory cytokines were found to be significant in patients with depression [13, 14]. Additionally, hypercortisolism was noted in depressive disorders and then linked to the increase in expression of numerous transcription factors (NF-kB, MAPK, JAK-STAT) involved in key inflammatory-related pathways [15]. Moreover, in patients with bipolar disorder increased concentrations of pro-inflammatory cytokines are correlated with poor cognitive function [16–18]. On the other hand, the poor cognitive functioning of HF patients was linked to the deterioration of overall adherence including those related to medication, appointments and dietary suggestions [19]. Summarizing the above, the physiological and behavioral changes observed in depression can affect nutritional status, condition and cardiovascular performance, and laboratory test results in patients with HF [20].

Aim

Until now, there is a lack of literature reports investigating nutritional, cardiac, and laboratory outcomes in chronic heart failure (CHF) patients affected by depression. Therefore, the aim of the study was to assess the relationship between depressive disorders and nutritional, cardiac, and laboratory outcomes in patients with CHF.

Material and methods

Study group

Ninety-four patients from Lubelskie Voivodeship (51 men and 43 women) aged 72 ±13 years with diagnosis of CHF were enrolled in the study group. All study participants were diagnosed and treated at the Clinic of Cardiology and Internal Medicine, Department of Cardiology, Military Hospital in Lublin, Poland between 2013 and 2014. Clinical guidelines issued by the European Society of Cardiology were applied for CHF diagnosis and included echocardiographic assessment (ejection fraction – EF%, tricuspid annular plane systolic excursion – TAPSE; right ventricular outflow tract – RVOT; left ventricular end-diastolic and end-systolic diameters – LVEDd and LVESd; left anterior descending artery – LAD), New York Heart Association (NYHA) functional classification and laboratory examination (serum concentration of N-terminal prohormone of brain natriuretic peptide (NT-proBNP), lipid profile, creatinine and hemoglobin concentration, CRP). The above-mentioned screening was complemented by clinical-demographic factors of the patients. The detailed baseline characteristics of the studied individuals are summarized in Table I.

The study protocol was defined with inclusion and exclusion criteria, as follows: Exclusion criteria – 1) coronary artery bypass grafting within the last 6 months; 2) presence of either hyperthyroidism or hypothyroidism; 3) condition after the implantation of metallic implants or cardioverter defibrillator; 4) acute coronary syndrome. Inclusion criteria – 1) newly diagnosed CHF; 2) signed informed consent to participate in the study; 3) ability to undergo bioimpedance analysis; 4) known medical history and collected full clinical data. The study protocol was approved by the Bioethical Commission in the Medical University of Lublin (no. of consent: KE-0254/64/2017).

Depression diagnosis

At the time of CHF diagnosis, the initial screening included the Beck Depression Inventory-II (BDI-II) to assess depression symptoms and measure their severity [21]. All patients completed a 21-question single-choice (scored from 0 to 3 points) self-report inventory and based of the obtained score they were diagnosed as depressive symptomatic or non-depressed. The following cut-off was applied to distinguish between symptomatic and non-depressed patients: BDI score ≥ 12 points (presence of depression symptoms). All patients with diagnosed symptoms of depression were examined by a psychiatrist at a hospital psychiatric ward in order to confirm the initial diagnosis of the disease. Regarding the obtained BDI score making it possible to distinguish mild from moderate or severe depression and to assign patients to study subgroups, the BDI cut-off scores were as follows: 12–19 points (mild depression) and ≥ 20 points (moderate or severe depression).

Nutritional screening

Anthropometric measurements (body weight, body mass index (BMI)) and laboratory tests (serum albumin level, CRP, hemoglobin) were followed by nutritional eval-
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Table I. Baseline characteristics of the study group

| Factor                  | Value (n = 94) |
|-------------------------|----------------|
| Gender:                 |                |
| Male                    | 51 (54.3%)     |
| Female                  | 43 (45.7%)     |
| Age, mean ± SD [years]  | 72 ±13         |
| Weight [kg]             | 82 ±19         |
| BMI [kg/m²]             | 29.3 ±6.1      |
| FM [kg]                 | 25.8 ±14.1     |
| FFM [kg]                | 51.4 ±18.2     |
| Albumin [g/dl]          | 3.41 ±0.61     |
| Triglycerides [mg/dl]   | 110 ±63        |
| Total cholesterol [mg/dl]| 156 ±43       |
| Creatinine [mg/dl]      | 1.27 ±0.60     |
| Hemoglobin [g/dl]       | 13.1 ±2.2      |
| CRP [mg/l]              | 16.9 ±12.4     |
| Systolic blood pressure [mm Hg] | 131 ±24 |
| Diastolic blood pressure [mm Hg] | 76 ±14 |
| EF%                     | 41 ±14         |
| NT-proBNP [pg/ml]       | 4810 ±1645     |
| LVEsd [cm]              | 4.4 ±1.1       |
| LVEDd [cm]              | 5.7 ±2.5       |
| LAD [cm]                | 4.5 ±0.6       |
| RVOT [cm]               | 3.5 ±0.6       |
| TAPSE [cm]              | 2.15 ±1.3      |
| PASP [mm Hg]            | 41 ±13         |
| NYHA:                   |                |
| I                       | 29 (30.9%)     |
| II                      | 32 (34%)       |
| III                     | 19 (20.2%)     |
| IV                      | 14 (14.9%)     |
| SGA:                    |                |
| A                       | 46 (48.9%)     |
| B                       | 38 (40.4%)     |
| C                       | 10 (10.7%)     |
| NRS:                    |                |
| < 3                     | 62 (66%)       |
| ≥ 3                     | 32 (34%)       |
| Diabetes mellitus       | 31 (33%)       |
| Renal failure           | 28 (29.8%)     |
| Smoking status:         |                |
| Smoker                  | 57 (60.6%)     |
| Non-smoker              | 37 (39.4%)     |
| Crm (nF)                | 1.28 ±0.8      |
| Pa [°]                  | 3.77 ±1.60     |

BMI – body mass index, Cm – capacitance of membrane, FM – fat mass, FFM – fat-free mass, EF – ejection fraction, LAD – left anterior descending artery, LVEDd – left ventricular end-diastolic diameter, LVEsd – left ventricular end-systolic diameter, NRS – nutritional risk score, NT-proBNP – N-terminal prohormone of brain natriuretic peptide, Pa – phase angle, PASP – pulmonary artery systolic pressure, RVOT – right ventricular outflow tract, SGA – subjective global assessment, TAPSE – tricuspid annular plane systolic excursion.

Statistical analysis

Version 15.3 of MedCalc (MedCalc, Belgium) computer software was applied for statistical analysis. Differences in the value of studied parameters between studied subgroups were analyzed by Student’s t-test. Fisher’s exact test and c² test were used to determine whether there were nonrandom associations between categorical variables. Pearson’s r correlation was applied to assess the relationship between BDI scores and studied parameters. The results with a value of p below 0.05 were considered to be statistically significant.

Results

Based on the patients’ medical history, BDI screening and further psychiatric examination, depression was diagnosed in 66 individuals (70.2% of the study group). Among the depressive patients, 45 individuals had previously confirmed depression and were treated for it. However, in 21 cases (31.8% of the depression group) the disease was newly diagnosed. The first aim of the study was to evaluate the association between clinical-demographic, cardiac or nutritional parameters and depression in patients suffering from CHF. Regarding parameters reflecting cardiac performance, we noted significantly lower EF% in the group of depressive patients compared to disease-free individuals (mean EF%: 42 ±12 vs. 49 ±9; p = 0.030). Interestingly, in individuals who were diagnosed with more advanced CHF according to NYHA classification occurrence of depression was significantly more common (NYHA III or IV vs. I or II: 84.8% vs. 62.3%, p = 0.033). The association between clinical-demographic or cardiac parameters and depression in CHF patients is presented in Table II.

Concerning nutritional and laboratory parameters, significant differences in body weight and BMI were noted between groups. Depressed patients demonstrated lower body weight (mean body weight: 75 ±14 kg and 89 ±19 kg; p = 0.023) and BMI (mean BMI: 27.3 ±4.4 kg/m² and 30.9 ±8.4 kg/m²; p = 0.044) compared to the

Evaluation of the patients using subjective global assessment (SGA) and nutritional risk score index (NRS-2002) questionnaires. Body composition parameters including fat mass (FM) and fat-free mass (FFM) were collected from bioelectrical impedance analysis (BIA). Parameters reflecting nutritional status at the cellular level including phase angle (Pa) measured at a frequency of 50 kHz and capacitance of the cell membrane (Cm) were also derived from BIA. Similar conditions of BIA measurements were provided for all study participants according to guidelines on reliable impedance measurements. The ImpediMed bioimpedance analysis SFB7 BioImp v1.55 device (Pinkenba, QLD, Australia) was used to measure the above-mentioned parameters. Cachexia was diagnosed according to the Evans criteria [22].
non-depressed group. There were no significant differences in the prevalence of normal BMI, overweight and obesity ($p = 0.874$) between groups. Laboratory tests revealed differences in serum albumin level, hemoglobin and CRP concentration between studied subgroups. Depressed individuals had reduced serum albumin concentration (mean albumin concentration: $3.21 \pm 0.60$ and $3.63 \pm 0.48$; $p = 0.015$), decreased hemoglobin concentration (mean hemoglobin concentration: $12.7 \pm 1.9$ g/dl and $14.0 \pm 2.3$ g/dl; $p = 0.042$) and an elevated level of CRP (mean CRP concentration: $15.9 \pm 7.5$ mg/l and $6.2 \pm 5.0$ mg/l; $p = 0.025$). Results of the association between the laboratory or nutritional measurements and the depression in CHF patients are presented in Table III.

Finally, we compared values of all studied parameters depending on the depression severity. For this purpose, patients were assigned to two subgroups, as follows: mild depression (BDI = 12–19 points) and moderate/severe depression (BDI ≥ 20 points). Overall, patients suffering from moderate or severe depression had worse outcomes reflected by cardiac and nutritional measurements. As regards cardiac parameters, significant differences were found for EF% and LAD. The moderately or severely depressed group had a lower level of EF% (mean EF%: $40 \pm 6$ and $49 \pm 10$; $p = 0.019$) and higher LAD (mean LAD: $4.9 \pm 0.9$ cm and $4.4 \pm 0.6$ cm; $p = 0.040$) compared to the group suffering from mild depression. We observed greater susceptibility to develop cachexia in patients diagnosed as moderately or severely depressed (cachexia prevalence: $64.3\%$ and $30.8\%$; $p = 0.030$), and these patients were at higher nutritional risk (NRS score ≥ 3) compared to patients with mild depression.

### Table II. Comparison of clinical-demographic and cardiac parameters depending on the depression presence in CHF patients

| Factor                        | Depression (n = 66; 70.2%) | Non-depression (n = 28; 29.8%) | $P$-value |
|-------------------------------|-----------------------------|-------------------------------|-----------|
| Age, mean ± SD [years]        | 73 ±14                      | 73 ±15                        | 0.887     |
| Gender:                       |                             |                               |           |
| Male                          | 36 (54.5%)                  | 15 (53.6%)                    | 1.0       |
| Female                        | 30 (45.5%)                  | 13 (46.4%)                    |           |
| Systolic blood pressure [mm Hg]| 134 ±23                     | 133 ±22                       | 0.883     |
| Diastolic blood pressure [mm Hg]| 75 ±14                     | 79 ±13                        | 0.296     |
| EF%                           | 42 ±12                      | 49 ±9                         | 0.030     |
| NT-proBNP [pg/ml]             | 1831 ±1124                  | 2213 ±782                     | 0.981     |
| LVESEd [cm]                   | 4.35 ±1.0                   | 4.0 ±0.8                      | 0.234     |
| LVEDd [cm]                    | 5.2 ±1.0                    | 5.2 ±0.9                      | 0.988     |
| LAD [cm]                      | 4.5 ±0.7                    | 4.5 ±0.7                      | 0.768     |
| RVOT [cm]                     | 3.5 ±0.5                    | 3.4 ±0.5                      | 0.668     |
| TAPSE [cm]                    | 2.0 ±0.4                    | 1.9 ±0.3                      | 0.749     |
| PASP [mm Hg]                  | 41 ±13                      | 38 ±12                        | 0.397     |
| NYHA:                         |                             |                               |           |
| I                             | 11 (16.6%)                  | 18 (64.3%)                    | <0.001    |
| II                            | 27 (40.9%)                  | 5 (17.9%)                     |           |
| III                           | 17 (25.9%)                  | 2 (7.1%)                      |           |
| IV                            | 11 (16.6%)                  | 3 (10.7%)                     |           |
| I and II                      | 38 (57.6%)                  | 23 (82.1%)                    | 0.033     |
| III and IV                    | 28 (42.4%)                  | 5 (17.9%)                     |           |
| Diabetes mellitus:            |                             |                               |           |
| Yes                           | 23 (34.8%)                  | 8 (28.6%)                     | 0.636     |
| No                            | 43 (65.2%)                  | 20 (71.4%)                    |           |
| Renal failure:                |                             |                               |           |
| Yes                           | 22 (33.3%)                  | 6 (21.4%)                     | 0.327     |
| No                            | 44 (66.7%)                  | 22 (78.6%)                    |           |
| Smoking status:               |                             |                               |           |
| Smoker                        | 37 (56.1%)                  | 20 (71.4%)                    | 0.177     |
| Non-smoker                    | 29 (43.9%)                  | 8 (28.6%)                     |           |

EF – ejection fraction, LAD – left anterior descending artery, LVESEd – left ventricular end-systolic diameter, LVESEd – left ventricular end-diastolic diameter, NT-proBNP – N-terminal prohormone of brain natriuretic peptide, PASP – pulmonary artery systolic pressure, RVOT – right ventricular outflow tract, TAPSE – tricuspid annular plane systolic excursion.
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Table III. Comparison of laboratory and nutritional measurements depending on the depression presence in CHF patients

| Factor                  | Depression (n = 66; 70.2%) | Non-depression (n = 28; 29.8%) | P-value |
|-------------------------|----------------------------|-------------------------------|---------|
| Weight [kg]             | 75 ±14                     | 89 ±19                        | 0.023   |
| BMI [kg/m²]             | 27.3 ±4.4                  | 30.9 ±8.4                     | 0.044   |
| Underweight [BMI < 18.5 kg/m²] | 0                           | 0                             | 0.874   |
| Normal BMI [18.5–24.99 kg/m²] | 19 (28.8%)          | 7 (25%)                       |         |
| Overweight [BMI ≥ 25 kg/m²] | 29 (43.9%)               | 12 (42.9%)                    |         |
| Obese [BMI ≥ 30 kg/m²]  | 18 (27.3%)                 | 9 (32.1%)                     |         |
| FM [kg]                 | 28.2 ±12                   | 29.4 ±15                      | 0.980   |
| FFM [kg]                | 52.6 ±15                   | 54.2 ±16                      | 0.802   |
| Albumin [g/dl]          | 3.21 ±0.60                 | 3.63 ±0.48                    | 0.015   |
| Triglycerides [mg/dl]   | 103 ±50                    | 109 ±55                       | 0.756   |
| Total cholesterol [mg/dl] | 156 ±40                  | 150 ±41                       | 0.604   |
| Creatinine [mg/dl]      | 1.22 ±0.45                 | 1.11 ±0.29                    | 0.441   |
| Hemoglobin [g/dl]       | 12.7 ±1.9                  | 14.0 ±2.3                     | 0.042   |
| CRP [mg/l]              | 15.9 ±7.5                  | 6.2 ±5.0                      | 0.025   |
| Cachexia:               |                            |                               |         |
| Yes                     | 25 (37.9%)                 | 13 (46.4%)                    | 0.495   |
| No                      | 41 (62.1%)                 | 15 (53.6%)                    |         |
| NRS:                    |                            |                               |         |
| < 3                     | 42 (63.6%)                 | 20 (71.4%)                    | 0.635   |
| ≥ 3                     | 24 (36.4%)                 | 8 (28.6%)                     |         |
| SGA:                    |                            |                               |         |
| A                       | 30 (45.5%)                 | 16 (57.1%)                    | 0.542   |
| B                       | 28 (42.4%)                 | 10 (35.7%)                    |         |
| C                       | 8 (12.1%)                  | 2 (7.2%)                      |         |
| A                       | 30 (45.5%)                 | 16 (57.1%)                    | 0.369   |
| B or C                  | 36 (54.5%)                 | 12 (42.9%)                    |         |
| Pa [°]:                 |                            |                               |         |
| Male                    | 3.83 ±1.93                 | 4.17 ±1.31                    | 0.662   |
| Female                  | 3.87 ±1.87                 | 4.12 ±1.33                    | 0.762   |
| Cm [nF]:                |                            |                               |         |
| Male                    | 1.22 ±0.9                  | 1.24 ±0.3                     | 0.960   |
| Female                  | 1.20 ±0.7                  | 1.21 ±0.5                     | 0.887   |

*BMI – body mass index, Cm – capacitance of membrane, FM – fat mass, FFM – fat-free mass, NRS – nutritional risk score, Pa – phase angle, PASP – pulmonary artery systolic pressure, SGA – subjective global assessment.*

Table III. Comparison of laboratory and nutritional measurements depending on the depression presence in CHF patients

The results obtained in our study seem to support the hypothesis that depression may be significantly correlated with the clinical picture of chronic heart failure. In our study, 70.2% of CHF patients suffered from depression. This percentage is consistent with the results of other authors as quoted below. In our study, the occurrence of depression was significantly more common in patients with a high BDI score (r = -0.128; p = 0.337), hemoglobin (r = -0.301; p = 0.027), albumin (r = 0.185; p = 0.222), BMI (r = -0.112; p = 0.495), body weight (r = -0.185; p = 0.145), NRS (r = 0.359; p = 0.033), FFM (r = 0.232; p = 0.102), EF% (r = -0.371; p = 0.017) and LAD (r = 0.141; p = 0.321).

Discussion

The results obtained in our study seem to support the hypothesis that depression may be significantly correlated with the clinical picture of chronic heart failure. In our study, 70.2% of CHF patients suffered from depression. This percentage is consistent with the results of other authors as quoted below. In our study, the occurrence of depression was significantly more common in patients with a high BDI score (r = -0.128; p = 0.337), hemoglobin (r = -0.301; p = 0.027), albumin (r = 0.185; p = 0.222), BMI (r = -0.112; p = 0.495), body weight (r = -0.185; p = 0.145), NRS (r = 0.359; p = 0.033), FFM (r = 0.232; p = 0.102), EF% (r = -0.371; p = 0.017) and LAD (r = 0.141; p = 0.321). Significant correlations were recorded for hemoglobin, NRS and EF%.
Table IV. Comparison of clinical-demographic, cardiac and nutritional parameters depending on the depression severity in CHF patients

| Factor                                | Mild depression (n = 52; 78.8%) | Moderate or severe depression (n = 14; 21.2%) | P-value |
|---------------------------------------|---------------------------------|-----------------------------------------------|---------|
| Age, mean ± SD [years]                | 82 ±7                           | 72 ±12                                        | 0.080   |
| Gender:                               |                                 |                                               |         |
| Male                                  | 30 (57.7%)                      | 6 (42.9%)                                     | 0.375   |
| Female                                | 22 (42.3%)                      | 8 (57.1%)                                     |         |
| Systolic blood pressure [mm Hg]       | 135 ±23                         | 134 ±23                                       | 0.926   |
| Diastolic blood pressure [mm Hg]      | 75 ±15                          | 70 ±12                                        | 0.446   |
| EF%                                   | 49 ±10                          | 40 ±16                                        | 0.019   |
| NT-proBNP [pg/ml]                     | 2100 ±1156                      | 1730 ±886                                     | 0.271   |
| LVEsd [cm]                            | 4.4 ±1.0                        | 4.1 ±0.8                                      | 0.395   |
| LVEDd [cm]                            | 5.3 ±1.0                        | 5.0 ±0.7                                      | 0.400   |
| LAD [cm]                              | 4.4 ±0.6                        | 4.9 ±0.9                                      | 0.040   |
| RVOT [cm]                             | 3.5 ±0.5                        | 3.5 ±0.6                                      | 0.968   |
| TAPSE [cm]                            | 2.0 ±0.5                        | 2.0 ±0.3                                      | 0.993   |
| PASP [mm Hg]                          | 42 ±14                          | 42 ±9                                         | 0.906   |
| NYHA:                                 |                                 |                                               |         |
| I                                     | 11 (21.1%)                      | 0                                             | 0.175   |
| II                                    | 20 (38.5%)                      | 7 (50%)                                       |         |
| III                                   | 14 (26.9%)                      | 3 (21.4%)                                     |         |
| IV                                    | 7 (13.5%)                       | 4 (28.6%)                                     |         |
| I and II                              | 31 (59.6%)                      | 7 (50%)                                       | 0.555   |
| III and IV                            | 21 (40.4%)                      | 7 (50%)                                       |         |
| Diabetes mellitus:                    |                                 |                                               |         |
| Yes                                   | 15 (28.8%)                      | 8 (57.1%)                                     | 0.063   |
| No                                    | 37 (71.2%)                      | 6 (42.9%)                                     |         |
| Renal failure:                        |                                 |                                               |         |
| Yes                                   | 18 (34.6%)                      | 4 (28.6%)                                     | 0.759   |
| No                                    | 34 (65.4%)                      | 10 (71.4%)                                    |         |
| Smoking status:                       |                                 |                                               |         |
| Smoker                                | 27 (51.9%)                      | 8 (57.1%)                                     | 0.772   |
| Non-smoker                            | 25 (48.1%)                      | 6 (42.9%)                                     |         |
| Weight [kg]                           | 79 ±17                          | 69 ±17                                        | 0.037   |
| BMI [kg/m²]:                          | 28.5 ±6.0                       | 27.1 ±5.1                                     | 0.584   |
| Normal BMI [18.5–24.99]               | 15 (28.8%)                      | 4 (28.6%)                                     | 0.992   |
| Overweight [BMI ≥ 25]                 | 23 (44.2%)                      | 6 (42.8%)                                     |         |
| Obese [BMI ≥ 30]                      | 14 (27%)                        | 4 (28.6%)                                     |         |
| FM [kg]                               | 27.0 ±11.0                      | 29.4 ±12.6                                    | 0.684   |
| FFM [kg]                              | 42.3 ±9.1                       | 54.5 ±12.4                                    | 0.022   |
| Albumin [g/dl]                        | 3.19 ±0.6                       | 3.14 ±0.5                                     | 0.805   |
| Triglycerides [mg/dl]                 | 100 ±53                         | 115 ±35                                       | 0.499   |
| Total cholesterol [mg/dl]             | 154 ±38                         | 168 ±48                                       | 0.388   |
| Creatinine [mg/dl]                    | 1.0 ±0.5                        | 1.3 ±0.3                                      | 0.105   |
| Hemoglobin [g/dl]                     | 13.3 ±1.7                       | 11.2 ±2.1                                     | 0.007   |
| CRP [mg/l]                            | 15.8 ±9.1                       | 17.2 ±7.4                                     | 0.171   |
| Cachexia:                             |                                 |                                               |         |
| Yes                                   | 16 (30.8%)                      | 9 (64.3%)                                     | 0.030   |
| No                                    | 36 (69.2%)                      | 5 (35.7%)                                     |         |
| NRS:                                  |                                 |                                               |         |
| < 3                                   | 38 (73.1%)                      | 4 (28.6%)                                     | 0.004   |
| ≥ 3                                   | 14 (26.9%)                      | 10 (71.4%)                                    |         |
with higher NYHA classes (NYHA III or IV vs. I or II). Husain et al., in a study including 1009 patients with CHF, found that 66% had depression (diagnosed based on the Beck Depression Inventory (BDI) and Clinical Interview Schedule-Revised (CIS-R)). They also noted that a higher NYHA class was significantly correlated with higher BDI score. Moreover, higher BDI scores in patients with depression were significantly correlated with higher all-cause mortality [23]. On the other hand, in a study by Yin et al. including 443 coronary heart disease (CHD) patients (38.8% with depression) it was found that the severity of anxiety was higher in patients classified as NYHA I/II compared to those classified as NYHA III/IV. However, they suggested that as CHD became unstable, anxiety developed quickly in these patients. Patients of NYHA class III/IV having unstable angina pectoris (AP) had significantly higher rates of anxiety and depression symptoms compared to those with stable AP. Interestingly, in the cited study, a significant correlation between NYHA class and the severity of depression was not observed [24].

In our study, depressive episode severity determined on the basis of Beck’s scale demonstrated a correlation with cardiological disorders defined using the EF% index. CHF patients with depression had significantly lower values of EF%. Additionally, lower EF% and higher LAD were observed in the group of patients with moderate or severe depression compared to those with its mild manifestation. These results support the hypothesis of a correlation existing between the severity of depression and CHF. On the other hand, in a study by Warraich et al., patients with heart failure with preserved ejection fraction (HFpEF) compared to those with reduced ejection fraction (HFrEF) had significantly more depressive symptoms according to Geriatric Depression Scale (GDS) score. Additionally, based on the EuroQol-5D-5L (EQ-5D-5L) questionnaire, self-reported depression and anxiety were significantly more common in patients with HFpEF compared to those with HFrEF (58% vs. 39%). Similarly, in patients with HFpEF, the clinical diagnosis of depression was observed significantly more frequently (22% vs. 11%). Although only 16% of patients had a clinical diagnosis of depression in their medical records, an additional 38% had symptomatic depression according to GDS criteria (≥ 5) without any depression-related symptoms in the medical history. Moreover, a significant, strong negative correlation was found between depression severity and QoL (measured using the Kansas City cardiomyopathy questionnaire (KCCQ) and physical composite score (PCS)) (r = –0.58, r = –0.63, respectively) [25]. Zuzarte et al. suggested that NT-proBNP may potentially act as a mediator linking HFrEF with the presence of psychiatric symptoms in HF patients. The authors reported a significant weak positive correlation between NT-proBNP and the severity of depression (rho = 0.22) as well as the severity of anxiety (rho = 0.18) [26]. However, notably, no such correlation was found in our study.

Interestingly, when patients with CHF and depression were compared to those without the psychiatric disorder, several statistically significant differences in terms of laboratory parameters were observed in our study. Patients with depression had significantly lower levels of albumin and hemoglobin but significantly higher CRP. Despite the fact that the lower albumin levels in the group of patients with depression have already been confirmed in the studies, this correlation constitutes an interesting observation in the group of patients with depression and accompanying chronic diseases (e.g., CHF). Moreover, it should be kept in mind that antidepressants may contribute to lowering the hemoglobin level [27].

The increased values of inflammatory markers in the course of depression are not a new observation, and the

**Table IV. Cont.**

| Factor | Mild depression  | Moderate or severe depression | P-value |
|--------|-----------------|-------------------------------|---------|
|        | (n = 52; 78.8%) | (n = 14; 21.2%)               |         |

**SGA:**

|        |                 |                  |         |
|--------|-----------------|-----------------|---------|
| A      | 26 (50%)        | 4 (28.6%)        | 0.080   |
| B      | 22 (42.3%)      | 6 (42.8%)        |         |
| C      | 4 (7.7%)        | 4 (28.6%)        | 0.228   |
| A      | 26 (50%)        | 4 (28.6%)        |         |
| B or C | 26 (50%)        | 10 (71.4%)       |         |

**Pa [°]:**

|        |                 |                  |         |
|--------|-----------------|-----------------|---------|
| Male   | 3.92 ±0.9       | 4.24 ±1.1       | 0.737   |
| Female | 3.87 ±0.7       | 4.15 ±0.9       | 0.633   |

**Cm [nF]:**

|        |                 |                  |         |
|--------|-----------------|-----------------|---------|
| Male   | 1.15 ±0.6       | 1.29 ±0.9       | 0.474   |
| Female | 1.19 ±0.6       | 1.28 ±0.8       | 0.566   |

**BMI** – body mass index, **Cm** – capacitance of membrane, **FM** – fat mass, **FFM** – fat-free mass, **EF** – ejection fraction, **LAD** – left anterior descending artery, **LVEDd** – left ventricular end-diastolic diameter, **LVESd** – left ventricular end-systolic diameter, **NRS** – nutritional risk score, **NT-proBNP** – N-terminal prohormone of brain natriuretic peptide, **Pa** – phase angle, **PASP** – pulmonary artery systolic pressure, **RVOT** – right ventricular outflow tract, **SGA** – subjective global assessment, **TAPSE** – tricuspid annular plane systolic excursion.
CRP level is only one of them (others include TNF-α, IL-1, IL-6 and IL-2R). Valkanova et al., in their systematic review and meta-analysis of longitudinal studies, found that elevated inflammatory markers (CRP, IL-6) have a minor, yet significant, relationship with the development of depressive symptoms [28]. Moreover, Del Giudice et al. suggested that some effects of IL-6 and CRP may not be specifically related to inflammation. Additionally, they stated that a high level of IL-6 stimulated the production of CRP, pointing to the biological relationship between the functions of both cytokines [29].

Patients diagnosed with depression seem to develop cachexia more easily, but such a correlation has not yet been confirmed in the light of the available data. According to our results, patients with depression had significantly lower body weight and BMI compared to those not suffering from depression. On the other hand, we did not observe a significant difference in the incidence of cachexia between depressed and non-depressed patients. However, it should be noted that a significantly higher percentage of cachexia (64.3% vs. 30.8%) and nutritional risk cases (≥ 3 according to NRS) was observed in the group of patients with severe and moderate depression compared to patients with mild depression. Comparing the group of patients diagnosed with moderate and severe depression with the group with mild depression, significantly lower body weight and FFM were observed. A study by Sun et al. demonstrated a correlation between cachexia and psychiatry-related changes in the clinical course of the underlying chronic disease (depression and anxiety accompanied by the deterioration of QoL). However, it should be noted that the cited study was conducted in patients with cancer and not with CHF [30]. Nevertheless, the correlation between depression and nutritional status has also been observed in a rural elderly population. Based on their results, Vafaei et al. concluded that patients with depression had significantly (over 15-fold) higher risk of malnutrition than those not suffering from depression [31]. Moreover, a number of markers seem to be correlated both with the nutritional status and the level of depression, including IGF-1, NPY, BDNF, ghrelin, leptin, CCK, GLP-1, AGE and glycermia, suggesting that the two conditions might share triggering molecular pathways [32].

**Conclusions**

Although our study focused on the incidence of depression depending on the occurrence of specific cardiovascular, nutritional and laboratory changes, it should be considered that depression may also cause the above-mentioned alterations. This issue significantly impedes drawing unambiguous conclusions. Nevertheless, we believe that our study provides interesting and innovative data on clinical parameters in a group of patients with depression and concomitant CHF. Since depression and its severity may affect the somatic state of the patient with CHF and reduce the potential benefits of treatment, further studies regarding this correlation seem to be warranted.

**Conflict of interest**

The authors declare no conflict of interest.

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