pagepress

GLOBAL CARDIOLOGY
Global Cardiology 2024; **3**
Published online 5 November 2024 | **DOI**: 10.4081/cardio.2024.47

ARTICLE

Depression, health-related quality of life and life satisfaction in patients with heart failure

Natasa Sedlar Kobe,[1] Daniel Omersa,[2] Mitja Lainscak,[3,4] Jerneja Farkas[1,3,4]

[1]National Institute of Public Health, Ljubljana; [2]General Hospital Jesenice, Jesenice; [3]General Hospital Murska Sobota, Murska Sobota; [4]Faculty of Medicine, University of Ljubljana, Slovenia

Abstract

Background: The Patient Health Questionnaire 9 (PHQ-9) has been recognized as an effective tool for identification of patients with heart failure (HF) at risk for lower health-related quality of life (HRQoL). We aimed to compare HRQoL levels, overall satisfaction with health and life, disease severity variables, sociodemographic variables and behavioural risk factors between patients with HF with different levels of depressive symptomatology.

Methods: In a >55 years-old general population cross-sectional HF prevalence study, 1851 subjects were screened and those with NT-proBNP ≥125 pg/mL (n=930) underwent detailed diagnostic visit to confirm or rule out HF as per 2016 European Society of Cardiology guidelines. HRQoL (the Short-Form 12 Health Survey, SF-12; EQ-5D-3L), depressive symptoms (Patient Health Questionnaire, PHQ-9) and satisfaction with life (Satisfaction With Life Scale, SWLS) were also assessed. Patient with HF (75±8 years, 54 % male, New York Heart Association (NYHA) functional class I-III, with mean left ventricular ejection fraction (LVEF) 56±13) were divided into three groups based on the severity of depressive symptomatology as per PHQ-9 score (none: score 0-4, mild: score 5-9, and moderate-to-severe: score 10-27). Multiple group comparisons and pairwise *post-hoc* analyses were performed.

Results: Results indicated significant between group differences in NYHA status (p<0.001), number of comorbidities (p=0.006), functional capacity (p=0.01), as well as HRQoL variables (p=0.05 to 0.001) and SWLS score (p<0.05), with non-depressed group generally showing better physical and subjective indicators of health and well-being compared with the mild and moderate-to-severe group.

Conclusions: Results indicate that even patients with HF with clinically non-significant levels of depressive symptomatology show significantly impaired psychosocial status (diminished HRQoL, lower life satisfaction).

Key words: heart failure; depressive symptoms; Patient Health Questionnaire 9; health-related quality of life; disease severity.

Received: 30 November 2023; Accepted: 14 October 2024.
**Correspondence to: Jerneja Farkas, MD, PhD, General Hospital Murska Sobota, Ulica dr. Vrbnjaka 6, Rakican, SI-9000 Murska Sobota, Slovenia. Tel. +386.02.5123731.*
E-mail: jerneja.farkas@sb-ms.si

Introduction

Heart failure (HF) represents a serious burden to both patients and healthcare system due to its increasing prevalence and association with poor functioning, impaired health-related quality of life (HrQoL), frequent hospitalizations and high healthcare costs.[1-5]

Multimorbidity is highly prevalent in patients with HF, with depression and anxiety being of common occurrence in this population.[6] According to the meta-analysis of 36 studies,[7] clinically significant depressive symptoms affect 21.5% of patients with HF. Therefore, the prevalence of depression in patients with HF is two-to-three times higher compared to the general population.[8] Also, research indicated that the prevalence of depression in patients with HF increases with New York Heart Association (NYHA) functional class.[7]

Depression in patients with HF has been related to adverse medical outcomes, including development and progression of HF. In a prospective observational study of 1.9 million healthy adults,[9] history of depression (defined by a billing diagnosis of depression or prescription of an antidepressant) was prospectively associated with 18% elevated risk of HF development over the subsequent 7 years, even after controlling for other cardiovascular risk factors. Furthermore, in patients with HF research

indicates prospective link of both elevated depressive symptoms and depressive disorders to frequent hospitalizations,[10] recurrent cardiac events,[7] mortality,[7,11,12] limitations in daily functioning and impaired health-related quality of life,[13] independent of other biomedical risk factors. There is also strong and consistent evidence of an independent causal association between depression, social isolation and lack of quality social support.[3]

Despite the growing evidence of high rates of depression in patients with HF and its adverse impacts on physical and psychological outcomes, depression often remains underdiagnosed and undertreated.[14] Accurately diagnosing depression in this population might be even more challenging given the overlap between cardiac and psychiatric symptoms. To address these issues, the European Society of Cardiology (ESC) guidelines[3] have recommended systematic screening for depression in patients with HF to increase its recognition. The use of validated instruments such as the Beck Depression Inventory (BDI) and the Patient Health Questionnaire (PHQ-9) is recommended, followed by referral of patients with depression for appropriate treatment.

Our study aimed to contribute to the growing body of knowledge about rates of depressive symptom severity from PHQ-9 questionnaire in population with HF and to compare three subgroups with different levels of depressive symptomatology (none, mild and moderate-to-severe) on a range of clinical, sociodemographic variables, behavioral risk factors and psychosocial variables. In particular, we expected better physical and psychosocial status in non-depressed group of patients with HF, according to the PHQ-9 proposed cut-off values.

Methods

Study design and participants

This was a secondary analysis of the data from a ≥55 years old general population cross-sectional HF prevalence study Screening Of adult urBan pOpulation To diAgnose Heart Failure (SOBOTA-HF). The detailed study protocol and initial results have been published elsewhere.[15] Briefly, all together 1851 subjects were screened and those with NT-proBNP ≥ 125 pg/mL (n=930) and 108 healthy controls with NT-proBNP <125 underwent detailed diagnostic visit to confirm or rule out HF as per 2016 ESC guidelines. A diagnostic visit included history and physical examination, electrocardiogram, echocardiography, blood and urine sampling, ankle brachial index, pulmonary function tests, body composition measurement, physical performance tests, and questionnaires to measure HRQoL, depressive symptoms and satisfaction with life. An external center validated echocardiography results, and the HF diagnosis was adjudicated within an international HF expert panel.

The SOBOTA-HF study protocol was evaluated and approved by the National Medical Ethics Committee of the Republic of Slovenia (Approval No. 0120-656/2016) and the study was performed in accordance with the Declaration of Helsinki. All participants gave their written informed consent for participation in the study prior to the study.

Instruments and data collection

Demographic and clinical data

All participants were examined by a physician who conducted the standardized interview protocol. Basic demographic (age, gender, education level, marital status, socioeconomic class) and clinical data (history of disease, history of interventions, symptoms of HF, medication, HF signs) were collected and standard measurements were performed (blood pressure, heart rate, height, weight, waist and hip circumference). Likelihood for HF was evaluated in accordance with the ESC guidelines[3] with findings of history and physical examination and with results of NT-proBNP. Body mass index (BMI) was calculated from weight (kg) and height (m) in kg/m^2.

Behavioral risk factors

Smoking status was assessed by asking participants about their current and past daily smoking. Alcohol consumption was assessed by the first three questions on the well-validated Alcohol Use Disorders Identification Test[16] (AUDIT-C): 'drinking frequency', 'typical quantity per occasion', and 'high intensity or 'binge' drinking frequency'. All questions are rated using a five-point response scale. Higher risk consumption was indicated by a score ≥5.[17]

For the assessment of the functional capacity of patients with HF, a widely used six-minute walk test (6MWD)[18] was performed according to the standard protocol.[19] The distance walked in 6 minutes was transformed into percent predicted value (PPV) by dividing the actual 6MWD by the expected value of 6MWD and then multiplying by 100, using standardized norm-referenced equations[20]. Handgrip strength measured in both hands using the JAMAR® Hydraulic Hand Dynamometer (Patterson Medical Ltd., Nottinghamshire, UK) was another physical performance test. The best of three measurements was used, as already performed in patients with HF.[21] Cut-off points for low grip strength were <27 kg for men and <16 kg for women.[22]

Psychosocial variables

Participants reported their symptoms of depression during the last 2 weeks on the 9-item Patient Health Questionnaire (PHQ-9).[23,24]. Each item describes one symptom corresponding to DSM-IV diagnostic criteria for major depressive disorder (i.e., sleep, concentration, energy problems, low self-esteem, anhedonia, *etc.*). Items are rated using a four-point response scale (0 = not at al, 1 = several days, 2 = more than half the day, 3 = nearly every day). Löwe and colleagues[24] recommend the use

of screening cut-off score of ≥9, which allows for the diagnosis of any depressive disorder with a sensitivity of 87% and a specificity of 76%. In the group of patients with HF Hammash and colleagues[25] report 70% sensitivity and 92% specificity in identifying depressive symptoms at the cut-off score of 10. In addition to its utility as a short screener, the PHQ-9 allows for an assessment of depression severity. A summary score ranges from 0 to 27 points, with scores corresponding to five different disease severity categories: *none* (PHQ-9 scores 0-4), *mild* (PHQ-9 scores 5-9), *moderate* (PHQ-9 scores 10-14), *moderately severe* (PHQ-9 scores 15-19), and *severe* (PHQ-9 scores 20-27).[23]

HRQoL was assessed with two well-validated generic questionnaires: the 12-item Short Form Medical Outcomes Study Survey (SF-12)[26,27] and The EQ-5D-3L[28,29] that have been used in several studies with cardiac population.[13,30] The SF-12 is a shorter, 12 item subset of the widely used SF-36 health-status instrument.[31] It measures eight health concepts of the SF-36 and allows the calculation of two summary measures: physical component summary 12 (PCS-12) and mental component summary 12 (MCS-12). Higher PCS/MCS scores indicate higher self-perceived physical/mental quality of life. Both SF-12 summary measures have been shown to replicate well SF-36 summary measures in heart disease patients.[32] The EQ-5D-3L consists of two parts. The first part includes five items, relating to five dimensions of mobility, self-care, usual activities, pain/discomfort, anxiety/depression. Using three-level ordinal scale participants report their perceived health status as: *no problem* (scored 1), *moderate problem* (scored 2), *severe problem* (scored 3). The EQ-5D-3L index score was calculated according to Slovenian population norms,[33] in which lower results demonstrate lower HRQoL. The second part of the instrument is visual analog scale (VAS) used to assess self-perceived global levels of health (0 = *worst imaginable state of health*, 100 = *the best imaginable state*).

The Satisfaction With Life Scale (SWLS),[34,35] was used to measure cognitive component of subjective well-being, life satisfaction. The scale consists of five multiple-choice items rated on a scale from: 1 = *strongly disagree* to 7 = *strongly agree*. A summary score of the scale ranges from 5 to 35. A total score corresponds to different levels of life satisfaction *average* (SWLS scores 20-24), *high* (SWLS scores 25-29), *slightly below average* (SWLS scores between 15-19), *extremely low* (SWLS scores 5-14), *extremely high* (SWLS scores 30-35). Studies indicate good psychometric properties of the scale in different non-clinical and clinical populations;[36-38] generally lower life satisfaction scores are reported in people with chronic illnesses compared to general population.

Missing items were imputed using the EM algorithm, which has been demonstrated to be an effective method of dealing with missing data.[39] However, the proportion of replaced items was small (ranging from 0.0% to 6.7% across items).

Analysis of data

The data analysis was performed using SPSS 21.0 statistical software (IBM). Descriptive data are presented for the entire sample of study participants with HF (n=221) and by all three subgroups based on the self-reported severity of depressive symptomatology: *none* (PHQ-9 scores 0-4), *mild* (PHQ-9 scores 5-9) and *moderate-to-severe* (PHQ-9 scores 10-27) [23]. Categorical data are presented as frequencies (percentages), and continuous data are presented as the mean values ± SD. To explore differences in characteristics across the three groups the chi-square test or Fisher's exact test were used for categorical variables and Kruskal-Wallis test for non-parametric continuous variables. When a significant difference was found, *post-hoc* testing using Bonferroni comparisons was used to identify specific group differences. Spearman's rank-order correlations were used to compare the relationships between PHQ-9 score and other psychosocial variables. Multiple regression models were used to further investigate the cross-sectional association between depression severity categories and self-perceived health-related quality of life (EQ-5D-3L index), global levels of health (EQ-5D-3L VAS) and general life satisfaction (SWLS score). To account for the possible confounding effects demographics (age, gender, education, SES, marital status) and clinical covariates (NYHA, BMI, number of comorbidities, SMWT) were added to regression models based on prior literature.[40-43] Dummy variables were built for all categorical variables. All statistical tests were two-tailed and utilized a 5% significance level.

Results

Table 1 displays descriptive information for the entire sample of study participants with HF (n=221), which were predominately older (on average 75±8 years) and had a NYHA classification of class I or II (85%). Approximately half of the sample were male (54%), married (61%), middle class (61%), had less than 12 years of education (49%), and reported three or more comorbidities (53%). According to the PHQ-9 score criteria,[28] 114 (52%) of the participants with HF were classified as non-depressed, while 84 (38%) reported mild and 23 (10%) moderate-to-severe levels of depressive symptomatology at the time of the diagnostic visit.

Three subgroups classified according to the self-reported severity of depressive symptomatology did not significantly differ in demographical variables. Also, clinical variables (LVEF, type of HF, NT-proBNP levels, BMI, specific comorbidities) and some behavioral variables (smoking, higher risk alcohol consumption) were not significantly different among these groups. However, there were significant between-group differences in NYHA status ($p<0.001$) and number of comorbidities ($p=0.006$); the group of participants without depressive symptomatology showed significantly better NYHA status (a greater proportion of participants had NYHA 1 and lower proportion had NYHA 3) compared to the other two groups (Figure 1), and reported significantly lower number of comorbidities compared to the group with mild depressive symptomatology. Physical performance variables of functional capacity measured by SMWT ($p=0.003$) and handgrip strength ($p<0.001$) were also significantly different among the three groups. Participants without depressive symp-

tomatology showed significantly better levels of functional capacity compared to the other two groups, and significantly better handgrip strength of dominant and non-dominant hand compared to the group with moderate-to-severe depressive symptomatology. Figure 2 shows discrepancies in the PHQ-9 item response pattern between three groups with different self-reported levels of depressive symptomatology. Compared to the other two groups, significantly higher proportion of participants in moderate-to-severe group reported experiencing depressed mood (item 1) and anhedonia (item 2) more than half the days or nearly every day (78% and 56% respectively). Similar pattern was noticed in all other items, including suicidal ideation (item 9) (Table 2).

Three subgroups with different severity of self-reported depressive symptomatology differed significantly by SF-12 MCS ($p<0.001$), EQ-5D-3L VAS ($p<0.001$) and EQ-5D-3L index score ($p<0.001$); the lowest scores on these scales were obtained in the group with moderate-to-severe depressive symptomatology, while the highest scores were noticed in the non-depressed group. Compared to other two groups, participants without depressive symptomatology also had the highest scores on SF-12 PCS and SWLS; according to post hoc tests the differences between moderate-to-severe and non-depressed group and between mild and non-depressed group were significant ($p<0.05$) (Table 3). For the comparison of EQ-5D-3L items and levels of life satisfaction as measured by SWLS between the three groups

Table 1. Characteristics of study participants with HF.

		Depressive symptomatology			p-value
	All sample (n=221)	None (n=114)	Mild (n=84)	Moderate to severe (n=23)	
Demographics					
Age (years), M±SD	74.7±7.7	73.9±7.8	74.8±7.6	77.9±6.9	0.087
Male, n (%)	120 (54.3)	63 (55.3)	42 (50.0)	15 (65.2)	0.412
<12 yrs of education, n (%)	84 (48.9)	43 (37.7)	33 (39.3)	8 (34.8)	0.912
Married/living together, n (%)	104 (62.3)	57 (50.0)	37 (44.0)	10 (43.5)	0.664
Lower/working SES, n (%)	40 (22.6)	19 (16.7)	18(21.3)	3 (13.0)	0.554
Clinical variables					
LVEF (%), M±SD	55.7±13.2	57.3±12.9	53.5±12.7	56.2±15.5	0.084
Type of HF, n (%)					
HFpEF	141 (63.8)	81 (71.1)	47 (56.0)	13 (56.6)	0.068
HFrEF	35 (15.8)	15 (13.2)	16 (19.0)	4 (17.4)	0.521
HFmrEF	45 (20.4)	18 (15.8)	21 (25.0)	6 (26.1)	0.218
NT-proBNP, M±SD	1251.0±1592.7	1024.4±1314.0	1357.6±1560.0	1984.4±2538.7	0.222
NYHA class, n (%)					<0.001
I	80 (36.4)	54 (47.4)[a]	22 (26.2)	5 (21.7)	
II	108 (49.1)	54 (47.4)	41 (48.8)	13 (56.5)	
III	32 (14.5)	6 (5.3)[a]	21 (25.0)	5 (21.7)	
IV	0 (0)	0 (0)	0 (0)	0 (0)	
BMI (kg/m^2), M±SD	30.5±5.0	30.3±5.1	30.9±5.0	30.0±4.7	0.678
Self-reported comorbidities M±SD	2.8±1.6	2.5±1.5d	3.2±1.6	2.5±1.6	0.006
Arterial hypertension, n (%)	182	92 (80.7)	70 (83.3)	20 (87.0)	0.739
Atrial fibrillation, n (%)	78	36 (31.6)	37 (44.0)	5 (21.7)	0.069
Ischaemic heart disease, n (%)	52	25 (21.9)	23 (27.4)	4 (17.4)	0.093
Diabetes mellitus, n (%)	51	22 (19.3)	27 (32.1)	2 (8.7)	0.091
Behavioural risk factors					
Physical performance					
SMWT (mean), M±SD	371.2±141.8	407.7±128.8[a]	345.4±143.6	284.5± 44.0	0.011
SMWT (PPV), M±SD	68.8±24.6	75.1±22.5[a]	63.7±24.7	55.9±25.9	0.003
HGS, M±SD	22.7±9.4	24.3±9.4[e]	21.8±8.6	17.9±10.6	0.010
HGS dominant, M±SD	24.7±9.0	26.1±9.2	24.2±8.5	19.3±8.1[c]	<0.001
HGS non-dominant, M±SD	22.7±9.4	24.3±9.5[e]	21.7±8.6	17.9±10.6	<0.001
Handgrip lower, n (%)	172 (78.2)	83 (72.8)	73 (86.9)[b]	16 (69.6)	0.048
Smoking, n (%)					
Current	18 (8.1)	9 (7.9)	8 (9.5)	1 (4.3)	0.143
Former	64 (29.0)	34 (29.8)	27 (32.1)	3 (13.0)	0.053
Higher risk alcohol consumption, n (%)	6 (2.7)	2 (1.8)	3 (3.6)	1 (4.3)	0.151

Percentages may not total 100 due to missing data or rounding; significant difference was set at $p<0.05$; *post-hoc* comparisons between individual groups: [a]*None* significantly different from *mild* and *moderate-to-severe*; [b]*Mild* significantly different from *none* and *moderate-to-severe*; [c]*Moderate-to-severe* significantly different from *none* and *mild*; [d]*None* significantly different from *mild*; [e]*None* significantly different from *moderate-to-severe*; [f]*Mild* significantly different from *moderate-to-severe*; SES, socioeconomic status; LVEF, left ventricular ejection fraction; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HFmrEF, heart failure with mid-range ejection fraction; NT-proBNP, N-terminal pro b-type natriuretic peptide; NYHA, New York Heart Association; BMI, Body Mass Index, SMWT, Six Minute Walk Test; PPV, Percent Predicted Value; HGS, Handgrip strength.

see Figure 1. Compared to other two groups, significantly lower proportion (p<0.05) of individuals in the group without depressive symptomatology had higher NYHA class, reported problems in all five HRQoL domains and reported low satisfaction with life levels. Correlation tests revealed large negative associations between the PHQ-9 score and SF-12 Mental composite summary (r = -0.556) and EQ-5D-3L Index score (r = -0.563). Associations between the PHQ-9 score and other included psychosocial variables were moderately negative with values between -0.50 and -0.30 (Table 4).[44] Depressive symptomatology severity was found to have significant negative relationship (p=0.05 to p<0.001) with level of self-perceived health-related quality of life (EQ-5D-3L index), global level of health (EQ-5D-3L VAS) and general life satisfaction (SWLS score) (adjusted R^2 = 10.0 to 23.0%) (Table 5).

After adjusting for covariates, the relationship between depressive symptomatology levels and all three psychosocial variables was still statistically significant (p=0.05 to p<0.001) (Table 6). Compared to the group without depressive symptomatology, stronger negative association with level of self-perceived health-related quality of life, global level of health and general life satisfaction level was found in a group with mild and moderate-to-severe depressive symptomatology. The total variance explained by the model with demographic and clinical covariates is 16% for general life satisfaction, 22% for self-perceived global levels of health and 43% for self-perceived health-related quality of life.

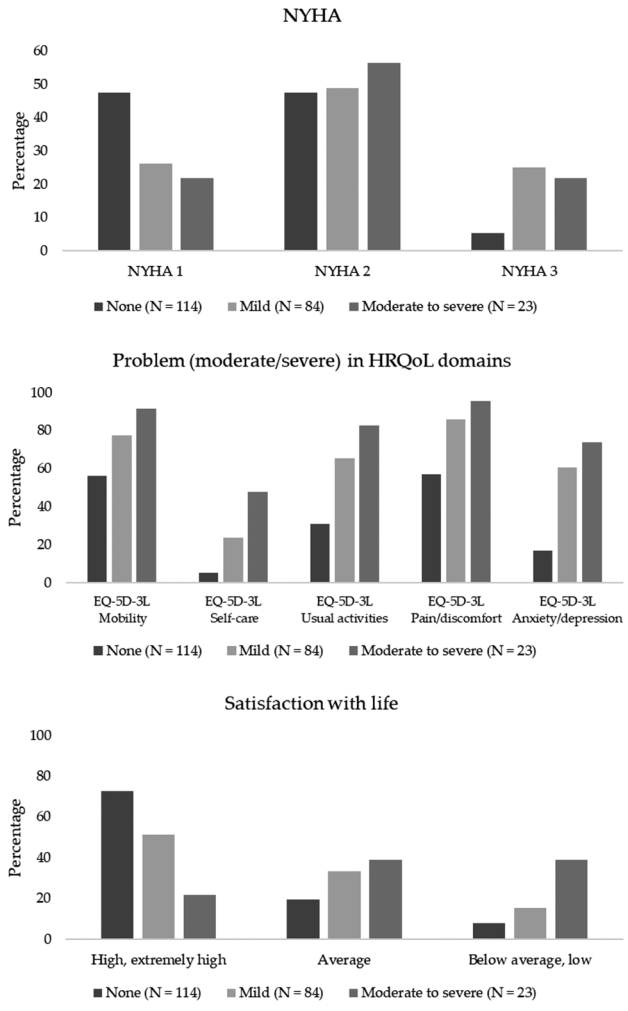

Figure 1. NYHA class, moderate/severe problems in EQ-5D-3L HRQol domains and satisfaction with life levels measured by SWLS scale in three groups with different depressive symptomatology levels.

Discussion

Our study assessed rates of depressive symptom severity in a sample of 221 patients with HF identified through a cross-sectional HF prevalence study SOBOTA-HF conducted in a ≥55 years old general population. Depressive symptom severity was assessed with the use of depression screening questionnaire PHQ-9, that has been suggested as one of the validated screening tools in this population.[3] Using proposed severity categories,[23] 38 % of the patients with HF reported mild and 10 % moderate-to-severe levels of depressive symptomatology at the time of study inclusion. Furthermore, differences between patients

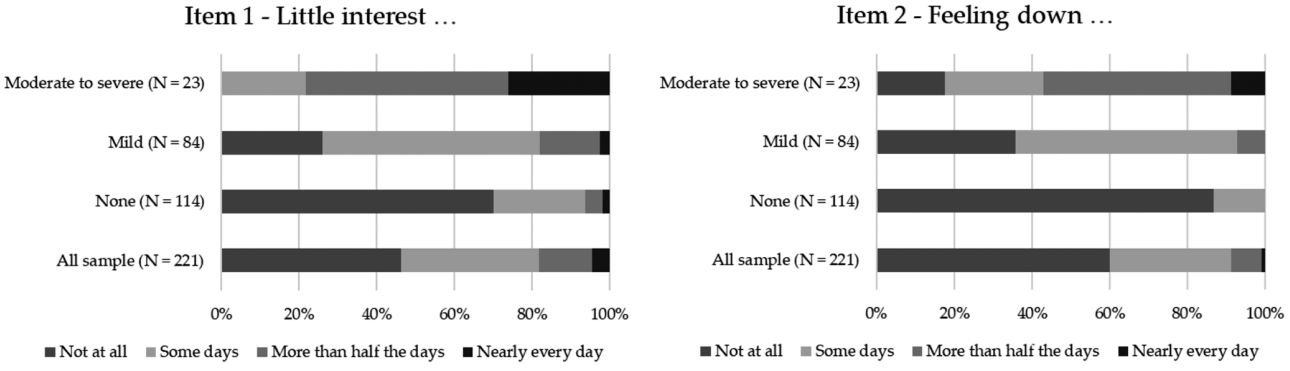

Figure 2. PHQ-2 item response frequency distribution by groups based on self-reported severity of depressive symptomatology.

with HF with different depressive symptom severity levels on a number of clinical, behavioral and psychosocial variables were examined. We found that the patients in non-depressed group (PHQ-9 score 0-4) reported better physical and subjective indicators of health and well-being than the group with mild and group with moderate-to-severe depressive symptomatology levels. Therefore, the overall findings from our study are consistent with a large body of research suggesting associations of depressive symptoms/depression and various negative psychosocial outcomes.[7,13] However, it adds to these findings suggesting that even patients with HF with mild, clinically non-significant depressive symptomatology level, may experience significantly impaired psychosocial capacities, compared to those that report no depressive symptomatology.

The prevalence of clinically significant depressive symptoms in patients with HF has been estimated to be approximately 21.5%,[7] which is two-to-three times higher compared to the general population.[8] However, the prevalence rates reported across 36 studies included into meta-analytic review by Rutledge and colleagues[7] widely varied, ranging from 9% to 60%; also, studies using solely self-report questionnaires to assess depression reported prevalence rates ranging from 30% to 44%. Using the PHQ-9 cut-off score of 10, proposed by Hammash and colleagues,[25] the prevalence obtained in our study is on the

Table 2. Percent of participants answering individual PHQ-9 items with most severe response categories ('more than half the days', 'nearly every day') for total sample and three groups.

n (%)		Depressive symptomatology			p-value
Answering with response categories ' more than half the days', 'nearly every day'	All samples (n=221)	None (n=114)	Mild (n=84)	Moderate to severe (n=23)	
Item 1 - Little interest…	40 (18.1)	7 (6.2)	15 (17.9)	18 (78.3)	<0.001
Item 2 – Feeling down…	19 (8.6)	0 (0)	6 (7.1)	13 (56.5)	<0.001
Item 3 – Trouble fallingasleep …	70 (31.7)	11 (9.6)	39 (46.5)	20 (87.0)	<0.001
Item 4 – Feeling tired…	58 (26.3)	5 (4.4)	34 (40.5)	19 (82.6)	<0.001
Item 5 – Poor appetite…	17 (7.7)	1 (0.9)	11 (13.1)	5 (21.7)	<0.001
Item 6 – Feeling bad about yourself…	13 (6.3)	0 (0)	4 (4.8)	9 (39.1)	<0.001
Item 7 – Trouble concentrating…	14 (6.3)	1 (0.9)	6 (7.2)	7 (30.4)	<0.001
Item 8 – Mowing or speaking slowly…	22 (10.0)	0 (0)	10 (11.9)	12 (52.2)	<0.001
Item 9 – Better off dead…*	21 (9.6)	1 (0.9)	12 (14.3)	8 (34.7)	<0.001

Post-hoc comparisons between individual groups revealed significant differences between all three groups on all items (p<0.001); *includes response categories 'several days', 'more than half the days', 'nearly every day'.

Table 3. Psychosocial variables of study participants with heart failure.

		Depressive symptomatology			p-value
M±SD (range)	All samples (n=221)	None (n=114)	Mild (n=84)	Moderate to severe (n=23)	
SF-12 MCS-12* (0-100)	51.4±10.2	56.2±7.3[a]	47.8±9.9[b]	40.2±9.2[c]	<0.001
SF-12 PCS-12* (0-100	38.2±10.1	41.4±9.7[a]	35.7±9.5	32.0±8.2	<0.001
EQ-5D-3L VAS score (1-100)	60.0±17.0	66.0 ±14.8[a]	56.8 ±15.8[b]	42.0±15.6[c]	<0.001
EQ-5D-3L index score° (0-1)	0.7±0.2	0.7±.02[a]	0.6±0.1[b]	0.5 ±0.1[c]	<0.001
SWLS (5-35)	25.6±5.6	27.1±4.5[a]	24.7±5.1	21.3±7.4	<0.001
SWLS ladder (1-10)	6.3±1.7	6.8±1.7[a]	5.9±1.4	5.6±2.1	<0.001

*SF-12 component scores are represented as *z* score (mean 50 + standard deviation 10); °EQ-5D-3L index score is calculated according to Slovenian population norms[33]; *post-hoc* comparisons between individual groups (significant difference was set at p<0.05): [a]*None* significantly different from *mild* and *moderate-to-severe*, [b]*Mild* significantly different from *none* and *moderate-to-severe*, [c]*Moderate-to-severe* significantly different from *none* and *mild*.; SF-12, the Short-Form 12 Health Survey; PCS, Physical Component Score; MCS, Mental Component Score; SWLS, the Satisfaction With Life Scale; EQ-5D-3L VAS, EQ-5D Visual Analog Scale.

Table 4. Correlation coefficients among psychosocial variables.

	PHQ-9 score	SF-12 MCS-12	SF-12 PCS-12	EQ-5D-3L VAS score	EQ-5D-3L index score	SWLS score
PHQ-9 score						
SF-12 MCS-12	-0.556**					
SF-12 PCS-12	-0.411**	0.097				
EQ-5D-3L VAS score	-0.423**	0.328**	0.425**			
EQ-5D-3L Index score	-0.563**	0.411**	0.493**	0.445**		
SWLS score	-0.351**	0.283**	0.245**	0.372**	0.202**	
SWLS ladder	-0.294**	0.176**	0.304**	0.472**	0.247**	0.499**

SF-12, Short-Form 12 Health Survey; PCS, Physical Component Score: MCS, Mental Component Score; SWLS, the Satisfaction With Life Scale; EQ-5D-3L VAS, EQ-5D Visual Analog Scale; **p<0.001.

lower side of the range (10% of the patients with HF at the time of study inclusion). This might be primarily explained by HF severity as research indicates increase in depression prevalence with NYHA functional class;[7] majority of participants in our study had NYHA class 1 or 2, and therefore lower symptom severity and degree of disability. Other possible explanations may have to do with stigma attached to mental health issues, resulting in social desirability bias.

Our study indicated moderate to large negative associations between depressive symptoms as measured by the PHQ-9 questionnaire, and both generic HRQoL questionnaires used (SF-12, EQ-5D-3L). This is consistent with the findings of Dickens and colleagues[45] reporting that association between depression and HRQoL in people with coronary heart disease is mostly significant, irrespective of the measure used. It is also worth mentioning that Al Sayah[46] and colleagues found that the reversed is true, as EQ-5D and SF-12 have been found to perform well in screening for depressive symptoms in chronic disease patients. What is more, de Jonge and colleagues[47] reported more severe depression being associated with greater impairment of HRQoL. Similarly, our results show that the level of self-reported disability on all EQ-5D-3L domains is the lowest in group without depressive symptomatology and the highest in group with moderate-to-severe depressive symptomatology level. Additionally, after adjustment for covariates, the negative association of depressive symptomatology levels (mild, moderate-to-severe as compared to none) and self-perceived health-related quality of life (as measured by EQ-5D-3L) remained statistically significant. Our findings are therefore in line with other studies demonstrating effect of depression on HRQoL,[48] independent of other biomedical risk factors. These findings can however be broadened by the obtained significant negative association of depressive symptomatology levels (mild, moderate-to- severe as compared to none) and general life satisfaction (as measured by SWLS). This relationship was as well present even when considering covariates and should prompt clinicians to consider using instruments for evaluation of psychosocial capacities even in those patients with HF who do not present with depressive symptoms.

In addition to non-depressed group generally showing better subjective indicators of health and well-being compared with the mild and moderate-to-severe group, our results also indicated between group differences in some physical indicators of health. Namely, NYHA class, number of comorbidities and functional capacity measured by the SMWT and handgrip strength; non-depressed group generally showed lower NYHA class, less comorbidities and better physical capacity compared to mild and moderate-to-severe group.

The cross-sectional nature of the study should be considered when interpreting results as the causality between the variables cannot be determined. Therefore, it is possible that lower HRQoL (or other variables, including HF) affect depressive symptom severity level; also, negative appraisals in depressed individuals (resulting in reporting health status more negatively) might affect worse self-reported HRQol levels. Due to the observational nature of the study, we acknowledge that the association between PHQ-9 score and psychosocial variables could be due to other factors that were not controlled in our study. Another limitation is related to the estimation of depression on the basis of elevated symptom severity from PHQ-9 question-

Table 5. Unadjusted regression analyses predicting self-perceived health-related quality of life (EQ-5D-3L index), global levels of health (EQ-5D-3L VAS) and general life satisfaction (SWLS score) from the severity of depressive symptomatology.

Predictors	Health-related quality of life (EQ-5D-3L index) β	Global levels of health (EQ-5D-3L VAS) β	General life satisfaction (SWLS score) β
Depressive symptomatology			
Mild *vs* none	-0.40***	-0.26*	-0.21*
Moderate-to-severe *vs* none	-0.40***	-0.43***	-0.32***
Total R^2	0.24	0.20	0.11
Corrected total R^2	0.23	0.19	0.10

R^2, variance; corrected total R^2, variance corrected for the number of predictors; β, standardized regression coefficient;*p<0.05; ***p<0.001.

Table 6. Regression analyses predicting self-perceived health-related quality of life (EQ-5D-3L index), global levels of health (EQ-5D-3L VAS) and general life satisfaction (SWLS score) from the severity of depressive symptomatology, adjusted for selected demographics and clinical covariates.

Predictors	Health-related quality of life (EQ-5D-3L index) β	Global levels of health (EQ-5D-3L VAS) β	General life satisfaction General life satisfaction (SWLS score) β
Depressive symptomatology			
Mild *vs* none	-0.28**	-0.19*	-0.23**
Moderate-to-severe *vs* none	-0.37***	-0.37***	-0.28**
Total R^2	0.47	0.28	0.23
Corrected total R^2	0.43	0.22	0.16

Adjusted for age, gender, education, SES, marital status, NYHA, BMI, number of comorbidities, SMWT; R^2, variance; corrected total R^2, variance corrected for the number of predictors; β, standardized regression coefficient;*p<0.05; ***p<0.001.

naire rather than a diagnostic interview[7]. Finally, we did not evaluate the potential effect of frailty; in patients with HF, no definite approach to diagnose frailty is accepted[50] and our database cannot meet any of the criteria commonly used in the clinical practice.

Conclusions

Our study assessed depressive symptoms rather than depressive disorder with the use of PHQ-9. Non-depressed group generally showed better subjective indicators of health and well-being compared with the group with mild and moderate-to-severe depressive symptomatology level. Significant between group differences were obtained in some physical indicators of health as well; compared to the other two groups, non-depressed group generally showed lower NYHA class, less comorbidities and better physical capacity. Our results also indicate significant association between depressive symptom severity levels and psychosocial variables (HRQoL, satisfaction with life), independent of other sociodemographic and clinical variables. Despite the clinically relevant depressive symptoms in patients with HF being recognized at a PHQ-9 cut-off score of 10,[25] our research indicates that even mild - clinically non-relevant - level of depressive symptom severity is associated with worse clinical and psychosocial status.

Contributions

NSK, JF, DO, conceptualization; NSK, DO, methodology and analysis; N. SK, ML, writing - original draft preparation; JF, ML, DO, writing - review and editing; ML, funding acquisition. All authors read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflicts of interest

The authors declare no conflict of interest.

Ethics approval and informed consent

The SOBOTA-HF study protocol was evaluated and approved by the National Medical Ethics Committee of the Republic of Slovenia (approval no. 0120-656/2016) and the study was performed in accordance with the Declaration of Helsinki. All participants gave their written informed consent for participation in the study prior to the study.

Funding

This research was funded by the Slovenian Research Agency, project ID J3-7405 Heart failure epidemiology in Slovenia: prevalence, hospitalizations and mortality, and by Roche Diagnostics International through research grant.

Acknowledgments

We would like to thank the SOBOTA-HF research team from General Hospital Murska Sobota and for this subanalysis we would especially like to acknowledge Klaudija Cimbola, RN.

References

1. Bui, AL, Horwich TB, Fonarow GC. Epidemiology and risk profile of heart failure. Nat Rev Cardiol 2011;8:30-41.
2. van Riet EE, Hoes AW, Wagenaar KP, Limburg A, Landman MA, Rutten FH. Epidemiology of heart failure: the prevalence of heart failure and ventricular dysfunction in older adults over time. A systematic review. Eur J Heart Fail 2016;18:242-52.
3. Ponikowski P, Voors AA, Anker SD, et al. Guidelines for the diagnosis and treatment of acute and chronic heart failure The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution. Eur J Heart Fail 2016;18:891-975.
4. Omersa D, Farkas J, Erzen I, Lainscak M. National trends in heart failure hospitalization rates in Slovenia 2004-2012. Eur J Heart Fail 2016;18:1321-8.
5. Ambrosy AP, Fonarow GC, Butler J, et al. The global health and economic burden of hospitalizations for heart failure: lessons learned from hospitalized heart failure registries. J Am Coll Cardiol 2014;63:1123-33.
6. Celano CM, Villegas AC, Albanese AM, Gaggin MD, Huffman JC. Depression and anxiety in heart failure: a review. Harv Rev Psychiatry 2018;26:175-84.
7. Rutledge T, Reis VA, Linke SE, Greenberg BH, Mills PJ. Depression in heart failure: a meta-analytic review of prevalence, intervention effects, and associations with clinical outcomes. J Am Coll Cardiol 2006;48:1527-37.
8. Lim GY, Tam WW, Lu Y, Ho CS, Zhang MW, Ho RC. Prevalence of depression in the community from 30 countries between 1994 and 2014. Sci Rep 2018;8:2861.
9. Daskalopoulou M, George J, Walters K, et al. Depression as a risk factor for the initial presentation of twelve cardiac, cerebrovascular, and peripheral arterial diseases: data linkage study of 1.9 million women and men. PLoS One 2016; 22:e0153838.
10. Song EK, Lennie TA, Moser DK. Depressive symptoms increase risk of rehospitalisation in heart failure patients with preserved systolic function. J Clin Nurs 2009;18:1871-7.
11. Frasure-Smith N, Lespérance F, Habra M, et al. Elevated depression symptoms predict long-term cardiovascular mortality in patients with atrial fibrillation and heart failure. Circulation 2009; 120:134-40.
12. Pelle AJ, Gidron YY, Szabó BM, Denollet J. Psychological predictors of prognosis in chronic heart failure. J Card Fail 2008;14:341-50.
13. Müller-Tasch T, Peters-Klimm F, Schellberg D, et al. Depression is a major determinant of quality of life in patients with chronic systolic heart failure in general practice. J Card Fail 2007;13:818-24.
14. Huffman JC, Smith FA, Blais MA, Beiser ME, Januzzi JL, Fricchione GL. Recognition and treatment of depression and anxiety in patients with acute myocardial infarction. Am J Cardiol 2006;98:319-24.
15. Lainscak M, Omersa D, Sedlar N, Anker SD, Farkas J. Heart failure prevalence in the general population: SOBOTA-HF study rationale and design. ESC Heart Fail 2019;6:1077-84.
16. Babor TF, Higgins-Biddle JC, Monteiro MG. AUDIT: The alcohol use disorders identification test: Guidelines for use in primary care (second edition). Geneva, World Health Organization; 2001.

17. Bradley KA, DeBenedetti AF, Volk RJ, Williams EC, Frank D, Kivlahan DR. AUDIT-C as a brief screen for alcohol misuse in primary care. Alcohol Clin Exp Res 2007;31:1208-17.
18. Demers C, McKelvie RS, Negassa A, Yusuf S. Reliability, validity, and responsiveness of the six-minute walk test in patients with heart failure. Am Heart J 2001;142:698-703.
19. ATS Statement: Guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002;166:1117.
20. Balashov K, Ehrmann Feldman D, Savard S, et al. Percent predicted value for the 6-minute walk test: using norm-referenced equations to characterize severity in persons with CHF. J Card Fail 2008;14:75-81.
21. Emami A, Saitoh M, Valentova M, et al. Comparison of sarcopenia and cachexia in men with chronic heart failure: results from the Studies Investigating Co-morbidities Aggravating Heart Failure (SICA-HF). Eur J Heart Fail 2018;20:1580-7.
22. Dodds RM, Syddall HE, Cooper R, et al. Grip strength across the life course: normative data from twelve british studies. PLoS One 2014;9:e113637.
23. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 2001;16:606-13.
24. Löwe B, Spitzer RL, Gräfe K, et al. Comparative validity of three screening questionnaires for DSM-IV depressive disorders and physicians' diagnoses. J Affect Disord 2004;78:131-40.
25. Hammash MH, Hall LA, Lennie TA, et al. Psychometrics of the PHQ-9 as a measure of depressive symptoms in patients with heart failure. Eur J Cardiovasc Nurs 2013;12: 446-53.
26. Ware J, Kosinski MM, Keller S. A 12-item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996;34:220-33.
27. Gandek B, Ware JE, Aaronson NK, et al. Cross-validation of item selection and scoring for the SF-12 Health Survey in nine countries: results from the IQOLA Project. J Clin Epidemiol 1998;51:1171-8.
28. Group EuroQol. EuroQol - a new facility for the measurement of health-related quality of life. Health Policy 1990;16:199-208.
29. Brooks R, Rabin R, De Charro F. The measurement and valuation of health status using EQ-5D: a European perspective: evidence from the Euroqol Biomed Research Programme. Dordrecht, Springer; 2013.
30. Boczor S, Daubmann A, Eisele M, Blozik E, Scherer M. Quality of life assessment in patients with heart failure: validity of the German version of the generic EQ-5D-5L™. BMC Public Health 2019;19:1464.
31. Ware JE, Snow KK, Kosinski MG. SF-36 health survey. Manual and interpretation guide. Boston, The Health Institute, New England Medical Center; 1993.
32. Müller-Nordhorn J, Roll S, Willich SN. Comparison of the short form (SF)-12 health status instrument with the SF-36 in patients with coronary heart disease. Heart 2004;90:523-7.
33. Prevolnik Rupel V, Srakar A, Rand K. Valuation of EQ-5D-3l health states in Slovenia: VAS based and TTO based value sets. Zdr Varst 2019;59:8-17.
34. Diener ED, Emmons RA, Larsen RJ, Griffin S. The Satisfaction with life scale. J Pers Assess 1985;49:71-5.
35. Pavot W, Diener E. Review of the Satisfaction with life scale. Psycol Assess 1993;5:164-72.
36. Meyer C, Rumpf HJ, Hapke U, John U. Impact of psychiatric disorders in the general population: satisfaction with life and the influence of comorbidity and disorder duration. Soc Psychiatry Psychiatr Epidemiol 2004;39:435-41.
37. Rosengren L, Jonasson SB, Brogårdh C, Lexell J. Psychometric properties of the Satisfaction with life scale in Parkinson's disease. Acta Neurol Scand 2015;132:164-70.
38. Serafini G, Pompili M, Innamorati M, et al. The impact of anxiety, depression, and suicidality on quality of life and functional status of patients with congestive heart failure and hypertension: an observational cross-sectional study. Prim Care Companion J Clin Psychiatry 2010;12:pcc09m00916.
39. Graham JW. Missing data analysis: making it work in the real world. Annu Rev Psychol 2009;60:549-76.
40. Evangelista LS, Moser DK, Westlake C, Hamilton MA, Fonarow GC, Dracup C. Impact of obesity on quality of life and depression in patients with heart failure. Eur J Heart Fail 2006;8:750-5.
41. Nesbitt T, Doctorvaladan S, Southard J, et al. Correlates of quality of life in rural patients with heart failure. Circ Heart Fail 2014;7: 882-7.
42. Peters-Klimm F, Kunz CU, Laux G, Szecsenyi J, Müller-Tasch T. Patient- and provider-related determinants of generic and specific health-related quality of life of patients with chronic systolic heart failure in primary care: a cross-sectional study. Health Qual Life Outcomes 2010;8:98.
43. Mårtensson J, Dracup K, Canary C, Fridlund B. Living with heart failure: depression and quality of life in patients and spouses. J Heart Lung Transplant 2003;22:460-67.
44. Cohen J. A power primer. Psychol Bull 1992;112:155-9.
45. Dickens C, Cherrington A, McGowan L. Depression and health-related quality of life in people with coronary heart disease: a systematic review. Eur J Cardiovasc Nurs 2012;11:265-75.
46. Al Sayah F, Ohinmaa J, Johnson JA. Screening for anxiety and depressive symptoms in type 2 diabetes using patient-reported outcome measures: comparative performance of the EQ-5D-5L and SF-12v2. MDM Policy Pract 2018;3:2381468318799361.
47. de Jonge P, Spijkerman TA, van den Brink RHS, Ormel J. Depression after myocardial infarction is a risk factor for declining health-related quality of life and increased disability and cardiac complaints at 12 months. Heart 2006;92:32-9.
48. Volz A, Schmid JP, Zwahlen M, Kohls S, Saner H, Barth J. Predictors of readmission and health-related quality of life in patients with chronic heart failure: a comparison of different psychosocial aspects. J Behav Med 2011;34:13-22.
49. Giannitsi S, Bougiakli M, Bechlioulis A, Kotsia A, Michalis LK, Naka KK. 6-minute walking test: a useful tool in the management of heart failure patients. Ther Adv Cardiovasc Dis 2019;13:1 753944719870084.
50. Vitale C, Jankowska E, Hill L, et al. Heart Failure Association/European Society of Cardiology position paper on frailty in patients with heart failure. Eur J Heart Fail 2019;21:1299-305.