

RESEARCH ARTICLE

Relationship between free fatty acids, body mass index and depressive symptoms in patients with chronic heart failure

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Abstract

Aim: To explore the prevalence of depressive symptoms among patients with chronic heart failure (CHF) and analyse the relationship between free fatty acids (FFAs), body mass index (BMI) and depressive symptoms among patients with CHF.

Design: A cross-sectional study.

Methods: Questionnaires were distributed to 200 patients with CHF in the department of Cardiology at a tertiary first-class hospital in Shandong province. A total of 195 hospitalized patients completed the survey. Data collected from February 2017–November 2017 were analysed by using Pearson's correlation and multiple linear regression. The depressive status of the patients was assessed by the Zung Self-rating Depression Scale (SDS), and the relationships between FFA, BMI and depressive symptoms were analysed using SPSS 20.0.

Results: The results showed that 71.28% CHF patients have depressive symptoms. The serum FFA level was significantly higher in CHF patients with depressive symptoms than those without depressive symptoms ($p = .003$), and FFA level was significantly positively correlated with the SDS score ($r = .242$, $p = .001$). The differences in SDS scores were statistically significant between two different BMI groups ($p < .01$), and BMI was negatively correlated with the SDS score ($r = -.139$, $p = .040$). Regression analysis showed that high FFAs ($\beta = 0.184$, $p = .009$) and low BMI ($\beta = -0.116$, $p = .049$) were risk factors for depressive symptoms in CHF patients. Gender, age, FFA and BMI were associated with depressive symptoms, accounting for 7.1% of the variance in depressive symptoms.

Conclusions: The prevalence of depressive symptoms in CHF patients is very high, and high FFAs and low BMI are risk factors for depressive symptoms. Targeted interventions to strengthen nutritional support in CHF patients may be benefit to improve depression-related outcomes.

KEYWORDS

body mass index, chronic heart failure, depressive symptoms, free fatty acids, psychological nursing

Hua Yang and Yan Li contributed equally to this work, they are co-lead authors.

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1 | INTRODUCTION

The chronic heart failure (CHF) is a terminal stage of cardiovascular disease, with various causes and a complicated pathogenesis. Although improvement of medical level had prolonged the survival of patients with cardiovascular disease, most patients would eventually develop into CHF. With ageing population of China, the incidence of chronic diseases such as coronary heart disease, hypertension and diabetes is rising, which further causes the epidemic of heart failure and a heavy social and public health economic burden. The prevalence of heart failure in China has been increasing to about 4.5 million patients. In 2000, the prevalence of CHF in the population of 35–74 years old was about 0.9% (Lichtman et al., 2014). However, patients with CHF have a high mortality rate. The 5-year mortality rate in the United States is 40%–65% (Hobbs et al., 2007), and the annual mortality rate in China is 19.5% (Li, 2019). In recent years, cardiovascular disease and mental and psychological problems have attracted more and more attention.

2 | BACKGROUND

With the development of modern medicine, the hospitalization and mortality rates for CHF patients have declined; currently, the 5-year mortality rate is still close to 50%. Depressive symptoms not only lead to poorer quality of life in patients with CHF, but also are associated with higher mortality and hospitalization rate. However, few studies have reported the correlations between free fatty acids (FFAs), as well as body mass index (BMI), and depressive symptoms in patients with CHF. One study showed that 21.5% of CHF patients had depressive symptoms (Rutledge et al., 2006). Depressive symptoms not only worsen the patients' life quality but also are related to high mortality and hospitalization rates (Ramos et al., 2016). Treating the depressive symptoms can improve both the quality of life and the long-term prognosis of patients. FFAs are the main source of energy in the human body. Under normal conditions, fatty acids provide 60%–70% of energy, and the rest is supplied by glucose (Chen et al., 2014). Therefore, under normal circumstances, the heart prioritizes the use of FFAs via beta oxidation. Serum level of FFAs in CHF patients was found to be higher than that in healthy subjects (Chen et al., 2014). The level of serum FFAs is a risk factor for the survival of patients with heart failure and has predictive value for the outcome (Wei et al., 2017). One study found that plasma FFA levels were elevated using intralipid plus heparin infusion, impaired cardiac structure and function (Han et al., 2018). Most studies have supported that BMI and depressive symptoms were correlated. In addition, different BMI categories (divided into low weight, normal weight, overweight and obesity) had a significant u-shaped relationship with depression (de Wit et al., 2009). However, whether FFAs and BMI have an effect on depressive symptoms in patients with CHF has not yet been studied. In this study, we aimed to analyse the relationship between FFAs, as well as BMI, and depressive symptoms in CHF patients.

3 | METHODS

3.1 | Aim

To explore the prevalence of depressive symptoms among patients with CHF and analyse the relationship between FFAs, BMI and depressive symptoms among patients with CHF.

3.2 | Design

A cross-sectional study.

3.3 | Participants

The study was a cross-sectional study which conducted using field questionnaires. A total of 195 patients with CHF who were admitted to the Department of Cardiology at a tertiary first-class hospital in Shandong province from February 2017–November 2017 were screened. Specifically, the selected criterion was: (a) adults over 18 years; (b) patients who were diagnosed with CHF; (c) patients with decompensation of cardiac function symptoms or signs; and (d) New York heart association (NYHA) class II–IV. The exclusion criteria were: (a) patients with severe acute diseases such as acute myocardial infarction, acute pulmonary embolism and acute attack of chronic obstructive pulmonary disease; (b) patients with serious diseases such as malignant tumours, diseases of the blood system, and severe liver and kidney dysfunction that may affect the patients' psychological state; and (c) patients with mental disorders, such as consciousness disorders, communication disorders and dysgnosia.

3.4 | Data collection

Data were collected from February 2017–November 2017 in the department of Cardiology at a tertiary first-class hospital in Shandong province. Those with CHF who met the criterion completed the Zung self-rating depression scale (SDS) by themselves. For patients with a low educational level, advanced age, poor vision or other conditions that prevented them from completing the questionnaire independently, researchers helped them complete the questionnaire by asking questions and taking notes. The formula of the sample size of the present prevalence rate is as follows: $n = \frac{z_{\alpha}^2 \times pq}{d^2}$ (p is the present prevalence rate, $q = 1 - p$, d is the allowable error, generally take $0.1p$, Z_{α} is the significance test statistic, $\alpha = 0.05$, $Z_{\alpha} = 1.96$, then the calculation formula is $n = 400 \times \frac{pq}{d^2}$). After a large number of literature reviews, the prevalence of depression in CHF patients is about 70%. The minimum sample size of this study is 171.43. Considering no response and questionnaire loss, the sample size was increased up to 200 participants. A total of 200 questionnaires were distributed, and 195 effective questionnaires were recovered, with an effective response rate of 97.5%.

3.5 | Ethical considerations

The study was approved by the ethics committee of Qilu Hospital of Shandong University (grant number: KYLL-2017-110), and all patients gave their written informed consent.

3.6 | Data analysis

Data analysis was performed using SPSS version 20.0 (SPSS Inc.). Categorical variables are expressed by frequency and percentage, while continuous variables are expressed by mean and standard deviation. Normally distributed data were analysed using *t* test, one-way ANOVA and Pearson correlation analysis. Non-parametric tests and Spearman correlation analysis were used for data that did not satisfy the normal distribution. Depression score was used as the dependent variable, and gender, age, FFA, BMI, NYHA functional class, RDW, FBG, K⁺, NT-proBNP logarithm, Hcy, LVEF (%), LVEDD (mm) and TC with statistical significance were used as independent variables in the univariate analysis. Pearson correlation analysis was used to explore the association between FFAs, BMI and depressive symptom. Multiple stepwise regression analysis was conducted to analyse the factors influencing depressive symptoms among CHF hospitalized patients. A value of $p < .05$ was considered statistically significant.

3.7 | Validity and reliability

The demographic characteristics included the patient's age, sex, New York cardiac function scale, BMI, blood glucose (GLU), homocysteine (Hcy), FFAs, left ventricular ejection fraction (LVEF), red blood cell distribution width (RDW), medical history and other indicators. The patients' fasting blood was extracted on the morning of the second day after admission, and indicators such as Hcy, FFA, RDW and GLU were tested. Routine cardiac ultrasonography was performed in our hospital within 3 days after admission, and LVEF was measured by the biplane Simpson's method. NYHA score was determined via medical chart documentation. According to the 2002 China Obesity Working Group, the data of 21 provinces and cities in China were summarized and the Guidelines for Prevention and Control of Overweight and Obesity in Chinese Adults were issued by the Department of Disease Control of the Ministry of Health. A BMI between 18.5–23.9 kg/m² was defined as normal weight, 24.0–27.9 kg/m² as overweight and greater than or equal to 28.0 kg/m² as obese.

Depressive symptoms were measured with the SDS (Duan & Sheng, 2012). The SDS includes 10 items that use positive words required to be scored in reverse order, while 10 items use negative words which are graded rated from 1–4. Depressive symptoms index = the cumulative score of each item $\times 1.25$. The depressive symptoms index is directly proportional to the degree of depressive symptoms, and the higher the index is, the heavier the depressive

symptoms are. According to Chinese norms, SDS standard score below 50 is generally defined as free of depression, and a standard score above 50 (including 50) is defined as depression. Mild depressive symptoms disorder ranged from 50–59, moderate depressive symptoms disorder ranged from 60–69, and severe depressive symptoms disorder ranged from 70 to above. In this study, the Cronbach's α of the SDS was 0.75.

4 | RESULTS

4.1 | Socio-demographic characteristics

A total of 195 hospitalized patients with CHF who met our criteria were investigated, including 121 males (62.1%) and 74 females (37.9%), aged between 21–88 years old, including 139 patients (71.28%) with depressive symptoms.

4.2 | Single factor analysis of influencing factors

4.2.1 | Analysis of qualitative data

Table 1 shows the baseline characteristics of the study population, and most of clinical characteristics differ across the three categories. The SDS scores of patients were different between different gender, age and BMI groups ($p = .018$, $p = .020$, $p = .001$, respectively); among these groups, the overweight group had the lowest scores among the three groups. Female patients had a higher depression score than male patients, indicating that females were more prone to depressive symptoms. In addition, elderly patients over 60 years old had higher depression scores than those under 60 years old, indicating that older patients were more prone to depressive symptoms. Interestingly, the overweight group had lower scores than the normal weight group and the obesity group, indicating that patients with a BMI between 24.0–27.9 kg/m² had a lower depressive symptoms risk (Table 1).

4.2.2 | Analysis of quantitative data

The influencing factors between patients with and without depressive symptoms

Normally distributed data (FFA, LVEF, blood glucose) were analysed with a *t* test, while non-normally distributed data (heart function grade, RDW, Hcy) were analysed using a non-parametric *z* test (FFAs and grade of cardiac function, LVEF, RDW, blood sugar, Hcy). The results showed that the combined FFA level was markedly higher in depressive symptoms patients than in patients without depressive symptoms; the difference was statistically significant ($p = .003$). However, there was no significant difference in the other indicators ($p > .05$). These results indicated that depressive symptoms are positively correlated with FFAs in patients with CHF (Table 2).

Value	Number	Percentage	SDS	t or F value	p value
Gender					
Male	121	62.1	53.19 ± 8.71	-2.394	.018 [†]
Female	74	37.9	56.37 ± 9.43		
Age					
<60	69	35.4	52.36 ± 9.24	-2.346	.020 [†]
≥60	126	64.6	55.52 ± 8.86		
Hypertension					
Yes	104	53.3	54.24 ± 8.44	0.253	.800
No	91	46.7	54.57 ± 9.84		
Alcohol					
Yes	75	38.5	53.63 ± 8.94	53.63	8.94
No	120	61.5	54.87 ± 9.20		
BMI grading					
Normal weight	87	44.6	56.85 ± 8.95	7.706	.001 ^{**}
Overweight	77	39.5	51.46 ± 8.91		
Obese	31	15.9	54.80 ± 8.03		
Diabetes history					
Yes	58	29.7	55.06 ± 9.52	-0.665	.507
No	137	70.3	54.12 ± 8.94		
CHD history					
Yes	98	50.3	54.99 ± 8.69	-0.909	.364
No	97	49.7	53.80 ± 9.51		
AF history					
Yes	56	28.7	55.18 ± 9.68	0.760	.448
No	139	71.3	54.08 ± 8.87		
Smoking history					
Yes	76	39.0	54.84 ± 8.76	0.556	.579
No	119	61.0	54.11 ± 9.34		
NYHA grading					
Grade II	31	15.9	55.89 ± 9.52	0.574	.564
Grade III	109	55.9	53.91 ± 8.65		
Grade IV	55	28.2	54.52 ± 9.79		
LVEF					
<40%	133	68.2	54.25 ± 9.30	1.346	.263
40%-50%	26	13.3	51.44 ± 13.67		
≥50%	36	18.5	55.56 ± 8.69		

Abbreviations: AF, atrial fibrillation; BMI, body mass index; CHD, coronary heart disease; NYHA, New York Heart Association.

[†] $p < .05$, ^{**} $p < .01$.

Correlation coefficients of study variables

Pearson correlation analysis was used for normally distributed data such as age, FFA, BMI; otherwise, Spearman's correlation analysis (RDW, Hcy) was used. The results showed that the SDS score was positively correlated with gender ($r = .167$, $p = .018$) and age ($r = .141$, $p = .046$) and FFAs ($r = .242$, $p = .001$) and negatively correlated with BMI ($r = -.139$, $p = .040$), which was consistent

TABLE 1 General information of patients ($N = 195$)

with the results of the scatter plot (Table 3; Figures 1 and 2). There was no significant correlation between the SDS score and NYHA functional class, RDW, GLU, K^+ , NT-proBNP logarithm, Hcy, LVEF (%), LVEDD (mm), TC ($r = -.065$, $p = .366$; $r = .075$, $p = .290$; $r = .055$, $p = .435$; $r = -.075$, $p = .302$; $r = .034$, $p = .638$; $r = .035$, $p = .623$; $r = .050$, $p = .479$; $r = .035$, $p = .622$; $r = -.102$, $p = .149$; Table 3).

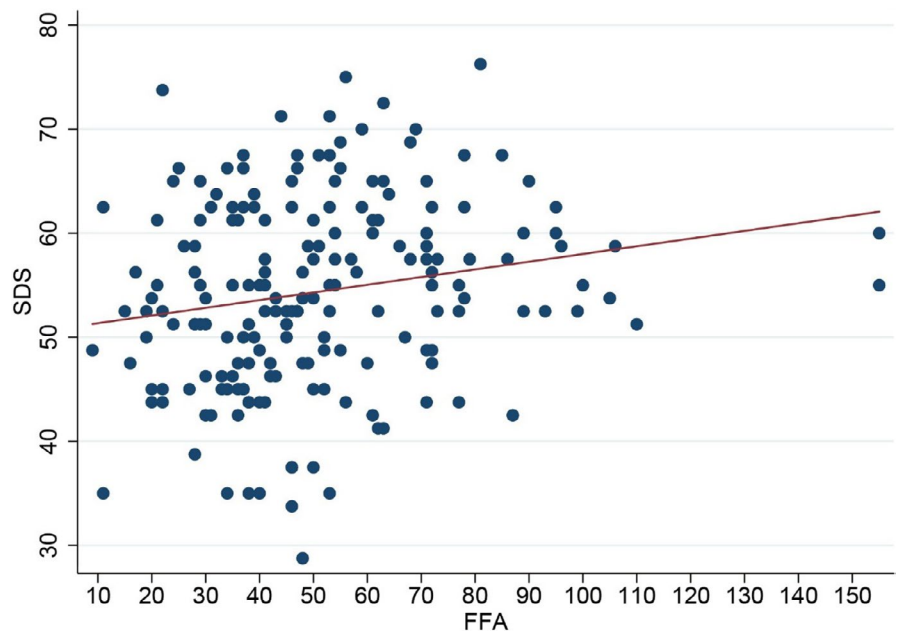
TABLE 2 Comparison of disease-related factors between patients with or without depression (N = 195)

Item	With depression	Without depression	t or z value	p
Number	139	56		
FFA (μmol/L)	54.55 ± 25.37	42.93 ± 16.57	-2.959	.003*
NYHA functional class	3.08 ± 0.66	3.23 ± 0.63	-1.462	.144
LVEF (%)	35.12 ± 13.85	35.29 ± 15.61	-0.487	.626
RDW	14.06 ± 1.86	13.88 ± 2.02	-0.877	.372
GLU (mmol/L)	5.68 ± 2.04	5.75 ± 1.94	-0.634	.549
Hcy	19.90 ± 6.69	18.39 ± 5.4	-1.412	.142

Abbreviations: BMI, body mass index; FFA, free fatty acid; GLU, blood glucose; HCY, homocysteine; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; RDW, red cell distribution width.

*p < .01.

FIGURE 1 Scatter plots of free fatty acid (FFA) and self-rating depression scale (SDS)



The correlation between NYHA grade and SDS

As shown in Figure 3, there were significant differences in SDS scores between the three obesity groups with different cardiac functions ($p < .01$). In the obesity group, the patients whose heart function score was grade II (NYHA grade) had higher SDS depression scores than patients with grade III and IV. Therefore, the NYHA grade and SDS were negatively correlated in the obesity group. There were significant differences in SDS scores between the different cardiac functional groups.

4.3 | Multivariate regression analysis of depression among patients with CHF

The SDS evaluation score of CHF patients was used as the dependent variable, and the factors with statistical significance in the univariate analysis were used as the independent variable. During the analysis, the SDS evaluation score, FFA and BMI were all measured

values, and gender was the categorical variable, with male encoding 1 and female encoding 2. The results showed that FFAs ($\beta = 0.184, p = .009$) and BMI ($\beta = -0.116, p = .049$), suggesting that high FFAs and low BMI are risk factors for depressive symptoms among patients with heart failure (see Table 4).

5 | DISCUSSION

To our knowledge, this is the first study to report the relationship between CHF and FFAs and BMI. The incidence of depression among patients with CHF is high; high FFAs and low BMI are risk factors for depressive symptoms among patients with CHF.

The current study found that 71.28% of HF patients had depressive symptoms. However, it was higher than that (50.7%) reported by Bhatt et al. (2016). One possible explanation is that this study sampled hospitalized patients, whereas Bhatt appears to have sampled and followed outpatients; in addition, the variation in prevalence be

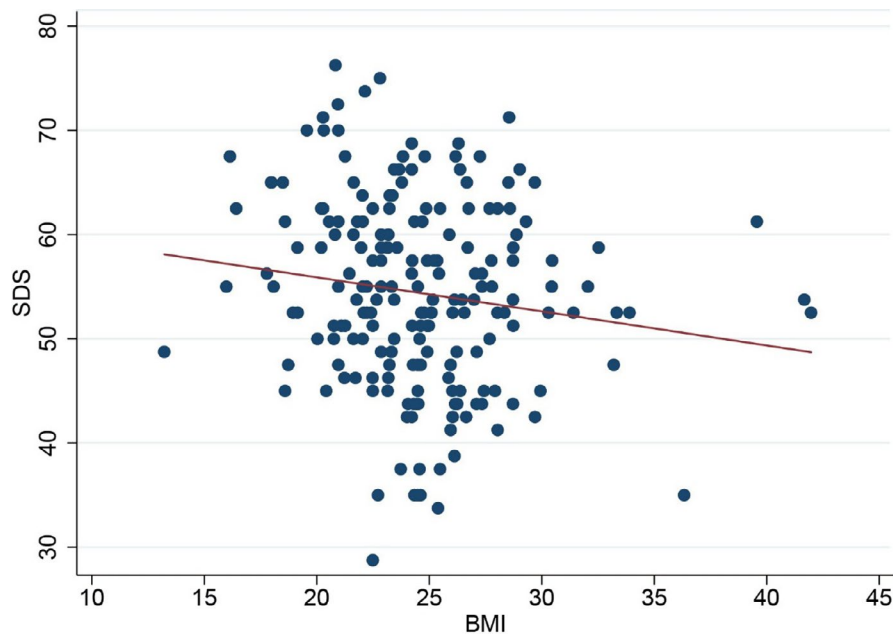


FIGURE 2 Scatter plots of body mass index (BMI) and self-rating depression scale (SDS)

TABLE 3 Correlation between SDS standard score and disease-related factors

Item	SDS	
	Regression coefficient	<i>p</i>
Gender	0.167	.018
Age	0.141	.046
BMI (kg/m ²)	-0.139	.040
FFA (μmol/L)	0.242	.001
NYHA functional class	-0.065	.366
RDW	0.075	.290
GLU (mmol/L)	0.055	.435
K ⁺	-0.075	.302
NT-proBNP logarithm	0.034	.638
Hcy	0.035	.623
LVEF (%)	0.050	.479
LVEDD (mm)	0.035	.622
TC	-0.102	.149

Abbreviations: BMI, body mass index; FFA, free fatty acid; GLU, blood glucose; HCY, homocysteine; NYHA, New York Heart Association; RDW, red cell distribution width; TC, Total cholesterol.

likely to attribute to the different screening tools and self-perception (Chen et al., 2020). Since depressive symptoms contribute to the increase in patients' hospitalization rates, readmissions and mortality, and poor life quality, it is imported to recognize and control the depressive symptoms in patients with heart failure (Gathright et al., 2017; Morys et al., 2016; Xu et al., 2018).

Studies have showed that depressive symptoms can be regarded as a risk factor predicting cardiovascular adverse events (Ehlert et al., 2001; Rutledge et al., 2006). This study included 195 patients with CHF. They found that the incidence of depressive

symptoms in these patients was 139 (71.28%). The results showed that depressive symptoms incidence was very high in patients with CHF, which deserved the attention of clinicians and nurses. According to statistics, coronary heart disease, rheumatic heart disease and hypertension accounted for 45.6%, 18.6% and 12.9% of the causes of heart failure, respectively, in China. And death caused by heart failure was mainly pump failure (59%), sudden death (13%) and arrhythmia (13%) and cryptogenic (15%; Duan & Sheng, 2012). Women with CHF were more likely to be depressed than men. Previous studies have shown that the incidence of depressive symptoms in female was relatively high. The exact cause of the difference in the incidence of mood disorders between men and women is currently unclear (Peng et al., 2012). The main explanations may be related to women's endocrine factors, physiological characteristics, social status, education level, family status and other social psychological factors. Although sex and age had a relationship with depressive symptoms, these factors cannot be manipulated.

A study found that plasma FFA levels, which were elevated using intralipid plus heparin infusion, impaired cardiac structure and function (Han et al., 2018). The increase in FFAs was related to the poor prognosis of patients with heart failure and may be a response to disordered energy utilization in patients with heart failure. The increase in FFAs results in lipid toxicity in the myocardium, leading to the vicious circle that accelerates the deterioration of cardiac function in patients with heart failure (Bianchi, 2020). Studies have shown that inhibition of fat decomposition in the short term reduces serum FFA levels, which aggravates cardiac dysfunction. The reduction in oxidative metabolism did not influence the work efficiency of the heart in healthy people. Interestingly, oxidative metabolism was not downregulated in heart failure patients, but the work efficiency was reduced, suggesting that heart failure was more dependent on available FFAs (Tuunanen et al., 2006). Although the relationship between FFAs and risk factors including hypertension,

FIGURE 3 The correlation between New York heart association (NYHA) grade and self-rating depression scale (SDS)

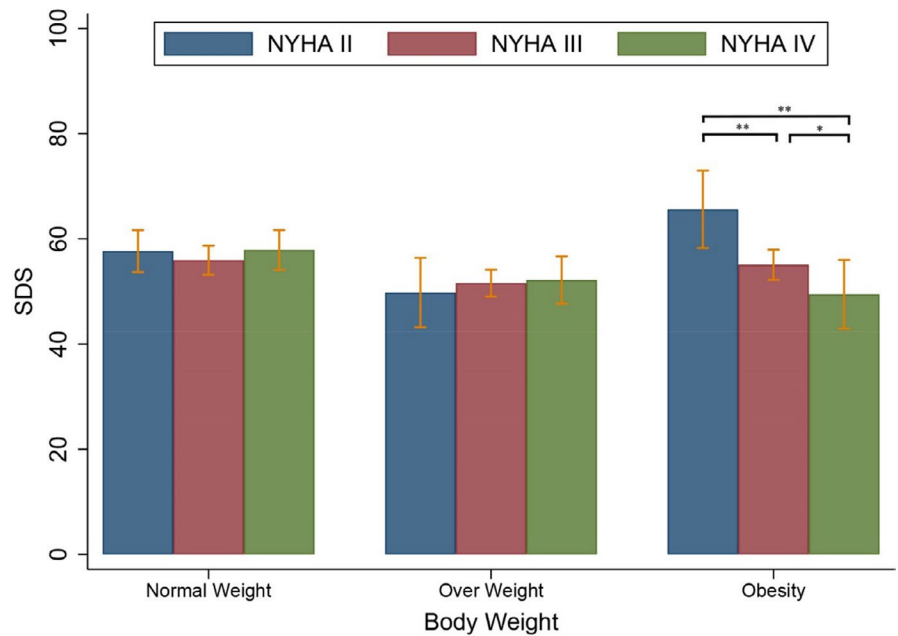


TABLE 4 Multiple regression analysis of SDS in patients with CHF

Variable	B	SE	β	t value	p value	95.0% confidence interval	
						Lower limit	Upper limit
Gender	2.550	1.328	0.136	1.920	.056	-0.070	5.170
Age	0.063	0.045	0.098	1.381	.169	-0.027	0.152
FFA	0.071	0.027	0.184	2.659	.009	0.018	0.123
BMI	-0.257	0.155	-0.116	-1.657	.049	-0.563	0.049

Abbreviations: BMI, body mass index; FFA, free fatty acid; SE, standard error. Adjust R² = .071.

atrial fibrillation, diabetes mellitus and CHD for HF had seldom been reported (Zhu et al., 2018), our study found that the level of FFAs in heart failure patients with depression was significantly higher than that in heart failure patients without depressive symptoms. In addition, the level of FFAs was positively correlated with the degree of depressive symptoms. To that extent, the level of FFAs may be a risk factor for depressive symptoms among patients with heart failure. We found that the lipid toxicity caused by high FFA levels may have an effect on the mental state of patients, suggesting that reducing FFA levels may be an effective method to improve the depressive symptoms status of patients with heart failure.

This study found that BMI and SDS were negatively correlated in patients with HF, suggesting that low BMI may be correlated with depression in patients with CHF and that overweight has a protective effect against depression in patients with CHF. A study of 178 patients with HF found that overweight and obese patients had a lower depressive symptoms risk (Meng et al., 2012). Another study of 447 hospitalized patients with type 2 diabetes found that BMI was an independent risk factor for depressive symptoms among type 2 diabetes patients (Yang, 2011). Additionally, a study involving 386 patients with acute coronary syndrome also found that low weight and normal weight were influencing

factors of depressive symptoms among the studied patients (Chen et al., 2013). A study of 580 coronary heart disease patients obtained the same conclusion and found that the depressive symptoms status of overweight and obese patients was significantly lower than that of low-weight and normal-weight patients (Lu et al., 2017). Patients were divided into low weight, normal weight, overweight and obesity group according to BMI. The results showed that the SDS scores of different BMI groups were statistically significant ($p < .01$). Multiple regression analysis showed that BMI was a risk factor for depressive symptoms among patients with CHF, suggesting that we may reduce the degree of depressive symptoms by modifying BMI. Most studies have supported that BMI and depressive symptoms are correlated. Wit et al. found that different BMI categories (divided into low weight, normal weight, overweight and obesity) had a significant u-shaped relationship with depressive symptoms (Wit et al., 2009). At present, no studies have clearly investigated the relationship between BMI and depressive symptoms among patients with CHF. Considering the influence of the “obesity paradox” on the prognosis of patients with heart failure, we believed that it was necessary to further study the relationship between BMI and depressive symptoms among patients with CHF (Baena-Diez et al., 2010; Mosterd

et al., 2001). At present, the mechanism of the obesity paradox is still unclear, and some researchers have suggested that it may be related to the energy metabolism of patients (Chase et al., 2014). Similar to previous studies, we found that the depressive symptoms of patients with heart failure conformed to the "obesity paradox". Therefore, we proposed the hypothesis that compared with heart failure patients with a low BMI, heart failure patients with a high BMI had a relatively low risk of depressive symptoms or mild depressive symptoms. Previous studies found that compared with normal and low-weight patients with CHF, overweight and obese patients with CHF had better heart function. Part of that may be due to the relative increased resistance to inflammatory factors in circulation, decreased B-type natriuretic peptide concentration and higher secretion of plasma apelin levels among the overweight and obese patients with CHF (Berger et al., 2002; de Denus et al., 2004; Horwich et al., 2006; Oreopoulos et al., 2008; Scheen, 2004; Zheng et al., 2008). Therefore, it can be inferred that patients with CHF of a low BMI are prone to poor heart function, severe heart failure symptoms, depressed mood and severe depressive symptoms (Meng et al., 2012).

6 | CONCLUSIONS

FFAs are positively associated with the SDS score, and BMI is negatively associated with the SDS score. Therefore, psychological interventions ahead of time and strengthen nutrition in patients with CHF may be benefit to improve depressive symptoms.

7 | STUDY LIMITATIONS

This study reports the correlation between FFAs, BMI and depression in patients with CHF; thus, we performed our research by SDS. The result we found would optimize the management of patients with heart failure to benefit more. This study has several limitations that should be considered. First, our study design was a cross-sectional study which was conducted using field questionnaires; therefore, cause-and-effect relationships could not be suggested in our analysis. Second, the patients were from a large general hospital in China with NYHA class II–IV, and the sample size was not large enough, which reduced the representativeness of the research. Third, the depressive symptoms were based on patients' self-reports and may affect the measurements' precision.

ACKNOWLEDGMENTS

The authors would like to acknowledge the tertiary first-class hospital in Shandong province. We also thank patients who participated in this study.

CONFLICT OF INTEREST

The authors declare no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

CL designed the study and drafted the manuscript. HY participated in the data collection and analysed the data. YL analysed the data and revised the draft manuscript. XS critically revised the manuscript for methodological and intellectual content. All authors read and approved the final version of the manuscript.

DATA AVAILABILITY STATEMENT

The data sets used for the current study are available from the corresponding author on reasonable request.

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How to cite this article: Yang H, Li Y, Su X, Li C. Relationship between free fatty acids, body mass index and depressive symptoms in patients with chronic heart failure. *Nurs Open*. 2021;8:2877–2885. <https://doi.org/10.1002/nop2.877>