Original Article

Impact of citrus fruit intake on the mental health of patients with chronic heart failure

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Abstract

Backgrounds: The full impact of the intake of citrus fruits on the risk of depression in individuals with chronic heart failure (HF) has been unknown. Here, we examined the associations between the estimated habitual intakes of citrus fruits and depressive symptoms in patients with chronic HF.

Methods: We enrolled 150 stable outpatients with chronic HF who had a history of worsening HF. To assess the patients' daily dietary patterns, we used a brief self-administered diet-history questionnaire (BDHQ) to calculate the daily consumption of foods and nutrients. To assess the patients' mental state, we used a nine-item Patient Health Questionnaire (PHQ-9).

Results: Twelve patients (8%) were identified as having moderate-to-severe depression (PHQ-9 score ≥10). The patients with PHQ-9 ≥10 had lower daily intakes of citrus fruits compared to those with no or mild depressive symptoms (PHQ-9 <10). The daily intakes of various antioxidants, including vitamin C, β-carotene, and β-cryptoxanthin, all of which are abundant in citrus fruits, were reduced in the patients with PHQ-9 ≥10, accompanied by higher serum levels of 8-isoprostane (an oxidative stress marker). A multivariate logistic regression analysis using forward selection showed that a lowered daily intake of citrus fruits was an independent predictor of the comorbidity of moderate-to-severe depression in patients with chronic HF, after adjustment for age, gender, and the hemoglobin value.

Conclusions: A lower daily consumption of citrus fruits was associated with higher prevalence of depression in patients with chronic HF. Our findings support the hypothesis that a daily

consumption of citrus fruits has a beneficial effect on the prevention and treatment of depression in chronic HF patients.

Keywords: Antioxidant, Chronic heart failure, Citrus fruits, Depression, Oxidative stress, Vitamin C, β-carotene, β-cryptoxanthin

Introduction

Chronic heart failure (HF) is a complex progressive clinical syndrome that is affected by multiple systemic disorders such as anemia, renal failure, and skeletal muscle abnormalities after the initial onset of acute HF. Among the non-cardiac comorbidities, depression is known as a major contributor to the progression of HF, as it independently increases the risk of all-cause death [1, 2]. Individuals with chronic HF have been shown to have a higher prevalence of depression than the general population [3], and healthcare providers have recognized the importance of their patients' mental health in HF management. However, the mechanisms that underlie the susceptibility of chronic HF patients to depression are not known.

It has been demonstrated that systemic oxidative stress characterized by lowered antioxidant defense capacity and/or increased reactive oxygen species (ROS) is related to depression in a general population [4]. In chronic HF, systemic oxidative stress is also reported to play a crucial role in disease progression [5-7]. Previous studies have shown that several circulating oxidative stress markers may predict adverse clinical events (including all-cause death and hospitalization) in patients with chronic HF [8, 9]. Accordingly, a disturbed redox balance may be related to the increased rate of the comorbidity of depression in chronic HF patients.

Despite recent advances in pharmacological and non-pharmacological treatment, the mortality rate of chronic HF patients is still high, and thus the importance of diet and exercise therapy has been reconsidered for the prevention and treatment of HF. In particular, patients' dietary

patterns in daily life are important, and a higher dietary intake (or blood concentration) of vitamin C, carotenoids, and α-tocopherol (as markers of fruits and vegetables) is associated with a reduced risk of cardiovascular disease, cancer, and all-cause mortality [10].

Previous studies have shown that a decreased intake of fruits, which are rich sources of antioxidants, is associated with depressive symptoms in general populations [11, 12]. A systematic review revealed that fruits have beneficial effects on mental health [13], and a meta-analysis demonstrated that every 100-g increase in the daily consumption of fruits is associated with a 3% reduced risk of depression [14]. Among the many commercially available types of fruits, citrus fruits contain various antioxidants, such as vitamin C, β-carotene, and β-cryptoxanthin, and are thus a good candidate for the prevention of depression [13, 15]. However, the influence of the daily consumption of fruits (including citrus fruits) on mental health in patients with chronic HF remains unclear.

We conducted the present study to determine whether daily dietary patterns, including fruit intake, might be associated with the depressed mental state in patients with chronic HF. To assess the patients' daily dietary patterns, we used a brief self-administered diet-history questionnaire (BDHQ) to calculate the daily consumption of foods and nutrients. To assess the patients' mental state, we used a nine-item Patient Health Questionnaire (PHQ-9). We also measured the patients' serum levels of 8-isoprostane to evaluate their systemic oxidative stress.

Methods

Study design

This was a multi-center, prospective, observational study to investigate the effects of dietary patterns on clinical outcomes in patients with chronic HF, and thus some of the data used herein were obtained from the same patients whose data were published previously but in a different context [16-18]. The study was approved by the ethics committees of Hokkaido University Hospital (approval no. 012-0224) and the other nine participating hospitals: Hakodate National Hospital, Hikone Municipal Hospital, Kitami Red Cross Hospital, Keiwakai Ebetsu Hospital, Kushiro City General Hospital, Obihiro Kyokai Hospital, Otaru Kyokai Hospital, Saiseikai Fukuoka General Hospital, and Tottori University Hospital. The study was conducted in accord with the ethical principles described in the Declaration of Helsinki. Written informed consent was obtained from each patient before his or her participation in the study.

Patients

A total of 150 Japanese patients with New York Heart Association (NYHA) functional class I–III compensated chronic HF who were regularly visiting an outpatient ward for >1 month after hospital discharge were enrolled between December 2012 and September 2014. These patients had a history of hospitalization due to HF worsening at least once within the 5 years before the initiation of the clinical study at each research institute. The exclusion criteria included nephrotic

syndrome, liver cirrhosis, uncontrolled diabetes (glycosylated hemoglobin [HbA1c] >7.0%), and cancer. We excluded patients who were taking steroids or antidepressants, which could influence their appetite and dietary pattern. Patients who underwent surgery within 3 months before the study and dialysis-dependent patients were also excluded.

Study protocol

At baseline, the patients underwent a complete clinical and physical examination including laboratory measurements, echocardiography to evaluate the left ventricular ejection fraction (LVEF) and left ventricular end-diastolic diameter (LVEDD), a 6-min walk test to evaluate exercise capacity, an evaluation of the dietary pattern, and a depression assessment using the PHQ-9. For the laboratory measurements, blood samples were collected from patients after a 10-hr overnight fast at each research institute, and residual samples were stored at −80°C for the later analysis of systemic oxidative stress conducted at the central laboratory of Hokkaido University Hospital. The participants were then followed up for 1 year for the assessment of clinical adverse events including all-cause death and rehospitalization (**Fig. 1**).

Laboratory measurements

After blood collection, the hemoglobin and plasma levels of B-type natriuretic peptide (BNP) were determined by routine in-house analyses. The estimated glomerular filtration rate

(eGFR) was calculated from the serum creatinine values and the patient's age with the use of the Japanese equation [19]: eGFR = 194 × (serum creatinine, mg/dL)$^{-1.094}$ × (age, yrs)$^{-0.287}$ × (0.739 if female). Chronic kidney disease (CKD) was defined as an eGFR <60 mL/min/1.73m^2.

Nutritional status assessment

The nutritional status of each patient was assessed by the Controlling Nutritional Status (CONUT) score [20] and a Geriatric Nutritional Risk Index (GNRI) that accounts for the patient's body mass index (BMI) [21]. Briefly, the CONUT score was calculated based on the patient's serum albumin concentration, total peripheral lymphocyte count, and total cholesterol level. The CONUT scores are classified into four groups: normal (0–1), mild risk (2–4), moderate risk (5–8), and severe risk (9–12) of malnutrition. The GNRI, known as a modified nutritional risk index for elderly patients that includes two nutritional indicators (the serum albumin level and BMI), was calculated as follows: GNRI = 14.89 × serum albumin (g/dL) + 41.7 × BMI/22. The GNRI values are classified into four grades of nutrition-related risk: major risk (GNRI <82), moderate risk (GNRI 82–91), low risk (GNRI 92–98), and no risk (GNRI >98).

Dietary pattern evaluation

Each patient's dietary pattern was evaluated using the BDHQ, a well-validated questionnaire that is adjusted to Japanese diets [22, 23]. The BDHQ is a four-page fixed-portion questionnaire

that calculates the frequency of the consumption of selected foods to estimate the intake of 58 food and beverage items during the preceding month. The BDHQ consists of five sections: (1) the intake frequency of food and nonalcoholic beverage items, (2) the daily intake of rice and miso soup, (3) the frequency of alcoholic beverage consumption and the amount per drink, (4) usual cooking methods, and (5) general dietary behavior.

Depression assessment

The chronic HF patients' depressive symptoms were assessed using the PHQ-9 [24]. A PHQ-9 score ≥5 denotes mild depression, and a score ≥10 is indicative of major depressive disorder. Accordingly, we used a PHQ-9 score ≥5 to define "presence of depressive symptoms," while a PHQ-9 score ≥10 was used to define "presence of moderate-to-severe depression."

Measurement of systemic oxidative stress

Systemic oxidative stress was evaluated by the measurement of the serum level of 8-isoprostane, a lipid peroxidation product of arachidonic acid, which is one of the most commonly used oxidative stress markers [25]. Because of the limited blood samples, the number of patients in the PHQ-9 <10 group and those in the PHQ-9 ≥10 group, respectively, was 93 and 11. The serum concentrations of 8-isoprostane were quantified by a standard sandwich enzyme-linked immunosorbent assay (ELISA) (Cayman Chemicals, Ann Arbor, MI) according to the

manufacturer's instructions.

Statistical analyses

Continuous variables except for serum 8-isoprostane (presented as the mean ± standard deviation) are expressed as the median (interquartile range), and categorical variables are expressed as numbers (percentages). We divided the 150 patients with chronic HF into two groups based on their PHQ-9 scores: a PHQ-9 <10 group (normal or with mild depression) and a PHQ-9 ≥10 group (with moderate-to-severe depression). Continuous variables were compared between these groups with an unpaired Student's *t*-test or Mann-Whitney U-test as appropriate, and the Chi-square test was used for group comparisons of categorical variables. We performed a multivariate analysis to identify independent variables that predict the comorbidity of moderate-to-severe depression in chronic HF patients, including the hemoglobin value and the intakes of citrus fruits (both of which were identified as relevant variables [$p<0.05$] using forward selection) in addition to age and gender. The adjusted odds ratios (OR) and 95% confidence interval (CI) were calculated for each variable from the logistic regression model. A Kaplan-Meier analysis with log-rank test was performed to assess the rates of all-cause death and rehospitalization. All analyses were conducted using JMP Pro 13.1.0 software (SAS Institute, Cary, NC). Probability (p)-values <0.05 were considered significant.

Results

Patient characteristics

The patient characteristics are summarized in **Table 1**. The median age of the total population of chronic HF patients was 68 years. The ratios of NYHA functional classes in the total chronic HF population were 29% class I, 61% class II, and 10% class III. The primary causes of the patients' HF were an ischemic cause (31%), dilated cardiomyopathy (31%), or others (38%) including hypertrophic cardiomyopathy, hypertensive heart disease, and valvular heart disease. The number of chronic HF patients without depression (PHQ-9 <5) was 116 (77%); 22 patients (15%) showed mild depression (PHQ-9 5–9), and 12 (8%) showed moderate-to-severe depression (PHQ-9 ≥10).

Most of these chronic HF patients were being treated with an angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB) and β-blockers. The LVEF (a parameter of LV systolic function), the CONUT score, and the GNRI value (parameters of nutritional status) were comparable between the PHQ-9 ≥10 and PHQ-9 <10 groups. There was no significant difference in exercise capacity evaluated by the 6-min walk test between the two groups. The hemoglobin values were significantly lower and the plasma levels of BNP (a parameter of HF severity) were higher in the PHQ-9 ≥10 patients compared to the PHQ-9 <10 patients.

Daily intakes of foods and beverages

Table 2 provides the patients' daily intakes of foods and beverages as estimated using the BDHQ. The daily intake of citrus fruits was lower in the PHQ-9 ≥10 group than in the PHQ-9 <10 group. Similarly, the intake of citrus fruits was significantly lower in the PHQ-9 ≥5 patients than in the PHQ-9 <5 patients (median [1st–3rd quartile]: 13 [0–32] vs. 37 [7–74] g, p=0.02). However, there was no significant difference in the daily intake of other fruits or 100% fruit and vegetable juice. The daily consumption of carrots/pumpkins was decreased in the PHQ-9 ≥10 group compared to the PHQ-9 <10 group.

Daily intakes of nutrients

Table 3 provides the daily intakes of nutrients estimated by the BDHQ. The daily intakes of vitamin C, α- and β-carotenes, and β-cryptoxanthin, all of which are antioxidants, were lower in the PHQ-9 ≥10 group compared to the PHQ-9 <10 group.

Systemic oxidative stress

The serum levels of 8-isoprostane, an oxidative stress marker, were higher in the chronic HF patients with PHQ-9 scores ≥10 than in those with PHQ-9 scores <10 (**Fig. 2**).

Adverse clinical events

Among the 150 patients with chronic HF, 145 patients were followed up for 1 year for the evaluation of adverse clinical events (**Fig. 1**). During the median follow-up period of 365 days, the combined clinical events of all-cause death and rehospitalization occurred in 19 patients (14%) (5 deaths and 14 rehospitalizations). The Kaplan-Meier analysis revealed that the PHQ-9 ≥10 patients had a significantly higher risk of adverse clinical events than the PHQ-9 <10 patients (33% vs. 11%, respectively; $p<0.05$) (**Fig. 3**).

Predictors of depression in patients with chronic HF

Among various potential variables including hemoglobin, log BNP, the intakes of citrus fruits, and carrots/pumpkins (all of which differed significantly between the PHQ-9 <10 and PHQ-9 ≥10 patients), hemoglobin and the intakes of citrus fruits were only identified as relevant variables ($p<0.05$) in the forward selection. The results of the multivariate logistic regression analysis demonstrated that a decreased intake of citrus fruits was an independent predictor of moderate-to-severe depression in patients with chronic HF, after adjustment for the hemoglobin value plus age and gender, with 0.54 as the OR for a 10 g/day increase of citrus fruit intake (95%CI: 0.30–0.97) (**Table 4**).

Discussion

The patients with moderate-to-severe depression (i.e., PHQ-9 scores ≥10) had lower daily intakes of citrus fruits than the patients with no or mild depressive symptoms (i.e., PHQ-9 scores <10). In addition, the daily intakes of the antioxidants, β-carotene, vitamin C, and β-cryptoxanthin, were lower in the PHQ-9 ≥10 group compared to the PHQ-9 <10 group, accompanied by enhanced systemic oxidative stress (i.e., increased serum levels of 8-isoprostane) in the PHQ-9 ≥10 patients. The patients with moderate-to-severe depression had a higher rate of adverse clinical events including all-cause death and rehospitalization during the 1-year follow-up period. The multivariate analysis revealed that a lowered daily intake of citrus fruits was an independent predictor of the comorbidity of moderate-to-severe depression in patients with chronic HF.

In general populations, decreased consumption of citrus fruits has been shown to be related to a higher prevalence of depression [26, 27]. A large cohort study showed that a daily intake of citrus fruits, which are known as flavonoid-rich foods, had a beneficial effect on the risk of incident depression in women without a prior history of depression during a 10-year follow-up [28]. That study also showed that the hazard ratio (95%CI) of incident depression was 0.82 (0.74–0.91) among their participants who consumed ≥2 servings of citrus fruits (including juices) per day compared to those who consumed <1 serving of citrus fruits per week [28]. Despite the accumulated evidence of the relationship between citrus fruit intake and mental health in healthy subjects, little has been known about the effects of citrus fruit intake on the mental health of

patients with chronic HF. Our present findings are the first to demonstrate that a lowered citrus fruit intake is associated with a higher prevalence of depression in chronic HF patients.

Chronic HF patients are more susceptible to depression than general populations [3]. One of the possible reasons for this is a redox imbalance, because oxidative stress plays a crucial role in disease progression in both chronic HF [5, 6] and depression [29]. Citrus fruits (e.g., oranges, mandarins, limes, lemons, and grapefruits) and their metabolites have various antioxidants, including vitamin C and carotenoids such as β-carotene and β-cryptoxanthin [30, 31]. Here, we observed enhanced systemic oxidative stress and reduced intakes of vitamin C, β-carotene, and β-cryptoxanthin in chronic HF patients who had moderate-to-severe depression. Other investigations have shown that decreased plasma vitamin C levels are associated with disturbed mental states, including anxiety and depression [32], and supplementation with high-dose vitamin C improved the depressive mood in healthy subjects [33]. It was also reported that reduced serum levels of carotenoids including β-carotene and β-cryptoxanthin independently predicted depressive symptoms in a general population [34]. Taken together, these past and present findings indicate that a lowered antioxidant capacity may underlie the association between decreased citrus fruit intake and depressive symptoms in patients with chronic HF.

Other factors related to citrus fruit intake may also influence the mental health of chronic HF patients. First, accumulated evidence suggests that systemic inflammation plays a role in depression [35]. As citrus fruits have an anti-inflammatory effect [36], a reduced consumption of

citrus fruits may result in increased systemic inflammation in patients with chronic HF. Second, citrus fruits have plenty of flavonoids, which can increase the level of brain-derived neurotrophic factor (BDNF), a neuroprotective growth factor [37]. The plasma level of BDNF was shown to be decreased in patients with depression [38], and lowered serum BDNF levels independently predicted adverse clinical events in patients with chronic HF [39]. Accordingly, decreased circulating BDNF may mediate the relationship between a reduced daily intake of citrus fruits and depression in chronic HF patients. Further studies are necessary to clarify the detailed mechanisms underlying the effects of citrus fruit intake on mental health in chronic HF.

Besides the difference in patient's dietary preference, we could not clarify the underlying mechanism by which chronic HF patients with moderate-to-severe depression had a reduced daily consumption of citrus fruits. Although depressive symptoms may cause appetite loss, total energy intake and daily consumption of other fruits were not decreased in these patients, suggesting that their appetite loss did not directly affect the lowered daily intake of citrus fruits. Given that HF patients have high vulnerability to suffering from mental illness, our present findings reaffirm HF patients as an important target for mental health intervention, including dietary intervention such as increased habitual intake of citrus fruits.

Our present analyses revealed that the median value of citrus fruit consumption was 32 g/day (i.e., 224 g/week) in the PHQ-9 <10 group and 6 g/day (i.e., 42 g/week) in the PHQ-9 ≥10 group. The weight per one citrus fruit is often assumed to be as follows: an orange (131 g), a

mandarin (84 g), a lime (67 g), a lemon (58 g), a grapefruit (white, 236 g; pink and red, 246 g) [40]. In our multivariate analysis conducted to identify independent variables that predict the comorbidity of moderate-to-severe depression in chronic HF patients, the OR for a 10 g/day increase in the intake of citrus fruits was 0.54, indicating that an increase in the weekly consumption of citrus fruits by 70 g (approximately 1/2 orange; 1 mandarin, lime, or lemon; or 1/3 grapefruit) might reduce the potential risk of depression by nearly half in these patients. However, patients with CKD who had a risk of hyperkalemia should be careful not to eat potassium-rich foods (including citrus fruits) too much.

In the multivariate analysis, we observed that anemia was also an independent predictor of moderate-to-severe depression in chronic HF patients, with 1.81 as the OR for an 1 g/dL decrease of hemoglobin (95%CI: 1.14–2.87). The most common cause of anemia in HF is iron deficiency [41], but in the present patient cohort, the daily intake of iron was not lowered in the chronic HF patients with moderate-to-severe depression. It has been reported that anemia deteriorates chronic HF patients' quality of life and increases adverse clinical events [42]. Impaired functional capacity (e.g., exertional dyspnea and fatigue) due to anemia is likely to affect the mental state of HF patients.

There are some study limitations that should be acknowledged. First, the number of patients who had moderate-to-severe depression was small (n=12). Second, the BDHQ that we used to estimate the dietary intake of patients does not directly assess the portion size of each food, and

thus the calculation of food intake might have been less accurate than in other questionnaires which evaluate portion sizes as well as the frequency of the intake of food and beverages. Finally, we did not evaluate the social, economic, or environmental conditions of patients, although these factors may also affect mental health.

Conclusions

A lowered daily intake of citrus fruits was revealed to be an independent predictor of the comorbidity of moderate-to-severe depression in patients with chronic HF. Our findings support the hypothesis that a daily consumption of citrus fruits has a beneficial effect on the prevention and treatment of depression in HF patients. Further studies that investigate the effect of citrus fruit supplementation on the mental health of HF patients are necessary.

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Disclosures

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Figure legends

Fig. 1. A flow chart of the chronic HF cohort. PHQ-9, Patient Health Questionnaire-9.

Fig. 2. Systemic oxidative stress in the chronic HF patients with a PHQ-9 score <10 (normal or mild depression; n=93) and those with a PHQ-9 score ≥10 (moderate-to-severe depression; n=11). Data are mean ± standard deviation (SD). *p<0.05 vs. PHQ-9 <10.

Fig. 3. Kaplan-Meier curves for the cumulative event (all-cause death and rehospitalization)-free ratio in the chronic HF patients with PHQ-9 scores ≥10 (moderate-to-severe depression) and PHQ-9 scores <10 (normal or mild depression).

Table 1. Baseline characteristics of the chronic HF patients with and without moderate-to-severe depression

	All patients (n = 150)	PHQ-9		*p*-value
		<10 (n = 138)	≥10 (n = 12)	
Demographic findings:				
Age, yrs	68 (60–77)	68 (61–77)	67 (49–77)	0.625
Male	103 (69%)	97 (70%)	6 (50%)	0.146
BMI, kg/m^2	22.9 (20.3–25.7)	23.0 (20.7–25.8)	22.4 (16.8–24.5)	0.212
NYHA functional class:				0.160
I	44 (29%)	42 (30%)	2 (17%)	
II	91 (61%)	84 (61%)	7 (58%)	
III	15 (10%)	12 (9%)	3 (25%)	
Primary cause of HF:				
Ischemic cause	47 (31%)	44 (32%)	3 (25%)	0.622
Dilated cardiomyopathy	46 (31%)	42 (30%)	4 (33%)	0.834
Others	57 (38%)	52 (38%)	5 (42%)	0.785
Hypertension	83 (55%)	79 (57%)	4 (33%)	0.110
Diabetes mellitus	39 (26%)	35 (25%)	4 (33%)	0.546
Dyslipidemia	105 (70%)	99 (72%)	6 (50%)	0.115
CKD	94 (63%)	85 (62%)	9 (75%)	0.357
Echocardiographic findings:				
LVEDD, mm	56 (49–63)	55 (48–63)	58 (53–61)	0.469
LVEF, %	45 (30–57)	45 (31–57)	38 (23–52)	0.189
Laboratory measurements:				
Hemoglobin, g/dL	13.2 (11.8–14.3)	13.4 (11.9–14.4)	11.6 (10.5–12.6)	0.007

Serum albumin, g/dL	4.2	(3.9–4.4)	4.2	(4.0–4.4)	4.2	(3.8–4.4)	0.906
Serum creatinine, mg/dL	0.99	(0.82–1.31)	0.98	(0.82–1.29)	1.28	(0.85–1.83)	0.132
eGFR, mL/min/1.73m^2	54.2	(39.5–67.3)	54.2	(40.6–67.6)	39.4	(25.1–71.1)	0.369
Total cholesterol, mg/dL	173	(149–193)	173	(151–193)	173	(120–241)	0.798
Plasma BNP, pg/mL	154	(76–373)	147	(74–336)	383	(121–589)	0.038
CONUT score	2	(1–2)	2	(1–2)	2	(1–3)	0.388
GNRI	106	(100–112)	106	(100–113)	106	(93–111)	0.463
6-min walk test	432	(347–499)	435	(350–501)	395	(303–433)	0.075
PHQ-9	2	(0–4)	2	(0–4)	15	(12–16)	<0.001
Medications:							
ACE inhibitors or ARBs	114	(76%)	104	(75%)	10	(83%)	0.732
β-blockers	130	(87%)	121	(88%)	9	(75%)	0.202
MRAs	87	(58%)	79	(57%)	8	(67%)	0.762
Statins	72	(48%)	68	(49%)	4	(33%)	0.373

Data are expressed as median (1st–3rd quartile) or n (%). CKD (chronic kidney disease) was defined as an eGFR <60 mL/min/1.73m^2. ACE: angiotensin-converting enzyme; ARB: angiotensin II receptor blocker; BMI: body mass index; BNP: B-type natriuretic peptide; CONUT: controlling nutritional status; eGFR: estimated glomerular filtration rate; GNRI: Geriatric Nutritional Risk Index; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; MRAs: mineralocorticoid receptor antagonists; NYHA: New York Heart Association; PHQ: Patient Health Questionnaire.

Table 2. Daily intakes of foods and beverages estimated using the BDHQ

	All patients (n = 150)	PHQ-9		*p*-value
		<10 (n = 138)	≥10 (n = 12)	
Citrus fruits, g	15 (6–44)	32 (7–64)	6 (0–14)	0.002
Carrots/pumpkins, g	17 (7–34)	17 (8–34)	6 (3–17)	0.019
Seaweeds, g	6 (3–14)	6 (3–14)	4 (1–11)	0.060
Green leaved vegetables, g	26 (9–48)	26 (9–54)	12 (6–23)	0.076
Coffee, g	61 (0–173)	84 (9–173)	12 (0–120)	0.078
Tofu/atsuage, g	36 (15–73)	36 (15–73)	15 (13–33)	0.081
Lean fish, g	15 (8–34)	15 (12–35)	12 (6–29)	0.099
Persimmons/strawberries, g	7 (0–32)	7 (0–32)	3 (0–11)	0.115
Western-type confectioneries, g	5 (0–25)	5 (0–25)	2 (0–10)	0.118
Cabbage/Chinese cabbage, g	19 (13–48)	19 (14–48)	16 (7–34)	0.150
Squid/octopus/shrimp/shellfish, g	12 (6–17)	12 (6–17)	9 (0–14)	0.235
Potatoes, g	24 (16–58)	25 (16–58)	22 (12–46)	0.267
Spaghetti/macaroni, g	9 (0–16)	9 (0–16)	4 (0–16)	0.365
Oily fish, g	14 (6–30)	14 (6–30)	13 (6–24)	0.378
Japanese radish/turnip, g	22 (5–31)	22 (5–34)	11 (5–25)	0.384
Ice cream, g	8 (0–20)	8 (0–20)	13 (0–48)	0.443
Tomatoes, g	20 (5–49)	21 (5–46)	10 (5–51)	0.451
Pork/beef, g	28 (11–34)	28 (11–36)	28 (6–32)	0.468
Cola drink/soft drink, g	7 (0–82)	13 (0–82)	0 (0–69)	0.488
Bread, g	26 (9–65)	26 (9–64)	33 (9–115)	0.528

Japanese wheat noodles, g	17	(7–40)	16	(7–40)	20	(9–40)	0.557
Other fruits, g	37	(7–74)	37	(7–74)	23	(2–72)	0.569
Buckwheat noodles, g	11	(0–21)	11	(0–22)	10	(2–18)	0.593
Japanese-type confectioneries, g	4	(0–8)	4	(0–8)	5	(0–15)	0.621
Mushrooms, g	9	(2–14)	9	(2–16)	7	(2–12)	0.660
Egg, g	26	(11–53)	26	(12–52)	31	(9–68)	0.682
100% fruit and vegetable juice, g	0	(0–33)	0	(0–33)	0	(0–28)	0.699
Black tea/oolong tea, g	0	(0–15)	0	(0–15)	0	(0–21)	0.735
Rice, g	240	(150–360)	240	(150–360)	240	(130–382)	0.739
Ham/sausage/bacon, g	4	(2–11)	4	(2–11)	4	(2–8)	0.739
Other root vegetables, g	31	(22–57)	30	(22–57)	51	(20–63)	0.763
Mayonnaise/dressing, g	5	(1–9)	5	(1–10)	5	(2–5)	0.789
Whole milk, g	36	(0–156)	46	(0–156)	10	(0–154)	0.790
Rice crackers, g	4	(0–18)	4	(0–18)	8	(0–15)	0.838
Small fish with bones, g	5	(0–11)	5	(0–11)	4	(0–21)	0.897
Dried fish/salted fish, g	19	(7–31)	23	(7–31)	13	(7–42)	0.901
Miso soup, g	96	(55–125)	96	(55–125)	71	(55–175)	0.909
Chicken, g	14	(7–32)	14	(6–32)	26	(7–32)	0.923
Chinese noodles, g	9	(0–18)	9	(0–18)	10	(2–16)	0.952
Green tea, g	150	(0–433)	150	(0–433)	148	(5–433)	0.992

Data are expressed as median (1st–3rd quartile). BDHQ: self-administered brief diet-history questionnaire; PHQ: Patient Health Questionnaire.

Table 3. Daily intakes of nutrients estimated using the BDHQ

	All patients (n = 150)	PHQ-9		*p*-value
		<10 (n = 138)	≥10 (n = 12)	
Total energy, kcal	1636 (1275–2005)	1657 (1276–2026)	1421 (1172–1983)	0.398
Total protein, g	63 (48–84)	63 (48–84)	58 (44–69)	0.319
Total fat, g	46 (32–57)	46 (34–57)	39 (26–68)	0.714
Total dietary fiber, g	10.4 (7.6–14.1)	10.4 (7.6–14.1)	10.0 (7.4–11.1)	0.195
β-cryptoxanthin, μg	269 (92–567)	278 (104–607)	83 (24–176)	0.003
α-carotene, μg	325 (139–644)	326 (148–650)	126 (63–314)	0.013
β-carotene, μg	2594 (1243–4132)	2690 (1307–4354)	1183 (645–2503)	0.014
Vitamin C, mg	108 (71–148)	115 (79–152)	77 (51–111)	0.020
Potassium, g	2.3 (1.6–3.0)	2.3 (1.6–3.0)	1.9 (1.4–2.2)	0.042
Vitamin B6, mg	1.2 (0.8–1.6)	1.2 (0.8–1.6)	1.0 (0.7–1.1)	0.079
Vitamin A, μg	555 (359–813)	574 (372–827)	475 (211–622)	0.090
Magnesium, mg	231 (169–310)	234 (169–310)	186 (154–237)	0.092
Vitamin B1, mg	0.7 (0.5–0.9)	0.7 (0.5–0.9)	0.6 (0.4–0.7)	0.117
Folate, μg	311 (207–409)	319 (207–416)	239 (204–306)	0.122
Vitamin K, μg	208 (124–332)	214 (128–345)	153 (100–250)	0.122
Niacin, mg	15.6 (11.7–21.4)	16.0 (11.7–21.6)	12.8 (8.7–15.8)	0.135
Soluble dietary fiber, g	2.5 (1.8–3.6)	2.6 (1.7–3.7)	2.4 (2.1–2.7)	0.181
Vitamin B2, mg	1.2 (0.8–1.5)	1.2 (0.8–1.5)	0.9 (0.7–1.4)	0.190
Calcium, mg	501 (319–713)	515 (339–712)	373 (267–676)	0.210
Pantothenic acid, mg	5.9 (4.2–7.3)	6.0 (4.2–7.3)	4.8 (4.0–6.2)	0.210

Phosphorus, mg	959	(697–1284)	986	(700–1300)	752	(655–1117)	0.228
Insoluble dietary fiber, g	7.5	(5.7–10.0)	7.5	(5.7–10.1)	7.4	(5.3–8.3)	0.234
α-tocopherol, mg	6.7	(4.9–8.7)	6.8	(5.0–8.9)	6.3	(3.3–7.6)	0.236
Ash, g	16	(13–21)	16	(13–22)	15	(11–19)	0.245
Animal protein, g	37	(28–53)	38	(28–54)	30	(21–40)	0.262
Copper, mg	1.0	(0.8–1.3)	1.0	(0.8–1.3)	1.0	(0.7–1.1)	0.268
Iron, mg	7.0	(5.0–8.9)	7.1	(5.1–9.1)	6.2	(4.5–7.7)	0.271
Vitamin B12, μg	10.3	(6.2–14.2)	10.6	(6.3–14.2)	7.1	(4.5–13.7)	0.283
Zinc, mg	7.1	(5.8–9.1)	7.1	(5.8–9.1)	6.4	(5.4–7.7)	0.315
Vegetable protein, g	25	(19–32)	25	(19–33)	23	(18–30)	0.315
Manganese, mg	2.8	(2.2–3.9)	2.9	(2.2–3.9)	2.5	(2.2–3.7)	0.379
Vitamin D, μg	14.5	(9.2–23.5)	14.6	(9.5–24.6)	9.8	(7.2–19.8)	0.394
σ-tocopherol, mg	2.5	(1.8–3.3)	2.5	(1.8–3.5)	2.5	(1.6–2.9)	0.434
β-tocopherol, mg	0.30	(0.23–0.41)	0.31	(0.23–0.41)	0.28	(0.20–0.39)	0.459
Vegetable fat, g	23	(16–30)	23	(16–30)	20	(13–29)	0.467
γ-tocopherol, mg	10.6	(7.4–13.9)	10.6	(7.4–14.2)	10.1	(5.9–12.5)	0.471
Carbohydrate, g	219	(174–270)	219	(175–272)	220	(154–260)	0.519
Sucrose, g	8.0	(3.2–13.6)	7.8	(3.2–13.5)	12.2	(3.0–17.5)	0.554
Polyunsaturated fat, g	10.8	(8.2–13.9)	10.9	(8.3–13.9)	10.2	(6.3–14.2)	0.673
Animal fat, g	22	(15–30)	22	(15–30)	21	(13–31)	0.698
Cholesterol, mg	313	(216–487)	313	(222–487)	296	(181–506)	0.745
Retinol, μg	263	(170–406)	270	(176–396)	221	(119–453)	0.771
Monounsaturated fat, g	16.2	(11.3–20.2)	16.4	(11.7–20.2)	14.3	(9.9–23.4)	0.776

Sodium, g	3.7	(2.9–4.8)	3.7	(2.9–4.8)	3.9	(2.5–4.7)	0.792
Salt, g	9.3	(7.3–12.0)	9.2	(7.4–12.2)	9.8	(6.2–11.8)	0.814
Saturated fat, g	11.5	(8.4–16.2)	11.5	(8.4–16.2)	10.9	(6.9–19.9)	0.846

Data are expressed as median (1st–3rd quartile). Abbreviations are as shown in Table 2.

Table 4. Multivariate analysis of predictors of moderate-to-severe depression (PHQ-9 ≥10)

	OR	95%CI	*p*-value
Citrus fruits, 10 g/day increase	0.54	0.30 – 0.97	<0.001
Hemoglobin, 1 g/dL decrease	1.81	1.14 – 2.87	0.007

In addition to the variables displayed, age and gender were included in the analysis.

Figure 1

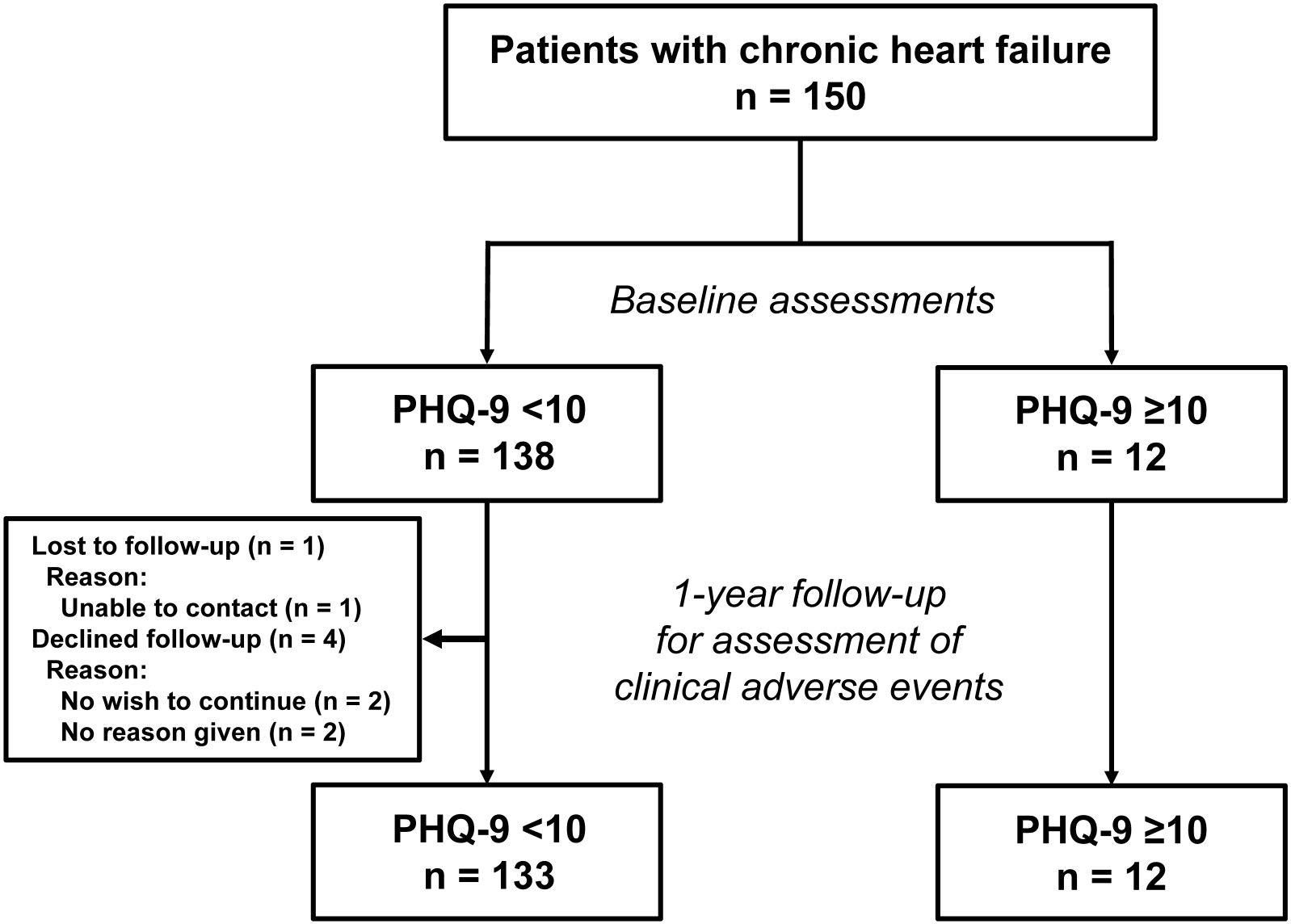

Patients with chronic heart failure
n = 150
Baseline assessments
PHQ-9 <10
n = 138
PHQ-9 ≥10
n = 12
Lost to follow-up (n = 1)
Reason:
Unable to contact (n = 1)
Declined follow-up (n = 4)
Reason:
No wish to continue (n = 2)
No reason given (n = 2)
1-year follow-up
for assessment of
clinical adverse events
PHQ-9 <10
n = 133
PHQ-9 ≥10
n = 12

Figure 2

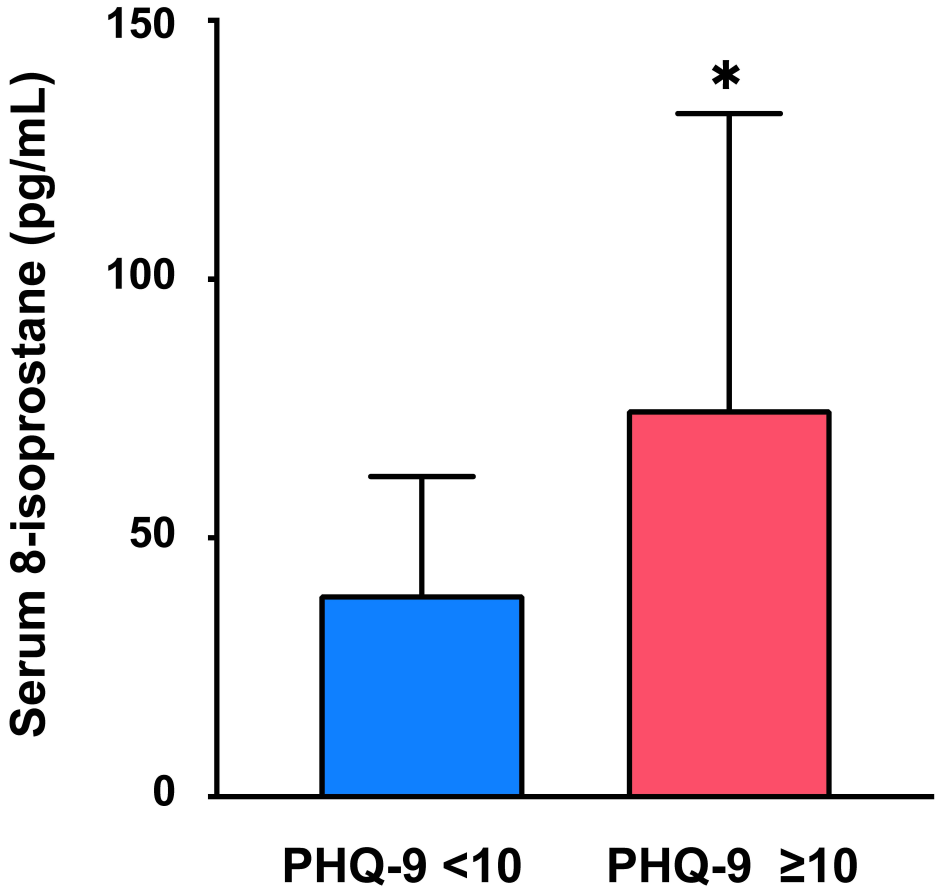
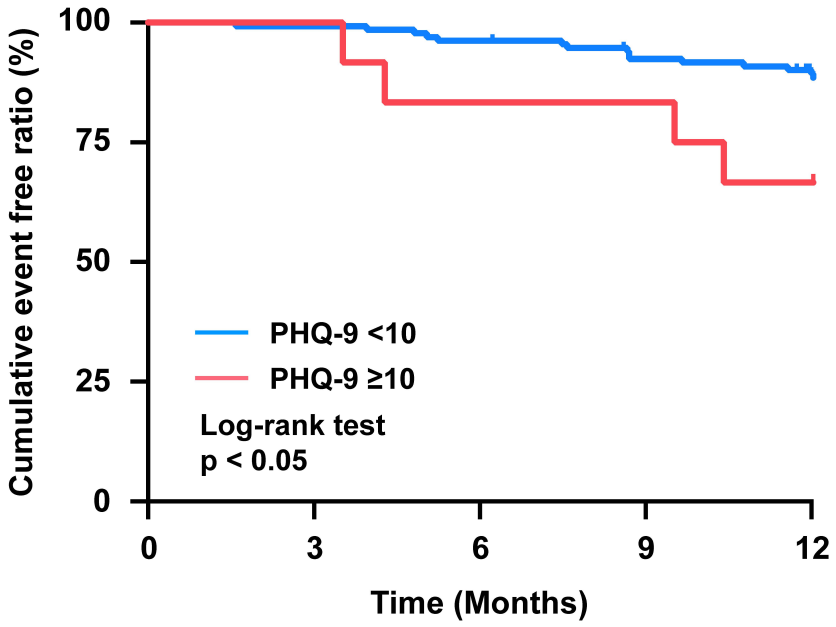


Figure 3



Number at risk

PHQ-9 <10	133	132	128	123	118
PHQ-9 ≥10	12	12	10	10	8