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Dietary sodium restriction below 2 gram per day predicted shorter event-free survival in patients with mild heart failure

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Abstract

Background—Despite a growing recognition that a strict low sodium diet may not be warranted in compensated heart failure (HF) patients, the link between sodium restriction below 2g/day and health outcomes is unknown in patients at different levels of HF severity.

Purpose—To compare differences in event-free survival among patients with < 2g/day, 2–3g/day, or > 3g/day sodium intake stratified by New York Heart Association (NYHA) class.

Method—A total of 244 patients with HF completed a four-day food diary to measure daily sodium intake. All-cause hospitalization or death for a median of 365 follow-up days and covariates on age, gender, etiology, body mass index, NYHA class, ejection fraction, total comorbidity score, the presence of ankle edema, and prescribed medications were determined by patient interview and medical record review. Hierarchical Cox hazard regression was used to address the purpose.

Results—In NYHA class I/II (n=134), patients with < 2g/day sodium intake had a 3.7-times higher risk ($p = .025$), while patients with > 3g/day sodium intake had a 0.4-times lower risk ($p = .047$) for hospitalization or death than those with 2–3g/day sodium intake after controlling for covariates. In NYHA class III/IV (n=110), > 3g/day sodium intake predicted shorter event-free

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survival ($p = .044$), whereas there was no difference in survival curves between patients with $< 2\text{g/day}$ and those with $2\text{--}3\text{g/day}$ sodium intake.

Conclusion—Sodium restriction below 2g/day is not warranted in mild HF patients, whereas excessive sodium intake above 3g/day may be harmful in moderate to severe HF patients.

INTRODUCTION

Prior researchers have reported that excessive sodium intake is associated with exacerbation of heart failure (HF) secondary to volume overload, resulting in preventable hospitalization.^{1,2} Consequently, a low sodium diet is recommended for HF patients under the current guidelines of the Heart Failure Society of America³ and the American College of Cardiology/ American Heart Association (ACC/AHA).^{4,5} However, the current guideline recommendations do not consider whether different levels of sodium restriction may be appropriate for patients with different levels of HF severity.

There is evidence that a low sodium diet less than 2g/day may be not warranted in compensated patients with HF optimized on medication therapy.^{6,7} It has been suggested that less than 2g sodium diet in patients with compensated HF may trigger neurohormone compensatory responses due to intravascular volume depletion that may interfere with drug therapy.⁸ Accordingly, it is possible to assume that compensated HF patients with less than 2g of sodium intake may have higher rate of hospitalization or death compared to compensated HF patients with more than 2g of sodium intake. However, there is little evidence that the link between low sodium diet and health outcomes varies among patients at different levels of HF severity.^{6,9}

Therefore, the purpose of this study was to compare differences in event-free survival among patients at different levels of HF severity with a daily sodium intake above and below 2g to 3g , the recommended range in current guidelines. We hypothesized that less than 2g of daily sodium intake would be independently associated with higher risk for hospitalization or death in patients in New York Heart Association (NYHA) Class I/II compared to $2\text{--}3\text{g}$ of daily sodium intake, but not patients in NYHA Class III/IV.

METHODS

Design and settings

This was a prospective study from baseline measurement of nutritional intake including sodium and caloric intake. Patients were recruited from outpatient HF clinics in three regional tertiary medical centers located in Kentucky, Indiana, and Georgia.

Participants

Eligibility criteria for participation included: 1) a confirmed diagnosis of chronic HF with either non-preserved systolic function, left ventricular ejection fraction (LVEF) $<40\%$ or preserved systolic function, LVEF $\geq 40\%$; 2) no change in prescribed doses of drugs during prior three months; and 3) ability to read and speak English. Exclusion criteria were: 1) referred for heart transplantation; 2) valvular heart disease, peripartum HF, or myocarditis as

the primary HF etiology; 3) history of cerebrovascular accident or recent myocardial infarction within the previous three months; and 4) any co-existing terminal illness such as cancer, liver or renal failure.

The lowest basal energy expenditure was estimated at 1,000 Kcal in this study using the Harris-Benedict equation.¹⁰ Therefore, we excluded patients who had an average energy intake of less than 1,000Kcal per day because this level of caloric intake is associated with suppressed appetite or inadequate food intake to meet the required energy.

A total of 265 patients were eligible for this study. Six patients declined to participate, two patients withdrew, nine patients were lost to follow-up, and four were determined to have incomplete food diaries. Subsequently, a total of 244 patients were included in this study.

Variable measurements

Dietary sodium intake—Patients completed a four-day food diary that included three weekdays and one weekend day to account for difference in eating behaviors between weekday and weekend days. Food diary is a comparably objective indicator of dietary sodium intake as 24-hour urine sodium excretion.¹¹ Dietary sodium intake was defined as the averaged four-day intake. Nutritional Data System for Research (NDSR, Minneapolis MN) software was used to analyze food diaries and determine dietary sodium intake.¹² The recommended range of sodium intake in the HFSA guidelines for patients with HF is 2g to 3 g.⁴ Accordingly, patients were divided into three groups: those with dietary sodium intakes less than 2g, those with intakes between 2 to 3g, and those with greater than 3g of daily sodium intake.

New York Heart Association (NYHA) Functional Class—This symptom based classification is used to determine the severity of HF through patients interview.¹³ Patients were classified into one of four categories based on the degree to which symptoms (i.e., dyspnea, fatigue) limit ordinary physical activities: NYHA Class I (no symptoms and no limitation), Class II (only mild symptoms with ordinary physical activities), Class III (symptoms with less than ordinary physical activities), and Class IV (symptoms at rest).¹⁴ Patients were collapsed into two groups: patients in NYHA class I/II and patients in NYHA class III/IV.

Covariates—To control for factors that can affect event-free survival, data on age, gender, HF etiology, body mass index (BMI), LVEF, total co-morbidity score using by Charlson comorbidity index,¹⁵ the level of serum N-terminal B-type pro natriuretic peptide (NT-pro BNP) and creatinine, hospitalization in the year prior to inclusion, the presence of lower leg or ankle edema, and prescribed medications were obtained through patient interview and medical record review. Averaged daily caloric intake was included as a covariate to control the relationship between amount of food consumed and sodium intake.¹⁶

Event-free survival—The primary outcome of this study was the composite end-point of time to first event of all-cause hospitalization or death. Patients were called monthly to track hospitalizations. Data about death were obtained from family members, physicians, medical

records or death certificates. Any reported hospitalizations were confirmed via hospital record review by a nurse with expertise in HF.

Procedures

The study was approved by the Institutional Review Boards at each enrollment site. Eligible patients were referred by cardiologists and nurse practitioners to the investigators. Written informed consent was obtained from each patient prior to participating. Patients were visited in their homes by a trained research assistant who provided digital scales with detailed oral and written instructions for measuring the weight of each food and recording all food consumed during the four-day food diary collection. Food models were also provided to patients for estimating serving sizes when the weight of foods could not be measured (e.g., when eating at a restaurant). To assure accurate and complete four-day food diaries, patients were asked to provide a return demonstration of food measurement and recording in food diary. A research assistant called patients on the first day of the four-day food diary to answer any questions. The morning after completion, patients brought their four-day food diary to the General Clinical Research Center (GCRC) at each site. The dietitian reviewed the completed food diary to verify serving sizes, obtain any missing information, and clarify food preparation techniques. These reviews lasted approximately 30–45 minutes. Total caloric and sodium intake were then determined using the NDSR software program for nutrient analysis. Patients were followed by telephone interview every month to collect event-free survival data.

Statistical Analysis

Data were analyzed using SPSS for Windows 18.0. Descriptive statistics including frequencies with percents and means with standard deviations were used to describe patient characteristics. Independent *t*-test or Chi-square tests were used to compare differences in sample characteristics between patients in NYHA class I/II and those in NYHA class III/IV. Analysis of variance (ANOVA) or Chi-square tests were used to determine dietary sodium intake-based differences in sample characteristics among three groups categorized by dietary sodium intake; those with < 2g/day, those with 2 to 3g/day, and those with > 3g/day of sodium intake. Hierarchical Cox proportional hazard regression with survival curves was used to compare differences in adjusted event-free survival among patients with less than 2g, 2 to 3g, and greater than 3g of daily sodium intake stratified into NYHA class I/II and class III/IV while controlling for age, gender, HF etiology, BMI, LVEF, total co-morbidity score, total caloric intake, the presence of lower leg or ankle edema, and use of ACE inhibitors and diuretics. The proportional hazard assumption was confirmed through visual inspection of log (–log) survival curves. The time-dependent covariate analysis was not statistically significant ($p = 0.835$), indicating that the assumption of proportionality is reasonable. A hazard ratio (HR) for event-free survival was obtained for all independent variables along with 95% confidence intervals (CIs).

RESULTS

Patient characteristics

Patient characteristics are presented in Table 1. The median age of the patients was 61 years with a range of 23 to 97 years (25th, 75th percentile; 53–67 years). Approximately, a half of the patients were obese. Sixty-eight patients (28%) had preserved systolic function, LVEF 40%. Average daily caloric intake was 1,837 kcal with a range of 1,010 to 4,363 kcal. As a group, patients were primarily in NYHA class II and III. A majority of patients were prescribed angiotensin-converting enzyme inhibitors, beta blockers, and diuretics.

Patients in NYHA class III/IV had more ischemic heart disease as the etiology of HF, higher BMI, lower LVEF, and greater total co-morbidity scores than patients in NYHA class I/II. However, there were no differences in ACE inhibitors, beta blockers, or diuretics use between NYHA class I/II and class III/IV (Table 1).

Dietary sodium intake-based differences

The average intake of dietary sodium was approximately 3.2 g. Forty-six percent of patients had greater than 3g of daily sodium intake, and 13.5 % had less than 2g of daily sodium intake.

Table 2 shows the differences in sample characteristics among three groups categorized by dietary sodium intake; those with < 2g/day, those with 2 to 3g/day, and those with > 3g/day of sodium intake. Men had higher sodium intake than women ($p < .001$). Patients with greater than 3g of daily sodium intake consumed the highest daily caloric intake among three groups ($p < .001$). Prescribed medications were similar among three groups, except for ACE inhibitors; the percentage of ACE inhibitor use was the highest in patients with greater than 3g/day of sodium intake as 79% ($p = .004$). However, there was no difference in daily sodium intake between NYHA class I/II and class III/IV ($p = .772$) (Table 2).

Event-free survival

Over a median follow-up of 365 days (25th, 75th quartile; 225–413 days), 6 patients (2.5%) died and 86 patients (35.2%) were hospitalized. One patient died due to decompensated HF, two died from cardiac-related problems, and three died from other causes. Twenty-two patients (9.0%) were hospitalized for decompensated HF, and 34 patients (13.9%) were hospitalized due to cardiac-related problems. The average time to the first event of hospitalization, or mortality was 214 days. The incidence of total events and 25th, 75th percentile of time to first cardiac event among patients categorized by daily sodium intake and NYHA class is shown in Table 3.

Dietary sodium intake and event-free survival

Table 4 presents the results from hierarchical proportional hazard regression analysis to predict event-free survival in each group of NYHA class I/II and class III/IV. In NYHA class I/II, patients with less than 2g of daily sodium intake had shorter event-free survival (HR = 3.68, 95% CI = 1.18–11.50), while patients with greater than 3g of daily sodium intake had longer event-free survival (HR = 0.39, 95% CI = 0.16–0.98), compared to those

with 2 to 3g of daily sodium intake after controlling for age, gender, BMI, HF etiology, preserved LVEF, total co-morbidity score, total caloric intake, presence of lower leg or ankle edema, and prescribed ACE inhibitors, diuretics, and beta blockers. Patients with < 2g of daily sodium intake had 3.7-times higher risk for hospitalization or death than those with 2 to 3g of daily sodium intake ($p = .025$). In contrast, patients with greater than 3g of daily sodium intake had a 60% lower risk for hospitalization or death ($p = .047$) in NYHA class I/II (Figure 1).

In NYHA class III/IV, patients with greater than 3g of daily sodium intake had a 2.1-times higher risk for hospitalization or death than those with 2 to 3g of daily sodium intake ($p = .044$). However, as demonstrated in Figure 2, there was no significant difference in adjusted survival curves between patients with less than 2g and those with 2 to 3g of daily sodium intake ($p = .418$) after adjusting for the same covariates (Figure 2).

DISCUSSION

Arcand and colleagues¹⁷ reported that compensated HF patients with greater than 2.8 g/day of dietary sodium intake had a 2.5-fold increased risk for all-cause hospitalization and mortality compared to those with less than 1.9 g/day. Their study provided some of the best evidence that dietary sodium is related to patient outcomes. However, Arcand et al.¹⁷ did not consider patient outcomes according to different levels of HF severity. Our results suggest that recommendations for sodium restriction may need to vary by severity of HF. A highly restrictive low sodium diet may not be indicated for patients in NYHA class I and II, while greater than 3g of daily sodium intake may not be beneficial for patients in NYHA class III and IV. Similar differences in the impact of dietary sodium intake on event-free survival of patients with different levels of HF severity were found in a previous prospective observational study using 24-hour urinary sodium excretion as a marker of dietary sodium intake support this conclusion. Lennie and colleagues¹⁸ reported that patients in NYHA class I and II with < 3g of urinary sodium excretion had shorter event-free survival than those in class I and II with greater urinary sodium excretion; while patients in NYHA class III and IV with > 3 g sodium excretion had shorter event-free survival than those with < 3g.

Evidence from prior experimental studies^{8,19–21} has shown that intravascular volume depletion induced by less than 2g of daily sodium intake can compromise renal function, especially in patients who are well compensated by treatment with ACE inhibitors and diuretics. Serum aldosterone and rennin levels were reported to be significantly higher in patients with approximately 1.8 g of daily sodium intake, compared to patients with 2.8 g of daily sodium intake. These data are consistent with our hypothesis that less than 2 g of daily sodium intake can result in increased risk of hospitalization or death by triggering a compensatory responses in patients with NYHA class I/II.

There were several limitations in this study that should be noted. Our data were based on sodium intake determined by patient recorded of food diaries. Leiba and colleagues²² reported that urinary sodium excretion was more accurate compared to patient recall for measuring sodium intake because of the difficulty of tracking added salt and sodium in processed foods. Average sodium intake over the four days may not reflect long-term

sodium intake. Four-day food diary was also done at one time point in all prior studies demonstrating nutritional intake of patients with HF,^{23,24} indicating that a single measure of four-day food diary is a robust measure for the role of four-day food diary in nutritional intake. This was not an interventional study that patients were randomly assigned to low, medium or high daily intake of sodium limiting our ability to fully draw a causal relationship between sodium intake and event-free survival. Although we adjusted for important clinical variables in our analysis, differences in other factors among the groups with different levels of daily sodium intake may be, at least in part, responsible for our findings. The relatively young age of this sample could be related to low comorbidity burden and low incidence rate of cardiac events, while high obesity rate could be associated with moderate to advanced NYHA functional class. In this regard, it is difficult to make a simple comparison with results of other HF studies. Furthermore, only 12% and 15% had less than 2g of daily sodium intake in NYHA class I/II and in class III/IV, respectively. The study needs to be replicated with a larger sample to fully determine the adverse impact of sodium on health outcomes. Lastly, patients were on consistent doses of all medications for three months before enrollment in this study. However, all patients were not treated with diuretics and ACE inhibitors. Our findings should be interpreted in light of these limitations.

CONCLUSIONS

Our data demonstrated that patients in NYHA class I/II consuming an average of less than 2g of daily sodium intake were approximately 3.7 times more likely to be hospitalized or die, while those in NYHA class III/IV eating greater than 3g per day of sodium were about 2.1 times higher likely to have hospitalization and death after controlling for covariates. These finding suggests that sodium restriction below the currently recommended 2g limit may not be indicated in mild to moderately symptomatic patients with HF, whereas excessive sodium intake above the upper 3g limit may be harmful in moderately to severe symptomatic patients with HF. Additional research would be needed prior to making definitive recommendations in dietary sodium intake.

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IMPLICATIONS FOR PRACTICE

- Sodium intake < 2g/day is not warranted in mild symptomatic HF patients, whereas sodium intake > 3/day is harmful in moderately to severe symptomatic patients with HF.
- A nonspecific recommendation for sodium intake is provided in the current guidelines.
- Future research would be needed prior to making definitive recommendations in sodium intake.

Figure 1.

Adjusted differences in event-free survival among patients with less than 2 g, 2 to 3 g, and greater than 3g of dietary sodium intake in NYHA class I/II

Figure 2.

Adjusted differences in event-free survival among patients with less than 2 g, 2 to 3 g, and greater than 3 g of dietary sodium intake in NYHA class III/IV

Table 1

Patient characteristics

		N = 244		
		N (%) or Mean $\pm$ SD		
Characteristics		Total	NYHA class I/II (n = 134)	NYHA class III/IV (n = 110)
Age (years)		61 $\pm$ 12	61 $\pm$ 12	61 $\pm$ 12
	< 70 years	197 (80.7)	109 (81.3)	88 (80.0)
	70 years	47 (19.3)	25 (18.7)	22 (20.0)
Gender	Male	162 (66.4)	93 (69.4)	69 (62.7)
	Female	82 (33.6)	41 (30.6)	41 (37.3)
Body mass index (kg/m ²)		30.4 $\pm$ 7.1	29.2 $\pm$ 6.1	31.8 $\pm$ 8.1 *
	Normal weight (< 25)	59 (24.1)	38 (28.4)	21 (19.1)
	Overweight (25 – 29.9)	68 (27.9)	41 (30.6)	27 (24.5)
	Obese ($\geq$ 30)	117 (48.0)	55 (41.0)	62 (56.4)
HF etiology	Non-ischemic heart disease	130 (53.3)	81 (60.4)	49 (44.5)
	Ischemic heart disease	114 (46.7)	53 (39.6)	61 (55.5) *
Left ventricular ejection fraction (%)		34 $\pm$ 13	35 $\pm$ 12	33 $\pm$ 14 *
	< 40%	176 (72.1)	95 (70.9)	81 (73.6)
	$\geq$ 40%	68 (27.9)	39 (29.1)	29 (26.4)
Total comorbidity score		3.1 $\pm$ 1.9	2.5 $\pm$ 1.5	3.8 $\pm$ 2.2 *
	Hypertension	169 (70.1)	91 (68.9)	78 (71.6)
	Diabetes mellitus	88 (36.1)	42 (31.3)	46 (41.8)
Total energy (Kcal/day)		1,837 $\pm$ 654	1,839 $\pm$ 638	1,834 $\pm$ 677
Medication	ACE inhibitors	166 (68.0)	91 (67.9)	75 (68.2)
	Angiotension II receptor blocker	50 (20.5)	27 (20.1)	23 (20.9)
	Digoxin	57 (23.4)	23 (17.2)	34 (30.9)
	β -blocker	216 (88.5)	121 (90.3)	95 (86.4)
	Diuretics	184 (75.4)	96 (71.6)	88 (80.0)
	Aldosterone antagonist	63 (25.8)	31 (23.1)	32 (29.1)

ACE; angiotensin-converting enzyme, HF; heart failure, NYHA; New York Heart Association

* ; $p < 0.05$ by independent t-test between NYHA classes I/II vs. III/IV.

Table 2

Patient characteristics among 3 groups categorized by daily sodium intake

		N = 244		
		N (%) or Mean $\pm$ SD		
Characteristics		< 2g/day of sodium intake (n = 33)	2 to 3g/day of sodium intake (n = 99)	> 3g/day of sodium intake (n = 112)
Age (years)		63 $\pm$ 12	62 $\pm$ 13	60 $\pm$ 11
Gender *	Male	14 (42.4)	60 (60.6)	88 (78.6)
	Female	19 (57.6)	39 (39.4)	24 (21.4)
Body mass index (kg/m ²)		29.0 $\pm$ 8.3	30.3 $\pm$ 7.2	30.9 $\pm$ 6.7
	Normal weight (< 25)	13 (39.4)	26 (26.3)	20 (17.9)
	Overweight (25 – 29.9)	6 (18.2)	26 (26.3)	36 (32.1)
	Obese ($\geq$ 30)	14 (42.4)	47 (47.5)	56 (50.0)
HF etiology	Non-ischemic heart disease	17 (51.5)	56 (56.6)	57 (50.9)
	Ischemic heart disease	16 (48.5)	43 (43.4)	55 (49.1)
NYHA Class	I/II	20 (60.6)	54 (54.5)	60 (53.6)
	III/IV	13 (39.4)	45 (45.5)	52 (46.4)
Left ventricular ejection fraction (%)		33 $\pm$ 12	35 $\pm$ 14	34 $\pm$ 13
	< 40%	25 (75.8)	70 (70.7)	81 (72.3)
	$\geq$ 40%	8 (24.2)	29 (29.3)	31 (27.7)
Total comorbidity score		3.2 $\pm$ 1.8	3.0 $\pm$ 1.9	3.2 $\pm$ 2.0
	Hypertension	24 (72.7)	66 (66.7)	79 (72.5)
	Diabetes mellitus	10 (30.3)	33 (33.3)	45 (40.2)
Hospitalization in the year prior to inclusion		9 (27.3)	31 (31.3)	31 (27.7)
Serum NT-pro BNP (pg/mL)		979 $\pm$ 901	832 $\pm$ 862	751 $\pm$ 596
Serum creatinine (mg/dl)		1.2 $\pm$ 0.5	1.2 $\pm$ 0.3	1.3 $\pm$ 0.9
Lower leg or ankle edema	No	15 (45.5)	57 (57.6)	58 (51.8)
	Yes	18 (54.5)	42 (42.4)	54 (48.2)
Total energy (Kcal/day) *		1,174 $\pm$ 372	1,625 $\pm$ 376	2,220 $\pm$ 673
Medication	ACE inhibitor *	18 (54.5)	60 (60.6)	88 (78.6)
	ARB II	9 (27.3)	25 (25.3)	16 (14.3)
	Digoxin	9 (27.3)	21 (21.2)	27 (24.1)
	β -blocker	29 (87.9)	87 (87.9)	100 (89.3)
	Diuretics	25 (75.8)	74 (74.7)	85 (75.9)
	Furosemide equivalent (mg/day)	39 $\pm$ 18	42 $\pm$ 23	42 $\pm$ 23
	Hydrochlorothiazide (mg/day)	28 $\pm$ 9	23 $\pm$ 9	27 $\pm$ 11
	Aldosterone antagonist	11 (33.3)	23 (23.2)	29 (25.9)

ACE; angiotensin-converting enzyme, ARB II; Angiotensin II receptor blocker, HF; heart failure, NYHA; New York Heart Association, NT-pro BNP; N-terminal pro B-type natriuretic peptide

* ; $p < 0.05$ by analysis of variance (ANOVA) or Chi-square tests among patients with < 2 g, 2 to 3 g, and > 3 g of daily sodium intake

Table 3

Event-rates and median time to first event in patients classified by different sodium intake and New York Heart Association class

	Total (N = 244)	NYHA class I/II (n = 134)			NYHA class III/IV (n=110)		
		<2g (n = 20)	2 to 3g (n = 54)	> 3g (n = 60)	<2g (n = 13)	2 to 3g (n = 45)	> 3g (n = 52)
All-cause death	6 (2.5)	1 (5.0)	1 (1.9)	0 (0.0)	0 (0.0)	1 (2.2)	3 (5.8)
HF-related hospitalization	22 (9.0)	0 (0.0)	4 (7.4)	3 (5.0)	4 (30.8)	6 (13.3)	5 (9.6)
Cardiac-related hospitalization	34 (13.9)	2 (10.0)	9 (16.7)	6 (10.0)	1 (7.7)	5 (11.1)	11 (21.2)
Other hospitalization	30 (12.3)	5 (25.0)	3 (5.6)	2 (3.3)	1 (7.7)	8 (17.8)	11 (21.2)
Total events	92 (37.3)	8 (40.4)	17 (31.5)	11 (18.3)	6 (46.2)	20 (44.4)	30 (57.7)
Median time to first event (days)	214 (90, 333)	93 (70, 234)	200 (95, 298)	250 (119, 494)	220 (92, 338)	208 (89, 329)	208 (89, 329)

Values are n (%) or median (25th, 75th quartile)

Adjusted differences to event-free survival among patients with < 2 g, 2 to 3 g, and > 3 g of dietary sodium intake in NYHA class I/II and NYHA class III/IV

Table 4

Variables	NYHA class I/II (n = 134)				NYHA class III/IV (n = 110)			
	Adjusted HR	95% CI	p	Adjusted HR	95% CI	p	Adjusted HR	95% CI
Age (years)	1.00	0.97 – 1.03	.996	1.00	0.97 – 1.02	.712		
Female gender	0.32	0.13 – 0.83	.018	1.41	0.66 – 3.00	.381		
BMI (kg/m ²)	1.03	0.95 – 1.11	.515	1.02	0.98 – 1.06	.408		
Ischemic heart disease	1.43	0.58 – 3.53	.436	0.99	0.52 – 1.94	.998		
Preserved LVEF 40%	0.92	0.38 – 2.26	.860	0.53	0.25 – 1.22	.093		
Total comorbidity	0.79	0.60 – 1.04	.095	1.13	0.98 – 1.30	.089		
ACE inhibitors	1.07	0.45 – 2.53	.878	1.04	0.54 – 1.99	.907		
Diuretics	1.95	0.72 – 5.32	.190	1.07	0.49 – 2.36	.868		
Beta blockers	0.82	0.29 – 2.31	.702	1.90	0.85 – 4.24	.118		
Total energy (Kcal)	1.00	0.99 – 1.00	.352	0.98	0.96 – 1.01	.114		
Lower leg or ankle edema	0.63	0.24 – 1.62	.333	1.26	0.50 – 3.17	.626		
2g–3g/day of sodium intake	1.00		1.00					
< 2g/day of sodium intake	3.68	1.18–11.50	.025	0.65	0.23 – 1.83	.418		
> 3g/day of sodium intake	0.39	0.16 – 0.98	.047	2.06	1.02 – 4.17	.044		

ACE; angiotensin-converting enzyme, BMI; body mass index, HR; hazard ratio, LVEF; left ventricular ejection fraction, NYHA; New York Heart Association