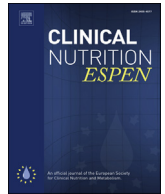




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## Original article

## Changes in dietary intake and nutritional status associated with a significant reduction in sodium intake in patients with heart failure. A sub-analysis of the SODIUM-HF pilot study

Eloisa Colin-Ramirez <sup>a,1</sup>, Finlay A. McAlister <sup>b</sup>, Yinggan Zheng <sup>c</sup>, Sangita Sharma <sup>a</sup>, Justin A. Ezekowitz <sup>a,c,d,\*</sup>

<sup>a</sup> Medicine Department, University of Alberta, Edmonton, Canada

<sup>b</sup> Division of General Internal Medicine, University of Alberta, Edmonton, Canada

<sup>c</sup> Canadian VIGOUR Centre at the University of Alberta, Edmonton, Canada

<sup>d</sup> Heart Function Clinic, Division of Cardiology, University of Alberta, Edmonton, Canada

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## SUMMARY

**Background & aims:** Concerns have been raised about the impact of dietary sodium restriction on the overall dietary intake and nutritional status in patients with heart failure (HF). The objective of this study was to evaluate the association between a significant reduction in sodium intake and dietary changes and nutritional status in patients with chronic HF.

**Methods:** This is a secondary analysis of 38 patients enrolled in a pilot study of dietary sodium reduction. Patients were classified into two groups according to a level of sodium reduction achieved ( $\geq 25\%$  [ $n = 21$  patients] and  $< 25\%$  [ $n = 14$  patients]) at 6 months. Between group changes in energy, nutrient intake, weight loss, and hand grip strength from baseline to 6 months were compared.

**Results:** Patients had a median age of 65 years, 51% were male, median body mass index was 30.7 kg/m<sup>2</sup> and median ejection fraction was 39%. Over 6 months, the group with  $\geq 25\%$  sodium reduction exhibited a greater increase in folate intake [median change 50 mcg/day (25th–75th percentiles: –101, 167) vs. –31 mcg/day (25th–75th percentiles: –221, 51),  $p = 0.04$  between groups] and a larger reduction in calcium intake [median change –262 (25th–75th percentiles: –585, –9) vs. 91 (25th–75th percentiles: –114, 210),  $p = 0.01$  between groups], and were more likely to meet the parameters of the DASH diet compared to the  $< 25\%$  sodium reduction group. No significant differences between groups were seen for caloric intake and other relevant nutrients and no significant weight loss was found in either group.

**Conclusions:** Dietary sodium reduction may be achieved without compromising overall dietary intake and nutritional status in patients with HF when an individualized and comprehensive dietary approach is used.

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### 1. Introduction

Dietary sodium restriction is the primary nutritional recommendation in heart failure (HF) [1–3]. Despite this recommendation, the most suitable level of restriction for this population is still unclear [4]. In addition, concerns have been raised about the impact that dietary sodium restriction may have on the overall dietary intake and nutritional status in patients on a low-sodium diet [5,6]. Previous studies have reported that dietary inadequacies (e.g.

\* Corresponding author. 2-132 Li Ka Shing Centre for Health Research Innovation, Edmonton, Alberta, Canada. Tel.: +1 7804078719; fax: +1 7804076452.

E-mail address: [jae2@ualberta.ca](mailto:jae2@ualberta.ca) (J.A. Ezekowitz).

<sup>1</sup> Present/permanent address: National Institute of Cardiology 'Ignacio Chavez', Mexico City, Mexico.

calories, protein, and several vitamins and minerals) are common in patients with HF [7–13], and several factors have been associated with decreased food intake in these patients, including decreased hunger sensations, fatigue, shortness of breath, nausea, anxiety, sadness, and medically-recommended diet restrictions [14]. Additionally, retrospective observational studies have linked dietary sodium consumption of <2000 mg/day to poor overall nutrient intake [5,6].

In patients with HF, a sodium-restricted diet is often described as unpalatable and subsequently related to decreased appetite, leading to higher risk of poor nutritional intake [14]. However, patients with more advanced HF are also more likely to reduce their overall dietary intake, including sodium, due to impaired appetite, introducing confounding to this association [15]. Additionally, poor nutritional status [16] and micronutrient deficiencies [17] have been shown to have a strong association with a shorter survival in patients with HF. Therefore, it is important to investigate whether a reduction in dietary sodium intake, the primary dietary strategy in HF, has an impact on overall dietary intake and nutritional status in this patient population.

We conducted a randomized controlled trial of dietary sodium reduction in patients with chronic HF [18], and collected detailed dietary and HF-related information over 6 months. The objective of this analysis was to evaluate the association between a significant reduction in sodium intake and changes in macro and micronutrients intake and markers of nutritional status in patients with chronic heart failure.

## 2. Materials and methods

### 2.1. Study design and population

This is a secondary analysis of the SODIUM-HF pilot study. The SODIUM-HF pilot was a randomized controlled trial (RCT) to determine the feasibility of conducting an RCT comparing a low-sodium diet (65 mmol or 1500 mg daily) to a moderate-sodium diet (100 mmol or 2300 mg daily) and to explore the effects of a low sodium diet on quality of life and B-type natriuretic peptide (BNP) levels in patients with chronic HF.

Patients were recruited from the Heart Function Clinic of the Mazankowski Alberta Heart Institute in Edmonton, Canada. After providing informed consent to participate in the study, participants were randomly assigned to either the low- or moderate-sodium diet. Details on the study design and patient's selection criteria were reported elsewhere [18]. The study was approved by the Health Research Ethics Board of the University of Alberta and all the patients provided written informed consent to participate in the study.

Overall, 38 patients ( $n = 19$  in the low-sodium diet,  $n = 19$  in the moderate-sodium diet) were enrolled in this pilot trial from May to December 2012, and 35 completed the 6-month follow-up. Two patients withdrew consent (one in each group) and one died.

### 2.2. Dietary intervention

Dietary intervention used in the SODIUM-HF pilot trial was described in detail previously [18]. In brief, regardless of the level of sodium restriction each patient was randomized to <2300 or <1500 mg/day, participants in both groups were prescribed a normocaloric diet with the following energy distribution as percentage of daily energy intake: carbohydrates, 50–55%; protein, 15–20%; fat, 25–30%; and saturated fat, <7%; consistent with the guidelines for a cardiovascular healthy diet [19].

Patients in both groups were provided with a meal plan containing specific dietary recommendations to achieve the targeted

level of sodium restriction. In addition, all patients were given a set of six daily sample menus according to their energy requirements, energy distribution, and level of sodium restriction.

Patients in both groups received conventional pharmacological and non-pharmacologic treatment for HF according to current Canadian Cardiovascular Society HF guidelines [1]. Also, patients were asked to follow the recommendations for fluid restriction provided by their clinician as per clinical practice – typically 2000–3000 ml/day in Canada. No specific recommendations for fluid restriction were provided as part of the dietary intervention.

### 2.3. Classification of study participants according to level of sodium reduction

In the pilot trial, both groups reported a significant reduction in dietary sodium intake at follow-up, with an average daily intake of less than 1500 mg/day at 6 months. Therefore, and for the purpose of this secondary analysis, all 35 participants that completed the 6-month follow-up were combined regardless of the dietary treatment allocation. Patients were further *a priori* classified into two groups according to level of sodium reduction from baseline to 6 months split at 25% reduction. A 25% reduction was chosen based on prior cut-offs used in hypertension trials of lifestyle interventions reduced sodium intake by about 25–35%, and this decrease in sodium intake has been associated with cardiovascular risk reduction [20]. The median sodium reduction in the entire study population was 34.4%, thus a sensitivity analysis of dietary changes was tested with a sodium reduction split at 35%.

### 2.4. Dietary information and assessments

#### 2.4.1. Dietary intake

Dietary intake, including sodium intake, was assessed by using 3-day food records (including 2 week days and 1 weekend day). For the purpose of this analysis, food records collected at baseline and 6-months were analyzed. Patients were instructed to record all food and beverages consumed using standard household measures (e.g. cups, tablespoons) or commercial measures (e.g. weight of commercially packaged foods as given on the label, number of servings or pieces consumed). Patients were asked to provide the *Nutrition Facts Label* of the packaged foods, when possible. Patients also recorded if any condiments or salt were added at the table or during cooking. If the amount of salt could not be measured in household measures, patients were asked to record the number of pinches or shakes added to the food so that sodium could be estimated. All food records were reviewed by the dietitian during interview with the patient to clarify food-item descriptions and portion sizes and to identify any missing food items. Food records were analyzed by trained personnel, with a nutrient software program (ESHA Food Processor SQL v.10.11; ESHA Research, Salem, OR). Additional food items were added to the ESHA database when none of the food items contained in the current database reflected the actual food consumed by the patient (e.g. no salt added homemade food, restaurant meals, etc.). Food records entered for analysis were checked twice for accuracy by independent coders. A mean dietary intake from the 3 days was estimated for energy, fiber, macro and micronutrients, and total fluids.

In addition, dietary intake was evaluated according to the DASH diet daily nutrient goals for daily nutrient intake (total fat  $\leq 27\%$  of daily energy intake [DEI]; saturated fat  $\leq 6\%$  of DEI; protein  $\geq 18\%$  of DEI; carbohydrates  $\leq 55\%$  of DEI; cholesterol  $\leq 150$  mg; potassium  $\geq 4700$  mg; calcium  $\geq 1250$  mg; magnesium  $\geq 500$  mg; and fiber  $\geq 30$  g) [21]. Proportion of patients meeting the DASH diet daily nutrient goals at baseline and 6 months was described for both groups.

#### 2.4.2. Nutritional status markers

Percentage weight change at follow-up was calculated and patients were classified according to a weight loss of 5% or greater in 6 months [22]. Hand-grip strength was measured at baseline and 6 months with a calibrated Jamar Hydraulic Hand Dynamometer (Sammons Preston Roylan, Bolingbrook, IL); the measurement was repeated twice, and the highest score was recorded in kilograms [23].

#### 2.5. Statistical analysis

Continuous variables were expressed as median (25th–75th percentiles), and categorical variables were presented as percentages. Changes from baseline to 6 months (deltas) were compared between groups of achieved sodium reduction by using the Mann–Whitney *U* test for continuous data, and chi-square test or Fisher's exact test for categorical data. All statistical tests were two-sided, and were considered statistically significant when  $p < 0.05$ . Analyses were performed using SPSS Version 17.0 (SPSS, Inc., Chicago, IL, USA).

Study data were collected and managed using REDCap electronic data capture tools hosted at the Faculty of Medicine & Dentistry at the University of Alberta.

### 3. Results

Of the 35 patients included for analysis, 21 achieved a reduction in dietary sodium intake  $\geq 25\%$  at 6 months, with a median change in sodium intake of  $-49\%$  (25th–75th percentile:  $-67, -41$ ), while 14 patients did not achieve this level of reduction, with a median

change in sodium intake of  $-8\%$  (25th–75th percentile:  $-17, 17$ ). Baseline characteristics by achieved sodium reduction are described in Table 1. Patients in both groups were similar; except for baseline dietary sodium intake was nearly twice as high in the group of patients who ultimately achieved sodium reduction  $\geq 25\%$  than in those who achieved less sodium reduction.

#### 3.1. Changes in dietary intake at follow-up

Over 6 months, the group of patients with sodium reduction  $\geq 25\%$  increased intake of folate and trended to increased intake of protein (as percentage of DEI), compared to a decrease in these two nutrients in the group achieving sodium reduction  $< 25\%$ , who also showed a greater decrease in intake of vitamin B6. Intake of calcium was significantly reduced in patients with sodium reduction  $\geq 25\%$ , while increased in those with sodium reduction  $< 25\%$ . In addition, there was a trend towards a greater reduction in saturated fat intake (as percentage of DEI) in the group of sodium reduction  $\geq 25\%$  compared to the group of sodium reduction  $< 25\%$ . Changes in caloric intake and other nutrients included in this analysis were not different between groups of sodium reduction (Table 2).

Compared to baseline, the proportion of patients that met the DASH diet goals for sodium (1500 and 2300 mg/day), total fat, saturated fat, protein and fiber increased at 6 months in the group of sodium reduction  $\geq 25\%$ , while a reduced number of patients achieved the goal for cholesterol and none of the patients met the goal for calcium in this same study group at 6 months. Importantly, no patients in this group met the goal for potassium or magnesium either at baseline or 6 months. The group of patients with sodium reduction  $< 25\%$  reported an increased proportion of patients that

**Table 1**  
Select baseline characteristics for patients included in analysis by groups of sodium reduction.

Characteristics	Overall (n = 35)	Dietary sodium reduction $\geq 25\%$ (n = 21)	Dietary sodium reduction $< 25\%$ (n = 14)	p
<b>Demographics, history and physical examination</b>				
Age, y	65 (56–72)	65 (54.5–73)	66.5 (55.8–73)	0.727
Male, %	51.4	52.4	50	0.890
BMI, kg/m <sup>2</sup>	30.7 (27.1–35.9)	32.5 (25.2–37.4)	29.9 (27.5–35.6)	0.654
NYHA class, %				1.0
II	91.4	90.5	92.9	
III	8.6	9.5	7.1	
Ischemic etiology of HF, %	34.3	38.1	28.6	0.561
Cerebrovascular disease, %	8.6	9.5	7.1	1.0
Diabetes mellitus, %	31.4	38.1	21.4	0.461
Hypertension, %	57.1	57.1	57.1	1.0
Dyslipidemia, %	62.9	66.7	57.1	0.568
Ejection fraction, %	39 (25–50.5)	37 (25–49)	45 (25–55)	0.550
Baseline sodium intake, mg/day	2354 (1699–3042)	2927 (2325–3668)	1594 (1280–2173)	<0.001
<b>Laboratory</b>				
Sodium, mmol/L	139 (137–140)	138 (136–139)	139 (139–140)	0.083
Potassium, mmol/L	4.2 (3.9–4.6)	4.2 (3.9–4.6)	4.5 (4.0–5.0)	0.210
Creatinine, $\mu\text{mol/L}$	104 (75–131)	96 (73.5–134.5)	106 (83.3–131.3)	0.855
Albumin, g/L	42 (38–43)	42 (38–43)	42 (40–44)	0.434
<b>Cardiac medications, %</b>				
ACEi or ARB	91.4	95.2	85.7	0.551
Beta-blockers	94.3	95.2	92.9	1.0
MRA	54.3	57.1	50	0.678
Loop diuretics	80	76.2	85.7	0.676
Non-loop diuretics	17.1	14.3	21.4	0.664
Anti-platelet agents	60	57.1	64.3	0.673
Anticoagulants	40	28.6	57.1	0.091

BMI, body mass index; NYHA, New York Heart Association; ACE inhibitors, angiotensin-converting-enzyme inhibitor; ARB, angiotensin receptor blockers; MRA, mineralocorticoid receptor antagonist.

Loop diuretics include only furosemide; non-loop diuretics include metolozone and thiazide, anti-platelet agents include aspirin and clopidogrel.

Values are medians (25th–75th percentiles) unless otherwise stated.

Data with median (25th–75th percentiles): *p*-values determined by Mann–Whitney *U* test between groups.

Data with %: *p*-values determined by Pearson's chi square or Fisher's exact test between groups.

**Table 2**  
Changes in dietary intake from baseline to 6 months by groups of dietary sodium reduction.

Dietary factor	Dietary sodium reduction $\geq 25\%$ ( $n = 21$ )			Dietary sodium reduction $< 25\%$ ( $n = 14$ )			*P value
	Baseline	6 Months	Absolute change ( $\Delta$ )	Baseline	6 Months	Absolute change ( $\Delta$ )	
Energy, kcal/day	1778 (1454, 2443)	1321 (1135, 1865)	-356 (-840, 91)	1488 (1257–1883)	1423 (1331–1758)	-20 (-261, 192)	0.118
Fiber, g/day	19 (16, 24)	19 (14–26)	1 (-7, 6)	20 (14–27)	19 (15–21)	-1 (-9, 4)	0.454
Sugar, g/day	99 (63, 130)	74 (52–92)	-18 (-59, -6)	90 (64–115)	81 (57–103)	-12 (-40, 25)	0.606
Fluid, ml/day	1560 (1389, 2035)	1620 (1205–2104)	-70 (-346, 219)	1694 (1523–2264)	1659 (1268–2425)	-18 (-354, 242)	0.960
<b>Macronutrients</b>							
Carbohydrates, g/day	223 (182, 290)	173 (138–225)	-41 (-84, -3)	200 (142–264)	212 (172–225)	-9 (-72, 65)	0.249
Carbohydrates, % of daily energy	50 (46, 54)	49 (46–51)	-0.45 (-5.56, 1.46)	54 (46–59)	54 (43–61)	0.25 (-8.74, 8.85)	0.907
Protein, g/day	78 (61, 115)	76 (61–111)	-0.95 (-18.22, 18.82)	66 (57–88)	66 (54–83)	-0.62 (-15.52, 9.85)	0.881
Protein, % of daily energy	18 (16, 21)	22 (19–27)	4 (-0.17, 10)	20 (14–22)	18 (15–22)	0.16 (-4, 2)	<b>0.056</b>
Total fat, g/day	65 (49, 92)	43 (37–59)	-14 (-43, -1)	54 (44–58)	51 (33–60)	-1 (-16, 10)	0.154
Total fat, % of daily energy	33 (28, 39)	31 (25–37)	-5 (-12, 3)	29 (26–33)	32 (22–33)	-0.27 (-5.55, 3.83)	0.342
Saturated fat, g/day	27 (13, 32)	14 (9–19)	-8 (-15, 3)	15 (11–19)	14 (11–20)	-0.38 (-7.70, 5.75)	<b>0.077</b>
Saturated fat, % of daily energy	11 (9, 13)	9 (6–12)	-2 (-5, 0.32)	9 (7–10)	8 (7–10)	-0.20 (-4.05, 2.75)	0.210
Cholesterol, mg/day	321 (135, 432)	258 (166–348)	33 (-145, 120)	217 (119–260)	193 (102–275)	-7 (-80, 88)	0.855
<b>Micronutrients</b>							
Thiamin, mg/day	0.95 (0.64, 1.10)	0.80 (0.62–1.02)	-0.09 (-0.33, 0.30)	0.94 (0.55–1.45)	0.94 (0.68–1.22)	0.03 (-0.46, 0.22)	0.702
Niacin, mg/day	15 (8, 24)	17 (10–26)	-2 (-5, 7)	23 (15–25)	17 (12–33)	-2 (-7, 6)	0.538
Folate, mcg/day	189 (129, 273)	218 (131–335)	50 (-101, 167)	206 (141–513)	177 (140–290)	-31 (-221, 51)	<b>0.044</b>
Vitamin B6, mg/day	0.93 (0.48, 1.44)	0.90 (0.48–1.47)	-0.04 (-0.31, 29)	1.34 (0.85–3.18)	1.32 (0.43–1.88)	-0.53 (-1.19, 0.15)	<b>0.031</b>
Vitamin C, mg/day	87 (41, 119)	88 (51–118)	-0.44 (-40, 38)	77 (49–148)	79 (61–174)	-5 (-45, 35)	0.881
Sodium, mg/day	2927 (2325, 3668)	1348 (894–1539)	-1472 (-2202, -996)	1594 (1280–2173)	1820 (1328–2124)	-176 (-245, 255)	<b>&lt;0.001</b>
Potassium, mg/day	1778 (1180, 2390)	1783 (1553–2452)	34 (-524, 959)	1994 (1583–2910)	1893 (1417–2960)	-236 (-1082, 449)	0.325
Calcium, mg/day	790 (575, 1245)	550 (447–738)	-262 (-585, -9)	669 (542–1068)	755 (564–972)	91 (-114, 210)	<b>0.012</b>
Magnesium, mg/day	174 (122, 226)	147 (112–241)	24 (-62, 59)	182 (123–284)	166 (125–284)	9 (-57, 46)	0.516

Values are medians (25th, 75th percentiles).

\*P-values represent the difference in changes between groups determined by Mann–Whitney *U* test.

met the goal for total fat and cholesterol at 6 months compared to baseline; however, a lower proportion of patients met the goal for sodium (1500 mg/day), protein and carbohydrates, and none of the patients in this group met the goals for potassium, magnesium, and fiber at 6 months. Differences between groups showed a higher proportion of patients that achieved the goal for sodium ( $< 1500$  mg/day), protein and carbohydrates at 6 months in the group of sodium reduction  $\geq 25\%$  compared to the group with sodium reduction  $< 25\%$  (Table 3).

### 3.2. Changes in nutritional status markers at follow-up

Two patients (9.5%) in the group of sodium reduction  $\geq 25\%$  and 1 (7.1%) in the group of sodium reduction  $< 25\%$  presented a body weight loss of 5% or more from baseline to 6 months ( $p = 1.0$  between groups).

**Table 3**  
Proportion of patients that met the DASH diet goals at baseline and 6 months by groups of sodium reduction.<sup>a</sup>

Component of the DASH diet goal	Dietary sodium reduction $\geq 25\%$ ( $n = 21$ )		Dietary sodium reduction $< 25\%$ ( $n = 14$ )		**P value
	Baseline	6 months	Baseline	6 months	
Sodium 1500 mg	4.8	76.2	50	35.7	0.033
Sodium 2300 mg	23.8	90.5	85.7	85.7	1.0
Total fat 27% of DEI	19	33.3	28.6	35.7	1.0
Saturated fat 6% of DEI	0	14.3	14.3	14.3	1.0
Protein 18% of DEI	47.6	81	57.1	50	0.073
Carbohydrates 55% of DEI	85.7	85.7	64.3	50	0.053
Cholesterol 150 mg	28.6	19	28.6	42.9	0.151
Potassium 4700 mg	0	0	7.1	0	
Calcium 1250 mg	23.8	0	14.3	14.3	0.153
Magnesium 500 mg	0	0	7.1	0	
Fiber 30 g	14.3	19	21.4	0	0.133

\*\*P-values represent the difference between groups for frequencies at 6 months determined by Fisher's exact test.

<sup>a</sup> Data reflect percent of patients (%) per study group.

Over six months, grip strength trended to increase (28–31 kg; median change: 3 kg [0, 7 kg]) in the group of patients with sodium reduction  $\geq 25\%$  compared to the group of sodium reduction  $< 25\%$  (31–33 kg; median change: 2 kg [-3, 2]);  $p = 0.09$  between groups).

### 3.3. Sensitivity analysis

When patients were re-classified according to the median sodium reduction of 35% at 6 months, 17 (48.6%) achieved a sodium reduction  $\geq 35\%$  and 18 (51.4%) achieved less reduction. Contrary to that observed with a sodium reduction  $\geq 25\%$ , patients with a sodium reduction  $\geq 35\%$  exhibited significant decreases in energy, protein and total fat intakes (as percentage of DEI) at follow-up (Table 4).

**Table 4**

Changes in hand-grip strength, weight and select dietary factors according to 35% sodium reduction (defined by the median of reduction in the overall study population).

	Dietary sodium reduction $\geq 35\%$ ( $n = 17$ )			Dietary sodium reduction $< 35\%$ ( $n = 18$ )			P value*
	Baseline	6 Months	Absolute change ( $\Delta$ )	Baseline	6 Months	Absolute change ( $\Delta$ )	
Hand-grip strength, kg	28 (23–34)	31 (29–38)	3 (–1, 7)	31 (20–45)	33 (20–44)	2 (–2, 3)	0.274
Weight loss $\geq 5\%$ , %		11.8			5.6		0.603**
Dietary factors							
Energy, kcal/day	1778 (1454–2443)	1280 (1108–1533)	–391 (–1030, –293)	1542 (1295–1883)	1483 (1332–2038)	24 (–147, 302)	<b>0.006</b>
Carbohydrates, % of daily energy	50 (44–54)	49 (45–52)	–0.12 (–6, 4)	54 (47–58)	52 (46–57)	–0.52 (–8, 5)	0.832
Protein, % of daily energy	18 (16–22)	25 (20–27)	5 (2, 10)	18 (15–21)	17 (15–21)	0.16 (–4, 3)	<b>0.025</b>
Total fat, % of daily energy	33 (28–41)	28 (24–33)	–6 (–14, 1)	30 (27–37)	33 (25–34)	2 (–4, 4)	<b>0.049</b>
Saturated fat, % of daily energy	11 (9–13)	7 (6–13)	–2 (–6, 0.28)	9 (8–11)	9 (8–11)	–0.26 (–4, 2)	0.195
Thiamin, mg/day	0.96 (0.64–1.19)	0.80 (0.62–1.02)	–0.09 (–0.38, 0.24)	0.88 (0.55–1.25)	0.86 (0.68–1.22)	0.03 (–0.42, 0.30)	0.807
Niacin, mg/day	17 (9–25)	17 (10–26)	–2 (–6, 7)	21 (12–24)	17 (12–31)	–2 (–6, 8)	0.858
Folate, mcg/day	230 (136–273)	218 (131–363)	50 (–101, 168)	171 (128–449)	202 (140–301)	–9 (–149, 82)	0.110
Vitamin B6, mg/day	1.00 (0.54–1.52)	0.90 (0.48–1.53)	–0.04 (–0.38, 0.19)	1.04 (0.62–2.95)	1.20 (0.45–1.63)	–0.32 (–0.84, 0.63)	0.219
Vitamin C, mg/day	90 (47–123)	99 (61–118)	–0.44 (–0.34, 38)	72 (44–119)	77 (43–148)	–5 (–55, 35)	0.757
Sodium, mg/day	2927 (2325–3668)	1115 (811–1444)	–1607 (–2202, –1066)	2011 (1329–2699)	1870 (1404–2124)	–225 (–509, 219)	<b>&lt;0.001</b>
Potassium, mg/day	1805 (1220–2487)	1783 (1465–2452)	34 (–584, 959)	1927 (1491–2784)	1822 (1467–2909)	–128 (–674, 449)	0.613
Calcium, mg/day	790 (575–1245)	546 (447–683)	–262 (–585, –81)	735 (542–1068)	751 (564–935)	81 (–183, 210)	<b>0.015</b>
Magnesium, mg/day	179 (135–232)	147 (107–227)	–4 (–90, 53)	175 (112–234)	166 (125–284)	25 (–46, 62)	0.858

Values are medians (25th, 75th percentiles).

\*P-values represent the difference in changes between groups determined by Mann–Whitney U test.

\*\*P-value represents the difference proportion of patients that presented a weight loss  $\geq 5\%$  in 6 months between groups determined by Fisher's exact test.

#### 4. Discussion

In this secondary analysis of a pilot trial of dietary sodium reduction, we have demonstrated that it is feasible to reduce dietary sodium intake  $\geq 25\%$  without causing a significant negative impact on the nutrient intake profile and nutritional status in patients with chronic HF. For example, using our individualized and comprehensive dietary approach, dietary sodium intake dropped from 2927 mg/day to 1348 mg/day in the group of patients that reduced sodium intake by 25% or more after 6 months of the dietary intervention. This reduction was observed along with an improvement in dietary intake profile as suggested by an increase in folate intake and a trend towards an increased protein and a decreased saturated fats intake from baseline to 6 months. This was also achieved without causing a major reduction in other relevant nutrients such as thiamin, niacin, vitamin C, potassium, and magnesium.

Our results confirm other studies that dietary sodium intake can be reduced and other dietary factors can be improved when a comprehensive and individualized dietary treatment plan is instituted. For example, a decreased intake of dietary fat (total or saturated) [24–26] and calories [24,26] was found at the end of follow-up in patients that received individualized dietary treatment for sodium reduction. In addition, The 2010 Dietary Guidelines for Americans Advisory Committee conducted a modeling study of dietary patterns that achieve nutrient adequacy while meeting sodium goals [27]. They determined that nutrient adequacy could be achieved at a sodium intake of 1500 mg/day when foods with lower sodium content were chosen in place of higher-sodium options.

It is important to mention that patients with a significant reduction in sodium intake in this study also significantly reduced intake of calcium. Several studies have reported a high frequency of inadequate calcium intake in patients with HF when compared to different established intake recommendations [7,9–11]. Akin to the findings of this analysis, a reduced calcium intake after dietary treatment for sodium reduction has been previously reported in a HF population [25]. Therefore, it seems that calcium

needs more attention when dietary counseling is provided to HF patients, and the prognostic significance of this nutritional deficiency in the HF setting needs to be further studied. However, it is reassuring that two recent studies failed to find an association between deficient calcium intake and mortality [28,29] in HF patients.

In our study, there was a low rate of compliance to most of the DASH diet daily goals in both groups, either at baseline or 6 months. Higher compliance with the DASH diet has been associated with lower mortality in women with HF [30]. It is worth noting that at 6 months, none of the patients in both groups of our study met the DASH goals for potassium and magnesium. Even though a sodium reduction  $\geq 25\%$  was not found to induce a significant decrease in the intake of these two micronutrients, patients reported a low baseline intake of potassium and magnesium that remained low at follow-up. This may be due to the fact that many patients with HF are told to reduce their intake of rich-potassium foods due to the risk of hyperkalemia with the use of potassium-sparing cardiac medications and/or to the co-existence of renal disease. Additionally, some foods rich in potassium are also good source of magnesium, such as certain legumes, nuts and seeds. Therefore, using the DASH diet as dietary reference in HF may not be appropriate in patients with a prescribed restriction of potassium intake.

Few studies have reported the prospective association between sodium restriction and dietary intake in HF [24–26] and to our knowledge, this is the first study that provides information about changes in intake of macro and several micronutrients associated with dietary sodium reduction in this patient population. Further studies that evaluate the prognostic importance of sodium restriction and dietary intake in HF are still needed; the ongoing Study of Dietary Intervention Under 100 MMOL in Heart Failure (SODIUM-HF; clinical trials.gov NCT02012179) will provide this answer.

Regarding nutritional status, no significant weight loss was found in either group, and a trend towards a greater improvement in hand grip strength was seen in the group with a significant sodium reduction compared to the group with less sodium reduction.

Hand grip strength is an emerging marker of muscle function that has been also employed as marker of nutritional status [23].

Finally, results of the sensitivity analysis suggest that a greater sodium reduction as high as 35% might lead to a significant reduction in energy, protein and fat; therefore, greater efforts should be done to keep an adequate dietary intake when a higher sodium intake reduction is being pursued.

#### 4.1. Limitations

This study is a secondary analysis of a randomized trial but is an observational study since study groups were formed based on dietary sodium intake achieved at follow-up. Relevant limitations associated to this work include: 1) small sample size, further hypothesis-driven studies should explore these questions in larger populations and account for potential confounding factors for this association such as ischemic etiology, presence of cardiovascular risk factors (diabetes and dyslipidemia), consumption of certain medications and ejection fraction; 2) patients with a sodium reduction achieved <25% had a lower sodium intake at baseline, thus had a narrow improvement threshold for sodium intake and therefore showed lower adherence to the overall dietary recommendations. However, this finding does not diminish the relevance of the results regarding the feasibility of sodium reduction without compromising overall dietary intake. Even when patients in the comparison group (sodium reduction <25%) were already following recommendations for sodium reduction, these showed an impaired dietary intake profile; 3) body weight assessment may not be sufficient to evaluate nutrition status in patients with heart failure due to alterations in fluid balances affecting body weight, and a body composition assessment may be more appropriate in this patient population; however, a marker of muscle function and nutritional status such as hand grip strength, was included in this analysis; and 4) although self-report of dietary intake using a 3-day food record has the potential for recall bias, these limitations were the same for both groups; additionally, methodology for collection of 3-day food records followed in this study included a detailed revision of the dietary information collected with the patient for completeness and accuracy in order to ensure quality of information.

## 5. Conclusion

Dietary sodium reduction may be achieved without compromising overall dietary intake and nutritional status in patients with HF when an individualized and comprehensive dietary approach is used. Special attention should be paid to dietary intake, particularly of calcium and magnesium, when pursuing a greater reduction in sodium intake.

#### Statement of authorship

ECR. Conception and design, analysis and interpretation of data, drafting of the manuscript and final approval of the manuscript submitted. FAM. Interpretation of data, revising manuscript critically for important intellectual content and final approval of the manuscript submitted. YZ. Analysis and interpretation of data, revising manuscript critically for important intellectual content and final approval of the manuscript submitted. SS. Interpretation of data, revising manuscript critically for important intellectual content and final approval of the manuscript submitted.

JAE. Conception and design, interpretation of data, drafting of the manuscript and final approval of the manuscript submitted.

#### Conflict of interest/disclosures

None.

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