

Aggressive Fluid and Sodium Restriction in Acute Decompensated Heart Failure

A Randomized Clinical Trial

Graziella Badin Aliti, RN, ScD; Eneida R. Rabelo, RN, ScD; Nadine Clausell, MD, PhD; Luís E. Rohde, MD, ScD; Andreia Biolo, MD, ScD; Luis Beck-da-Silva, MD, ScD

Importance: The benefits of fluid and sodium restriction in patients hospitalized with acute decompensated heart failure (ADHF) are unclear.

Objective: To compare the effects of a fluid-restricted (maximum fluid intake, 800 mL/d) and sodium-restricted (maximum dietary intake, 800 mg/d) diet (intervention group [IG]) vs a diet with no such restrictions (control group [CG]) on weight loss and clinical stability during a 3-day period in patients hospitalized with ADHF.

Design: Randomized, parallel-group clinical trial with blinded outcome assessments.

Setting: Emergency room, wards, and intensive care unit.

Participants: Adult inpatients with ADHF, systolic dysfunction, and a length of stay of 36 hours or less.

Intervention: Fluid restriction (maximum fluid intake, 800 mL/d) and additional sodium restriction (maximum dietary intake, 800 mg/d) were carried out until the seventh hospital day or, in patients whose length of stay was less than 7 days, until discharge. The CG received a standard hospital diet, with liberal fluid and sodium intake.

Main Outcomes and Measures: Weight loss and clinical stability at 3-day assessment, daily perception of thirst, and readmissions within 30 days.

Results: Seventy-five patients were enrolled (IG, 38; CG, 37). Most were male; ischemic heart disease was the predominant cause of heart failure (17 patients [23%]), and the mean (SD) left ventricular ejection fraction was 26% (8.7%). The groups were homogeneous in terms of baseline characteristics. Weight loss was similar in both groups (between-group difference in variation of 0.25 kg [95% CI, -1.95 to 2.45]; $P = .82$) as well as change in clinical congestion score (between-group difference in variation of 0.59 points [95% CI, -2.21 to 1.03]; $P = .47$) at 3 days. Thirst was significantly worse in the IG (5.1 [2.9]) than the CG (3.44 [2.0]) at the end of the study period (between-group difference, 1.66 points; time \times group interaction; $P = .01$). There were no significant between-group differences in the readmission rate at 30 days (IG, 11 patients [29%]; CG, 7 patients [19%]; $P = .41$).

Conclusions and Relevance: Aggressive fluid and sodium restriction has no effect on weight loss or clinical stability at 3 days and is associated with a significant increase in perceived thirst. We conclude that sodium and water restriction in patients admitted for ADHF are unnecessary.

Trial Registration: clinicaltrials.gov Identifier: NCT01133236

JAMA Intern Med. 2013;173(12):1058-1064.

Published online May 20, 2013.

doi:10.1001/jamainternmed.2013.552

Author Affiliations:

Postgraduate Program in Cardiovascular Sciences, Cardiology, Federal University of Rio Grande do Sul (Drs Aliti, Rabelo, Clausell, Rohde, Biolo, and Beck-da-Silva), Hospital de Clínicas de Porto Alegre, Cardiology Division, Heart Failure Clinic (Drs Aliti, Rabelo, Clausell, Rohde, Biolo, and Beck-da-Silva), and School of Nursing, Federal University of Rio Grande do Sul (Dr Rabelo), Porto Alegre, Brazil.

SODIUM AND FLUID RESTRICTION are nonpharmacologic measures widely used in the treatment of acute decompensated heart failure (ADHF).¹ Despite a lack of clear evidence on their therapeutic effect, these measures have been recommended in textbooks and clinical practice guidelines.²⁻⁵

The first randomized clinical trial⁶ (RCT) comparing the effect of a fluid-restricted diet vs liberal fluids in patients admitted for heart failure (HF) found no significant differences in time to clinical stabilization. A later RCT⁷ in patients whose condition was stabilized after hospitalization failed to find any benefit

in fluid restriction; furthermore, it stressed the potential harmful effects of this practice, including increased thirst, dry mouth, dysgeusia, dry skin, and pruritus. Therefore, the authors maintained that it may be

See Invited Commentary at end of article

beneficial and safe to recommend liberal fluid prescription in patients with HF after hospital discharge.

These 2 studies found no effect of this nonpharmacologic measure in patients with ADHF or stable HF after recent hospital admission. However, both studies may have been underpowered because of

a relatively small difference between interventions.^{6,7} Hence, doubts remain as to the benefit or potential harm of fluid and sodium restriction in patients with clinical congestion and ADHF treated in a hospital setting.

Several studies^{8,9} have assessed the effects of dietary sodium intake in patients with HF. Tested interventions have included daily sodium intake ranging from 230 to 5750 mg.¹⁰ Because of this heterogeneity, the current data are insufficient to support any specific sodium intake recommendations for patients with ADHF. In the absence of more definitive evidence, national and international practice guidelines continue to advocate a healthy diet^{4,11} with a mean sodium intake of 2.0 g⁵ to 2.4 g.⁴ In light of the inconclusive results of studies on the benefits of sodium and fluid restriction, the objective of this trial was to test the hypothesis that aggressive fluid restriction coupled with a low-sodium diet would have an effect on weight loss and clinical stabilization in patients hospitalized for ADHF. The control group (CG) followed a diet with liberal fluid and sodium intake.

METHODS

STUDY DESIGN

This was a randomized, blinded, parallel-group clinical trial. Outcome assessments were water and sodium restriction in patients with ADHF.

PARTICIPANTS

The sample comprised adult inpatients with a diagnosis of ADHF and systolic dysfunction (left ventricular ejection fraction $\leq 45\%$), Boston criteria¹² score of 8 or more points, and a length of stay of no more than 36 hours after hospital admission. The Boston criteria were used in the emergency department before inclusion in the study. Patients with an endogenous creatinine clearance rate of 30 mL/min/1.73 m² or less (by the Cockcroft-Gault formula)¹³ (to convert creatinine clearance to milliliters per second per meters squared, multiply by 0.0167), cardiogenic shock, survival compromised due to other underlying disease, and/or issues that might hinder treatment adherence (eg, dementia, cognitive deficits) were excluded from the sample. The study was carried out between July 6, 2009, and April 12, 2012, at a public teaching hospital and approved by the local Research Ethics Committee.

INTERVENTION

The study intervention consisted of fluid restriction (maximum fluid intake, 800 mL/d) and sodium restriction (maximum dietary intake, 800 mg/d), carried out until hospital day 7 or until discharge in patients whose length of stay was less than 7 days. Patients in the intervention group (IG) underwent a daily physical examination guided by a clinical congestion score (CCS).¹⁴ Perceived thirst (measured on a visual analog scale), body weight, and use of intravenous diuretics, vasodilators, and inotropes were also assessed daily. The CG received a standard hospital diet, with liberal fluid (at least 2.5 L) and sodium (approximately 3-5 g) intake.

STUDY PROTOCOL

After screening, potentially eligible patients were invited to take part in the study, and written informed consent was obtained from all participants (**Figure 1**). Data were then collected on

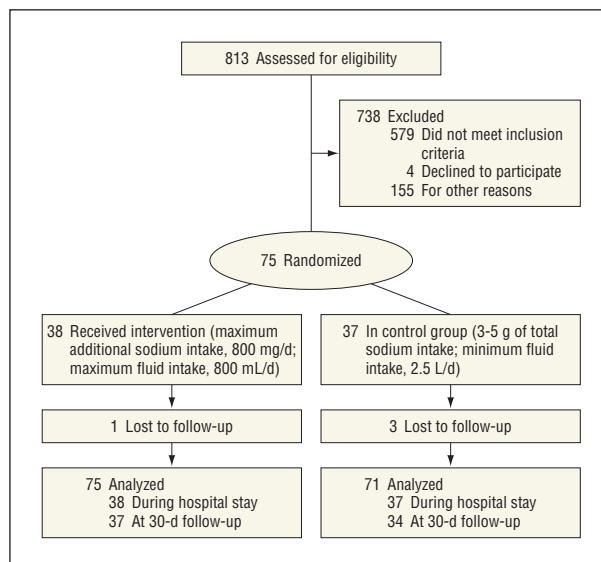


Figure 1. Consolidated Standards for Reporting of Trials flowchart.

sociodemographic and clinical variables, routine laboratory tests, and current prescriptions; the CCS was calculated; body weight and perceived thirst were measured; and a venous whole-blood sample was drawn for quantitation of brain-type natriuretic peptide (BNP) (Triage BNP Test; Biosite Diagnostics Inc).

Shortly after allocation, the on-call dietitian—previously briefed on the study protocol—was notified of randomization and tasked with changing each patient’s dietary prescription so that the randomized diet would be delivered at the next meal. In both groups, the prescribed study diet was entered into patients’ electronic medical records using the same wording: “Diet as per study protocol. Patient is to receive study diet until ___/___ or discharge. Do not change diet.” When patients required a special diet for other reasons, the electronic medical record was amended accordingly (eg, with addition of the wording “DM diet” for patients requiring a diabetic diet).

STUDY OUTCOMES

Primary End Point

Weight loss and clinical stability at 3-day assessment was the primary end point. Body weight was measured by the investigators using digital scales (Tanita). Patients were weighed standing at the center of the scale platform, wearing as little clothing as possible, while barefoot, and after micturition. Clinical stability was defined as improvement in clinical congestion and cessation of all intravenous pharmacotherapy for HF (diuretics, inotropes, or vasodilators).

The CCS is an instrument composed of 7 items that assess clinical signs and symptoms of congestion, including presence of rales, a third heart sound, jugular venous distension, peripheral edema, hepatojugular reflux, orthopnea, paroxysmal nocturnal dyspnea, and New York Heart Association functional class. The score ranges from 1 to 22 points, with higher scores being directly indicative of increased clinical congestion.¹⁴

Secondary End Points

Assessment of perceived thirst was performed using a visual analog scale. In this setting, patients are asked to grade their thirst on a scale of 0 to 10.¹⁵⁻¹⁷ Hospital readmissions were documented, defined as those occurring because of HF and within 30 days of hospital discharge.

Table 1. Sociodemographic and Clinical Profile of the Sample

Characteristic	No. (%)			P Value
	Overall (N = 75)	IG (n = 38)	CG (n = 37)	
Sociodemographic data				
Age, mean (SD), y	60 (11.0)	60.6 (10.5)	59.3 (12.2)	.59 ^a
Male sex	52 (69)	28 (74)	24 (65)	.56 ^b
White ethnicity	63 (84)	33 (87)	30 (81)	.37 ^b
Clinical data				
Duration of heart failure, median (IQR), y	2 (0.5-7.0)	3.5 (1.0-7.2)	1 (0.1-5.7)	.08 ^c
Ischemic source	17 (23)	8 (21)	9 (24)	.95 ^b
Nonischemic source	58 (77)	30 (79)	28 (76)	.78 ^b
Left ventricular ejection fraction, mean (SD), %	26.0 (8.7)	27.4 (8.9)	24.6 (8.4)	.16 ^a
Boston score, points, mean (SD)	11.9 (1.8)	11.9 (1.8)	12 (2.2)	.86 ^a
Endogenous creatinine clearance, mean (SD), mL/min/1.73 m ²	71.4 (28.0)	69.7 (29.1)	73.2 (27.1)	.58 ^a
NYHA class III	35 (47)	18 (47)	17 (46)	.67 ^b
NYHA class IV	34 (45)	16 (42)	18 (49)	.67
Current medications				
β-Blockers				
Metoprolol tartrate	42 (56)	23 (61)	19 (51)	.63
Carvedilol	2 (3)	0	2 (5)	.23
Angiotensin-converting enzyme inhibitors				
Captopril	36 (48)	19 (50)	17 (46)	.82
Enalapril maleate	22 (29)	13 (34)	9 (24)	.45
Angiotensin receptor blockers				
Spirolactone	8 (11)	4 (11)	4 (11)	>.99
Hydralazine	38 (51)	20 (53)	18 (49)	>.99
Furosemide	22 (29)	11 (29)	11 (30)	>.99
Hydrochlorothiazide	61 (81)	31 (82)	30 (81)	>.99
	9 (12)	7 (18)	2 (5)	.15

Abbreviations: CG, control group; IG, intervention group; IQR, interquartile range; NYHA, New York Heart Association (functional classification: III, dyspnea on minor exertion; IV, dyspnea at rest).

SI conversion factor: To convert creatinine clearance to milliliters per second per meters squared, multiply by 0.0167.

^aDetermined using unpaired, 2-tailed *t* test for between-group comparisons.

^bDetermined using Fisher exact test.

^cDetermined using Mann-Whitney test.

SAMPLE SIZE

Sample size was calculated with WinPepi, version 11.1 (<http://www.brixtonhealth.com/pepi4windows.html>). We used the weight loss values reported by Travers et al,⁶ who assessed weight loss in patients hospitalized for ADHF and clinical congestion. For a significance level of $\alpha = .05$, a statistical power of 80%, and a substantial difference in weight loss of 2 kg within 3 days, the minimum sample size was calculated as 74 participants (IG, 37; CG, 37).

RANDOMIZATION

A simple sequential randomization plan was generated online using the <http://www.randomization.com> website. An external investigator was responsible for the randomization plan used for patient allocation.

BLINDING

Professionals involved in patient care were blinded to allocation throughout the study period. All initial assessments were performed before randomization by the same investigator (G.B.A.). Clinical examinations during admission and at 30-day follow-up were performed by a nurse who was also blinded to allocation.

STATISTICAL ANALYSIS

The objective of the statistical analysis was to compare within-patient changes between treatment groups. Therefore, mixed-

effects models were undertaken to measure such changes. Continuous variables are expressed as mean (SD) if normally distributed or as median (interquartile range [IQR]) if skewed. Between-group differences in quantitative variables were assessed with the *t* test (for normal distribution) or the Mann-Whitney test (for skewed variables). A paired 2-tailed *t* test was used for analysis of within-group differences in body weight and CCS. The Fisher exact test or Pearson χ^2 test was used as appropriate for analysis of between-group differences in categorical variables. All analyses were performed by intention to treat. The significance level was set at $P < .05$. All analyses were performed using commercial software (SPPS, version 18; SPSS Inc).

RESULTS

From July 6, 2009, through April 12, 2012, a total of 813 patients were admitted with ADHF and assessed for eligibility. Seventy-five patients were randomized; 38 were allocated to the IG and 37 to the CG. There were no deaths or withdrawals during the study period (from admission to the seventh day). Four patients were lost to 30-day follow-up: 3 because of transportation issues to attend the 30-day follow-up visit (IG, 1; CG, 2) and 1 (CG) for an aortic surgery performed during the 30-day follow-up visit. A Consolidated Standards for Reporting of Trials flow diagram of patient progress through the trial is shown in Figure 1.

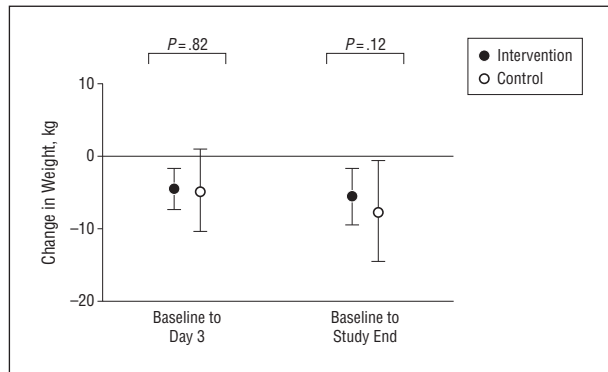


Figure 2. Change in body weight from baseline to 3-day reassessment and from baseline to the end of the study period in the intervention and control groups. Significance was determined using the Mann-Whitney test. Data points indicate the mean values; whiskers indicate SD.

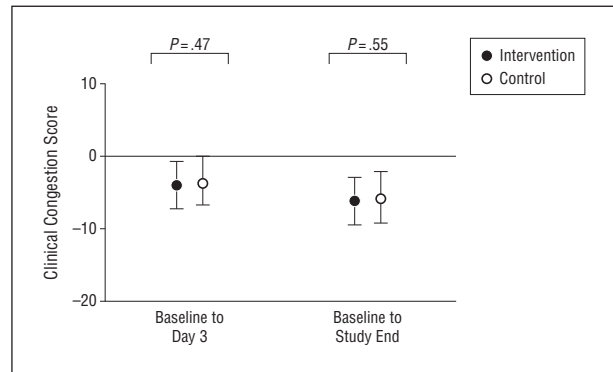


Figure 3. Change in clinical congestion score from baseline to 3-day reassessment and from baseline to the end of the study period in the intervention and control groups. Significance was determined using the Mann-Whitney test. Data points indicate the mean values; whiskers indicate SD.

SOCIODEMOGRAPHIC AND CLINICAL CHARACTERISTICS

Table 1 describes the sample profile at baseline. Mean age was 60.6 (10.5) years in the IG and 59.3 (12.2) years in the CG. In both groups, most patients were male. Mean left ventricular ejection fraction was 27.4 (8.9%) in the IG and 24.6 (8.4%) in the CG. In both groups, ischemic heart disease was the most prevalent cause of HF (IG, 21% CG, 24%). There were no significant between-group differences in baseline characteristics.

The overall median length of stay was 6 days (4-12): 7 days (3.8-13) in the IG, and 6 days (4-12.5) in the CG ($P = .89$). There were no statistically significant differences in length of stay among the patients who remained hospitalized after day 7, regardless of allocation ($P = .90$).

BODY WEIGHT LOSS

Mean baseline body weight was statistically similar in the 2 study groups (IG, 78 [14.6] kg vs CG, 82.4 [21.5] kg; $P = .29$). There were no significant between-group differences in change in body weight from baseline to 3-day reassessment (IG, -4.42 [2.85] kg vs GC, -4.67 [5.6] kg; $P = .82$). In other words, both groups lost a similar amount of weight (**Figure 2**).

CLINICAL STABILITY

The mean CCS at baseline was similar in both groups (IG, 12.6 [3.1] points vs CG, 12.8 [2.8] points; $P = .67$). There were no significant between-group differences in the change in CCS from baseline to 3-day reassessment (primary end point) (IG, -4.03 [3.3] points vs CG, -3.44 [3.35] points; $P = .47$). The between-group difference in CCS variation was 0.59 points (95% CI, -2.21 to 1.03; $P = .47$) at 3 days. In other words, both groups exhibited similar improvement in clinically overt congestion (**Figure 3**).

PERCEIVED THIRST

There were no significant between-group differences in mean perceived thirst at baseline as measured on a visual analog scale (IG, 4.08 [2.6] points vs CG, 3.95 [2.5]

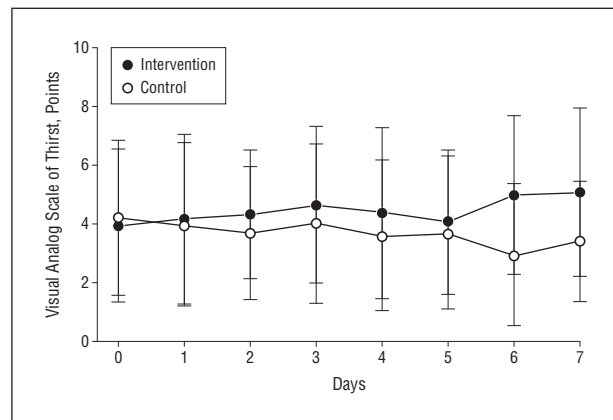


Figure 4. Progression of perceived thirst during the study (time, $P = .32$; group, $P = .25$; time \times group $P = .01$; by mixed-effects models). Data points indicate the mean values; whiskers indicate SD.

points; $P = .65$). Thirst was significantly worse in the IG (5.1 [2.9]) than in the CG (3.44 [2.0]) at the end of the study period (time, $P = .32$; group, $P = .25$; time \times group, $P = .01$); the standardized effect size was 0.67 (0.2-1.13), as shown in **Figure 4**.

INTRAVENOUS MEDICATIONS

During the first 3 days of admission, there were no significant between-group differences in the rate of intravenous administration of diuretics (IG, 94.7%; CG, 97.3%; $P > .99$), vasodilators (IG, 26.3%; CG, 18.9%; $P = .58$), or inotropes (only 1 patient, allocated to the IG, received dobutamine hydrochloride) for treatment of HF.

There were no significant between-group differences in the mean dose of loop diuretics administered as an intermittent intravenous bolus injection at baseline (IG, 84.7 [40.7] mg/d; CG, 79.1 [31.0] mg/d; $P = .50$) nor were there any significant differences in the percentage of patients receiving continuous intravenous infusion of loop diuretics or in the percentage of patients receiving intravenous vasodilators. The median time to transition from intravenous to oral diuretic therapy was similar in the IG (4 days; IQR, 2.0-7.2) and CG (4 days; IQR 2.0-7.0; $P = .97$).

Table 2. Progression of Laboratory Variables in the Intervention and Control Groups

Characteristic	Baseline		P Value	Study End		P Value ^a	P Value ^b
	IG	CG		IG	CG		
Creatinine, mean (SD), mg/dL	1.3 (0.5)	1.3 (0.6)	.86	1.3 (0.5)	1.2 (0.3)	.44	.55
Urea, median (IQR), mg/dL	56 (48-87)	58 (41-83)	.38	59 (43-88)	49 (42-71)	.06	.32
Sodium, serum, mean (SD), mEq/L	139 (4)	139 (5)	.54	139 (4)	139 (3)	>.99	.48
Sodium, urinary, median (IQR), mEq/L	74 (46-109)	81 (46-98)	.59	74 (45-94)	89 (51-119)	.13	.10
Potassium, mean (SD), mEq/L	4.3 (0.5)	4.3 (0.6)	.49	4.3 (0.6)	4.0 (0.5)	.52	.32
Hemoglobin, mean (SD), g/dL	13 (2)	13 (2)	.23	13 (3)	13 (2)	.13	.90
BNP, median (IQR), pg/mL	1084 (608-1820)	1425 (632-2297)	.67	954 (488-1331)	770 (4485-1400)	.92	.51

Abbreviations: BNP, brain-type natriuretic peptide; CG, control group; IG, intervention group; IQR, interquartile range.

SI conversion factors: To convert BNP to nanograms per liter, multiply by 1; creatinine to micromoles per liter, multiply by 88.4; hemoglobin to grams per liter, multiply by 10; potassium to millimoles per liter, multiply by 1; serum sodium to millimoles per liter, multiply by 1; and urea to millimoles per liter, multiply by 0.357.

^aMultiple comparison test with Bonferroni correction.

^bRepeated-measures analysis (generalized estimating equations method) for the between-group difference from baseline to the end of the study period.

Table 3. Clinical and Laboratory Variables at 30-Day Follow-up

Characteristic	Mean (SD)		P Value ^a
	IG (n = 37)	CG (n = 34)	
Clinical data			
Weight, kg	73.7 (13.3)	72.5 (19.0)	.76
Clinical congestion score	7.9 (3.8)	6.0 (3.1)	.02
Thirst, VAS score	4.21 (2.4)	3.91 (2.7)	.64
NYHA functional class	2.16 (0.9)	1.89 (0.8)	.16
Laboratory values			
Creatinine, mg/dL	1.34 (0.42)	1.29 (0.4)	.61
Urea, mg/dL	74.0 (39.0)	61.3 (24.6)	.11
Sodium, serum, mEq/L	139.4 (3.7)	140.4 (2.2)	.16
Sodium, urinary, mEq/L	73.7 (49.7)	72.3 (37.2)	.89
Potassium, mEq/L	4.51 (0.5)	4.44 (0.5)	.57
Hemoglobin, g/dL	13.7 (1.8)	12.8 (1.9)	.22

Abbreviations: CG, control group; IG, intervention group; NYHA, New York Heart Association; VAS, visual analog scale.

SI conversion factors: See Table 2.

^aSignificance determined using multiple comparison test with Bonferroni correction.

LABORATORY MONITORING

Laboratory tests, such as serum creatinine, urea, sodium, potassium, and hemoglobin, were performed at baseline and hospital discharge. There were no significant between-group differences in the results of laboratory tests at any time during the course of the study (**Table 2**).

FOLLOW-UP

Thirty-seven patients from the IG and 34 from the CG returned for 30-day follow-up (clinical and laboratory data reported in **Table 3**). Patients in the IG were significantly more congested ($P = .02$) than were those in the CG. There were no significant between-group differences in any other clinical or laboratory factors. The change in CCS between 30-day follow-up and the end of the study showed that patients in the IG had more severe congestion, with congestion scores 2.4 points higher (95% CI, 0.94-3.99; $P = .002$) than those of patients in the control group, as reported in **Table 4**.

Table 4. CCS at the End of the Study and at 30-Day Follow-up and the Difference Between These Periods in the IG and CG

Characteristic	Mean (SD)	
	IG	CG
CCS at study end	6.4 (3.0), n = 38	7.1 (2.6), n = 37
CCS at 30-d follow-up	7.9 (3.8), n = 37	6.0 (3.0), n = 34
$\Delta\text{CCS}_{\text{D30-End}}^a$	1.5 (3.6)	-1.2 (3.3)

Abbreviations: CCS, clinical congestion score; CG, control group; $\Delta\text{CCS}_{\text{D30-End}}$, difference in CCS between 30-day follow-up and the end of the study; IG, intervention group.

^aDifference significant at $P = .002$; adjusted covariance matrix for correction of different CCS at hospital day 7.

READMISSIONS AND EMERGENCY DEPARTMENT VISITS

All visits to the emergency department or hospital admission were computed within a 30-day period after the seventh day or discharge. There were no significant between-group differences in the number of readmissions occurring within 30 days of the end of the study (IG, 11 patients [29%]; CG, 7 patients [19%]; $P = .41$).

BRAIN-TYPE NATRIURETIC PEPTIDE

Median BNP levels at baseline were elevated and similar in both groups (IG, 1084 [608-1820] pg/mL; CG, 1425 [632-2297] pg/mL; $P = .67$) (conversion of BNP level to nanograms per liter is 1:1). By the end of the study, both groups had experienced similar reductions in median BNP levels (IG, 954 [488-1331] pg/mL; CG, 770 [448-1400] pg/mL; $P = .92$). However, the IG had more patients with a BNP level greater than 700 pg/mL at the end of the study, and this subset of patients had a higher readmission rate (7 of 22 patients) compared with controls (1 of 20) ($P = .04$).

COMMENT

To our knowledge, this was the first RCT to test the hypothesis of early, aggressive fluid and sodium restriction in patients hospitalized for ADHF. The results of this

combined intervention showed no benefit on weight loss or clinical stability at 3-day follow-up. As well as failing to provide benefit, the study intervention was associated with significantly greater perceived thirst during the hospital stay. There were no significant between-group differences in readmission rate at 30 days. Patients who were discharged with higher BNP levels (>700 pg/mL) appeared to be at greater risk for readmission; this was more frequently seen in the IG (1 vs 7 patients; $P = .04$). To the best of our knowledge, no other study has used a similar approach in patients with systolic dysfunction, clinical congestion, and ADHF.

CLINICAL TRIALS IN ACUTE HF

Fluid Restriction

Using a similar approach but focusing on fluid restriction, Travers et al⁶ conducted the first RCT of patients with ADHF and systolic dysfunction. The authors found no significant difference in time to clinical stabilization between the fluid-restricted and liberal-fluids groups. However, the between-group difference in fluid intake was only 392 mL/d. This trial prompted us to test a more aggressive intervention in an attempt to achieve a more substantial difference in fluid intake between groups. From a comparative standpoint, we may infer that our intervention was indeed more rigorous, since patients in our IG had an average weight loss of 4.5 kg during a 3-day period, whereas those in the IG of the study by Travers et al lost a mean (SD) of 2.6 (3.0) kg over the course of 8.3 (6.3) days. Our findings were otherwise similar, with no significant between-group differences in weight loss or clinical stability at 3-day follow-up.

In clinical practice, fluid and sodium restriction often are prescribed for patients hospitalized for ADHF for no other reason than to mirror nonpharmacologic care provided in the outpatient setting. In light of this practice, the findings of Holst et al,⁷ who published a crossover RCT comparing the effects of restricted fluid intake (1500 mL/d) vs rational fluid intake based on physiologic requirements (30-35 mL/kg/d) in outpatients with stable HF, are worth mentioning. The authors found no significant differences in clinical end points such as functional status, quality of life, or hospitalization, but patients in the fluid-restriction group experienced significantly greater thirst and difficulty adhering to the study intervention.

Currently, the scarce evidence available suggests that fluid restriction is unlikely to be of benefit in hospitalized patients with ADHF. Our study underscores the findings of Travers et al,⁶ with our findings continuing to show a neutral effect of fluid restriction despite the wider between-group difference in interventions. This contradicts the exaggerated importance afforded to this nonpharmacologic measure in the past, when management options for HF were few and fluid restriction provided a relatively plausible means of preventing congestion.¹⁸ It has been proposed¹⁹ that the effects of fluid restriction, if any, would be diluted by current therapeutic regimens, which include renin-angiotensin-aldosterone system blockers, high-dose loop diuretics, and, in the hospital environment, intravenous vasodilators.

Dietary Sodium Restriction

Research on sodium restriction has moved in the opposite direction of what had been postulated in recent decades. Recent data²⁰⁻²² have highlighted the alternative hypothesis that sodium restriction may be harmful in HF. One study²³ has shown that sodium restriction in patients with HF leads to activation of the antidiuretic and antinatriuretic systems, and the investigators concluded that such activation may be detrimental.

Since the late 1990s, a team of Italian researchers has developed a counterintuitive form of therapy that consists of administering hypertonic saline solution (HSS) to treat ADHF. This therapy is based on fluid restriction, increased sodium intake, high-dose diuretics, and rapid HSS infusion. According to the investigators, the efficacy of this combined administration of sodium and diuretics in the management of severe treatment-refractory HF is probably the result of instant mobilization of extravascular fluid into the intravascular compartment. The end result is increased diuresis and free water loss within minutes of infusion.²⁴ An RCT²⁵ compared the effects of the high-dose furosemide/low-volume HSS infusion vs intermittent high-dose furosemide and no HSS in patients hospitalized with refractory HF. The results showed improvements in clinical and hemodynamic variables and shorter lengths of stay in the HSS group. There was also evidence of long-term benefit (48 months), with a lower mortality rate among patients who had received furosemide and HSS (mortality, 45.3% vs 87%; $P < .001$).²⁶ Therefore, the current evidence suggests that increasing rather than restricting sodium intake may be beneficial in patients with ADHF.

In summary, the effect of fluid restriction appears neutral.^{6,7} There is evidence, drawn from a combination of multiple interventions, that increased sodium intake may provide benefits by reducing length of stay, improving clinical and hemodynamic variables, and lessening mortality.^{20,22-24}

THIRST

Prescription of a low-sodium, fluid-restricted diet in the presence of low cardiac output and increased activation of neurohormonal systems will lead to stimulation of the thirst center in the hypothalamus⁷ and may trigger sensations of thirst at different levels of perception. This sensation is often worsened by xerostomia secondary to diuretic use.

In view of the importance of this sensation in patients already experiencing discomfort with the symptoms of HF, this is a matter of concern. In our study, thirst-related findings were similar to those of Holst et al.⁷ On average, perceived thirst was moderate and significantly worse in the IG. This finding adds a negative component to an intervention that, thus far, had appeared neutral in terms of weight loss and relief of clinical congestion.

In summary, this RCT contributes to the field of HF research by showing that, in patients with ADHF, aggressive fluid and sodium restriction had no effect on weight loss or clinical stability compared with a diet with liberal fluid and sodium intakes. Furthermore, this aggressive intervention was associated with significantly higher rates of perceived thirst.

Accepted for Publication: January 12, 2013.
Published Online: May 20, 2013. doi:10.1001/jamainternmed.2013.552

Correspondence: Luis Beck-da-Silva, MD, ScD, Cardiology Division, Heart Failure Clinic, Hospital de Clínicas de Porto Alegre, Rua Ramiro Barcelos, 2350 Sala 2060, Porto Alegre, RS 90035-903, Brazil (luisbeckdasilva@gmail.com).

Author Contributions: Drs Aliti, Rabelo, and Beck-da-Silva had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* All authors. *Acquisition of data:* Aliti and Rabelo. *Analysis and interpretation of data:* All authors. *Drafting of the manuscript:* Aliti, Rabelo, Biolo, and Beck-da-Silva. *Critical revision of the manuscript for important intellectual content:* All authors. *Statistical analysis:* Rabelo, Rohde, Biolo, and Beck-da-Silva. *Obtained funding:* Rabelo. *Administrative, technical, and material support:* Rabelo and Clausell. *Study supervision:* Rabelo, Rohde, Biolo, and Beck-da-Silva.

Conflict of Interest Disclosures: None reported.

Funding/Support: Financial support was provided by Fundo de Incentivo à Pesquisa e Eventos at Hospital de Clínicas de Porto Alegre (HCPA).

REFERENCES

1. Grady KL, Dracup K, Kennedy G, et al. Team management of patients with heart failure: a statement for healthcare professionals from the Cardiovascular Nursing Council of the American Heart Association. *Circulation*. 2000;102(19):2443-2456.
2. Teerlink JR. Diagnosis and management of acute heart failure. In: Braunwald E, Libby P, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2008:583-610.
3. Montera MW, Almeida RA, Tinoco EM, et al. II: Brazilian guidelines on acute cardiac insufficiency [in Portuguese]. *Arq Bras Cardiol*. 2009;93(3)(suppl 3):1-65.
4. McMurray JJV, Adamopoulos S, Anker SD, et al; ESC Committee for Practice Guidelines. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology: developed in collaboration with the Heart Failure Association (HFA) of the ESC. *Eur Heart J*. 2012;33(14):1787-1847.
5. Jessup M, Abraham WT, Casey DE, et al. 2009 Focused update: ACCF/AHA guidelines for the diagnosis and management of heart failure in adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines; developed in collaboration with the International Society for Heart and Lung Transplantation. *Circulation*. 2009;119(14):1977-2016.
6. Travers B, O'Loughlin C, Murphy NF, et al. Fluid restriction in the management of decompensated heart failure: no impact on time to clinical stability. *J Card Fail*. 2007;13(2):128-132.
7. Holst M, Strömberg A, Lindholm M, Willenheimer R. Liberal versus restricted

- fluid prescription in stabilised patients with chronic heart failure: result of a randomised cross-over study of the effects on health-related quality of life, physical capacity, thirst and morbidity. *Scand Cardiovasc J*. 2008;42(5):316-322.
8. Lennie TA, Song EK, Wu JR, et al. Three gram sodium intake is associated with longer event-free survival only in patients with advanced heart failure. *J Card Fail*. 2011;17(4):325-330.
9. Nakasato M, Strunk MC, Guimarães G, Rezende MVC, Bocchi EA. Is the low-sodium diet actually indicated for all patients with stable heart failure [in Portuguese]? *Arq Bras Cardiol*. 2010;94(1):92-101.
10. Gupta D, Georgiopolou VV, Kalogeropoulos AP, et al. Dietary sodium intake in heart failure. *Circulation*. 2012;126(4):479-485.
11. Bocchi EA, Marcondes-Braga FG, Bacal F, et al. Updating the Brazilian guideline for heart failure—2012 [in Portuguese]. *Arq Bras Cardiol*. 2012;98(1)(suppl 1):1-33.
12. Marantz PR, Tobin JN, Wassertheil-Smoller S, et al. The relationship between left ventricular systolic function and congestive heart failure diagnosed by clinical criteria. *Circulation*. 1988;77(3):607-612.
13. Gault MH, Longerich LL, Harnett JD, Wesolowski C. Predicting glomerular function from adjusted serum creatinine. *Nephron*. 1992;62(3):249-256.
14. Sauer J, Rabelo ER, Castro RA, et al. Nurses' performance in classifying heart failure patients based on physical exam: comparison with cardiologist's physical exam and levels of N-terminal pro-B-type natriuretic peptide. *J Clin Nurs*. 2010;19(23-24):3381-3389.
15. Flaherty SA. Pain measurement tools for clinical practice and research. *AANA J*. 1996;64(2):133-140.
16. Morita T, Tei Y, Tsunoda J, Inoue S, Chihara S. Determinants of the sensation of thirst in terminally ill cancer patients. *Support Care Cancer*. 2001;9(3):177-186.
17. Wirth JB, Folstein MF. Thirst and weight gain during maintenance hemodialysis. *Psychosomatics*. 1982;23(11):1125-1127, 1130-1131, 1134.
18. Holst M, Strömberg A, Lindholm M, Uden G, Willenheimer R. Fluid restriction in heart failure patients: is it useful? the design of a prospective, randomised study. *Eur J Cardiovasc Nurs*. 2003;2(3):237-242.
19. Rothberg MB, Sivalingam SK. The new heart failure diet: less salt restriction, more micronutrients. *J Gen Intern Med*. 2010;25(10):1136-1137.
20. Paterna S, Parrinello G, Cannizzaro S, et al. Medium term effects of different dosage of diuretic, sodium, and fluid administration on neurohormonal and clinical outcome in patients with recently compensated heart failure. *Am J Cardiol*. 2009;103(1):93-102.
21. Arcand J, Ivanov J, Sasson A, et al. A high-sodium diet is associated with acute decompensated heart failure in ambulatory heart failure patients: a prospective follow-up study. *Am J Clin Nutr*. 2011;93(2):332-337.
22. Paterna S, Gaspare P, Fasullo S, Sarullo FM, Di Pasquale P. Normal-sodium diet compared with low-sodium diet in compensated congestive heart failure: is sodium an old enemy or a new friend? *Clin Sci (Lond)*. 2008;114(3):221-230.
23. Alvelos M, Ferreira A, Bettencourt P, et al. The effect of dietary sodium restriction on neurohumoral activity and renal dopaminergic response in patients with heart failure. *Eur J Heart Fail*. 2004;6(5):593-599.
24. Di Pasquale P, Sarullo FM, Paterna S. Novel strategies: challenge loop diuretics and sodium management in heart failure—part II. *Congest Heart Fail*. 2007;13(3):170-176.
25. Paterna S, Di Pasquale P, Parrinello G, et al. Effects of high-dose furosemide and small-volume hypertonic saline solution infusion in comparison with a high dose of furosemide as a bolus, in refractory congestive heart failure. *Eur J Heart Fail*. 2000;2(3):305-313.
26. Licata G, Di Pasquale P, Parrinello G, et al. Effects of high-dose furosemide and small-volume hypertonic saline solution infusion in comparison with a high dose of furosemide as bolus in refractory congestive heart failure: long-term effects. *Am Heart J*. 2003;145(3):459-466.

INVITED COMMENTARY

Counterintuitive Evidence Concerning Salt and Water Restriction in Acute Decompensated Heart Failure Patients

Fluid retention manifested by peripheral edema, fluid in the lungs, and ascites has been recognized as a sign of congestive heart failure from earliest times. In fact, in 1775, Withering,¹ when describing the effects of the foxglove on patients with “dropsy,” believed that the major action of the drug was as a di-

uretic. Our present understanding of the pathophysiology of heart failure has evolved through the hemodynamic stage that focused on the heart as the primary cause with secondary effects on the kidney, where inotropic agents and diuretics were the mainstay of therapy to the neurohormonal stage. Here, activation of the