REVIEW

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Salt, No Salt, or Less Salt for Patients With Heart Failure?

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ABSTRACT

Restricting dietary sodium is a common recommendation given by clinicians to patients with heart failure and is one supported by current guidelines. However, the quality of evidence for this recommendation is suboptimal, and there is no consensus on the optimal level of sodium intake. Though excessive sodium intake is associated with left ventricular hypertrophy and hypertension, recent data have suggested that very low sodium intake is paradoxically associated with worse outcomes for patients with heart failure. This is possibly explained by the association between low sodium intake and activation of the sympathetic and renin-angiotensin-aldosterone systems. Nevertheless, sodium restriction is routinely recommended and remains a cornerstone of heart failure and blood pressure therapy. In this review we discuss the pros and cons of sodium restriction for patients with heart failure from the current literature.

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KEYWORDS: Blood pressure; Heart failure; Renin-angiotensin-aldosterone; Salt; Sodium intake

The prevalence of heart failure is increasing and now affects more than 25 million people globally.[1,2] Restricting dietary sodium is a common recommendation given by physicians to patients with heart failure. On average, Americans consume 3500-4000 mg of dietary sodium every day.[3] All current international heart failure guidelines recommend restriction in sodium intake.[4–12] However, the level of evidence in these guidelines is either not provided or is derived from expert opinion and lacks of high-quality data (Grade C; Table 1). Guidelines recommend sodium restriction ranging from 1500 to 3000 mg/d and reflect a lack of consensus on the maximum sodium intake.

Current American College of Cardiology (ACC)/American Heart Association (AHA) guidelines recommend sodium restriction as reasonable for patients with heart failure even though there are concerns whether low sodium intake is efficacious.[4] Observational studies and randomized controlled trials have suggested that low sodium intake may be harmful.[13–17] An executive summary from the US National Heart, Lung and Blood Institute and the National Institutes of Health Office of Dietary Supplements also noted the lack of high-quality evidence and concern about sodium intake.[18] Not to be forgotten are once fully embraced but erroneous recommendations about hormone replacement therapy, beta blockers in heart failure, and antiarrhythmic treatment.[19] There is no doubt that high sodium intake is associated with volume retention, high blood pressure, and cardiovascular morbidity.

However, in the case of heart failure, reasonable differences of opinion exist on salt restriction. What should you recommend to your patients with heart failure? In this review we discuss present evidence for and against sodium restriction to help you decide.

ARGUMENTS FOR SALT RESTRICTION IN PATIENTS WITH HEART FAILURE

Patients with heart failure have diminished renal perfusion, which in turn activates the sympathetic and renin-angiotensin-aldosterone system (RAAS) and leads to a vicious cycle

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of water and salt retention despite the fluid overload. Furthermore, the natriuretic system is impaired early in heart failure along with inappropriate levels of vasopressin causing further salt retention.[20] This physiological mechanism provides the basis for a low sodium diet in all patients with heart failure. Increased sodium intake is associated with high blood pressure, and it has been shown indirectly that diets consisting of low sodium intake such as the Dietary Approaches to Stop Hypertension (DASH) diet, improve all-cause mortality and risk of adverse cardiac events.[21–23] The International Study of Sodium, Potassium and Blood Pressure study enrolled more than 10,000 patients from 32 countries and showed that salt intake and blood pressure are directly correlated ($r = 0.0556$, $P < 0.001$).[24] A meta-analysis of 28 randomized controlled trials of salt reduction and blood pressure changes showed that salt reduction led to a roughly 25% reduction in stroke deaths and cardiovascular mortality.[25] Similarly, the Trial of Hypertension Prevention showed that a low sodium diet for 6 months achieved by education resulted in a lower incidence of cardiovascular diseases over a mean follow-up of 47 months.[26] Moreover, a prospective observational study showed that an increase in dietary sodium intake is linked to increased all-cause and cardiovascular mortality.[27]

There are 2 common arguments against the RAAS-based origin of heart failure hypothesis. First are observational data showing an inverse relationship with dietary sodium intake and heart failure that may be explained by the concept of reverse causation. Because patients with heart failure are commonly placed on a low sodium diet, the majority of the people who consume a low sodium diet will be more likely to have heart failure compared with the general population. Also, patients who comply with sodium restriction often have poor caloric intake and decreased nutritional status, which may confound heart failure outcomes.[28,29]

Second, some suggest that low sodium stimulates the sympathetic nervous system and RAAS could theoretically contribute to worsening of heart failure (Figure 1). Others respond by noting that low sodium intake mimics diuretic use. But despite activation of the RAAS by diuretics, heart failure mortality does not increase, and diuretics retain their status as the mainstay for symptom improvement in heart failure. If low sodium intake through activation of RAAS led to worse outcomes, similar results should occur when diuretics are compared with other antihypertensive agents. However, in the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack trial (ALLHAT), chlorthalidone as an antihypertensive agent resulted in a significantly lower rate of 6 year HF events compared with both calcium channel blockers ($P < 0.001$).[30] Despite activation of the RAAS and sympathetic systems by diuretics, diuretics outperformed ACEI in almost all of the secondary outcomes including heart failure in the ALLHAT Study.[30]

In the majority of the heart failure studies, which have shown an inverse relationship of dietary sodium intake and heart failure readmission rates, a significant proportion of patients were not on beta blockers and spironolactone.[13–15] Moreover, studies conducted in an outpatient setting[31–35] have also shown a trend toward improvement in signs and symptoms of heart failure in patients with low sodium intake.

CLINICAL SIGNIFICANCE

- The quality of evidence for recommending dietary sodium restriction in patients with heart failure is suboptimal, and there is no consensus on the optimal level of sodium intake.
- Although presently available scientific data fail to demonstrate the value of a very low sodium diet, a high sodium diet is not in patient's best interest either.

ARGUMENTS AGAINST SALT RESTRICTION IN PATIENTS WITH HEART FAILURE

In 3 randomized controlled trials,[13–15] reduced dietary sodium intake resulted in significantly increased mortality and readmission rates (Table 2). These trials were performed by the same group of investigators on patients with heart failure after hospital discharge. Studies in hospitalized

Table 1 Guideline Recommendations for Sodium Intake in Heart Failure

Guideline and Reference	Year	Sodium Intake Recommendation	Level of Evidence
Cardiac Society of Australia and New Zealand[9]	2018	<2 g/d	Not stated
Canadian Cardiovascular Society[8]	2017	2-3 g/d	Limited
Heart Failure Society, India[6]	2017	<3 g/d	Not stated
Royal College of Physicians[5]	2016	Reduce intake for patients with high salt intake	Limited
Scottish Intercollegiate Guidelines Network[11]	2016	Salt intake of <6 g/d	Not stated
American College of Cardiology/American Heart Association[4]	2013	Restriction as reasonable	C
European Society of Cardiology[7]	2012	Moderate restriction	Not stated
American Dietetic Association[12]	2011	<2 g/d	Fair
Heart Failure Society of America[10]	2010	2-3 g/d; <2 g/d in severe heart failure	C

Level of Evidence: C = consensus opinion of experts. Limited population evaluated; Fair = benefits more than harms, but quality of evidence is weak; Limited = more research is required

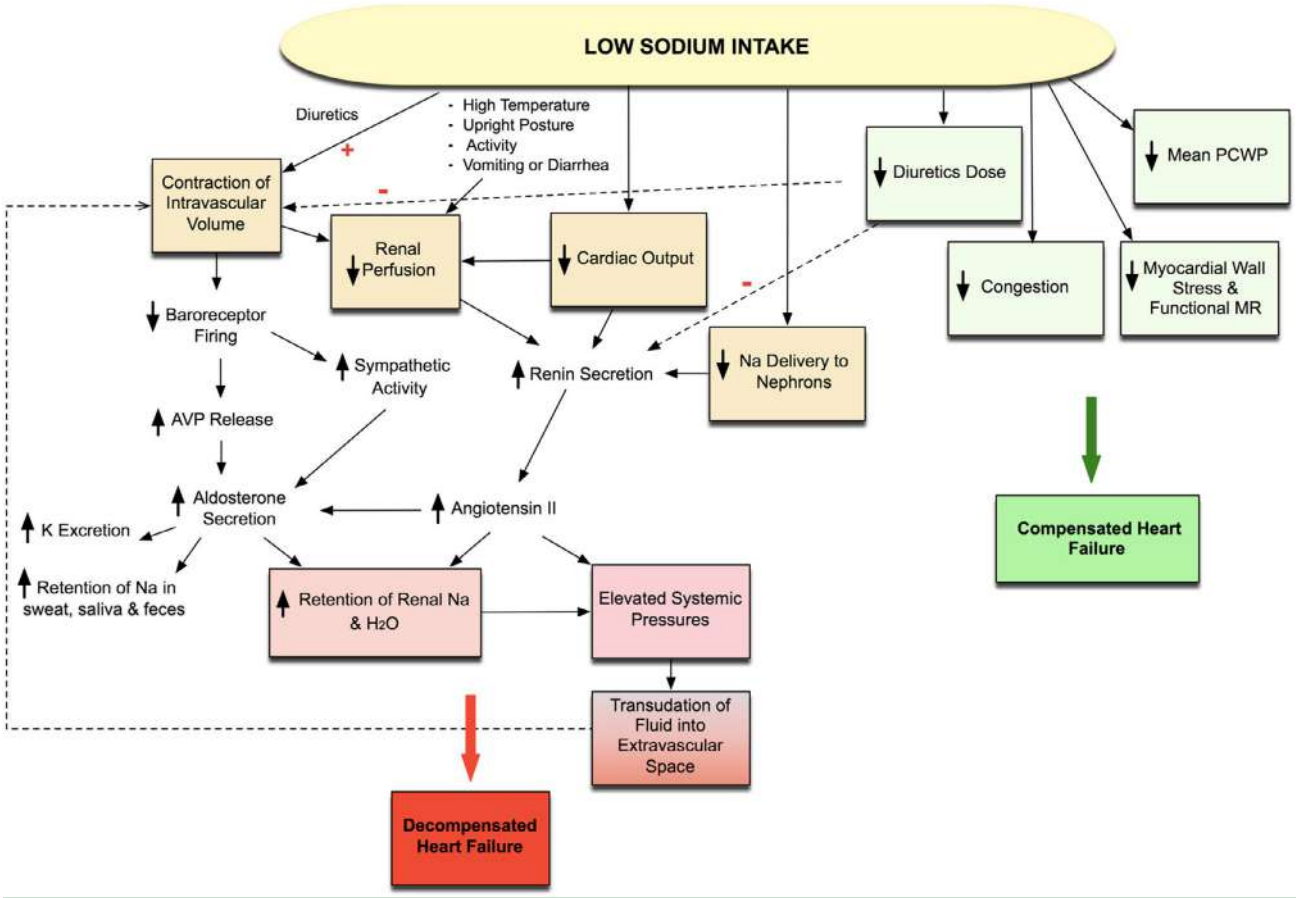

Figure 1 Physiological effects of low sodium intake in heart failure. Low sodium intake may have varied effects on heart failure. Intravascular volume contraction improves hemodynamics and reduces diuretic requirement, congestion, and myocardial wall stress, leading to compensated heart failure. Intravascular volume contraction, however, may also lead to a vicious cycle of increased sodium and water retention through neurohormonal activation predisposing to decompensated heart failure. AVP = arginine vasopressin; K = potassium; MR = mitral regurgitation; Na = sodium; PWCP = pulmonary wedge capillary pressure; red plus = diuretic action enhances contraction of intravascular volume; red minus = low diuretic doses reduce hormonal activation and contraction of intravascular volume. Reproduced with permission from Circulation 2012;126:479-485.[22]

patients with heart failure have also shown that low sodium intake is associated with increased mortality and heart failure–related hospitalizations.[36–39] In one of the studies, patients on a low sodium diet without hypertonic saline infusion had significantly lengthier hospital stays and higher rates of rehospitalization compared with those who were on moderate to high sodium diet with hypertonic saline infusion.

Restricted dietary sodium might lead to worse outcomes in heart failure patients for 2 reasons (Table 3). Low sodium intake can cause neurohormonal activation leading to worsening of heart failure.[40] Multiple animal studies have shown that low sodium intake can cause RAAS activation.[41] Though these may not be that pronounced in the setting of beta blockers and RAAS inhibition, higher plasma renin activity has been shown to be an independent predictor of outcomes in patients with heart failure regardless of the baseline therapy.[40] Moreover, although blockage of RAAS improves renal blood flow, it cannot increase glomerular filtration rate in the presence of a low sodium diet.

Low sodium intake reduces cardiac output and stroke volume and increases epinephrine and vascular resistancem resulting in worsening of hemodynamic effects in patients with Stage C heart failure.[42–44] Sodium restriction leads to increased plasma renin activity, norepinephrine, angiotensin II, and urinary aldosterone as well.[42–44] Low sodium intake also causes undesirable effects on insulin resistance and serum lipids, factors that predispose patients to cardiovascular diseases. Patients with moderate (2300 mg/d) sodium diet have more natriuresis and diuresis, resulting in a decreased creatinine compared with patients who had low sodium intake.[23] Could this be explained by the apparent U-shaped association between heart failure risk and urine sodium excretion in healthy men and women with the lowest incidence of heart failure in the group of 3000-3400 mg/d?[45] That association was confirmed in a meta-analysis of 23 cohort studies and 2 clinical trials.[46] However, reverse causation in the observational studies might have been a confounding factor.

Patients find compliance to diets with sodium restriction lower than 1500 mg/d difficult or impossible. Recent

Table 2 Randomized Controlled Trials Investigating the Impact of Sodium Intake in Patients With Heart Failure

Author, Year	Sample Size	Country	Patients	Intervention	Outcomes
Inpatient Studies					
Aliti,[34] 2013	75	Brazil	Patients with acute HF with LVEF < 45% and LOS < 36 h after hospital admission	2 g/d salt and 800 mL/d water versus 7.5-12.5 g salt and > 2500 mL water	No difference in clinical congestion score
Paterna,[36] 2011	1927	Italy	Hospitalized patients with HF (EF < 40%)	2760 mg/d Na diet vs 1840 mg/d Na diet	Group with lower Na diet had 24% mortality compared with 13% in higher Na diet at mean follow-up of 37 ± 15 months
Licata,[37] 2003	107	Italy	Hospitalized patients with HF (EF < 35%)	2760 mg/d Na diet versus 1840 mg/d Na diet	Group with lower Na diet had 13% survival compared with 55% in higher Na diet at mean follow-up of 31 ± 14 mo
Velloso,[35] 1991	32	Brazil	Admitted with acute illness due to chronic HF	2 g/d salt versus < 10 g/d salt	No difference in time needed for compensation of HF symptoms
Outpatient Studies					
Alvelos,[35] 2004	24	Portugal	Chronic HF (LVEF < 40%) with no exacerbations in previous 2 months	100 mmol/d salt vs usual salt intake	No difference in NYHA class change
Colin-Ramirez,[31] 2004	65	Mexico	Confirmed HF (systolic or diastolic)	2-2.4 g/d Na vs traditional management with no specific prescription	Edema and fatigue decreased in the intervention group
Paterna,[14] 2008	232	Italy	Patients with NYHA Class II HFrEF recently discharged (EF < 35%)	Group 1: 2760 mg/d Na diet Group 2: 1840 mg/d Na diet Fluid intake: 1 L/d	6 mo (death, death + readmission): Group 1: 7.6%, 12.7% Group 2: 26.3%, 39.5%
Paterna,[15] 2009	410	Italy	Patients with NYHA Class II HFrEF recently discharged (EF < 35%)	Group A & B: 2760 mg Na + 500/250 mg F Group C & D: 1840 mg Na + 500/250 mg F fluid Intake: 1 L/d Group E & F: 2760 mg Na + 500/250 mg F Group G & H: 1840 mg Na + 500/250 mg F fluid Intake: 2 L/d	6 mo (death, death + HF readmission): A: 1.9%, 7.7% B: 3.9%, 29.4% C: 9.8%, 49.0% D: 13.7%, 54.9% E: 9.6%, 51.9% F: 12.0%, 58.0% G: 11.5%, 71.1% H: 15.7%, 78.4%
Parrinello,[13] 2009	173	Italy	Patients with NYHA Class II HFrEF recently discharged (EF < 35%)	Group 1: 2760 mg/d Na + (250—500) mg F Group 2: 1840 mg/d Na + (250—500) mg F Fluid Intake: 1 L/d	12 months (readmission, death+ readmission): Group 1: 12%, 16% Group 2: 44%, 64%
Philipson,[33] 2013	97	Sweden	History of CHF (NYHA Classes II and IV)	Advise to reduce Na intake to 2-3 g/day vs nurse-led standard advice	No difference
Colin-Ramirez,[32] 2015	38	Canada	Patients with HF (NYHA Class II or III) receiving optimum medical therapy as per CSS guidelines	1.5 g/d Na vs 2.3 g/d NA	No difference in the clinical change
Hummel,[34] 2017	66	United States	Patients who were discharged after primary or secondary diagnosis of HF exacerbation	1.5 g/d Na with compliant meals vs usual care	No difference in KCCQ CSS

CHF = Congestive heart failure; CSS = Clinical Summary Score; EF = ejection fraction; F = Furosemide; HFrEF = Heart failure with reduced ejection fraction; HF = heart failure; KCCQ = Kansas City Cardiomyopathy Questionnaire; LVEF = left ventricular ejection fraction; Na = Sodium; NYHA = New York Heart Association.

Table 3 Pro and Con Arguments for Salt Restriction

Pros	Cons
Inhibits RAAS	Increased HF-related readmission rates
Lowers blood pressure	Increased mortality
Reduces cardiovascular mortality	Decrease in cardiac output, stroke volume, and increased pressor hormones
	Intolerability

HF = heart failure; RAAS = renin-angiotensin-aldosterone system.

Table 4 Unanswered Questions and Future Research Direction Regarding Dietary Sodium Intake in Patients With Heart Failure

Unanswered Questions	Future Directions
How "low" sodium intake is suitable for patients with HF	Dose ranging sodium intake studies
Impact of low sodium intake in patients with HFpEF	Dedicated studies for patients with HFpEF
Effect of low sodium intake in certain subgroups such as African Americans	Enrollment of higher number of ethnic minorities
Impact of strict sodium intake on nutrition and frailty in elderly	Studies investigating the association between strict sodium intake and nutrition in elderly
Impact of low sodium intake in various comorbid conditions	Comparison of the impact of low sodium intake in patients with and without chronic kidney disease

HF = heart failure; HFpEF = heart failure with preserved ejection fraction.

studies have suggested that only 15% of the patients have <2000 mg/d sodium intake based on 24-hour urinary sodium excretion. Even in symptomatic patients, the estimated adherence rate to sodium restriction is only 33%.[47] The cut off of 1500 mg/d is difficult to achieve even with the help of dietician and may be an unrealistic goal for patients in today's food environment. A more plausible approach could be to move toward a DASH diet in heart failure and focus on totality of nutritional support instead of focusing on just 1 nutrient.

UNANSWERED QUESTIONS AND FUTURE DIRECTION

All studies, except 1,[48] have focused on patients with heart failure with reduced ejection fraction (HFrEF). Moreover, all of the studies have had overwhelming majority of white patients. Because RAAS physiology differs among racial groups, especially the black population, the impact of low sodium intake may be different.[22] Selecting an optimum sodium intake is also crucial. For example, in the ongoing Prevent adverse Outcomes in Heart Failure by Limiting Sodium (PROHIBIT) study, sodium intake of 1500 mg/d will be compared with 3000 mg/d, which is far less than what an average American consumes in 1 day. However, creating arms with very high or very low sodium intake would cause ethical and logistical concerns. There are more unanswered questions regarding dietary sodium intake in patients with heart failure (Table 4).

WHAT IS THE CLINICIAN TO RECOMMEND TODAY?

Now that you have seen what we think is the most pertinent data on the topic, how much salt should your patients ingest per day? We agree with the approach for salt intake provided in the ACC/AHA heart failure guidelines until better evidence is available.[7] Because excessive sodium intake is associated with left ventricular hypertrophy, worse renal function, hypertension, and cardiovascular diseases,[49,50] patients who are at risk for heart failure (Stages A and B) should restrict sodium intake to 1500 mg/d, and those patients who already have heart failure (Stages C and D) should have some degree of sodium restriction for symptom improvement. Currently, there is too little evidence to recommend a particular cut off for Stage C and D heart failure patients. We make sure our patients know that although presently available scientific data fail to demonstrate the value of a very low sodium diet, a high sodium diet is not in their best interest either.

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