Dietary sodium restriction is arguably the most frequent self-care behavior recommended to patients with heart failure (HF)\(^1,2\) and is endorsed by all HF guidelines.\(^3-10\) However, the data on which this recommendation is drawn are modest, and the limited trials conducted have produced inconsistent findings. Americans consume \(\approx3700\) mg sodium daily,\(^11\) whereas the US Department of Agriculture and the Department of Health and Human Services recommend 2300 mg daily intake for the general population, with a stricter recommendation of 1500 mg/d for those \(>50\) years of age, blacks, or individuals with hypertension, diabetes mellitus, or chronic kidney disease.\(^12\) According to a recent report from the National Health and Nutrition Examination Survey, although 47.6% of persons aged \(\geq2\) years meet the criteria to limit daily sodium intake to 1500 mg, the usual intake for 98.6% of those persons was \(>1500\) mg; in 88.2% of the remaining population, daily intake was greater than the recommended \(<2300\) mg.\(^13\) The American Heart Association now recommends sodium intake of 1500 mg/d for all Americans,\(^14\) similar to the recommendation by the Institute of Medicine.\(^15\) Interestingly, and paradoxically, the suggested 1500 mg daily sodium intake for the general population is less than the limit proposed for HF patients by most guidelines, which appears as a contradiction. Whether this contradiction suggests inconsistent policy or a limited understanding of sodium homeostasis in the HF versus non-HF state is debatable. Sodium homeostasis physiology is altered in HF as opposed to healthy individuals and those with hypertension, and may partially explain these incongruous recommendations. This review summarizes the studies assessing the effects of sodium restriction in HF, highlighting knowledge gaps and future directions.

Sodium Intake Recommendations and Patterns

Excessive sodium intake is associated with fluid retention. Therefore, all HF management guidelines recommend sodium restriction. In 2005, the American College of Cardiology and the American Heart Association HF guidelines recommended 3000 to 4000 mg daily sodium intake,\(^16\) and, for patients with volume overload, restriction to 2000 mg/d. This recommendation was subsequently updated to moderate sodium restriction.\(^2\) The Heart Failure Society of America recommends 2000 to 3000 mg daily sodium intake and \(<2000\) mg for patients with moderate to severe HF symptoms. The Table summarizes the most current recommendations by multiple organizations. Expert opinion and level of evidence C has been largely the basis for these recommendations. The inconsistency of guidelines underlines the weak database that supports this cornerstone treatment for such a serious condition. Data on sodium consumption among HF patients indicate limited compliance with recommended sodium restriction. In a recent study, when instructed to limit sodium intake to 2000 mg/d, HF patients averaged a daily intake of 2671 mg/d with a wide range, spanning between 522 and 9251 mg/d.\(^18\) In another study, the reported sodium intake among HF patients was 3190 mg/d.\(^19\) Sodium reduction is difficult to adhere to even among patients with symptomatic HF, with an estimated compliance rate of only 33% as noted by 3-day food diaries.\(^18\) Congruent with this observation, a recent study reported that only 34% of patients consume \(<3000\) mg and only 15% consume \(<2000\) mg daily based on their 24-hour urinary sodium excretion.\(^20\) Sodium consumption \(<2000\) mg/d is difficult to achieve even with dietician education,\(^21\) and studies have demonstrated that sex\(^22\) and race\(^23\) affect dietary preferences and adherence to sodium restriction recommendations in patients with HF.

Sodium Homeostasis in HF

Heart failure may be associated with reduced cardiac output, elevated systemic venous pressures, or shunting of blood away from the kidneys; all may lead to diminished renal perfusion, in turn, activating the sympathetic nervous system\(^24\) and the renin angiotensin aldosterone system,\(^25\) and
creating a vicious cycle of sodium and water retention despite fluid overload (Figure).\textsuperscript{25} Moreover, considering the hypovolemic, volume-overloaded state, inappropriate physiological vasopressin levels are seen in HF. The natriuretic peptide system in HF is inadequate to counteract this dynamic because of decreased efficacy and inadequate cleaving of natriuretic peptides,\textsuperscript{26,27} downregulation of renal natriuretic peptide receptors,\textsuperscript{28} and degradation of natriuretic peptides by endopeptidases in the renal tubule.\textsuperscript{28} Therefore, despite the need for sodium and water excretion, sodium-retaining factors prevail.\textsuperscript{29}

Dietary sodium restriction is associated with further neurohormonal activation in HF. In animal studies, a sodium-restricted diet leads to a decrease in cardiac output and increased vascular resistance owing to renin angiotensin aldosterone system activation.\textsuperscript{29} Also, although blocking renin angiotensin aldosterone system does provide an improvement in renal blood flow, it is not associated with an increase in glomerular filtration rate or natriuresis when accompanied by a low-sodium diet.\textsuperscript{30} Recently, the Valsartan in Heart Failure Trial investigators reported that higher plasma renin activity (PRA) was a strong and independent predictor of mortality regardless of angiotensin-converting enzyme inhibitor or \( \beta \)-blocker treatment.\textsuperscript{31} Of note, in the Heart Outcomes Prevention Evaluation trial, high PRA was also an independent predictor of mortality in high-risk patients with atherosclerosis or diabetes mellitus without HF, regardless of allocation to ramipril.\textsuperscript{32} These data question the view that neurohormonal activation in HF has limited prognostic importance in the presence of neurohormonal blockade.

### Table. Guideline Recommendations for Dietary Sodium and Fluid Restriction in Heart Failure

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Year</th>
<th>Sodium Restriction Recommendation</th>
<th>Fluid Restriction Recommendation</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Heart Foundation of Australia/Cardiac</td>
<td>2006</td>
<td>&lt;3 g/d for NYHA class II without peripheral edema/</td>
<td>&lt;2 g/d for NYHA class III and IV/</td>
<td>C</td>
</tr>
<tr>
<td>Society of Australia and New Zealand</td>
<td></td>
<td>&lt;2 L/d for all patients and &lt;1.5 L/d during fluid retention episodes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart Failure Society, India</td>
<td>2007</td>
<td>&lt;2 g/d</td>
<td>&lt;2 L/d</td>
<td>Not Stated</td>
</tr>
<tr>
<td>European Society of Cardiology</td>
<td>2008</td>
<td>Moderate restriction</td>
<td>1.5–2 L/d in patients with severe symptoms and especially with hyponatremia</td>
<td>C</td>
</tr>
<tr>
<td>Canadian Cardiovascular Society</td>
<td>2008</td>
<td>&lt;2 g/d</td>
<td>2 L/d</td>
<td>Not Stated</td>
</tr>
<tr>
<td>American College of Cardiology/American Heart</td>
<td>2009</td>
<td>Moderate restriction (=&lt;2 g/d, if volume overload, followed by fluid intake restriction to 2 L/d if fluid retention persists)</td>
<td></td>
<td>C</td>
</tr>
<tr>
<td>Royal College of Physicians</td>
<td>2010</td>
<td>Salt reduction</td>
<td>Fluid restriction</td>
<td>Limited; further research required</td>
</tr>
<tr>
<td>Heart Failure Society of America</td>
<td>2010</td>
<td>2–3 g/d; &lt;2 g/d may be considered in moderate to severe heart failure</td>
<td>&lt;2 L/d, if fluid retention persists and if severe hyponatremia (serum Na &lt;130 mEq/L) is present</td>
<td>C</td>
</tr>
<tr>
<td>Scottish Intercollegiate Guidelines Network</td>
<td>2010</td>
<td>&lt;2.4 g/d</td>
<td>tailored fluid restriction</td>
<td>1+</td>
</tr>
<tr>
<td>American Dietetic Association</td>
<td>2011</td>
<td>&lt;2 g/d</td>
<td>1.4–1.9 L/d depending on clinical symptoms</td>
<td>Fair</td>
</tr>
</tbody>
</table>

Level of Evidence: C = Limited populations evaluated. Only consensus opinion of experts, case studies, or standard of care; Fair = Benefits exceed the harms but quality of evidence is not as strong; 1+ = well-conducted meta-analysis, systematic reviews, or randomized controlled trials with low risk of bias. NYHA indicates New York Heart Association.

### Overview of Sodium Intake Studies in HF

Several studies have investigated the effects of dietary sodium in patients with HF, albeit randomized evidence is limited. Few studies evaluated outcomes, and most investigated the physiological effects of varying sodium in the diet. Most studies focused on dietary sodium restriction primarily, whereas others had additional features such as fluid restriction, diuretic dosing, and use of parenteral saline. To facilitate this discussion, sodium intake is classified into “very low” (230–800 mg/d), “low” (1610 mg/d to 2000 mg/d), and “moderate-to-high” (2300–5750 mg/d) dietary intake. Comparing these studies is challenging because of the variation in sample size, study design, sodium intervention, sodium intake assessment, and baseline HF therapy among the studies (online-only Data Supplement Table I).

### Physiological and Neurohormonal Responses

Decreased pulmonary artery and capillary wedge pressures without change in cardiac index and systemic vascular resistance was observed by Cody and colleagues\textsuperscript{33} in New York Heart Association (NYHA) class III to IV patients with a very low sodium diet, but Damgaard and colleagues\textsuperscript{34} noted a decrease in cardiac index and stroke volume and an increase in pulmonary vascular resistance with a low-sodium diet in NYHA class II to III patients. Two studies by Volpe and colleagues\textsuperscript{35,36} concluded that moderate-to-high sodium intake had no hemodynamic effects on NYHA I to II patients.
but predisposed patients to sodium retention. Natriuretic
peptide levels were affected inconsistently among studies;
levels did not change significantly with dietary sodium
modification in 4 studies using very low to moderate dietary
sodium restriction,34,36–38 decreased in 2 studies with a
moderate-to-high sodium diet,35,39 and increased in 3 studies
with a low-sodium diet.40–42 Levels of neurohormones, such
as PRA, norepinephrine, angiotensin-II, and urinary aldoste-
rone, increased with dietary sodium restriction regardless of
degree of restriction.33–36,40–42 Interestingly, Nakasato and
colleagues37 showed a differential effect on PRA according to
body mass index; only in patients with lower body mass
index did PRA increase with a very low sodium diet in
comparison with a moderate-to-high sodium diet.

Diuresis, Electrolyte, and Renal Responses
Licata and colleagues,43 Parrinello and colleagues,42 and
Paterna and colleagues40,41,44 performed a series of studies
with varied fluid restriction, diuretic dosing, low versus
moderate to high dietary sodium intake, and/or the use of
hypertonic saline infusion. Patients who received hypertonic
saline and a moderate-to-high sodium diet had more diuresis
and natriuresis in comparison with those who were not treated
with hypertonic saline and consumed a low-sodium diet.
Regardless of use of hypertonic saline, these studies demon-
strated that low dietary sodium intake was associated with a
significant increase in blood urea nitrogen and creatinine,
whereas moderate-to-high sodium intake was related to de-
creased creatinine and an insignificant increase in blood urea
nitrogen.40–44 The highest daily diuresis was observed among
those receiving 500 mg/d furosemide, 2760 mg/d sodium
diet, and strict fluid restriction (1000 mL/d). Those receiving
2760 mg/d sodium and 1000 mL/d fluid restriction, irrespec-
tive of diuretic dose, had better natriuresis and showed only a
modest increase in creatinine and stable blood urea nitrogen
levels, whereas other groups showed more increases in both
creatinine and blood urea nitrogen.40

Outcomes
Adverse event rates, defined as HF or non-HF readmission
rates and mortality rates, were higher with low-sodium diets
in several studies.40–44 Mortality rate was lower in the
moderate-to-high sodium group in 3 studies in comparison
with low-sodium diet.51–53 In studies evaluating the effects of
low and moderate-to-high dietary sodium intake with or
without hypertonic saline infusion, patients on the low-
sodium diet without hypertonic saline infusion had longer hospital stays\textsuperscript{43,44} and higher readmission rates in comparison with those on the moderate-to-high sodium diet with hypertonic saline infusion; these differences were observed as early as 30 days and continued up to 12 months.\textsuperscript{50–52} Patients not randomly assigned because of inability to follow the prescribed fluid intake restriction, but still receiving the moderate-to-high sodium diet, had a higher rate of HF-related readmissions, similar to that observed in those receiving low-sodium diets, in comparison with those who were able to comply with fluid restriction.\textsuperscript{41} Thus, restricted fluid intake may in part be responsible for these differences.

Two observational studies, however, showed different results.\textsuperscript{70,45} Arcand and colleagues\textsuperscript{45} showed that in a HF cohort consisting mostly of patients with NYHA class I to II symptoms, \( \geq 2800 \text{ mg/d sodium}\) resulted in more HF hospitalizations in comparison with those on lower intake. Lennie and colleagues\textsuperscript{52} interestingly showed \( <3000 \text{ mg/d sodium} \) was associated with better outcomes in NYHA class III to IV patients, whereas it was associated with significant increase in hospital visits, readmissions, and mortality in NYHA class I to II patients.

Critique

Clinical studies assessing the effect of sodium restriction on outcomes in HF are limited. Variances in protocols, fluid intake, actual measurement of sodium intake, and clinical and therapeutic characteristics among these studies make it challenging to compare data and draw definitive conclusions. Sodium intake is challenging to measure. Besides variable sodium intake among studies, another concern is that compliance with the prescribed sodium diets was not described in some studies or was subjectively assessed in others. Only in short-term studies in which the patients received a diet from a metabolic kitchen could sodium intake be strictly controlled. Concomitant fluid intake was described in some studies and it varied, whereas adherence to the recommended amount of fluid was either not reported or subjectively assessed. Earlier studies discontinued HF medications before randomization,\textsuperscript{33,35,36} and later studies did not consistently have patients on optimal medical therapy. Hemodynamic changes varied in these studies in response to a restricted sodium diet; however, statistically significant adverse neurohormonal changes were consistently noted. The multiinterventional approach of several of these studies, eg, altering diuretic dose, fluid allowance, and sodium restriction, confounds the effect of sodium intake.\textsuperscript{40–42} With the exception of 1 observational study that evaluated patients with preserved ejection fraction,\textsuperscript{36} all other studies focused on patients with HF and reduced ejection fraction. Thus, the physiological and clinical impact of dietary sodium restriction in HF with preserved ejection fraction is unknown. Finally, these data pertain almost exclusively to white patients. Considering the differences in neurohormonal activation, especially the renin angiotensin aldosterone system, and cardiovascular and renal pathophysiology among the races, especially blacks, the effects of sodium restriction in nonwhite HF patients cannot be ascertained from these studies.

Some studies have shown poor caloric intake and decreased nutritional status in patients who comply with sodium restriction,\textsuperscript{18,46–48} which may also impact HF outcomes. Whether dietary sodium intake in HF should be individualized, based on body weight, symptoms, renal function, or other characteristics, is uncertain.

These inconsistencies are in part related to studies with small sample sizes and conclusions based on nonrandomized data. Interestingly, the 3 larger randomized, controlled trials that assessed clinical outcomes showed congruent results,\textsuperscript{40–42} ie, lower sodium intake was associated with worse outcomes, including significantly higher mortality and readmission rates. However, all 3 of these studies were performed by the same group of investigators in a restricted geographic location enrolling postdischarge patients, and these effects were not independently confirmed by other investigators. In addition, in the largest of these studies,\textsuperscript{40} multiple groups were tested for sodium effects, increasing the potential for type I error, and therefore the results need to be interpreted with caution. Finally, clinical evidence suggests that sodium restriction is associated with neurohormonal activation in HF, which may not be an innocent phenomenon even among treated patients. However, no study to date has evaluated the effects of sodium restriction on neurohormonal activation and outcomes in optimally treated HF patients. Although a significant proportion of patients in these studies were on angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, few were on \( \beta \)-blockers or aldosterone antagonists. These data underscore the need for more definitive trials to assess the efficacy and safety of dietary sodium restriction in HF.

Conclusions

It is widely perceived that HF management should include dietary sodium restriction, a recommendation endorsed by all national and international guidelines. Given the generally accepted notion that increased sodium intake leads to increased fluid retention in HF, it has been assumed that a low-sodium diet as suggested for the general population would improve outcomes in HF patients also. Indeed, there are no conclusive data suggesting that the sodium intake recommended for the general population is unsafe for HF patients in the current era of medical therapy. Also, although adverse neurohormonal activation related to sodium restriction in HF remains a concern, its clinical relevance in an optimally treated patient is not known.

Currently, there are insufficient data to endorse any specific level of sodium intake with certainty, and differences among the various HF subpopulations are not known. Effects of sodium restriction in nonwhite HF patients and those with preserved ejection fraction are virtually unknown. The new American Heart Association recommendations for 1500 mg/d sodium appears to be appropriately applicable for patients with stage A and B HF, because of the data linking sodium intake with blood pressure,\textsuperscript{49} incidence of hypertension,\textsuperscript{50} left ventricular hypertrophy,\textsuperscript{51} cardiovascular disease,\textsuperscript{52} other HF risk factors,\textsuperscript{52–53} and even with incident HF per se.\textsuperscript{54} However, it becomes evident from this review that for stage C and D HF
patients, there are insufficient data to support a definitive recommendation. Physicians should consider some degree of sodium restriction in patients with stage C and D HF, but more data are needed to support a specific sodium intake level. The generation of guideline statements to support a fundamental recommendation such as dietary modifications in HF must not be relegated to consensus alone, but should be as evidence driven as drug and device therapy. The lack of a well-informed database puts patients with HF at risk for errant recommendations. We believe that there is a critical need for rigorously designed mechanistic, behavioral, and outcome trials to better study sodium homeostasis in HF and inform management of dietary intake of sodium in all severities of HF. This is especially true considering the signal for worse HF outcomes with sodium restriction in several studies.46-51,52

We do know that very high sodium intake is not optimal, but we do not know (1) what the lowest safest and most efficacious range is and (2) if that range would be applicable to all patients, or needs to be individualized. Thus, more “dose-ranging” sodium intake studies would be informative. At the minimum, a randomized clinical trial in patients with systolic HF should be considered that assess the effects of sodium restriction on clinical outcomes including mortality and hospitalization risk. Several different strategies are possible, one of which would be to randomly assign patients to moderate sodium restriction, ie, 2300 mg/d per the current recommendation, and 1500 mg/d, the strict recommendation for the general population proposed by the American Heart Association. However, these values are suggested more out of the concern to be consistent, if possible, with the national guidelines for the population at large. Importantly, these patients should undergo uniform fluid restriction according to current recommendations and be on optimal medical therapy when studying the effects of sodium intake.

Mechanistic studies can focus on effect of sodium restriction on the myocyte (both at the level of cellular signaling and also at the organ level), vasculature, renal function, and neurohormonal activation. However, these 4 physiological domains are directly affected by, or the effect of sodium on them can be modified by, baseline medical therapy. Thus, fundamental research with animal models and human studies on baseline standard therapy are likely to yield important insights. Moreover, mechanistic studies assessing the physiological effects and safety of dietary sodium restriction in patients with HF with preserved ejection fraction should also be conducted to inform larger outcome studies. It is also possible that the effect of sodium intake varies considerably among different individuals. Some ways to personalize sodium intake recommendations that could be assessed include studies based on genomic factors, body size, renal function, comorbidity burden, symptoms status, etc.

Beyond the mechanistic and clinical outcomes studies, further behavioral research is important. Heart failure patients, like the population at large, despite medical advice, continue to consume large quantities of sodium daily. Further research investigating reliable means of longer-term sodium intake assessment over time is important, because current means are either prone to recall bias (eg, food frequency questionnaires) or are episodic and reveal the status for the past 24 hours, which may not be reflective of the overall sodium intake pattern (eg, 24-hour urinary sodium measurements). How to best implement sodium intake recommendations so that the adherence rates improve, and how much that will involve advocacy versus behavior change interventions, needs further exploration. Alternate food-seasoning options that can satisfy taste preferences, but do not contain elements that in excess can be detrimental (eg, potassium content in individuals on angiotensin-converting enzyme inhibitor and aldosterone antagonists therapy), should be sought.

Disclosures

None.

References

Executive Summary: HFSA 2006 Comprehensive Heart Failure Practice Guideline.


46. Colín Ramírez E, Castillo Martínez L, Orea Tejeda A, Rebollar González V, Narvaez David R, Asensio Lafuente E. Effects of a nutritional inter-


Key Words: heart failure □ sodium restriction □ neurohormones □ outcomes
Dietary Sodium Intake in Heart Failure
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Circulation. 2012;126:479-485
doi: 10.1161/CIRCULATIONAHA.111.062430
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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Supplemental Material

Gupta et al.: Dietary Sodium Intake in Heart Failure
### studies evaluating sodium intake in heart failure

#### dietary sodium restriction only

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<tr>
<th>Source</th>
<th>Design</th>
<th>Meds D/C’d</th>
<th>Sodium Intake Determination</th>
<th>Intervention</th>
<th>Hemo-dynamic Effects</th>
<th>Neurohormonal Effects</th>
<th>Physiologic Effects</th>
<th>Clinical Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Damgaard 2006</strong>¹</td>
<td>Randomized crossover Low vs. Moderate-to-High Na Intake</td>
<td>No</td>
<td>24-h urine sodium levels</td>
<td>1610 mg/d vs. 5750 mg/d</td>
<td>CI ↓, SVI ↓, TPR ↑³</td>
<td>NE ↑, Epi (NS)</td>
<td>Na ↓, BUN ↑, Cr↑ while seated</td>
<td>Not Evaluated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Fluid intake: free Study Period: 14 days</td>
<td>PP ↓*</td>
<td>Ang II ↑, pro-BNP↑⁴</td>
<td></td>
<td></td>
</tr>
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<tr>
<td><strong>Arcand 2011</strong>²</td>
<td>Observational Low vs. Moderate vs. Moderate-to-High Na Intake</td>
<td>No</td>
<td>Food diary</td>
<td>Tertiles based on Na Group 1: ≤1900 mg/d Group 2: 2000-2700 mg/d Group 3: ≥2800 mg/d</td>
<td>Fluid intake: not mentioned Study Period: median follow-up 3 years</td>
<td>BP ↑⁵, NYHA class (NS)</td>
<td>NE ↑, Epi ↑, BNP↓⁶, Aldosterone↑⁷ = 0.09</td>
<td>- Lower cumulative ADHF event rate with &lt; 2800 mg/d Na at 1- and 3-y (log rank p = 0.001)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Lower mortality with &lt; 2800 mg/d Na (log rank p = 0.022)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- No significant difference in all-cause hospitalizations (log rank p =0.224)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Higher sodium intake associated with more ADHF events</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Alvelos 2004</strong>³</td>
<td>Single-Blind Randomized Moderate vs. Moderate-to-High Na Intake</td>
<td>No</td>
<td>24-h urine sodium levels</td>
<td>2300mg/d vs. &quot;usual diet&quot; Fluid intake: not mentioned Study Period: 15 days</td>
<td>BP ↑⁵, NYHA class (NS)</td>
<td>NE ↑, Epi ↑, BNP↓⁶, Aldosterone↑⁷ = 0.09</td>
<td>Urinary volume ↓, Cr (NS) CrCl ↓↑</td>
<td>Not Evaluated</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Sodium restriction leads to antinatriuretic, antidiuretic effects in HF</strong></td>
</tr>
</tbody>
</table>

¹ The observation that high sodium intake improves cardiac performance, induces peripheral vasodilatation, and suppresses the release of vasoconstrictor hormones does not support the advice for HF patients to restrict dietary sodium.
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Randomization</th>
<th>Very Low vs. Moderate-to-High Na Intake</th>
<th>N</th>
<th>NYHA</th>
<th>Age</th>
<th>EF</th>
<th>Fluid Intake</th>
<th>Study Period</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cody 1986</td>
<td>Randomized crossover</td>
<td>Yes</td>
<td>Metabolic kitchen provided all diets</td>
<td>10</td>
<td>NYHA III-IV</td>
<td>43-72</td>
<td>No Data</td>
<td>2300 mg/d vs. 2300 mg/d</td>
<td>7 days</td>
<td>Decreased sodium associated with lower weight, higher RAAS activation, and increased SNS activity with HF</td>
</tr>
<tr>
<td>Nakasato 2010</td>
<td>Single-Blind Randomized</td>
<td>No</td>
<td>Burke-type dietary history method</td>
<td>50</td>
<td>NYHA I-III</td>
<td>Group 1, 52±2(SE) Group 2, 52±2(SE)</td>
<td>Group 1, 27±1%(SE) Group 2, 31±1%(SE)</td>
<td>800 mg/d vs. 2400 mg/d</td>
<td>14 days</td>
<td>Improved QOL in all subjects</td>
</tr>
<tr>
<td>Philipson 2010</td>
<td>Single-Blind Randomized</td>
<td>No</td>
<td>24-h urine sodium levels</td>
<td>30</td>
<td>NYHA II-III</td>
<td>Control 74±9(SD) Intervention 74±8(SD)</td>
<td>Control 31.7±9.1%(SD) Intervention 34.7±11%(SD)</td>
<td>2000-3000 mg/d + 1.5 L/d vs. General Diet (ESC guidelines)</td>
<td>12 weeks</td>
<td>No negative impact on signs or symptoms of heart failure and quality of life</td>
</tr>
</tbody>
</table>
| Volpe 1993 | Sequential intervention | Yes | Metabolic kitchen provided all diets | 24 (12 HF/12 controls) | NYHA: I-II | Control 38±4(SE) HF 46±3(SE) | 2300 mg/d x 5 days then 5750 mg/d x 6 days | 11 days | Findings underscore a susceptibility to retain sodium and water early in the...

**Sodium and Fluid Restriction**

- **Lennie 2011**
  - Comparing Varying degrees of Moderate and Moderate-to-High Na Intake
  - N: 302 NYHA I-IV
  - Age: 62±12(SD)
  - EF: 33.8±14%(SD)
  - Fluid intake: not mentioned
  - Study Period: median follow-up 12 months

- **Cody 1986**
  - Randomized crossover
  - Very Low vs. Moderate-to-High Na Intake
  - N: 10
  - NYHA III-IV
  - Age: 43-72
  - Fluid intake: not mentioned
  - Study Period: median follow-up 12 months

- **Nakasato 2010**
  - Single-Blind Randomized
  - Very Low vs. Moderate-to-High Na Intake
  - N: 50 NYHA I-III
  - Age: Group 1, 52±2(SE) Group 2, 52±2(SE)
  - Fluid intake: not mentioned
  - Study Period: median follow-up 12 months

- **Philipson 2010**
  - Single-Blind Randomized
  - Moderate vs. High Na Intake
  - N: 30 NYHA II-III
  - Age: Control 74±9(SD) Intervention 74±8(SD)
  - Fluid intake: not mentioned
  - Study Period: median follow-up 12 months

- **Volpe 1993**
  - Sequential intervention
  - Study Moderate vs. High Na Intake
  - N: 24 (12 HF/12 controls)
  - NYHA: I-II
  - Age: Control 38±4(SE) HF 46±3(SE)
  - Fluid intake: not mentioned
  - Study Period: median follow-up 12 months

**NYHA I-II** - higher event rate
**NYHA III-IV** - lower event rate
(Events = mortality + cardiac-related hospitalization /ED visits)
Sodium restriction (< 3000 mg/d) best for NYHA III-IV
Volpe 1997

### Sequential Intervention Study

- **Moderate vs. High Na Intake**
- **N:** 20 (10 HF NYHA I-II/10 controls)
- **Age:** Control 45±4(SE); HF 51±2 (SE)
- **EF:** HF 29.7±2%(SE)

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Intervention</th>
<th>Study Period</th>
<th>EF:</th>
<th>Fluid Intake</th>
<th>Diuretic Intake</th>
<th>HR (NS)</th>
<th>BP (NS)</th>
<th>BNP</th>
<th>Aldo</th>
<th>Renin</th>
<th>GFR</th>
<th>CrCl</th>
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</thead>
<tbody>
<tr>
<td>Control</td>
<td>Metabolic kitchen provided all diets</td>
<td>14 days</td>
<td>75.7</td>
<td>1.5-1.8 L/d</td>
<td>250mg F BID</td>
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<tr>
<td>Group G</td>
<td>Metabolic kitchen provided all diets</td>
<td>6 months</td>
<td>76.5</td>
<td>2 L/d</td>
<td>125mg F BID</td>
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<tr>
<td>Group F</td>
<td>Metabolic kitchen provided all diets</td>
<td>12 months</td>
<td>76.0</td>
<td>1.5 L/d</td>
<td>125mg F BID</td>
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<tr>
<td>Group E</td>
<td>Metabolic kitchen provided all diets</td>
<td>18 months</td>
<td>75.6</td>
<td>2 L/d</td>
<td>125mg F BID</td>
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<tr>
<td>Group D</td>
<td>Metabolic kitchen provided all diets</td>
<td>24 months</td>
<td>75.5</td>
<td>1.5 L/d</td>
<td>125mg F BID</td>
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**Sodium Restriction + Fluid Restriction + Diuretic Dosing**

<table>
<thead>
<tr>
<th>Paterna 2008</th>
<th>Single-Blind Randomized</th>
<th>Study Period</th>
<th>EF:</th>
<th>Fluid Intake</th>
<th>Diuretic Intake</th>
<th>HR (NS)</th>
<th>BP (NS)</th>
<th>BNP</th>
<th>Aldo</th>
<th>Renin</th>
<th>GFR</th>
<th>CrCl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low vs. Moderate-to-High Na Intake</td>
<td>1840 mg/d vs. 2760 mg/d</td>
<td>6 months</td>
<td>75.2</td>
<td>2 L/d</td>
<td>125mg F BID</td>
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<tr>
<td>N: 232 NYHA II post discharge</td>
<td>Fluid Intake: 1 L/d</td>
<td>6 months</td>
<td>75.2</td>
<td>2 L/d</td>
<td>125mg F BID</td>
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<tr>
<td>Age:</td>
<td>Diuretic dose: 1 L/d</td>
<td>6 months</td>
<td>75.2</td>
<td>2 L/d</td>
<td>125mg F BID</td>
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<tr>
<td>Normal-Na 27.1±7(SD)</td>
<td>Diuretic dose: 1 L/d</td>
<td>6 months</td>
<td>75.2</td>
<td>2 L/d</td>
<td>125mg F BID</td>
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<tr>
<td>Low-Na 73.3±9(SD)</td>
<td>Diuretic dose: 1 L/d</td>
<td>6 months</td>
<td>75.2</td>
<td>2 L/d</td>
<td>125mg F BID</td>
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<tr>
<td>EF:</td>
<td>Diuretic dose: 1 L/d</td>
<td>6 months</td>
<td>75.2</td>
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</table>

**Sodium Depletion Has**

- **Detrimental neurohormonal and renal effects leading to worse clinical outcomes in those with compensated HF**
- **Low sodium diet leads to worsening renal function and increase in readmissions**

**Sodium Restriction**

- **development of heart failure and may indirectly support the usefulness of sodium restriction and of early therapeutic interventions even in the milder stages of the disease.**

**The exposure to salt loading may unmask an early predisposition to retain sodium in the milder stages of [heart failure].**
<table>
<thead>
<tr>
<th>Study Type</th>
<th>Study Design</th>
<th>Sodium Intake</th>
<th>Sodium Intake</th>
<th>Fluid Intake</th>
<th>Diuretic Dose</th>
<th>Study Period</th>
<th>Follow-up Period</th>
<th>Outcome</th>
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</thead>
<tbody>
<tr>
<td>Licata 2003</td>
<td>Single-blind Randomized Low vs. Moderate to High Na Intake</td>
<td>No</td>
<td>Diet provided during hospitalization and standardized hypertonic saline given based on randomization. Post-discharge assessment not noted</td>
<td>1840 mg/d vs. 2760 mg/d</td>
<td>Fluid intake: 1 L/d Diuretic dose: 500 mg -1000 mg F BID +/- HSS</td>
<td>Study Period: 6-12 days Follow-up Period: 31 +/-14 (SD) months</td>
<td>SBP ‡ BUN † § BUN † §</td>
<td>Na § -Significantly higher hospitalization days§ and readmission rates</td>
</tr>
<tr>
<td>Paterna 2005</td>
<td>Double-Blind Randomized Low vs. Moderate-to-High Na Intake</td>
<td>No</td>
<td>Diet provided during hospitalization and standardized hypertonic saline given based on randomization. Post-discharge assessment not noted</td>
<td>1840 mg/d vs. 2760 mg/d</td>
<td>Fluid intake: 1 L/d Diuretic dose: 500 mg -1000 mg F BID +/- HSS</td>
<td>Study Period: 6-12 days Follow-up Period: 30 days</td>
<td>SBP ‡ BUN † § BUN † §</td>
<td>Na § -Significantly higher hospitalization days§ and readmission rates</td>
</tr>
</tbody>
</table>

All values are means ± standard error (SE) or standard deviation (SD) as designated. * p<0.05; † p <0.02; ‡ p<0.01; § p<0.001; ¶ p< 0.0001; NS – no significant difference (ADHF - acutely decompensated heart failure; Age (years); Aldo - aldosterone; Ang II - angiotensin II; ANP - atrial natriuretic peptide; BNP - brain natriuretic peptide; BUN - blood urea nitrogen; CI - cardiac index; Cr - creatinine; CrCl - creatinine clearance; EF - Ejection Fraction (%); Epi - epinephrine; F - furosemide; GFR - glomerular filtration rate; HF - heart failure; HR - heart rate; MAP - mean arterial pressure; Na - sodium; NE - norepinephrine; PAP - pulmonary artery pressure; PCWP - pulmonary capillary wedge pressure; PP - pulse pressure; RAAS – renin-angiotensin-aldosterone system; RPF - renal plasma flow; RVR - renal vascular resistance; SNS – sympathetic nervous system; SV - stroke volume; SVI - stroke volume index; TPR - total peripheral resistance)
References


