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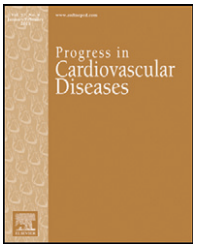

Dietary Salt Restriction in Heart Failure: Where Is the Evidence?

James J. DiNicolantonio[a,*], Subhankar Chatterjee[b], James H. O'Keefe[a]

[a]Mid-America Heart Institute at Saint Luke's Hospital, Kansas City, MO, USA
[b]R. G. Kar Medical College & Hospital, Kolkata, India

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ABSTRACT

Several dietary guidelines, health organizations and government policies recommend population-wide sodium restriction to prevent hypertension and related comorbidities like heart failure (HF). The current European Society of Cardiology and American College of Cardiology/American Heart Association Heart Failure guidelines recommend restricting sodium in HF patients. However, these recommendations are based on expert opinion (level C), leading to wide variability in application and lack of consensus among providers pertaining to dietary salt restriction. To evaluate the strength of current evidences to recommend dietary salt restriction among HF patients, we performed a comprehensive literature review and explored the safety and efficacy of such recommendations.

Notwithstanding substantial progress in the pharmacology and technology related to cardiovascular (CV) care, heart failure (HF) remains the most frequent cause of hospital admission and readmission.[1] Along with the wide pharmaceutical armamentarium and availability of devices, such as cardiac resynchronization therapy, physical exercise and dietary salt and fluid restriction remain essential steps in the management of HF and are recommended by nearly all HF guidelines.[2–6] The current 2013 ACCF/AHA guideline recommends sodium restriction to 1.5 g/day for patients with stage A and B HF, while for stage C and D HF AHA advises salt restriction <3 g/day,[7] which is much lower than what an average American diet contains (approximately 3.7 g/day).[8] Yet the recommendation for drastic reductions in the consumption of salt is still an unresolved issue in patients with HF. To evaluate the strength of the current evidence to recommend dietary salt restriction among HF patients, we performed a comprehensive literature review to explore the safety and efficacy of such recommendations.

Pathophysiology of HF

HF is defined as a decreased ability of the heart to fill (diastolic HF) and/or eject blood (systolic HF) due to structural and/or functional defects in the myocardium leading to a reduced cardiac output (CO).[2] The structural (as in dilated cardiomyopathy) or functional (as in myocardial infarction) insult to the heart is viewed as the index event. Following an index event, although pumping capacity of the heart starts to progressively decline, the patient remains largely asymptomatic or minimally symptomatic due to various compensatory mechanisms—that are orchestrated predominantly through activation of neurohormonal systems both within the heart and systemically. Reduced CO and the subsequently decreased effective intravascular volume lead to unloading of high pressure baroreceptors in left ventricle, aortic arch and carotid sinus. This results in loss of parasympathetic output with increased sympathetic discharge and non-osmotic

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* Address reprint requests to Dr. James J. DiNicolantonio, PharmD, Saint Luke's Mid America Heart Institute.
E-mail address: jjdinicol@gmail.com (J.J. DiNicolantonio).

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Abbreviations and Acronyms

ACM = all-cause mortality

AVP = arginine vasopressin

BP = blood pressure

CO = cardiac output

CV = cardiovascular

CVD = cardiovascular disease

HF = heart failure

HR = hazard ratio

HTN = hypertension

MAP = mean arterial pressure

NYHA = New York Heart Association

RAAS = renin angiotensin aldosterone system

SNS = sympathetic nervous system

secretion of arginine vasopressin (AVP) (also known as antidiuretic hormone). Activation of sympathetic nervous system (SNS) and/or reduced renal blood flow and/or a decrease in sodium delivery, results in the release of renin from the macula densa in the kidney, and leads to activation of the renin angiotensin aldosterone system (RAAS). Both RAAS and AVP act as powerful vasoconstrictors that increase the permeability of renal collecting ducts leading to increased salt and water reabsorption. On the other hand, in HF the natriuretic peptide system, which can modulate the effects of peptides such as angiotensin II and AVP, becomes inadequate to counteract the maladaptive effects of neurohormonal activation because of reduced efficacy and inadequate cleaving of natriuretic peptides,[9,10] downregulation of renal natriuretic peptide receptors and degradation of natriuretic peptides by endopeptidases present in the renal tubule.[11] Therefore, although these compensatory mechanisms try to maintain homeostasis even in the face of the failing heart, they ultimately cause end-organ damage by various mechanisms such as remodeling of the heart and excessive water retention (predisposing to hyponatremia, pulmonary congestion, and increased morbidity/mortality).[12]

Dietary sodium restriction: current practices and evidence

The Heart Failure Society of America Clinical Practice Guidelines state: "dietary sodium restriction (2000–3000 mg daily) is recommended for patients with the clinical syndrome of HF and preserved or depressed left ventricular ejection fraction. Further restriction (<2,000 mg daily) may be considered in moderate to severe HF (Strength of Evidence = C)."[13] In this section we explore that lack of existing evidence that lowering sodium in HF patients improves morbidity/mortality and where the recommendations for a lower sodium diet stem from.

The concept of restricting salt among the general population (to prevent the emergence of hypertension (HTN) as well as HTN-induced HF) and the associated comorbidities originated from the noted observational cross-sectional study INTER-SALT.[14] Across 52 "INTERSALT" centers, the median 24-h urinary sodium excretion ranged from 0.2 to 242.1 mmol. When the relation between blood pressure (BP) and salt intake (assessed by the 24-h urinary sodium excretion) was studied within each of the 52 INTERSALT centers (with adjustments for sex and age applied), a positive association was found in 39 of the 52 centers (significant in 15) and a negative association was revealed in 13 centers (significant in 2). Analyses across centers of median BP and the prevalence of HTN in relation to median sodium excretion showed a positive association when all 52 centers were included but not when 4 populations with low sodium values were excluded. In another prospective study[15] a group of 1499 participants was followed for more than 6 years and their BP and sodium excretion were measured. The annual increases in mean BP were 0.37 mm Hg systolic and 0.47 mm Hg diastolic ($p < 0.001$), but on average the 24-h urinary sodium excretion did not change over time. However, in multivariable-adjusted analyses of individual participants, a 100-mmol increment in 24-h sodium excretion was associated with a significant 1.71 mm Hg increase in systolic BP ($p < 0.001$), without concomitant change in diastolic BP. What this tells us is that among and within various populations, sodium intake appears to only weakly track with BP.

As described earlier, in HF the reduced CO and renal perfusion cause RAAS activation that causes salt and water retention, which in turn may cause or worsen the congestive symptoms in HF. In this regard, the recommendation of a low salt diet for HF patients seems appealing as water is thought to follow salt (more salt ingested leads to increased thirst and greater fluid retention). However, experimental evidence shows that for subjects who are not sodium deprived, sodium intake expands intravascular volume via fluid shift from the interstitial space into the blood vessels without increasing total body water.[16] In a study of 24 patients (12 compensated HF patients and 12 controls) randomized to 1 week of a low-sodium diet (70 mmol/day i.e., 1.575 mg/day) and 1 week of a high-sodium diet (250 mmol/day i.e., 5.625 mg/day); the high sodium group had a 9% increase in plasma volume, a 14% increase in cardiac index, a 21% increase in stroke volume index, and a 10% decrease in total peripheral resistance.[17] The authors concluded that a high sodium intake did not cause excessive sodium and water retention in medically treated compensated HF patients and thus, the improvements in cardiac status caused by a high sodium intake do not support the advice for a sodium-restricted diet in HF patients. Lennie et al. showed that 3 g dietary sodium restriction might be appropriate for patients in NYHA functional Classes III and IV, but harmful for NYHA Classes I and II patients (HR for event-free survival for 24-h Urinary Na $\geq$ 3 g in NYHA Class I/II was 0.44 (95% CI = 0.20–0.97) and 2.54 (95% CI = 1.10–5.84) for NYHA III/IV).[18] A meta-analysis of 58 studies looking at sodium restriction showed that in normotensive individuals, mean arterial BP (MAP) was reduced by only by 0.6 mmHg and in HTN by 3 mmHg.[19] Yet this small reduction of BP needs to be weighed against the activation of the SNS and RAAS. A recent Cochrane review performed by Adler et al. failed to demonstrate any benefit of salt restriction among normotensive and HTN individuals with respect to CV disease (CVD) morbidity and mortality.[20] The PURE investigators showed that sodium intake between 3 and 6 g/day was associated