JAMDA xxx (2017) 1–6

JAMDA

journal homepage: www.jamda.com

Original Study

Association Between Sodium Excretion and Cardiovascular Disease and Mortality in the Elderly: A Cohort Study

Diana Lelli MD [a,*], Raffaele Antonelli-Incalzi MD [a], Stefania Bandinelli MD [b], Luigi Ferrucci MD, PhD [c], Claudio Pedone MD, PhD, MPH [a]

[a] *Area di Geriatria, Università Campus Bio-Medico di Roma, Rome, Italy*
[b] *Geriatric Rehabilitation Unit, Azienda Sanitaria di Firenze, Florence, Italy*
[c] *Longitudinal Studies Section, Clinical Research Branch, National Institute on Aging, Baltimore, MD*

Keywords:
Aged
frail elderly
mortality
cardiovascular diseases
sodium
dietary

ABSTRACT

Objective: High dietary sodium intake is a risk factor for cardiovascular events and death. Recently, a J-shaped correlation between sodium intake and adverse outcomes has been shown. The evidence on the association between sodium intake and cardiovascular outcomes in the elderly is scant. The objective of this study was to evaluate the correlation between sodium intake and cardiovascular events and mortality in an elderly population, taking into account frailty status.
Design: Cohort study of community dwelling older people enrolled in the InCHIANTI (Invecchiare in Chianti - Aging in the Chianti) study from 1998 to 2000 and followed-up for 9 years.
Setting: Two communities in Tuscany, Italy.
Participants: A total of 920 participants 65 years of age and older, with 24-hour urinary sodium excretion data.
Measurements: Nine-year mortality and incident cardiovascular events were analyzed using Cox and nonlinear log-binomial models, stratified by frailty status. Sensitivity analysis in participants without hypertension and cardiovascular diseases was performed.
Results: Mean age of the population was 74.5 years (standard deviation 6.99); 55.4% were women. There was a bi-modal association between sodium excretion and mortality, with risk increasing only below sodium excretion of 6.25 g/d [hazard ratio (HR) 1.29, 95% confidence interval (CI) 1.20-1.38], confirmed in the adjusted model (HR 1.12, 95% CI 1.04-1.22). These results were confirmed in participants without cardiovascular diseases. After stratification for frailty phenotype, the association was stronger in frail participants (adjusted HR 1.23, 95% CI 1.02-1.50 vs HR 1.11, 95% CI 1.01-1.22 in robust participants). There was no association between 24-hour sodium excretion and 9-year incidence of cardiovascular diseases (adjusted risk ratio 0.96, 95% CI 0.90-1.02).
Conclusions: Reduced sodium excretion is associated with increased mortality in a sample of community-dwelling older people, especially among the frail participants. High levels of sodium excretion are not associated with adverse outcomes in this population; therefore, sodium restriction might not be beneficial in older people.

Excess dietary sodium intake is considered an important cause of hypertension,[1] and very recently an urinary sodium excretion >3.7 g/d has been associated with subclinical cardiovascular disease.[2] Several studies have shown a reduced risk of cardiovascular events in people with lower sodium intake,[3] and reducing sodium intake is recommended for cardiovascular prevention.[4] There is evidence, however, that a J-shaped or U-shaped relationship may exist between sodium intake and adverse outcomes, with risk increasing when sodium excretion is below ∼3 g/d or above ∼5 g/d.[5,6] The increased risk associated may be related to increased activity of renin-angiotensin-aldosterone system and sympathetic nerve activation.[7]

To our knowledge, only 1 study evaluated this association in an elderly population, finding no relationship between sodium intake and adverse outcomes.[8] In this study, sodium intake was evaluated

The authors declare no conflicts of interest.

* Address correspondence to Diana Lelli, MD, Area di Geriatria, Università Campus Bio-Medico di Roma, Via Alvaro del Portillo 200, Roma 00128, Italy.
E-mail address: d.lelli@unicampus.it (D. Lelli).

https://doi.org/10.1016/j.jamda.2017.09.004
1525-8610/

using a food frequency questionnaire rather than 24-hour urinary sodium excretion that is considered the most accurate method to estimate sodium intake.[9] Thus, the evidence on this issue in the elderly is still not clear. In this population, comorbidities, polypharmacotherapy, and frailty may act as an effect modifier, in the same way as it happens for hypertension, which does not seem to be associated with mortality in people with reduced gait speed.[10] The objective of our study was to evaluate the correlation between sodium intake (estimated using sodium urinary excretion), mortality, and cardiovascular events in an elderly population. The association was analyzed separately in people with and without frailty.

Methods

Data Source and Study Design

We analyzed data from the longitudinal InCHIANTI (Invecchiare in Chianti - Aging in the Chianti) study.[11] The baseline study was supported by the Italian Ministry of Health and also partly supported by the US National Institute on Aging. After obtaining informed consent, participants were randomly selected from the populations of 2 town areas; data collection started in September 1998 and was completed in March 2000. The eligible participants were interviewed at home by trained study researchers. The interview was followed by a physical examination at the study clinic as well as laboratory analysis. Follow-up visits were scheduled at 3, 6, and 9 years. The Italian National Institute of Research and Care on Aging Ethical Committee approved the study protocol.

Sample Selection

From 1170 participants with available 24-hour urinary sodium excretion data, we excluded participants younger than 65 years (N = 250). Follow-up data at 9 years were available for 920 participants. For the analysis on incident cardiovascular events, we selected participants without history of cardiovascular disease at baseline (N = 514).

Definition of Exposure and Outcome

Sodium intake was estimated using the 24-hour sodium urinary excretion. On the day of the study visit, participants were provided with a plastic bottle containing 1 g of boric acid as preservative, and instructed to collect all the urine produced in the following 24 hours, making the maximum effort to avoid dispersing urine during the collection period.

We considered mortality for all causes and incident cardiovascular events (angina pectoris, myocardial infarction, heart failure, and stroke) as outcome measures. Cardiovascular events were ascertained using a questionnaire and reviewing clinical documentation at the follow-up visits. Data on mortality were collected from mortality registers.

Analytic Approach

We reported the characteristics of the study sample using descriptive statistics (mean and standard deviation for continuous variables, proportion for categorical variables), according to quartiles of 24-hour urinary sodium excretion. We took into account associated diseases (eg, hypertension, diabetes), cigarette smoke (pack-years), blood pressure, total cholesterol, and estimated creatinine clearance [chronic kidney disease epidemiology collaboration (CKD-EPI)]. Total caloric intake, macronutrients and micronutrients intake, and alcohol intake were evaluated using the European Prospective Investigation into Cancer and Nutrition Questionnaire; a food frequency intake questionnaire validated in an Italian elderly population.[12,13] Finally, we took into account years of education and physical activity.

Mortality risk across quartiles of sodium excretion was calculated using the Kaplan-Meier method. We used Cox regressions to evaluate the relationship between sodium excretion and mortality. Both linear and polynomial (restricted cubic splines) models were fitted; the goodness of fit of these models was evaluated using the log-likelihood test; and the best fitting unadjusted model was then adjusted for potential confounders, selected on the base of the clinical significance, prior knowledge, and results of the univariate analysis. To explore the different role of demographic and clinical variables, we first adjusted for age and sex, and then for the other potential confounders [education, CKD-EPI, pack/y, hypertension, diabetes, body mass index (BMI), caloric intake/body weight, and antihypertensive drugs and diuretics]. Finally, we repeated the analysis in participants with and without frailty, defined according to the Fried frail phenotype as the presence of 3 or more of the following criteria: unintentional weight loss (10 lbs in past year), self-reported exhaustion, reduced grip strength, slow walking speed, and low physical activity.[14] Because cardiovascular diseases (angina pectoris, myocardial infarction, heart failure, and stroke) and hypertension may significantly influence the relationship between sodium excretion and mortality, we planned a

Table 1
General Characteristics of the Population Distributed by Quartiles of 24-Hour Sodium Excretion

	I Quartile (n = 230)	II Quartile (n = 230)	III Quartile (n = 230)	IV Quartile (n = 230)	*P*
Age, mean (SD), years	77.4 (7.6)	74.9 (6.9)	73.2 (6.4)	72.5 (6)	<.001
Female sex, No. (%)	156 (68)	136 (60)	125 (55)	88 (38)	<.001
Education, mean (SD), years	5.3 (3.6)	4.9 (2.9)	5.5 (3.4)	5.6 (3)	.094
Sedentary, No. (%)	170 (74)	149 (65)	132 (58)	120 (52)	<.001
BMI, mean (SD), kg/m^2	26.6 (4)	27.4 (4.4)	27.5 (3.9)	28.1 (3.6)	.002
CKD-EPI, mean (SD), mL/min/1.73 m^2	68.4 (15.6)	71.1 (14.2)	72.5 (12.8)	72.5 (13)	.005
Total cholesterol, mean (SD), mg/dL	215.6 (36.8)	217.5 (40.5)	218.4 (40)	218.8 (38.1)	.819
Systolic blood pressure, mean (SD), mmHg	155.6 (20.4)	148.9 (17.8)	148.6 (18.6)	149.5 (20.3)	<.001
Diastolic blood pressure, mean (SD), mmHg	85.6 (8.2)	83 (7.8)	83.9 (9)	83.7 (8.6)	.01
Smoke, mean (SD), pack/year	11.2 (21)	10.4 (19.5)	13.6 (21.8)	16 (22.3)	.021
Hypertension, No. (%)	145 (63)	149 (65)	133 (58)	141 (61)	.462
Diabetes, No. (%)	26 (11)	27 (12)	21 (9)	42 (18)	.021
Peripheral Arteriopathy, No. (%)	36 (16)	29 (13)	21 (9)	23 (10)	.128
COPD, No. (%)	19 (8)	17 (7)	14 (6)	21 (9)	.652
Metabolic syndrome, No. (%)	48 (21)	59 (26)	53 (23)	57 (25)	.635
Dementia, No. (%)	18 (8)	12 (5)	4 (2)	4 (2)	.002

COPD, chronic obstructive pulmonary disease.