Dietary Sodium Restriction Rapidly Improves Large Elastic Artery Compliance in Older Adults With Systolic Hypertension

Phillip E. Gates, Hirofumi Tanaka, William R. Hiatt, Douglas R. Seals

Abstract—We determined the temporal effects of dietary sodium restriction on large elastic artery compliance and systolic blood pressure (SBP) in 12 untreated, older (64 ± 2 years) men and women (6 each) with stage 1 systolic hypertension. After baseline measurements subjects were assigned to 4 weeks of low or normal sodium intake (randomized, crossover design). Urinary sodium excretion was reduced by 60% by the end of week 1 of sodium restriction (54 ± 11 mmol/d, \( P < 0.01 \)) versus baseline (135 ± 14). Compared with baseline (0.11 ± 0.01 mm/mm Hg), carotid artery compliance was increased by 27% (to 0.14 ± 0.02, \( P < 0.05 \)) at the end of week 1 of sodium restriction, attaining peak levels by week 2 (+46%, to 0.16 ± 0.02, \( P < 0.01 \)). Similarly, supine resting brachial artery SBP was reduced by >5 mm Hg by week 1 of sodium restriction, attaining peak reductions by week 2 (−12 mm Hg, \( P < 0.01 \) versus baseline). The 24-hour ambulatory SBP was ≈3 mm Hg lower at week 1 of sodium restriction and ≈6 mm Hg lower by week 2 (\( P < 0.01 \) versus baseline). The reductions in resting SBP from baseline to week 2 of sodium restriction were strongly related to the corresponding increases in carotid compliance (\( r = 0.80, P < 0.01 \)). Urinary sodium excretion, carotid artery compliance, and SBP were not different during normal sodium intake versus baseline. Other subject characteristics were not different across conditions. Sodium restriction rapidly improves large elastic artery compliance in older adults with stage 1 systolic hypertension. These improvements in central arterial compliance appear to be a key mechanism in the rapid normalization of SBP by sodium restriction in these patients. (Hypertension. 2004;44:35-41.)

Key Words: sodium, dietary ■ aging ■ renin ■ angiotensin

It is now recognized that systolic, not diastolic, hypertension represents the greatest blood pressure–related risk for cardiac and cerebrovascular diseases in adults older than 50 years.\(^1-3\) The primary mechanism contributing to the development of systolic hypertension with aging is believed to be a reduction in the compliance (increased stiffness) of the large elastic arteries in the central circulation (ie, aorta and carotid arteries).\(^4,5\) Accordingly, central arterial compliance has been identified as a key therapeutic target for the treatment of systolic hypertension in older adults.\(^4,6\)

In this context, aging is associated with an increased blood pressure sensitivity to dietary sodium intake,\(^7\) and reductions in salt intake decrease blood pressure, cardiovascular disease risk, and mortality.\(^8,9\) Taken together, we reasoned that dietary sodium restriction might reduce systolic blood pressure (SBP) in older adults by improving large elastic artery compliance. Consistent with this, recently\(^10\) we demonstrated that dietary sodium restriction markedly lowers SBP in postmenopausal women with high-normal SBP or stage 1 systolic hypertension. Indirect measures of arterial stiffness suggested that the reduction in SBP may have been mediated, in part, by corresponding increases in arterial compliance.

In the present follow-up investigation we used a double-blind, placebo-controlled, crossover study design to determine the effects of dietary sodium restriction on directly measured carotid artery compliance (combined high-resolution ultrasonography andplanation tonometry) in middle-aged and older men and women with stage 1 systolic hypertension. Subjects underwent dietary sodium restriction and sodium intake was manipulated by consumption of placebo or sodium chloride tablets. The target dietary sodium intake was ≈60 mmol/d, considered to be a low sodium intake by the Dietary Approaches to Stop Hypertension (DASH) Sodium Collaborative Research Group.\(^11\) To establish the temporal pattern of the changes in central arterial compliance and SBP, carotid artery compliance and BP were determined weekly during 4-week periods of reduced and normal sodium intake.

Methods

Subjects
Men and women older than 50 years participated in the study if they met the following inclusion criteria: stage 1 hypertension\(^12\); not using...
anthypertensive medications; no overt signs of disease on physical examination and medical history; normal blood chemistry; negative ECG-monitored exercise test; ankle–brachial index \( \leq 0.9 \); absence of plaque on ultrasound interrogation of the carotid and femoral arteries; nonsmoker for previous 2 years; body mass index \(<35\); not consuming a low-sodium diet; and postmenopausal if female (amenorrheic for at least 2 years). Procedures for screening subjects have been described previously.\textsuperscript{13-17} Seventy-one subjects responded to recruitment efforts, and 12 successfully completed screening (6 men and 6 women). All 12 subjects completed the intervention, and all were white. The human research committee of the University of Colorado at Boulder approved the study and all procedures, and volunteers gave their written informed consent before participation.

**Experimental Design**

We used a double-blind, placebo-controlled, randomized, crossover experimental design that had previously been shown to reduce BP in older normotensive and hypertensive subjects.\textsuperscript{18} Measurements were taken at baseline and then at each week of an 8-week dietary sodium intervention period. During the intervention period, subjects reduced dietary sodium intake and were asked to take a prescribed number of tablets with each meal. For 4 of the weeks, the tablet was placebo, and for the other 4 weeks the tablet was slow-release sodium chloride (HK Pharma, Hertfordshire, UK). The order of tablet administration was randomized. The number of tablets taken (10 mmol [0.23 g] sodium per tablet) was intended to return subjects to baseline sodium intake and was based on a once-weekly 24-hour urinary sodium excretion analysis in comparison to the average of 2 samples collected at baseline. Primary investigators and subjects were unaware of the order of tablet administration. Data are presented as baseline, low sodium condition (low), and normal sodium condition (normal). All procedures were conducted at the University of Colorado at Boulder General Clinical Research Center (GCRC), Blood/urine chemistries were measured using standard procedures at the Core Laboratory of the University of Colorado Health Sciences Center GCRC in Denver.

**Large Elastic Artery Compliance**

Carotid artery compliance and \( \beta \)-stiffness index were determined using high-resolution B-mode ultrasound and simultaneous estimates of carotid BP using planimetry, as described in detail previously.\textsuperscript{19} The carotid blood pressure waveform was calibrated using diastolic blood pressure (DBP) and mean brachial BP.\textsuperscript{20} Images were analyzed using automated analysis software (Medical Imaging Applications).

**Casual BP Measurements**

Resting casual brachial artery BP measurements were made after an overnight fast in the upright seated and supine positions, as described previously.\textsuperscript{10} Measurements were made during 3 weekly visits at baseline and once each week during the intervention period. An experienced GCRC research nurse made measurements using the same equipment and cuff on all subjects.

**Ambulatory BP Measurements**

BP recordings were made during normal daily activity in 11 subjects for 24 hours (Model 90217-1A; Spacelabs) as described in detail previously.\textsuperscript{10}

**Dietary Analysis**

Subjects were instructed how to keep 3-day dietary records by the GCRC bionutritionist. Records were analyzed using Food Processor software (ESHA Research) at baseline and at the end of each condition of the intervention.

**Dietary Sodium Restriction**

After screening and baseline measurements, subjects were given comprehensive dietary education and counseling by the GCRC bionutritionist to reduce dietary sodium intake without changing caloric intake or dietary composition. After initial education and counseling subjects met with the GCRC bionutritionist once per week throughout the intervention period.

**Data Analysis and Statistics**

All data were analyzed using SPSS v11. A 2-way within-subjects ANOVA was conducted to evaluate the effect of condition (low and normal) and time (weeks 1 to 4) on arterial compliance and casual resting BP. The condition \( \times \) time main effect was tested using Wilks \( \lambda \). Where a significant main effect was found, paired-samples \( t \) tests were conducted to determine differences between specific baseline and intervention weeks. Bivariate relations were determined using Pearson correlation coefficients. To determine whether the changes in carotid artery compliance and \( \beta \)-stiffness index at week 2 of the low sodium condition were independent of the change in mean arterial pressure, separate bivariate linear regression analyses were performed with mean carotid pressure entered as the predictor variable. Statistical significance was set at \( P < 0.05 \) for all analyses.

**Results**

**Subject Characteristics**

The mean age of the men and women was 63 ± 1 and 64 ± 4 years, respectively. Metabolic profile, body mass, and body composition did not change from baseline during the dietary sodium restriction intervention (Table 1). There were no sex (gender)-related differences in these responses to the intervention conditions or in any of the responses described.

**Dietary Sodium Restriction**

At baseline, mean dietary sodium intake was 135 mmol/d, higher than the 100 mmol/d intake currently recommended for the adult population,\textsuperscript{20} but slightly lower than the average intake in the United States (148 mmol/d).\textsuperscript{21} Dietary sodium intake was reduced to 57 mmol/d during the intervention period, without any changes in dietary macronutrient or potassium intake (Table 2). Urinary sodium excretion was lower (\( P < 0.05 \)) during each week of the low sodium condition compared with baseline and any week of normal sodium intake.

### Table 1. Body Stature, Mass, and Composition and Metabolic Profile of the Subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Low Sodium</th>
<th>Normal Sodium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height, cm</td>
<td>170 ± 3</td>
<td>170 ± 3</td>
<td>170 ± 3</td>
</tr>
<tr>
<td>Body mass, kg</td>
<td>72.8 ± 3</td>
<td>71.8 ± 4</td>
<td>72.0 ± 3</td>
</tr>
<tr>
<td>Body fat, %</td>
<td>30.6 ± 2</td>
<td>30.6 ± 2</td>
<td>30.8 ± 2</td>
</tr>
<tr>
<td>Fat-free mass, kg</td>
<td>50.8 ± 3</td>
<td>50.1 ± 3</td>
<td>50.1 ± 3</td>
</tr>
<tr>
<td>Body surface area, m²</td>
<td>1.84 ± 0.06</td>
<td>1.83 ± 0.06</td>
<td>1.83 ± 0.06</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>25.1 ± 1</td>
<td>24.7 ± 1</td>
<td>24.7 ± 1</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>5.10 ± 0.4</td>
<td>5.09 ± 0.3</td>
<td>4.96 ± 0.4</td>
</tr>
<tr>
<td>HDL, mmol/L</td>
<td>1.48 ± 0.3</td>
<td>1.39 ± 0.2</td>
<td>1.44 ± 0.3</td>
</tr>
<tr>
<td>LDL, mmol/L</td>
<td>3.06 ± 0.3</td>
<td>3.10 ± 0.4</td>
<td>2.89 ± 0.3</td>
</tr>
<tr>
<td>VLDL, mmol/L</td>
<td>0.61 ± 0.2</td>
<td>0.58 ± 0.2</td>
<td>0.63 ± 0.2</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>1.32 ± 0.5</td>
<td>1.27 ± 0.3</td>
<td>1.36 ± 0.5</td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
<td>5.08 ± 0.3</td>
<td>5.00 ± 0.2</td>
<td>5.12 ± 0.4</td>
</tr>
<tr>
<td>Insulin, pmol/L</td>
<td>55 ± 15</td>
<td>42 ± 7</td>
<td>53 ± 15</td>
</tr>
</tbody>
</table>

Data are mean ± SE.
Thus, the slow-release sodium tablets were effective in supplementing dietary sodium during each week of the normal condition, maintaining urinary sodium excretion at levels not different from baseline.

Plasma renin activity was increased \( (P<0.05) \) in the low sodium condition compared with baseline and the normal sodium condition. However, dietary sodium restriction had no effect on other vasoactive substances (Table 3).

### Carotid Artery Compliance and Stiffness

Compared with baseline, carotid artery compliance was increased \( (P<0.05) \) by the end of the first week of low sodium \(+27\%)\, reached its highest value in week 2 \(+46\%, \ P<0.01\), and remained elevated during weeks 3 and 4 (Figure 2). The changes in carotid \( \beta \)-stiffness index inversely mirrored these changes in carotid artery compliance (Figure 2). During the normal sodium condition, carotid artery compliance and \( \beta \)-stiffness index were lower and higher, respectively, than during the low sodium condition and not different from baseline. Augmentation index, carotid systolic pressure, and carotid and brachial pulse pressures were reduced in the low sodium condition compared with baseline and the normal condition (Table 4). Resting heart rate was not different among conditions (Table 4).

### Casual Resting BP

The BP responses were similar for the random zero sphygmomanometry and semiautomated BP measurements; therefore, only the former values are presented (Figure 3). Mean baseline SBP/DBP was 148/84 mm Hg. Compared with baseline, supine SBP was reduced by \(+5 \text{ mm Hg} \) by the end of the first week of the low-sodium condition, attaining its nadir \(+12 \text{ mm Hg} \, P<0.01 \) by the end of week 2. Supine

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**TABLE 2. Subject Diet Composition**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Low Sodium</th>
<th>Normal Sodium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total kilojoules per day</td>
<td>9433±724</td>
<td>8402±703</td>
<td>8511±507</td>
</tr>
<tr>
<td>Carbohydrates, g/d</td>
<td>298±28</td>
<td>252±15</td>
<td>266±24</td>
</tr>
<tr>
<td>Protein, g/d</td>
<td>90±8</td>
<td>85±11</td>
<td>84±8</td>
</tr>
<tr>
<td>Fat, g/d</td>
<td>77±9</td>
<td>85±11</td>
<td>72±8</td>
</tr>
<tr>
<td>Calcium, mmol</td>
<td>45±8</td>
<td>32±5</td>
<td>32±5</td>
</tr>
<tr>
<td>Magnesium, mmol</td>
<td>21±4</td>
<td>21±4</td>
<td>29±8</td>
</tr>
<tr>
<td>Potassium, mmol</td>
<td>72±8</td>
<td>69±8</td>
<td>77±10</td>
</tr>
<tr>
<td>Sodium,* mmol</td>
<td>135±18</td>
<td>52±4†</td>
<td>57±1†</td>
</tr>
</tbody>
</table>

Dietary sodium does not include sodium chloride tablets given in the low sodium condition.

Data are mean±SE.

*Main effect of condition.

†\( P<0.01 \) vs baseline.

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**TABLE 3. Circulating Vasoactive Hormone Concentrations**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Low Sodium</th>
<th>Normal Sodium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma renin activity,*</td>
<td>0.49±0.06</td>
<td>0.70±0.08†‡</td>
<td>0.44±0.06</td>
</tr>
<tr>
<td>Angiotensin II, pg/mL</td>
<td>3.9±0.4</td>
<td>4.9±0.6</td>
<td>4.2±0.4</td>
</tr>
<tr>
<td>Arginine vasopressin, pg/mL</td>
<td>0.90±0.18</td>
<td>0.67±0.08</td>
<td>0.68±0.08</td>
</tr>
<tr>
<td>Atrial natriuretic peptide, pg/mL</td>
<td>80±12</td>
<td>68±10</td>
<td>73±7</td>
</tr>
<tr>
<td>Norepinephrine, pg/mL</td>
<td>316±38</td>
<td>290±23</td>
<td>297±31</td>
</tr>
<tr>
<td>Epinephrine, pg/mL</td>
<td>24±2</td>
<td>30±5</td>
<td>26±4</td>
</tr>
<tr>
<td>Endothelin-1, pg/mL</td>
<td>7.1±0.5</td>
<td>6.5±0.4</td>
<td>6.9±0.7</td>
</tr>
</tbody>
</table>

Data are mean±SE.

*Main effect of condition.

†\( P<0.05 \) vs baseline; ‡\( P=0.01 \) vs normal.

---

**Figure 1.** The 24-hour urinary sodium excretion at baseline (Base) in each of 4 weeks of the low sodium condition (L1–L4) and during the 4 weeks of the normal sodium condition (N1–N4). *Lower than baseline \( (P<0.05) \). †Lower than any given normal week \( (P<0.05) \).

**Figure 2.** Carotid artery compliance and \( \beta \)-stiffness index at baseline (Base) in each of 4 weeks of the low sodium condition (L1–L4) and during the 4 weeks of the normal sodium condition (N1–N4). *Lower than baseline \( (P<0.05) \). †Lower than any given normal week \( (P<0.05) \).
DBP was reduced by 3 to 6 mm Hg below baseline during the low sodium condition (P < 0.05). During the normal sodium condition, supine SBP and DBP were higher than during the low sodium condition and not different compared with baseline. The seated SBP and DBP responses to the intervention were qualitatively similar to those observed for supine BP (data not shown).

**Ambulatory BP**

Compared with baseline, 24-hour SBP was slightly lower (−3 mm Hg, NS) by the end of the first week of the low sodium condition, reached its nadir by week 2 (−6 mm Hg, P < 0.01), and remained lower during weeks 3 and 4 (Figure 4). Daytime and nighttime SBP also reached their nadir by week 2 of the low sodium condition (−6 and −7 mm Hg, respectively; Figure 4). The 24-hour DBP decreased (P < 0.05) below baseline values throughout the low sodium condition as a result of nonsignificant decreases in daytime and nighttime levels. During the normal sodium condition, 24-hour SBP and DBP were higher than during the low sodium condition and not different compared with baseline.

**Relations Between Changes in Carotid Artery Compliance and β-Stiffness Index and Changes in Resting SBP and Mean BP in Response to Dietary Sodium Restriction**

In the 11 subjects who responded to dietary sodium restriction by week 2, the reductions in casual supine SBP from baseline were strongly related to the corresponding increase in carotid artery compliance (r = −0.80, P < 0.01) and reduction in β-stiffness index (r = 0.62, P < 0.05; Figure 5). Bivariate regression analysis also indicated that the change in carotid mean arterial pressure predicted the change in carotid artery compliance (R² = 0.58; P < 0.01), but not the change in β-stiffness index (R² = 0.06; P = 0.47).

**Discussion**

The present study is the first to demonstrate that moderate dietary sodium restriction increases directly measured large elastic artery compliance in humans with systolic hypertension. Our results are also the first to show that these

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**Table 4. Hemodynamic Data**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Condition</th>
<th>Baseline</th>
<th>Low Sodium</th>
<th>Normal Sodium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, bpm</td>
<td></td>
<td>61 ± 3</td>
<td>60 ± 3</td>
<td>60 ± 3</td>
</tr>
<tr>
<td>Augmentation index,* %</td>
<td></td>
<td>40 ± 2</td>
<td>29 ± 2†‡</td>
<td>37 ± 2</td>
</tr>
<tr>
<td>Carotid artery systolic pressure,* mm Hg</td>
<td></td>
<td>134 ± 5</td>
<td>119 ± 5†‡</td>
<td>127 ± 4‡§</td>
</tr>
<tr>
<td>Carotid artery pulse pressure,* mm Hg</td>
<td></td>
<td>50 ± 6</td>
<td>40 ± 6†‡</td>
<td>46 ± 5</td>
</tr>
<tr>
<td>Brachial artery pulse pressure,* mm Hg</td>
<td></td>
<td>66 ± 3</td>
<td>58 ± 4†‡</td>
<td>62 ± 3§</td>
</tr>
</tbody>
</table>

Data are mean ± SE.

*Main effect of condition.
†P < 0.05, baseline vs low; ‡P < 0.05, normal vs low; §P < 0.05 baseline vs normal.
improvements in compliance occur rapidly. Indeed, an increase in compliance is observed by the end of the first week of reduced sodium intake and reaches peak values after only 2 weeks of sodium restriction. Our findings also establish that these rapid improvements in central arterial compliance with dietary sodium restriction are strongly related to corresponding reductions in SBP. Taken together, our results support the idea that increased large elastic artery compliance in the central circulation may be an important mechanism in the rapid normalization of SBP in response to dietary sodium restriction in middle-aged and older adults with untreated stage 1 systolic hypertension.

**Dietary Sodium Restriction and SBP in Older Adults**

The DASH trial recently demonstrated the efficacy of dietary sodium restriction for reducing SBP in some normotensive and hypertensive individuals across the adult age range. The greatest reductions in SBP occurred in subjects who reduced dietary sodium intake from a moderate to a low level compared with subjects who reduced sodium intake from a high to a moderate level. This is consistent with the present results and previous studies from our laboratory in which subjects demonstrated baseline dietary sodium intake comparable to the DASH moderate level and reduced dietary sodium to a low level.

The present findings complement our recent observations in postmenopausal women by demonstrating that dietary sodium restriction produces mean reductions in supine resting SBP in middle-aged and older men and women with stage 1 systolic hypertension to high normal levels, while also reducing DBP. Importantly, peak reductions occur within 2 weeks of initiating sodium restriction. We established that significant reductions in SBP and DBP occur under these conditions using both casual (resting) and 24-hour ambulatory recordings. The 24-hour recordings revealed that similar absolute reductions in SBP occurred during the daytime and nighttime hours. We were also able to show that the BP-lowering effects of dietary sodium restriction were independent of other changes in diet composition, metabolic risk profile, and body mass and composition. Thus, these findings establish a rapid and robust primary SBP-lowering effect of dietary sodium restriction in older hypertensive men and women.

**Dietary Sodium Restriction, Large Elastic Artery Compliance, and SBP**

We recently reported that moderate dietary sodium restriction lowers aortic pulse wave velocity and augmentation index, indirect measures of arterial compliance, in postmenopausal women with elevated baseline SBP. The present findings confirm (eg, reductions in augmentation index) and extend these original observations in at least 3 important ways. First, we demonstrate for the first time to our knowledge that directly measured large elastic artery compliance is increased by dietary sodium restriction in middle-aged and older men and women with stage 1 systolic hypertension. Second, we have established that this novel adaptation occurs within the first week of reduced sodium intake and appears to be fully developed by the end of week 2 of sodium restriction. Carotid artery compliance increased by almost 50% above baseline values within this brief period. Third, we found that these rapid, marked reductions in resting SBP after 2 weeks of sodium restriction were strongly related to the corresponding improvements in large elastic artery compliance, suggesting that the latter may be a key mechanism mediating the SBP-lowering effects of dietary sodium restriction. To further test this assertion, we attempted to determine arterial stiffness independently of blood pressure, because arterial compliance is improved by a reduction in mean arterial pressure. The β-stiffness index is, in theory, a pressure-independent expression of carotid artery distensibility. Regression analysis revealed that some of the change in compliance was predicted by the change in central mean arterial pressure alone, but the reduction in carotid β-stiffness index was not. Taken together, these findings support the concept that sodium restriction exerts a primary effect on arterial compliance that contributes to corresponding reductions in SBP.

The rapid improvement in large elastic artery compliance in response to sodium restriction suggests that the mechanisms underlying salt-sensitive hypertension in this population are labile. Structural changes involving extracellular matrix proteins in the arterial wall are believed to play a major role in the reductions in central arterial compliance and consequent increases in SBP with human aging. Given that
a reversal of such changes would take considerable time (months or, perhaps, years), it is unlikely that structural adaptations contributed significantly to the improvements in carotid artery compliance observed over the initial 2 weeks of dietary sodium restriction. A more likely explanation is that the favorable changes in carotid compliance were mediated by a mechanism that tonically modulates vascular smooth muscle cell tone. Candidates would include reduced sympathetically mediated nerve activity/salpha-adrenergic stimulation, reduced oxidative stress/increased nitric oxide bioavailability, and reduced local vascular endothelin 1 and/or renin-angiotensin system bioactivity, all of which have been implicated in vascular changes associated with salt-sensitive hypertension. We did not observe any changes in circulating angiotensin II, vasopressin, atrial natriuretic factor, catecholamines, or endothelin 1 in response to sodium restriction in the present study. However, this does not rule out the possibility that sodium restriction produced effects at the local vascular level in 1 or more of these modulating influences. There is experimental evidence linking sodium restriction to reduced oxidative stress and increased nitric oxide bioavailability, although we have no data concerning these possible mechanisms in the present study.

A putative mechanism for an increase in smooth muscle cell tone in a salt-loaded state involves the endogenous ligand of the alpha-1 sodium pump, marinobufagin. In the Dahl salt-sensitive rat model, salt loading resulted in an increase in an ouabain-like compound that was followed by an increase in levels of marinobufagin. In this proposed mechanism, high levels of marinobufagin inhibit vascular Na,K-ATPase, resulting in an increase in intracellular sodium. High levels of intracellular sodium increase intracellular calcium because of reduced sodium-calcium exchange, ultimately leading to greater smooth muscle cell tone. If our subjects were in a relatively salt-loaded state at baseline (daily dietary sodium intake was six times that considered to be an optimal minimum), sodium depletion may have reduced the influence of marinobufagin on Na,K-ATPase, with consequent reductions in vascular smooth muscle cell tone and increases in arterial compliance. Presumably, this would also affect the smooth muscle cells surrounding resistance arterioles, explaining the reduction in diastolic blood pressure via a decrease in systemic vascular resistance.

Conclusions
The results of the present study support the concept that the rapid normalization of SBP in response to dietary sodium restriction in middle-aged and older adults with untreated stage 1 systolic hypertension may be mediated by an increase in the compliance of the large elastic arteries in the central circulation.

Perspectives
Systolic hypertension is a major contributor to the risk of coronary and cerebrovascular diseases in middle-aged and older adults. Reductions in the compliance (ie, increased stiffening) of the large elastic arteries in the cardiothoracic circulation are believed to be the primary mechanism responsible for the development of systolic hypertension with aging in humans. The results of the present investigation and our recent study together establish the efficacy of moderate dietary sodium restriction for producing rapid and marked reductions in SBP in middle-aged and older men and women with untreated systolic hypertension. Importantly, the findings of the present study demonstrate that this robust SBP-lowering effect of sodium restriction is temporally related to a rapid increase in central arterial compliance. Although this association does not prove cause and effect per se, the present observations provide additional evidence supporting the possibility that sodium restriction may exert its favorable effects on SBP in middle-aged and older hypertensive adults, at least in part, by improving the distensibility of the large elastic arteries.

Acknowledgments
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References


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