Are Low Intakes of Calcium and Potassium Important Causes of Cardiovascular Disease?

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Inadequate levels of calcium and potassium intake have long been associated with higher blood pressures. Epidemiologic data have suggested these associations and many clinical trials have indicated causal relationships. However, the intervention data are plagued with inconsistent study designs, populations, and results, and there remain many questions regarding dietary recommendations of these nutrients for cardiovascular health. Until recently, nutrition research focused on single-nutrient interventions, generally with disparate results. Recognizing that nutrients are not consumed individually but as combined constituents of a varied diet, efforts in this area have shifted to the role of the overall diet, or dietary patterns, in blood pressure and cardiovascular disease. The suggestions of epidemiologic surveys nearly two decades ago that the total diet has a greater influence on cardiovascular health than do specific components, are now being borne out by randomized controlled trials demonstrating this effect.

Hypertension, which affects approximately 50 million Americans, is a primary risk factor for cardiovascular disease, as well as for stroke and end-stage renal disease. Inadequate levels of dietary calcium and dietary potassium have been implicated in the development of hypertension for several decades. Observational studies have repeatedly suggested inverse relationships between each of these minerals and blood pressure; clinical trials have generally supported these relationships but have also produced conflicting and even contradictory results. In light of the major role of hypertension in cardiovascular disease and the potentially beneficial effects of calcium and potassium on blood pressure, these two minerals have been subjects of extensive investigation in the area of nutrition and cardiovascular research for > 20 years.

Calcium Epidemiology

A relationship between dietary calcium and blood pressure was reported by McCarron et al in the early 1980s. These investigators assessed nutrient intake in persons with and without hypertension, and observed that those with hypertension had significantly lower dietary calcium intakes than those who did not. Based on dietary recall data, of the nutrients measured (including sodium and potassium), calcium was the only nutrient that differed significantly in intake between the two groups. To further examine these results, these investigators conducted a similar analysis of the first National Health and Nutrition Examination Survey (NHANES I) comprising dietary data from > 10,000 individuals. A total of 17 nutrients were included in this analysis and, again, low calcium intake was the most consistent factor in the diet composition of persons with high blood pressure. Figure 1 depicts the negative correlation ($r = −0.604$) between calcium intake and mean systolic blood pressure for the total cohort.

These initial studies have been followed by numerous others reporting the inverse relationship between dietary calcium intake and blood pressure status. A meta-analysis of 23 of these studies, published between 1983 and 1993, was conducted by Cappuccio et al; that analysis was...
recently revised by Birkett.8 Whereas the meta-analysis by Cappuccio et al reported a modest inverse association between dietary calcium and arterial pressure, appropriate corrections to the analysis by Birkett revealed that the estimated effect was markedly greater than earlier reported. The Birkett meta-analysis revealed that systolic blood pressure was lowered by approximately \(20.4\) (95% confidence interval [CI] \(20.5\) to \(20.3\)) mm Hg per 100 mg of calcium, and diastolic pressure by an estimated \(20.4\) (95% CI \(20.7\) to \(20.02\)) mm Hg per 100 mg calcium.

**Intervention Studies**

Numerous clinical trials—which are necessary to establish causal relationships that observational studies can only suggest—have examined the effect of increased calcium intake on blood pressure regulation, with most showing at least a minimal effect.3,9–11 However, as with all dietary intervention trials, this effect has not been demonstrated in all studies, with some producing no effect and others a negative effect. In a meta-analysis of the 33 appropriately designed, randomized, controlled clinical trials (n = 2412) published before mid-1994, Bucher et al10 reported that increased calcium intake resulted in average blood pressure reductions of 1.3 mm Hg systolic and 0.2 mm Hg diastolic in the general population, and 4.3 mm Hg and 1.5 mm Hg in hypertensive persons. A recent update of that meta-analysis included 42 studies (n = 4560), and again identified a beneficial effect of calcium on blood pressure.11 In addition, this latter analysis demonstrated a greater blood pressure-lowering effect when the increased calcium was derived from foods, primarily dairy products, rather than from supplements (ie, tablets).

**Potassium Epidemiology**

An inverse relationship between potassium intake and blood pressure has been suggested by the results of several epidemiologic studies. In their report published in 1979, Walker et al12 observed that urinary potassium concentrations were lower in persons with hypertension compared with those with normal blood pressures. Because sodium and creatinine concentrations were similar between the two groups, these researchers concluded that the intakes of sodium or water did not account for the differences in urinary potassium, and they were among the first to suggest the possibility of a pathogenetic role of potassium on high blood pressure.

This report was followed by many other observational surveys providing further evidence of the connection between potassium intake and blood pressure. A study of electrolyte excretion and blood pressure in young African American and white women identified the inverse relationship, as well as a positive correlation between the sodium–potassium ratio and blood pressure.13 In their population-based study assessing potassium intake and blood pressure, Khaw and Barrett-Connor14 observed negative correlations between dietary potassium and blood pressure in adult men and women. In a later study, these investigators also reported an inverse association between dietary potassium intake and stroke-associated mortality.15 As shown in Fig. 2, they found that the relative risk of stroke was significantly less at higher potassium intake levels compared with the lowest intake levels; multivariate analysis suggested that a 10-mmol increase in dietary potassium was associated with a 40% lower stroke-associated mortality risk.

Large-scale population surveys have reported similar findings. In the 52-center Intersalt Study, which comprised more than 10,000 participants throughout the world, uri-
nary potassium excretion, urinary sodium excretion, and the sodium–potassium ratio were each found to be independently related to blood pressure. More recently, both the Nurses’ Health Study and the Scottish Heart Health Study demonstrated the inverse association between potassium and blood pressure within their study populations of 41,541 and 11,629 respectively.

**Intervention Studies**

As noted above regarding calcium, observational studies are limited to identifying associations between factors, whereas clinical trials are required to determine actual cause and effect. The potassium–blood pressure relationship has been addressed in a multitude of intervention studies of varying sizes, designs, and results. To reconcile these variations and to obtain more precise estimates of the effects of intervention, Whelton et al conducted a meta-analysis of the 33 randomized controlled clinical trials that met their carefully defined criteria for analysis. With potassium supplementation (median 75 mmol/day), mean (95% CI) blood pressure reductions were $-2.3 \, (2.1 \text{ to } -4.3)$ mm Hg systolic and $-2.0 \, (0.5 \text{ to } -3.4)$ mm Hg diastolic. Notably, treatment effects appeared to be greater at higher sodium intakes.

**Inconsistent Findings**

As described above, focused studies of the relationships between blood pressure and calcium and potassium have been conducted for more than two decades; yet, we still do not have full consensus regarding the actual effects and benefits of these electrolytes on cardiovascular health. Whereas inadequate intakes of potassium and calcium have been clearly associated with increased hypertension risk in population studies, the results of clinical trials have produced both inconsistent results and conflicting interpretations of those results.

**Contributing Factors**

The discrepancies in the results of the studies, the heterogeneity of response commonly observed in clinical trials assessing electrolytes, as well as the subsequent lack of consensus regarding the blood pressure effects of these nutrients, have a number of possible, related explanations. It is likely that the blood pressure effects of single nutrients are small and thus require large-scale trials for their detection. In contrast, the results of epidemiologic surveys and clinical trials that include modifications of more than one nutrient may reflect larger, more easily detected additive effects. Intercorrelations between nutrients may also play a major role in the inconsistency of results in all studies in which intake levels of one or more nutrients are manipulated. Additional confounding factors in dietary studies include the degree that baseline intake of the nutrient under study may influence individual blood pressure responses, and the likely possibility that supplemented nutrients used in many studies may not have the same effect on blood pressure as those present in food sources.

**Multicollinearity**

Each of these explanations likely contributes, in part, to the unresolved questions regarding the role of specific nutrients in blood pressure regulation. Paramount among these, however, is the high degree of intercorrelation among dietary factors. As emphasized by Reed et al in their analyses of the Honolulu Heart Study, identifying the individual and conjoined actions of dietary nutrients is complicated by multicollinearity, making it inherently difficult to isolate clearly the effects of one nutrient from those consumed concurrently. Examples of this include the 1989 report from the Nurses’ Health Study in which Witteman et al observed that dietary calcium and magnesium had strong, independent inverse associations with hypertension, and that adjusting for their intakes elimi-
nated the observed crude inverse association of dietary potassium and fiber with hypertension risk. Also, from the Health Professionals Follow-up Study, it was reported that nutrient effects on blood pressure that were observed when assessed individually were obliterated when the nutrients were considered together.24

The suggestion that it is the adequate intake of multiple nutrients—rather than the intake of any single nutrient—that influences optimal blood pressure regulation exists throughout the nutrition literature. Based on the results of our 1984 analysis of dietary components and hypertension from the NHANES database,6 we concluded that nutritional emphasis should be placed on “consumption of a diet balanced in all the essential nutrients.” Reed et al22 concluded, in their article on diet and multicollinearity, that “If recommendations are to be made concerning nutritional prevention of hypertension, these data suggest that the focus be on a mixture of nutrients rather than on a specific item.” These and numerous other epidemiologic and clinical study reports of interrelationships between nutrients served as the catalysts for the redirection that has recently taken place in nutrition research, from assessing individual nutrient effects to the current approach of examining the effects of the total diet.

Accepting the hypothesis that micronutrients express their physiologic actions through integrated pathways, it is unrealistic to expect a uniform benefit in terms of blood pressure control by altering the intake of a single nutrient. Considering that nutrients are not ingested in isolation, but as combined constituents of a total diet, it is not surprising that manipulations of a single nutrient would produce inconsistent results. We now recognize that nutrients function interactively in the body and in their impact on blood pressure regulation. The recent redirection of investigative efforts on total diet influences on blood pressure may well provide the answers needed to reach the long-sought consensus on dietary recommendations for cardiovascular health.25,26

### Dietary Patterns

#### Blood Pressure

The NHLBI-sponsored Dietary Approaches to Stop Hypertension Study (DASH) was designed in the early 1990s to assess the effects of the total diet, or dietary patterns, on blood pressure.20 Acknowledging the complexities inherent in single-nutrient interventions and the myriad of conflicting results that they produced, DASH was a large multicenter, randomized, controlled feeding study that compared three dietary patterns in persons with high-normal and mildly elevated blood pressure. After 3 weeks on a control diet, considered a typical Western diet—low in fruits, vegetables, and dairy products, and high in fat—participants were randomly assigned to one of the following: 1) the control diet; 2) a diet rich in fruits and vegetables (eight to 10 servings/day); or 3) a combination diet rich in fruits and vegetables (10 servings/day) and low-fat dairy products (three servings/day) (Table 1). Sodium intake and body weight were maintained at constant levels in all three diets.

As shown in Table 2, both the fruits-and-vegetables diet and the combination diet significantly reduced both systolic and diastolic blood pressures compared with the control diet.27 With the combination diet, systolic pressure was reduced by 5.5 mm Hg more and diastolic pressure by 3.0 mm Hg more than with the control diet. Blood pressure reductions with the fruits-and-vegetables diet compared with the control diet were also highly significant, but were only about half (2.8 mm Hg systolic and 1.1 mm Hg diastolic) of those achieved with the combination diet. The reductions with both intervention diets were observed within the first 2 weeks of study and were sustained for the remaining 6 weeks of the intervention.

Falkner et al28 recently assessed the effects of dietary micronutrients on blood pressure in 180 African American and Hispanic adolescents at high risk for hypertension. Using folic acid intake as an index of fruit, vegetable, and

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### Table 1. DASH study calcium and potassium intake targets and average daily servings of their primary food sources*

<table>
<thead>
<tr>
<th>Item</th>
<th>Control Diet</th>
<th>Fruits-and-Vegetables Diet</th>
<th>Combination Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nutrient Target</td>
<td>Nutrient Target</td>
<td>Nutrient Target</td>
<td>Nutrient Target</td>
</tr>
<tr>
<td>Calcium (mg/day)</td>
<td>450</td>
<td>450</td>
<td>1240</td>
</tr>
<tr>
<td>Potassium (mg/day)</td>
<td>1700</td>
<td>4700</td>
<td>4700</td>
</tr>
<tr>
<td>Fruits and juices</td>
<td>1.6</td>
<td>5.2</td>
<td>5.2</td>
</tr>
<tr>
<td>Vegetables</td>
<td>2.0</td>
<td>3.3</td>
<td>4.4</td>
</tr>
<tr>
<td>Grains</td>
<td>8.2</td>
<td>6.9</td>
<td>7.5</td>
</tr>
<tr>
<td>Low-fat dairy</td>
<td>0.1</td>
<td>0.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Regular-fat dairy</td>
<td>0.4</td>
<td>0.3</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Dash—Dietary Approaches to Stop Hypertension.

* Values are for diets designed to provide an energy level of 2100 kcal. Based on Ref. 27.
whole grain intake, they observed that diastolic blood pressures were significantly lower in the high folate group compared with the low folate group. In male participants, diastolic blood pressures in the high and low folate groups, respectively, were 67 versus 72 mm Hg, and in female participants 73 versus 76 mm Hg. Sodium intake and body mass index were not different between groups, whereas the low folate group had significantly lower intakes of potassium, calcium, magnesium, beta-carotene, cholecalciferol, vitamin E, and all B vitamins. The investigators concluded that higher intakes of a combination of nutrients derived from fruits, vegetables, and low-fat dairy products can contribute to early primary prevention of hypertension.

**Cardiovascular Disease**

Dietary patterns have been implicated in disease in the past. Low coronary heart disease rates and long life expectancies in Greece and surrounding areas focused attention in the 1980s on the “Mediterranean Diet.” The cardioprotective effects of the dietary pattern common in this part of the world were believed to be conferred by the total fat content, which is low in saturated fats and high in monounsaturated fats. However, when the clinical trials assessing the role of specific fats on cardiovascular health produced inconsistent results, it was recognized that other dietary components of the Mediterranean diet were likely also contributing to its beneficial cardiovascular effects, and the total dietary content then became the focus of subsequent investigations of the benefits of this diet. It is now generally agreed that it is the multiple nutrients consumed together in the Mediterranean diet that accord its protective effects.

A number of prospective studies have indicated a role of multiple dietary components in the development of cardiovascular disease. Most recently, dietary patterns were examined in two studies with regard to all-cause and cause-specific mortality in women and the risk of coronary heart disease in men. Kant et al assessed the association of mortality with the overall diet using a multifactorial diet quality index and data from the prospective Breast Cancer Detection Demonstration Project involving 42,254 women. These investigators developed the Recommended Foods Score (RFS) to measure overall diet quality, which scored the intake of recommended foods with emphasis on fruits, vegetables, whole grains, lean meats, and low-fat dairy products. They found that women reporting the highest intakes of these foods had a lower mortality risk. At the highest intake level, women had nearly a 30% lower risk of multivariate-adjusted all-cause mortality (Fig. 3A) and of coronary heart disease (Fig. 3B) compared with the lowest intake level.

In their study using data from the Health Professionals Follow-up Study (n = 44,875), Hu et al identified two

### Table 2. Mean changes in blood pressure in the intervention diets compared to the control diet in the DASH study

<table>
<thead>
<tr>
<th>Category</th>
<th>Combination Group (97.5% CI)</th>
<th>P Value</th>
<th>Fruits-and-Vegetables Group (97.5% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All subjects (n = 459)</td>
<td>-5.5 (-7.4 to -3.7)</td>
<td>&lt;.001</td>
<td>-2.8 (-4.7 to -0.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hypertensive (n = 133)†</td>
<td>-11.4 (-15.9 to -6.9)</td>
<td>&lt;.001</td>
<td>-7.2 (-11.4 to -3.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Nonhypertensive (n = 326)</td>
<td>-3.5 (-5.3 to -1.6)</td>
<td>&lt;.001</td>
<td>-0.8 (-2.7 to 1.1)</td>
<td>.33</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All subjects (n = 459)</td>
<td>-3.0 (-4.3 to -1.6)</td>
<td>&lt;.001</td>
<td>-1.1 (-2.4 to 0.3)</td>
<td>.07</td>
</tr>
<tr>
<td>Hypertensive (n = 133)†</td>
<td>-5.5 (-8.2 to -2.7)</td>
<td>&lt;.001</td>
<td>-2.8 (-5.4 to -0.3)</td>
<td>.01</td>
</tr>
<tr>
<td>Nonhypertensive (n = 326)</td>
<td>-2.1 (-3.6 to -0.5)</td>
<td>.003</td>
<td>-0.3 (-1.9 to 1.3)</td>
<td>.71</td>
</tr>
</tbody>
</table>

CI = confidence interval; DASH = Dietary Approaches to Stop Hypertension.
* Based on Ref. 27.
† Hypertension was defined as a baseline systolic blood pressure ≥ 140 mm Hg or a diastolic blood pressure ≥ 90 mm Hg.

![FIG. 3. Depicting the association between diet quality and mortality in women, this chart compares the relative risks of (A) all-cause mortality and (B) coronary heart disease-specific mortality by quartiles of the Recommended Food Score index. (Data derived from Ref. 33)](image)
major dietary patterns and assessed the cardiovascular disease risk associated with each of them. The prudent diet included higher intake of fruits, vegetables, whole grains, fish, and poultry; the Western pattern was characterized by higher intake of meats, refined grains, high-fat dairy products, and sweets. The relative risks from the lowest to the highest quintiles of the prudent diet pattern were 1.0, 0.87, 0.79, 0.75, and 0.70 (95% CI: 0.56, 0.86; \( P \) for trend < .001). These values for the Western pattern were 1.0, 1.21, 1.36, 1.40, and 1.64 (95% CI: 1.24, 2.17, \( P \) for trend < .0001). Based on their findings, which included adjustments for age, coronary heart disease risk factors, smoking, body mass index, and family history of myocardial infarctions, the authors concluded that these dietary patterns significantly predict the incidence of coronary heart disease and provide strong evidence of the cardioprotective effects of the prudent diet pattern.

**Stroke**

Recent studies of the effects of multiple nutrients consumed as part of the total diet on stroke risk have demonstrated lower risk in men and in women consuming nutrient-rich diets. In their continuing analyses of the Health Professionals Follow-up Study in men, Harvard researchers examined the association of potassium, magnesium, calcium, and fiber intakes with stroke risk. They found that the multivariate risk in the top quintile of potassium intake (median 4.3 g/day) was 0.62 (95% CI: 0.43, 0.88, \( P \) for trend = .07) compared with those in the bottom (median 2.4 g/day). Cereal fiber and magnesium, but not calcium intakes were also inversely related to the risk of total stroke.

In a similar analysis in women, in which calcium, potassium, and magnesium intakes were studied in relation to stroke risk, the Nurses’ Health Study database (n = 85,764) revealed an inverse association between age- and smoking-adjusted relative risk of ischemic stroke and each of these three minerals, particularly calcium. In the highest quintile of calcium intake, women had an adjusted relative risk of stroke of 0.69 (95% CI: 0.50, 0.95; \( P \) for trend = .03) compared with risk in the lowest quintile. Relative risk for women in the highest quintile of potassium intake compared to the lowest was 0.72 (95% CI: 0.51, 1.01; \( P \) for trend = .10). The inverse relationship between stroke risk and calcium intake was stronger for dairy calcium than for that from nondairy sources. This study demonstrated that “low calcium intake, and perhaps low potassium intake, may contribute to increased risk of ischemic stroke.”

**Summary**

Early observational data indicated that inadequate intake levels of calcium and of potassium were associated with higher blood pressures. Because of the direct and primary role of elevated blood pressure, both established and borderline, in the development and prevalence of cardiovascular disease, the potentially beneficial effects of these dietary components have been the subjects of extensive epidemiologic and clinical study during the past several decades. Although their individual roles have been assessed with varying results, recognition of their biologic interdependencies has resulted in the shift in current nutritional research to examining their combined roles within the total diet.

As described in this review, today we have clear evidence of significant positive effects of long-term adequate mineral intake—when these nutrients are derived in combination from foods—on blood pressure, cardiovascular disease, and mortality. The most health-promoting diets do not require extraordinary effort, cost, or complexity, but are simply those that have been consistently recommended by national health organizations, ie, those diets that provide the recommended daily allowances of dietary micro- and macronutrients.

Although much of the past effort to improve blood pressure and cardiovascular health focused on altering intakes of one or two dietary factors such as sodium or fat, this narrow approach is generally being replaced by the recognition that foods are consumed in combination and that nutrient actions are interrelated, thereby likely functioning synergistically in their effects on physiologic processes such as blood pressure regulation. According to the American Heart Association, their revised dietary guidelines for 2000 have been updated to “place increased emphasis on foods and an overall eating pattern.” As stated in the new guidelines: “Eating adequate amounts of essential nutrients, coupled with energy intake in balance with energy expenditure, is essential to maintain health and to prevent or delay the development of cardiovascular disease, stroke, hypertension, and obesity.”

**References**


