Total polyphenol excretion and blood pressure in subjects at high cardiovascular risk

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Acronyms: GFR, glomerular filtration rate; BP, blood pressure; TPs, total polyphenols; TPE, total polyphenol excretion; F&B, fruit and vegetables; SPE, solid phase extraction; F-C, Folin–Ciocalteu; GAE, gallic acid equivalent; CHD, coronary heart disease; ORs, odds ratios.

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Abstract  Background and aims: Dietary factors are critical for the prevention and treatment of hypertension, but data on the effects of specific nutrients on blood pressure (BP) are scarce. The aim of this study was to assess the relationship between total polyphenol excretion (TPE) in urine, as an objective measurement of total polyphenol intake and BP in an elderly population at high cardiovascular risk.

Methods and results: Cross-sectional substudy of 589 high-risk participants entering in the PREDIMED trial. BP was measured and TPE was determined in urine by Folin–Ciocalteau assay. A significant positive association was observed between TPE in urine and daily intake of fruit and vegetables (F&V), coffee or wine after adjusting for potential confounders. The intake of 100 g of F&V (Beta = 0.150; P < 0.001) had a greater contribution to TPE than 100 mL of coffee (Beta = 0.141; P = 0.001), and the latter two foods contributed more than the consumption of 100 mL of wine (Beta = 0.120; P = 0.019). An inverse association was observed between urinary TPE and the prevalence of hypertension. Participants in the highest quartile of urinary TPE had a reduced prevalence of hypertension compared to those in the lowest quartile (Odds Ratio = 0.64; 95% confidence interval 0.45 to 0.92; P = 0.015). Systolic and diastolic BP were inversely associated with urinary TPE after adjustment for potential confounders (P = 0.024 and P = 0.003, respectively).

Conclusions: Polyphenol intake, assessed via TPE in urine, was negatively associated with BP levels and prevalence of hypertension in an elderly Mediterranean population at high cardiovascular risk. Participants with the highest intake of polyphenol-rich foods showed the lowest BP measurements.

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Introduction

Hypertension is a major global public health problem [1]. A healthy diet and lifestyle modification are the first steps for the management of hypertension [2]. Adoption of a healthier food pattern such as the Mediterranean diet [3] or the DASH (Dietary-Approaches-to-Stop-Hypertension) diet has also been advocated. In addition, there is considerable evidence that the consumption of fruits and vegetables (F&V) is inversely associated with high BP, whereas a high consumption of refined cereals or of meat/meat products is associated with a higher risk [2,4,5].

However, besides sodium and potassium dietary intake, few studies have analyzed the effects of dietary nutrients, such as oleic acid [6,7] vitamin C or other antioxidant compounds [8,9] on BP. Some studies have also evaluated the effects of polyphenol-rich foods such as cocoa [10], however up to now no studies have evaluated the effects of total dietary polyphenol intake on this issue.

The total dietary amount of polyphenol is approximately 1 g/d [11], being an amount that is higher than any other known dietary antioxidants; in fact, it is around 10 times higher than dietary vitamin C and 100 times higher than vitamin E and carotenoid intake. On the other hand, epidemiologic data have shown an inverse association between the risk of overall mortality or cardiovascular disease and the consumption of polyphenol-rich foods such as fruit and vegetables, tea, olive oil and wine [12–14].

We undertook, therefore, a substudy within a larger clinical trial, the PREDIMED study [3,15], in order to evaluate whether polyphenol-rich food intake, assessed as the excretion of total polyphenols (TPs) in spot urine samples, and directly measuring BP in a large sample of elderly individuals at high cardiovascular risk.

Methods

Subjects and design

The PREDIMED (PREvención con Dieta MEDiterránea) study is a large, parallel-group, multicenter, randomized, controlled 5-year clinical trial aimed to assess the effects of the Mediterranean diet on the primary prevention of cardiovascular disease (www.predimed.org; ISRCTN35739639). The detailed recruitment method and study protocol have been described previously [3].

From October-2003 to July-2004, we selected 612 potential participants in primary health centers affiliated with the Hospital Clinic of Barcelona and the University of Navarra (Pamplona) in Spain. Eligible participants were free of cardiovascular disease at baseline and fulfilled at least one of the following two criteria: (1) type-2 diabetes mellitus and/or (2) three or more coronary heart disease (CHD) risk factors [16]. The participants provided written informed consent and the study protocol was approved by the Institutional Review Boards of the two participating centres.

Measurements

At baseline, all participants completed a validated semi-quantitative food frequency questionnaire (FFQ) with 136-items [17], the validated Spanish version [18] of the Minnesota Leisure Time Physical Activity Questionnaire, and a 47-item questionnaire about education, lifestyle, history of illnesses and medication use. Trained nurses measured BP thrice with a validated semi-automatic oscillometer (Omron HEM-705CP [19]; Hoofddorp, The Netherlands).
Netherlands). Creatinine-estimated glomerular filtration rate (GFR) was calculated using the Modification of Diet in Renal Disease (MDRD) formula in all participants [20]. Energy and nutrient intake was derived from Spanish food composition tables [21]. The morning urine samples were collected; the aliquots were immediately prepared, coded, shipped to a central laboratory and frozen at \( -80 ^\circ \text{C} \) until analysis. TP consumption from plant food and beverages (mg/g fresh matter) was quantified according to Saura-Calixto F et al. [22] and Brat P et al. [23], from the FFQ.

**Analysis of total polyphenols in urine**

Solid Phase Extraction (SPE) with 96-well plate cartridges (Oasis MAX) was performed in the urine samples to avoid any interference with F–C reagent. For all the spot urine samples TPs and creatinine were analyzed as described by Medina-Remón A. et al. [24]. TPE was expressed as mg gallic acid equivalent (GAE)/g of creatinine.

**Statistical analysis**

Analyses were performed using SPSS software v14.0 (Chicago, USA). The baseline characteristics of the participants were expressed as means or percentages and standard deviations (SD). Variables were examined for normality and skewness (Kolmogorov and Levene tests). The variable urinary TPE, which was not normally distributed and was not normalized by the logarithmic transformation, were Box–Cox transformed with \( \alpha = 0.00001 \) and \( \lambda = 0.25 \). Participants were divided into quartiles according to their urinary TPE (not normalized).

Pearson correlation coefficients were used to examine the unadjusted correlation between the urinary TPE and TP intake according to FFQ, as well as in the different food groups using units of 100 g/day. Multivariate linear regression models were used to test the relationship between the TPE normalized in urine as the dependent variable, and the TPE in urine was analyzed. In fact, a weak but significant Pearson correlation was obtained between dietary intake of TPs from FFQ and urinary TPE measured (\( r = 0.179; \quad P < 0.001 \)).

Table 1 shows the average food consumption of study participants divided according to quartiles of urinary TPE measured as mg GAE/g creatinine. Significant increasing trends across quartiles of TPE were observed for the intake of fruits, vegetables, total F&V, dairy products, fish and TP intake; whereas decreasing trends across TPE quartiles were observed for total alcohol intake, cereals, olive oil, pastries, cakes or sweets, as well as total energy intake.

The linear regression analyses of TPE in spot urine samples and TP intake (100 mg), total F&V intake (100 g), wine intake (100 mL) and coffee intake (100 mL) are presented in Table 2 with various models. The remaining variables are not shown because they did not exhibit any significant association with urinary TPE adjusted for potential confounding factors. We observed a significant positive association between urine TPE and daily intake of F&V, as well as with daily intake of coffee in the unadjusted model (\( \beta = 0.131; P < 0.001 \) and \( \beta = 0.261; P < 0.05 \), respectively). After adjusting for potential confounding factors in models 2, 3 and 4, the association remained statistically significant in the multivariate regression analysis. TPE concentration in spot urine samples showed a significant inverse association with the intake of wine, \( \beta = -0.090, \quad P < 0.05 \) in the unadjusted model; but after adjusting for potential confounding factors this association reversed and became positive and statistically significant (\( \beta = 0.121, \quad P = 0.019 \)).

The standardized coefficients (Beta) are the regression coefficients obtained with the regression model using the standardized values (measured in standard deviation units), and are therefore independent of measurement units. The standardized coefficients (Table 2) from this model showed that total phenol intake (Beta = 0.283), F&V intake (Beta = 0.150) contributed more to urinary TPE than coffee intake (Beta = 0.141), and both contributed to a greater extent than wine (Beta = 0.120).
Table 3 shows the profile of cardiovascular risk factors of participants according to the quartile of urinary TPE. A higher polyphenol excretion in urine was associated with older age (\( P \) for trend < 0.001), lower systolic (\( P \) for trend < 0.015) and diastolic BP (\( P \) for trend < 0.001), and a lower, but not significant, use of anti-hypertensive medication. However, participants in the highest quartile of TPE reported a lower educational level than those in the lower quartile categories, had a higher prevalence of diabetes, but were less likely to be smokers, and to have a family history of CHD.

On multivariate linear regression analyses, systolic and diastolic BP exhibited a monotonic inverse association with TPE in spot urine samples (quartiles) after adjustment for potential confounders (Table 4). The non-standardized coefficients, \( \beta = -1.731 (P = 0.024) \) and \( \beta = -1.264 (P = 0.003) \) represent the expected change of systolic and diastolic BP, respectively, corresponding to an increase from a TPE to the upper quartile.

Logistic regression analysis showed an inverse association between urinary TPE (by quartile) and the prevalence of hypertension (Table 5). Compared to the participants in the lowest quartile of TPE (\(< 89.00 \text{ mg GAE/g creatinine}\)), participants in the highest quartile (\(> 160.23 \text{ mg GAE/g creatinine}\)) had a significantly reduced prevalence of hypertension (OR = 0.71, CI 0.53 to 0.95; \( P = 0.022 \)) in the unadjusted model. In all three models, a significant difference was observed between the top and the bottom quartiles for the prevalence of hypertension, after adjustment for potential confounders. When the analysis was adjusted for all possible confounding factors (model 4), participants in the highest quartile had a 36% reduced odds of hypertension (OR = 0.64, CI 0.45 to 0.92; \( P = 0.015 \)), compared to those in the lowest quartile. Finally, BP correlated better with urinary TPE than with TP intake assessed by FFQ. In fact, a highly significant association between polyphenol intake assessed via TPE in urine and

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### Table 1 Daily intake of selected foods according to quartiles of excreted total urinary polyphenols, expressed as mg GAE /g creatinine.

<table>
<thead>
<tr>
<th>Urine mg GAE/ g creatinine concentration quartile</th>
<th>Q1 (&lt;89.0)</th>
<th>Q2 (89.1–119.5)</th>
<th>Q3 (119.6–160.2)</th>
<th>Q4 (&gt;160.3)</th>
<th>( P ) for trend*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine total polyphenol (mg GAE/ g creatinine)</td>
<td>72.8 (11.6)</td>
<td>103.1 (8.2)</td>
<td>138.2 (11.1)</td>
<td>226.1 (69.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. of subjects</td>
<td>147</td>
<td>148</td>
<td>147</td>
<td>147</td>
<td>0.742</td>
</tr>
<tr>
<td>Olive oil (g)</td>
<td>48.7 (14.3)</td>
<td>47.3 (13.7)</td>
<td>45.1 (14.6)</td>
<td>45.0 (15.7)</td>
<td>0.014</td>
</tr>
<tr>
<td>Total nuts (g)</td>
<td>8.6 (10.7)</td>
<td>9.2 (11.3)</td>
<td>9.6 (12.2)</td>
<td>9.1 (10.9)</td>
<td>0.680</td>
</tr>
<tr>
<td>Vegetables (g)</td>
<td>253.1 (80.2)</td>
<td>261.1 (81.1)</td>
<td>262.6 (84.0)</td>
<td>272.7 (92.1)</td>
<td>0.053</td>
</tr>
<tr>
<td>Legumes (g)</td>
<td>17.9 (7.0)</td>
<td>17.9 (7.5)</td>
<td>17.7 (7.0)</td>
<td>16.5 (7.6)</td>
<td>0.107</td>
</tr>
<tr>
<td>Fruits (g)</td>
<td>304.6 (143.6)</td>
<td>319.3 (141.3)</td>
<td>315.1 (132.9)</td>
<td>360.8 (151.2)</td>
<td>0.002</td>
</tr>
<tr>
<td>Total fruits and vegetables (g)</td>
<td>557.7 (176.8)</td>
<td>580.4 (173.3)</td>
<td>577.7 (162.1)</td>
<td>633.5 (190.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>Fish or seafood (g)</td>
<td>86.5 (34.0)</td>
<td>82.2 (35.8)</td>
<td>88.7 (36.9)</td>
<td>94.1 (39.0)</td>
<td>0.030</td>
</tr>
<tr>
<td>Meat or meat products (g)</td>
<td>132.0 (49.6)</td>
<td>129.7 (43.7)</td>
<td>134.3 (48.5)</td>
<td>134.2 (47.5)</td>
<td>0.531</td>
</tr>
<tr>
<td>Pastries, cakes or sweets (g)</td>
<td>34.8 (31.6)</td>
<td>27.9 (24.8)</td>
<td>25.3 (25.9)</td>
<td>23.7 (28.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cereals (g)</td>
<td>243.7 (106.7)</td>
<td>235.8 (91.6)</td>
<td>228.7 (98.3)</td>
<td>211.3 (83.3)</td>
<td>0.003</td>
</tr>
<tr>
<td>Milk and dairy products (mL)</td>
<td>352.1 (214.8)</td>
<td>378.8 (216.5)</td>
<td>396.5 (222.1)</td>
<td>403.1 (215.1)</td>
<td>0.033</td>
</tr>
<tr>
<td>Wine (mL)</td>
<td>121.1 (147.0)</td>
<td>81.5 (137.9)</td>
<td>101.1 (161.5)</td>
<td>81.3 (149.3)</td>
<td>0.071</td>
</tr>
<tr>
<td>Coffee (mL)</td>
<td>63.3 (47.7)</td>
<td>69.6 (52.9)</td>
<td>67.5 (48.3)</td>
<td>74.5 (56.0)</td>
<td>0.097</td>
</tr>
<tr>
<td>Tea (mL)</td>
<td>3.92 (16.4)</td>
<td>3.25 (11.4)</td>
<td>4.16 (12.6)</td>
<td>5.47 (20.4)</td>
<td>0.332</td>
</tr>
<tr>
<td>Chocolate (g)</td>
<td>3.1 (6.2)</td>
<td>2.4 (5.2)</td>
<td>2.3 (5.5)</td>
<td>1.9 (4.8)</td>
<td>0.063</td>
</tr>
<tr>
<td>Natural orange</td>
<td>23.3 (54.3)</td>
<td>25.19 (57.8)</td>
<td>13.4 (41.2)</td>
<td>19.1 (50.8)</td>
<td>0.199</td>
</tr>
<tr>
<td>Total polyphenol intake (mg GAE)</td>
<td>1075.6 (354.9)</td>
<td>1057.5 (320.2)</td>
<td>1086.2 (322.3)</td>
<td>1222.5 (439.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>Alcohol (g)</td>
<td>15.7 (17.9)</td>
<td>10.2 (16.0)</td>
<td>12.2 (18.5)</td>
<td>9.9 (17.8)</td>
<td>0.018</td>
</tr>
<tr>
<td>Fibre (g)</td>
<td>22.1 (6.2)</td>
<td>22.0 (5.5)</td>
<td>21.9 (5.2)</td>
<td>22.5 (6.2)</td>
<td>0.606</td>
</tr>
<tr>
<td>Cholesterol (g)</td>
<td>353.6 (119.7)</td>
<td>328.6 (93.7)</td>
<td>340.5 (113.4)</td>
<td>342.1 (89.4)</td>
<td>0.561</td>
</tr>
<tr>
<td>Sodium (mg/d)</td>
<td>3347.7 (959.2)</td>
<td>3088.0 (905.4)</td>
<td>3123.2 (1006.5)</td>
<td>3145.4 (877.2)</td>
<td>0.100</td>
</tr>
<tr>
<td>Potassium (mg/d)</td>
<td>3926.7 (722.3)</td>
<td>3929.4 (700.9)</td>
<td>3994.8 (805.5)</td>
<td>4029.7 (659.7)</td>
<td>0.161</td>
</tr>
<tr>
<td>Total energy, Kcal/d</td>
<td>2380.1 (586.8)</td>
<td>2238.0 (472.0)</td>
<td>2205.1 (547.4)</td>
<td>2138.5 (476.8)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

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* One-factor ANOVA was used for continuous variables and \( \chi^2 \)-test for categorical variables.

** Mean (standard deviation). GAE: gallic acid equivalent.
systolic (P for trend = 0.024) and diastolic BP (P for trend = 0.003) was observed (Table 4), whereas polyphenol intake assessed via FFQ tended to be associated with BP values, but here the association did not reach the statistical significance.

**Discussion**

In the current study, we observed an inverse association between urinary TPE, an objective measurement of polyphenol intake, and the risk of hypertension in a large Spanish cohort of elderly participants at high cardiovascular risk. In addition, systolic and diastolic BP measurements correlated negatively with urinary TPE after adjustment for potential confounders. The results from the present study also provide evidence that total phenol, F&V, coffee and wine intake in the Mediterranean diet are positively related with the excretion of TPs in spot urine samples. The intake of F&V contributed more to urinary TPE than coffee, and wine consumption. In addition, the absolute daily consumption of F&V in grams was 781% and 852% higher than the daily intake of coffee and wine, respectively.

F&V, and beverages such as coffee, tea and red wine, constitute the main sources of polyphenols [25]. Polyphenols represent a wide variety of structures from different subclasses, that explain the difficulties to estimate the TP content in these foods, mainly F&V [23]. Polyphenols are quantitatively the main dietary antioxidant source; however, the biological effects of these compounds depends on their bioavailability, their kinetics and exposure time [26]. The most common polyphenols in the human diet are not necessarily the most active in vivo, either because they have a lower intrinsic activity than others or because they are poorly absorbed from the intestine, highly metabolized, or rapidly eliminated [25].

Most dietary polyphenols (75–99%) are not found in urine, and the quantities detected intact vary from one phenolic compound to another [11]. This fact may be due to their reduced absorption through the gut barrier, their excretion to the bile or their metabolization by the colonic microflora or our own tissues. To acquire high plasma concentrations requires repeated ingestion of polyphenol-rich foods [27].

The BP lowering effects of fruit- and vegetable-rich diets in hypertensive patients have mainly been attributed to the presence of multiple antioxidants. Two different double-blind cross-over trials [10,28] with polyphenol rich food (dark chocolate versus white and a rich versus low flavonoid sweet juice) showed that the polyphenols rich food reduced BP.

The clinical relevance of the endothelium-dependent effects of plant polyphenols is dependent upon their systemic availability. For this reason, intestinal absorption and metabolism of the plant polyphenols are a rate-limiting step for the protective effects of this class of compounds. In healthy volunteers, the coronary flow-velocity reserve increased 30 min after drinking red wine (1 g/kg ethanol), a polyphenol-rich beverage, but not after drinking the same quantity of alcohol as vodka or white wine, a polyphenol-free beverage or an alcoholic beverage with medium quantity of alcohol as vodka or white wine, a polyphenol-rich beverage, but not after drinking the same quantity of alcohol as vodka or white wine, a polyphenol-rich beverage, but not after drinking the same quantity of alcohol as vodka or white wine [29]. Endothelium-dependent vasodilatation also improved in men, after the acute intake of 500 mL of red wine and de-alcoholized red wine [30]. In patients with mild isolated systolic...
ANOVA—one factor was used for continuous variables and χ²-test for categorical variables. BMI: body mass index (calculated as weight in kilograms divided by height in square meters); BP: blood pressure; ACE: angiotensin-converting enzyme; CHD: coronary heart disease.

Table 3  Baseline characteristics of the study participants by quartile of total polyphenol excretion expressed as mg GAE/g creatinine.

| Urine mg GAE/ g creatinine concentration quartile | Q1 (<88.99) | Q2 (89–119.46) | Q3 (119.47–160.22) | Q4 (>160.23) | P for trend
|---|---|---|---|---|---
| No. of subjects | 147 | 148 | 147 | 147 |
| Age, (y) mean (SD) | 66.0 (5.7) | 68.3 (6.1) | 68.0 (5.8) | 69.3 (6.0) | < 0.001
| Women, n (%) | 51 (34.7) | 83 (56.1) | 85 (57.8) | 107 (72.8) | < 0.001
| Weight (kg), mean (SD) | 80.0 (11.1) | 75.3 (11.2) | 74.1 (10.3) | 71.7 (11.2) | < 0.001
| BMI, (kg/m²), mean (SD) | 29.6 (2.9) | 29.6 (3.7) | 29.2 (3.7) | 29.1 (3.4) | 0.171
| Overweight or obese (BMI ≥25 Kg/m²), n (%) | 138 (93.9) | 137 (92.6) | 128 (87.1) | 135 (91.8) | 0.263
| Systolic BP (mmHg), mean (SD) | 156.0 (15.6) | 152.2 (18.3) | 155.0 (21.6) | 149.1 (16.0) | 0.015
| Diastolic BP (mmHg), mean (SD) | 88.9 (10.2) | 86.2 (9.8) | 85.5 (11.8) | 83.4 (8.5) | < 0.001
| Hypertension, n (%) | 123 (83.7) | 126 (85.1) | 113 (76.9) | 114 (77.6) | 0.067
| Diabetes, n (%) | 31 (21.1) | 47 (31.8) | 52 (35.4) | 62 (42.2) | 0.001
| Dyslipidemia, n (%) | 78 (53.1) | 103 (69.6) | 93 (63.3) | 96 (65.3) | 0.097
| Current smoker n (%) | 39 (26.5) | 20 (13.5) | 22 (15.0) | 14 (9.5) | < 0.001
| Family history of CHD, n (%) | 45 (30.6) | 46 (31.1) | 37 (25.2) | 47 (32.0) | 0.018
| ACE inhibitors, n (%) | 119 (81.0) | 114 (77.0) | 106 (72.1) | 107 (72.8) | 0.063
| Diuretics, n (%) | 11 (7.5) | 7 (4.7) | 7 (4.8) | 9 (5.8) | 0.639
| Statins or other hypolipidemic drugs, n (%) | 42 (28.6) | 70 (47.3) | 69 (46.9) | 65 (44.2) | 0.01
| Insulin, n (%) | 3 (2.0) | 4 (2.7) | 12 (8.2) | 9 (6.1) | 0.024
| Oral hypoglycemic drugs, n (%) | 17 (11.6) | 26 (17.6) | 26 (17.6) | 36 (24.5) | 0.006
| Aspirin or other antiplatelet drugs, n (%) | 29 (19.7) | 28 (18.9) | 37 (25.2) | 30 (20.4) | 0.582
| Medication, n (%) | | | | | |
| Educational level, n (%) | | | | | |
| Primary school | 104 (70.7) | 112 (75.7) | 108 (73.5) | 121 (82.3) | 0.041
| High school | 24 (16.3) | 18 (12.2) | 28 (19.0) | 18 (12.2) | 0.685
| University | 19 (12.9) | 17 (11.5) | 10 (6.8) | 7 (4.8) | 0.006
| Energy expenditure in physical activity (kcal/d), mean (SD) | 256.0 (215.5) | 245.9 (220.7) | 293.1 (231.0) | 255.3 (205.3) | 0.576
| Glomerular filtration rate, mL/min | 77.2 (16.4) | 78.1 (14.6) | 78.1 (18.1) | 79.5 (18.9) | 0.264

a ANOVA—one factor was used for continuous variables and χ²-test for categorical variables. BMI: body mass index (calculated as weight in kilograms divided by height in square meters); BP: blood pressure; ACE: angiotensin-converting enzyme; CHD: coronary heart disease.

Table 4  Multivariate linear regression analyses with systolic blood pressure and diastolic blood pressure as the dependent variables, and quartile of total polyphenol excreted in spot urine samples (mg GAE/g creatinine) as exposure variable, adjusted for potential confounders.

<table>
<thead>
<tr>
<th>Variables</th>
<th>β</th>
<th>SE</th>
<th>Beta</th>
<th>P</th>
<th>95 % CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 1</td>
<td>-1.743</td>
<td>0.712</td>
<td>-0.104</td>
<td>0.015</td>
<td>-3.141 to -0.345</td>
</tr>
<tr>
<td>Model 2</td>
<td>-1.895</td>
<td>0.741</td>
<td>-0.113</td>
<td>0.011</td>
<td>-3.350 to -0.440</td>
</tr>
<tr>
<td>Model 3</td>
<td>-1.895</td>
<td>0.743</td>
<td>-0.113</td>
<td>0.011</td>
<td>-3.354 to -0.436</td>
</tr>
<tr>
<td>Model 4</td>
<td>-1.731</td>
<td>0.765</td>
<td>-0.103</td>
<td>0.024</td>
<td>-3.233 to -0.228</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 1</td>
<td>-1.705</td>
<td>0.397</td>
<td>-0.180</td>
<td>&lt; 0.001</td>
<td>-3.298 to -0.875</td>
</tr>
<tr>
<td>Model 2</td>
<td>-1.438</td>
<td>0.408</td>
<td>-0.152</td>
<td>&lt; 0.001</td>
<td>-2.188 to -0.637</td>
</tr>
<tr>
<td>Model 3</td>
<td>-1.405</td>
<td>0.409</td>
<td>-0.148</td>
<td>0.001</td>
<td>-2.208 to -0.602</td>
</tr>
<tr>
<td>Model 4</td>
<td>-0.011</td>
<td>0.422</td>
<td>-0.013</td>
<td>0.003</td>
<td>-0.209 to -0.435</td>
</tr>
</tbody>
</table>

β: Non-standardized coefficient (regression line coefficient); SE: Standard error; Beta: Standardized coefficient; CI: Confidence interval; P: two-sided test of significance; Model 1: unadjusted; Model 2: adjusted by age and weight; Model 3 adjusted as in Model 2 plus smoking status, physical activity, and educational level; Model 4 adjusted as in Model 3 plus additionally adjusted for medication use (angiotensin-converting enzyme inhibitors, diuretics, statins or other hypolipidemic drugs, insulin, oral hypoglycemic drugs and aspirin or other antiplatelet drugs) consumed in the last month, sodium and potassium intake and glomerular filtration rate (GFR); GAE: Gallic acid equivalent.

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may improve endothelium function and reduce BP in hypertensive subjects.

F&V seem to be essential items in the prevention of dietary diseases. Some epidemiological evidence supports that a diet rich in F&V may help prevent BP from increasing and help decrease elevated BP levels for those with high normal BP or hypertension [33]. In the SUN study [4], the prevalence of non-previosly diagnosed hypertension was inversely associated with F&V consumption in a Mediterranean population with a very high intake of both fat- and plant-derived foods. In the Nurses’ Health Study, intake of F&V was also inversely associated with systolic and diastolic BP, whereas the intake of cereals and meat was directly associated with systolic BP [34]. After the 8-year follow-up in 1714 employed middle-aged men in the Chicago Western Electric Study, vegetable protein, beta-carotene, and an antioxidant vitamin score based on vitamin C and beta-carotene were inversely and significantly related to an average annual change in BP [35]. Thus, in all mentioned studies a high consumption of F&V was associated with a decrease in BP levels. In the current study performed in a free-living Spanish high-risk population, we observed a similar effect when consumption of F&V was high. However, until now, no study has tried to correlate the biomarker of TP intake, determined in spot urine samples, with BP measurements or with the prevalence of hypertension. Taking into account that greater excretion of polyphenols in urine is determined by high TP consumption, we suggest that the observed independent inverse association of objectively measured TPE in urine samples with BP measurements or with the prevalence of hypertension is determined by high TP consumption, polyphenols in urine is determined by high TP consumption.

### Table 5

<table>
<thead>
<tr>
<th>Urine mg GAE/g creatinine concentration quartile</th>
<th>Q1 (&lt;88.99)</th>
<th>Q2 (89–119.46)</th>
<th>Q3 (119.47–160.22)</th>
<th>Q4 (≥160.23)</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension, n (%)</td>
<td>123 (83.7)</td>
<td>126 (85.1)</td>
<td>113 (76.9)</td>
<td>114 (77.6)</td>
<td>0.867</td>
</tr>
<tr>
<td>Model 1</td>
<td>1.00</td>
<td>1.82 (0.33–10.13)</td>
<td>0.67 (0.29–1.55)</td>
<td>0.71 (0.53–0.95)</td>
<td>0.021</td>
</tr>
<tr>
<td>Model 2</td>
<td>1.00</td>
<td>1.40 (0.21–9.24)</td>
<td>0.61 (0.25–1.47)</td>
<td>0.64 (0.46–0.89)</td>
<td>0.006</td>
</tr>
<tr>
<td>Model 3</td>
<td>1.00</td>
<td>1.29 (0.19–8.49)</td>
<td>0.55 (0.22–1.37)</td>
<td>0.65 (0.47–0.91)</td>
<td>0.007</td>
</tr>
<tr>
<td>Model 4</td>
<td>1.00</td>
<td>1.39 (0.19–10.34)</td>
<td>0.55 (0.20–1.48)</td>
<td>0.64 (0.45–0.92)</td>
<td>0.047</td>
</tr>
</tbody>
</table>

Model 1, unadjusted; Model 2 was adjusted for sex, age and weight; Model 3 adjusted as in Model 2 plus smoking status, physical activity, educational level and energy expenditure in physical activity; Model 4 was adjusted as in Model 3 plus medication intake: ACE inhibitor, diuretics, statins (hypolipidemic drugs), insulin, oral hypoglycemic drugs, aspirin or other antiplatelet drug supplements taken in the last month, sodium and potassium intake and glomerular filtration rate (GFR); GAE: Gallic acid equivalent.

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References


