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Coffee in hypertensive women with asymptomatic peripheral arterial disease: a potential nutraceutical effect / Mattioli, Anna V; Migaldi, Mario; Farinetti, Alberto. - In: JOURNAL OF CARDIOVASCULAR MEDICINE. - ISSN 1558-2027. - 19:4(2018), pp. 183-185-185. [10.2459/JCM.0000000000000626]

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30/04/2024 02:29

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# Coffee in hypertensive women with asymptomatic peripheral arterial disease: a potential nutraceutical effect

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*J Cardiovasc Med* 2018, **19**:183–185

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Received 23 December 2017 Revised 14 January 2018  
Accepted 22 January 2018

Several studies suggest that coffee is associated with a lower risk of atherosclerosis.<sup>1,2</sup> Coffee contains polyphenol antioxidants, which have been hypothesized to act against free oxygen radicals and lipid peroxidation and to improve endothelial function.<sup>1–3</sup> Coffee is part of the Mediterranean diet, one of the healthiest diets. The characteristics and virtues of the Mediterranean diet were recently accompanied by a declaration from *United Nations Educational, Scientific and Cultural Organization*, which classified the Mediterranean diet as a ‘cultural heritage of humanity’.<sup>4</sup>

The current study aims to evaluate the relationship between coffee and asymptomatic peripheral arterial disease (PAD) in hypertensive women.

## Methods

A retrospective analysis on a group of 650 women was performed. Patients were referred to our clinic from general practitioners for screening and prevention of cardiovascular disease. We selected nondiabetic women with known hypertension<sup>5,6</sup> only if they were free of symptoms of PAD, had ankle–brachial index (ABI) evaluation, and a complete nutritional assessment. We excluded participants with a previous history of cardiovascular disease (ischemic heart disease, heart failure, and stroke), those who did not complete questionnaire, and those who did not undergo ABI evaluation and who did not sign the consent (flow chart in Supplemental material, <http://links.lww.com/JCM/A116>). From the initial group, we analyzed data from 237 women (age range 45–54 years).

The Local Ethical Review Board approved the study and participants signed an informed consent.

## Data collection

The prevalence of nutritional parameters was assessed by a self-administered food frequency questionnaire with 116 items and completed by an interviewer-administered 7-day diet recall questionnaire on the day of first visit.<sup>7</sup> For collection of nutritional parameters, we referred to a previous article.<sup>7</sup> Coffee consumption was investigated.<sup>1,8</sup>

## Statistical analysis

SPSS, V.21.0.1 (SPSS Inc., Chicago, Illinois, USA) was used for statistical analysis. To study the association of consumption of coffee with PAD, we used Cox proportional hazards regression analysis. For these analyses, consumption of coffee was used as continuous and categorical (0; 1–2; 3–4; >5 cups/day) variables, to obtain the best fitting model. We performed analyses in which we adjusted for age, BMI, smoking, physical activity, and adherence to a Mediterranean diet.

In interaction analysis, *P* interaction less than 0.05 was considered to indicate effect modifiers on the association of coffee consumption with ABI.

## Results

Clinical characteristics of patients according to categories of coffee consumption are shown in Table 1.

Patients were categorized according to coffee consumption, and we evaluated the distribution of ABI index within groups. A total of 27.4% of women who are not used to drinking coffee had an ABI lower than 0.9 compared with 16.8% of women who were heavy consumers (more than five cups/day); *P* less than 0.05. Obesity was also more frequent in abstainer from coffee compared with heavy consumers.

Coffee consumption was associated with a decreased risk of developing asymptomatic PAD (Table 2).

## Discussion

The current retrospective analysis was performed to evaluate the relationship between coffee consumption in premenopausal age and asymptomatic PAD. We found that a high intake of coffee was associated with a reduced risk of asymptomatic PAD. Previous studies found controversial data on the relationship between coffee consumption and atherosclerosis.<sup>3,4,8</sup>

**Table 1 Clinical characteristics of patients**

Clinical characteristics	0 cup/coffee (no drinkers)	1–2 cups/day	3–4 cups/day	>5 cups/day
Number of patients	47	83	70	37
Mean age (years)	56 ± 3	57 ± 5	55 ± 4	52 ± 6*
Weight (kg)	90.2 ± 5.7	89.9 ± 4.6	85.5 ± 3.1*	71.7 ± 4.2**
BMI (mean)	30.1 ± 3.8	26.8 ± 3.1*	24.6 ± 3.9*	21.3 ± 3.5**
Waist circumference (cm)	105 ± 6	93 ± 3*	88 ± 8**	88 ± 6**
Smoking (cigarette/day)	7 ± 7	11 ± 5.3*	10 ± 9	12 ± 10*
Sedentary (<200 kcal/week) (number of patients)	23 (48.9%)	26 (31.3%)	20 (28.6%)	5 (13.5%)**
Antihypertensive drugs (1)	34	75	65	29
Antihypertensive drugs (2)	10	2	3	5
Antihypertensive drugs (>2)	3	6	2	3

Significantly, different from first quartile (Bonferroni correction for multiple comparisons). \*  $P < 0.05$  versus no drinkers. \*\*  $P < 0.01$  versus no drinkers.

Drinking coffee was associated with acute increase in blood pressure (BP) in nonhabitual coffee drinkers; conversely, this effect was not reported in habitual coffee consumers.<sup>9,10</sup> However, many observational cohort studies identified no statistically significant association between daily coffee consumption at various levels and BP changes.<sup>11</sup>

The association between dietary intake and PAD has been evaluated in a recent analysis from the Atherosclerosis Risk in Communities (ARIC) study, a prospective cohort study.<sup>12</sup> Authors found that greater meat consumption was associated with a higher risk, and moderate alcohol consumption was associated with a lower risk of incident PAD. They concluded that whether these associations are causal remains to be seen. Moreover, they found that low coffee consumption was associated with a lower risk of incident PAD. The ARIC study included both women and men of different ethnicities. We analyzed a selected patient population of premenopausal women. In addition, we referred to espresso coffee; on the contrary, North American countries are used to drinking filtered American coffee. It is well known that intake of antioxidants changes with coffee preparation (espresso, filtered, percolated) as well as the composition of coffee and subsequently the concentration and bioavailability of antioxidant compounds.<sup>13</sup>

Women with high coffee consumption had a good adherence to a Mediterranean diet and high levels of physical activity suggesting a healthier lifestyle, a known factor for prevention of atherosclerosis.

The diet may affect vascular characteristics. For example, sodium intake is negatively correlated with arterial stiffness, whereas potassium intake is positively correlated with augmentation index.<sup>14</sup>

**Table 2 Association of coffee consumption with asymptomatic peripheral arterial disease in adjusted models**

PAD	0 cup/coffee References	1–2 cups/day HR (95% CI)	3–4 cups/day HR (95% CI)	>5 cups/day HR (95% CI)
Model 1	1	0.76 (0.42–1.43)	0.78 (0.32–0.98)	0.66 (0.44–1.1)*

HR, hazard ratio; CI, confidence interval; PAD, peripheral arterial disease.  
\*  $P < 0.05$  versus no drinkers.

However, the analysis adjusted for some cardiovascular risk factors suggests a direct action of coffee on vessels.<sup>3,14,15</sup> Rhee *et al.*<sup>16</sup> found that caffeinated coffee, decaffeinated coffee, and caffeine are not risk factors for hypertension in postmenopausal women. The European Food Safety Authority recently published a scientific opinion on the safety of caffeine and noted that caffeine consumption, at single doses ranging from 80 to 300 mg, acutely increases BP, which reaches a peak 30 min after consumption and then returns to baseline after 2–4 h in the adult population.<sup>17</sup> A single dose of caffeine up to 200 mg does not give rise to safety concerns, and habitual caffeine consumption up to 400 mg/day does not give rise to safety concerns for nonpregnant adults. Further research is needed to fully elucidate the role of chronic caffeine intake in hypertension. The beneficial effects we observed could be related to antioxidant compounds in coffee. Green coffee beans are a complex source of multiple bioactive constituents with characteristic free radical or antioxidant activity, which include, in varying quantities, caffeine, chlorogenic acid, trigonelline, cafestol, and kahweol, depending on the source. In addition, the process of roasting coffee beans produces a series of changes to the chemical composition of coffee, leading to the formation of substances with antioxidant activity.<sup>13</sup>

#### Limitation of the study

The major limitation is the retrospective evaluation of nutritional data and the use of questionnaire. The nutritional habits were self-reported, alcohol and coffee intake could be underestimated, and some misclassification of exposure was to be expected. All patients were given antihypertensive drugs; however, due to the many different kinds and doses of drugs, it was not possible to carry out a statistical analysis on subgroups.

These results need further evaluation with prospective trial to rule out the direct effect of coffee compounds on vessels and atherosclerosis.

#### Conclusion

In conclusion, it can be suggested that coffee consumption associated with a healthy lifestyle can help in the prevention of atherosclerosis in premenopausal women.

## Acknowledgements

We would like to thank Mrs Jane A. Carter for language editing and Dr Matteo B. Puviani for his help in graphical editing.

## Conflicts of interest

There are no conflicts of interest.

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