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Influence of dietary total antioxidant capacity on the association between smoking and hypertension in Brazilian graduates (CUME project)

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Abstract *Background and aims:* Hypertension (HTN) is a chronic non-communicable disease influenced by non-modifiable risk factors, such as sex and age, as well as modifiable risk factors such as lifestyle, including diet and smoking. Moreover, diet quality among smokers is worse than that of non-smokers, mainly in terms of antioxidant content. Thus, the current study aimed to investigate whether dietary total antioxidant capacity (dTAC) influences the association between smoking and HTN.
Methods and results: This cross-sectional study included 4303 graduates (69.35% women) from the Cohort of Minas Gerais Universities (CUME) project. An online food frequency questionnaire was administered to participants, and dTAC was estimated using the ferric reducing antioxidant power method. In the questionnaires, individuals reported smoking status, systolic and diastolic blood pressure values, previous HTN diagnosis, and use of antihypertensive drugs. Logistic regression models were used to estimate the odds ratio and 95% confidence interval between smoking and HTN, stratified by the median dTAC. Current and former smokers had higher dTAC values despite their lower fruit intake. Moreover, coffee was the main contributor to dTAC among them. Smoking was associated with a higher likelihood of HTN, mainly among individuals with a higher dTAC. However, after exclusion of coffee antioxidant capacity, there was an association between only smoking and HTN in individuals with lower dTAC.
Conclusions: The controversial association between higher dTAC and HTN can result from high coffee intake. Higher dTAC without coffee intake may mitigate the association between smoking and HTN in this population.

Abbreviations: CI, Confidence Interval; CUME, The Cohort of Minas Gerais Universities; dTAC, Dietary Total Antioxidant Capacity; FFQ, Food Frequency Questionnaire; FRAP, Ferric Reducing Antioxidant Power; HTN, Hypertension; NCDs, Non-Communicable Disease; OR, Odds Ratio; UFMG, Universidade Federal de Minas Gerais; UFV, Universidade Federal de Viçosa; UFOP, Universidade Federal de Ouro Preto; UFLA, Universidade Federal de Lavras; UFJF, Universidade Federal de Juiz de Fora.

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Introduction

Hypertension (HTN) is a highly prevalent non-communicable disease (NCDs) with low rates of control and has been associated with modifiable and non-modifiable risk factors [1], one of which is smoking. In addition, oxidative stress influences this association, since it predisposes individuals to develop NCDs [2]. Eating habits adopted by smokers have been characterized as high energy intake that derives from alcohol and food items with high cholesterol and saturated fatty acid content, as well as from lower vitamin and fiber content due to their fruit and vegetable lower intake [3,4], suggesting that the diet of these individuals has a lower antioxidant content than that of non-smokers.

Smoking combined with a low antioxidant content diet may enable additional oxidative stress and favor the occurrence of HTN. Several factors play a key role in the development of cardiovascular diseases, which represent a public health issue. Diet is the focus of preventive strategies because it is an important modifiable risk factor for these diseases [5]. Accordingly, there has been evidence regarding the beneficial effects of dietary antioxidants in preventing and reducing the risk of developing cardiovascular disease [6,7], as well as arterial injury, which is another risk factor for HTN [8,9]. Therefore, it is essential to investigate the antioxidant potential of diets since it helps increase the body's defenses against diseases [10]. Dietary total antioxidant capacity (dTAC) estimates have enabled the identification of good antioxidant sources [11] and their association with health outcomes such as obesity, inflammation, and hepatic steatosis [12–14].

The combination of all food items should be taken into consideration at the time of assessment of an individual's dietary antioxidant intake, based on dTAC. Therefore, it has a higher predictive capacity and biological importance than a single antioxidant [15].

There is an inverse association between dTAC and the prevalence/incidence of chronic diseases, suggesting that this methodology has a great potential for clinical and public health applications [2,16]. Longitudinal studies have confirmed that antioxidant-rich diets can indeed reduce blood pressure levels [2,17].

Hence, we aimed to investigate whether dTAC influences the association between smoking and HTN. Understanding this could help develop and implement nutritional strategies focused on managing this chronic disease and its clinical complications.

Methods

CUME project

The Cohort of Minas Gerais Universities (CUME) project, launched in 2016, aims to assess the impact of Brazilian dietary and nutritional transition patterns of NCDs among graduates and postgraduates from different universities in the Minas Gerais State, Brazil. The baseline data were collected through a self-completed electronic questionnaire in a virtual environment. Only participants who were invited via e-mail and signed the free informed consent form were allowed to complete the questionnaire. It was divided into two stages: 1) participants' demographic and socioeconomic features, lifestyle, and health conditions and 2) participants' food intake, based on a food frequency questionnaire (FFQ), as well as their dietary practices and eating environment.

The study was approved by the Human Research Ethics Committees of all participating institutions (UFMG: 07223812.3.3001.5153, UFV: 4483415.5.1001.5149, UFOP: 44483415.5.2003.5150, UFLA:44483415.5.2002.5148 and UFJF: 4483415.5.5133).

Project design, dissemination strategies, and first participants' baseline profiles were detailed in a previous study [18].

Study population

A cross-sectional, multicenter study was developed based on the 2016 and 2018 CUME project baseline data of participants who completed the online questionnaire, including an FFQ ($n = 4629$).

Participants whose energy intake was lower than 500 kcal ($n = 2$) and higher than 6000 kcal ($n = 128$) were excluded from the study [18,19]. Foreign participants ($n = 23$) and individuals living abroad during the survey period ($n = 173$) were also excluded. Thus, the final study sample comprised 4303 participants, 69.4% were women, 28.5% were >40 years old, and the mean age was 36 ($\pm$9.4) years.

Hypertension diagnosis

HTN, the dependent variable in the present study, was determined based on satisfaction of at least one of the following criteria [1]: systolic blood pressure $\geq$ 140 mmHg, diastolic blood pressure $\geq$ 90 mmHg, use of antihypertensive drugs, and previous diagnosis of HTN by a physician. Data regarding self-reported HTN under the CUME project were validated through in-person measurements, based on a standardized protocol by the laboratories involved in the project [20].

Dietary assessment and dTAC estimation

Participants' food intake and dTAC were estimated according to the data collected from March to August in 2016 and 2018 (when the baseline questionnaire was administered). The estimation was conducted through a quantitative FFQ with 144 food items previously validated for the Brazilian population [21] and some added food items. A photo album of serving sizes was developed for the current study and used alongside the questionnaire. The updated version was divided into food groups (dairy, meat and fish, cereals and legumes, oils and fats, fruits and vegetables, beverages, and other food items, which included food preparations, sugar, honey, and sweets). It

was also validated by a subsample study comprising of 146 CUME project participants, who provided all requested information via 24-h telephone recalls. Intraclass correlation coefficients (ICC) showed moderate agreement between the estimated intake and the reference tool (overall ICC = 0.44). It also evaluated the reproducibility of the self-reported FFQ, based on participants who completed the questionnaire twice within 1 year. There was a good agreement between the two assessments of participants' dietary intake (overall ICC = 0.76) (unpublished results).

The FFQ consisted of a list of the assessed food groups presented at the beginning of each page, and the participants were asked to select the foods they had eaten in the previous year, after which they were asked to report the portion size eaten, expressed in household measures often used in Brazil (e.g., a teaspoon, tablespoon, ladle, and cup) or traditional food portions (units, slices, or pieces) and intake frequency (daily, weekly, monthly or yearly).

Furthermore, all the intake frequencies were converted to measures of daily intake. Subsequently, daily food intake (grams or milliliters) was calculated by multiplying the serving size by intake frequency. The Brazilian food composition table [22] was used to calculate caloric (kcal) and nutrient intakes. Moreover, the United States Department of Agriculture's food composition table [23] was used for the same purpose when necessary.

The dTAC estimate was based on the ferric reducing antioxidant power (FRAP) assay, which measures the decrease in iron content in the presence of antioxidants [24]. Results were expressed in mmol per 100 g of food (mmol/100 g). Each participant's dTAC was calculated by multiplying the amount of FFQ-recorded food or drink by the corresponding FRAP value, and all food-item values were added. The FRAP values were obtained from a database previously published by Carlsen et al. (2010) [11] and combined with the supporting literature [25–29].

The following criteria were followed to assign a FRAP value to the FFQ items: 1) mean values were calculated for food items that presented more than one FRAP value available; 2) the values of similar food items that belonged to the same botanical group were assigned to those that did not have a value; 3) corresponding food FRAP values were used for items that did not have a value due to variations in preparing specific items or products (light, diet); and 4) no value was assigned to items that did not meet any of these criteria (15 items, such as meat and other animal-origin food). The dTAC without coffee was obtained through the same process, except for the exclusion of its antioxidant capacity.

Smoking status

The study compared mainly the "current and former smokers" to the "non-smokers" [30].

Covariates

Sociodemographic variables of interest in the present study comprised sex (male, female) and age (<40 years, ≥40 years).

Health status indicators adopted in the current study relied on weight status (non-overweight and overweight), which was determined based on individuals' body mass index (BMI), which was calculated as the self-reported weight in kilograms divided by the square of the height expressed in meters. Adult individuals were considered overweight when they had BMI ≥25 kg/m^2 [31], whereas elderly individuals were considered overweight when they had BMI ≥ 27 kg/m^2 [32]. Self-reported BMI was also previously validated [20].

Alcohol intake (yes/no) and physical activity level (insufficiently active or active) were the lifestyle variables. Participants who took at least 150 min of moderate-to-vigorous aerobic physical activity were classified as physically active [33].

Statistical analysis

Descriptive analysis was used for each variable. Variable normality was tested using the Shapiro–Wilk test. Inferential methods were used to assess the association between variables.

Differences in macro- and micronutrients and fruit and vegetable intake were investigated based on participants' smoking history using the Mann–Whitney test. The HTN explanatory model was achieved through multiple logistic regression based on the backward method. The odds ratio (OR) was estimated through logistic regression, which was performed based on the crude model (without adjustment) and multiple analyses (with adjustments).

Covariates associated with HTN, based on the literature, or statistical association through bivariate analysis (sex, age, academic background, physical activity, BMI, sodium, and alcohol intake) were used for adjustment purposes. All consumption variables were adjusted for total energy intake based on the residual method [34].

Logistic regressions were performed to assess the association between smoking and HTN, which was stratified based on the median dTAC (13.49 mmol/d) and dTAC without coffee (13.30 mmol/d), to evaluate whether dTAC affected this association. Data are reported as OR and 95% confidence interval (CI). The 'non-smoker' group was used as the reference.

Statistical analyses were performed using the STATA software version 13.0 (Stata Corporation, College Station, Texas, USA), using a statistical significance of 5%.

Results

Among the 4303 participants included in the study sample, 72.3% of participants reported drinking alcoholic beverages, and 36.6% were physically inactive. HTN and smoking had a prevalence of 11.9% and 8.4%, respectively. Both prevalence rates were higher in male participants (data not shown).

Model of HTN-associated factors

HTN prevalence was more associated with male sex, age ≥40 years, current and former smokers, higher dTAC

(≥13.49 mmol/d), no alcohol intake, insufficient physical activity and overweight (Table 1).

Dietary intake based on smoking

Energy and alcohol intake was higher among current and former smokers than among non-smokers. They also reported lower protein, carbohydrate, fiber, micronutrient intake (such as vitamin C and calcium) as well as higher sodium intake (Table 2).

Moreover, current and former smokers recorded lower fruit intakes than non-smokers, while, there was no difference in vegetable intake between these groups. They also recorded higher dTAC and dTAC without coffee than non-smokers (Table 2).

Groups and food items' rate of contribution to dTAC

We observed a higher contribution of coffee to dTAC; however, when it was excluded from the analysis, higher contributions of fruits, vegetables, and juice to dTAC was observed (Fig. 1).

Table 1 Prevalence of hypertension and its associated factors. The Cohort of Universities of Minas Gerais (CUME Project), 2016 and 2018.

Variables	Total		Hypertension		*p-values*[a]
	n	%	OR	CI (95%)	
Sex					
Female	2.984	69.4	1 (Ref.)	–	–
Male	1.319	30.6	1.29	(1.05–1.58)	0.015
Age (years)					
<40	3.078	71.5	1 (Ref.)	–	–
≥40	1.225	28.5	2.95	(2.42–3.59)	<0.001
Smoking					
Never smoked	3.425	79.6	1 (Ref.)	–	–
Current smoker and former smoker	878	20.4	1.31	(1.04–1.64)	0.021
dTAC (mmol/d)					
<13.49[b]	2.194	51.0	1 (Ref.)	–	–
≥13.49[b]	2.109	49.0	1.30	(1.06–1.59)	0.011
Alcohol intake					
Yes	3.112	72.3	1 (Ref.)	–	–
No	1.191	27.7	1.30	(1.04–1.62)	0.019
Physical activity level					
Active	2.730	63.4	1 (Ref.)	–	–
Insufficiently active[c]	1.573	36.6	1.30	(1.06–1.59)	0.010
Weight-status					
Not overweight	2.587	60.3	1 (Ref.)	–	–
Overweight	1.704	39.7	2.74	(2.24–3.37)	<0.001

OR: Odds Ratio; CI (95%): Confidence Interval of 95%; dTAC (mmol/d): Dietary total antioxidant capacity; Ref.: Reference.

[a] p-value from Logistic Regression.

[b] Median intake of the sample = 13.49 mmol/d.

[c] Insufficiently active: <150 min of moderate or vigorous activity per week (WHO, 2011a); Weight-status: Body Mass Index - not overweight (BMI < 25.0 kg/m^2 for adults and <27.0 kg/m^2 for elderly) and overweight (BMI≥ 25 kg/m^2 for adults and ≥27 kg/m^2 for elderly) (WHO, 1998; LIPSCHITZ, 1994).

Smoking, dTAC and hypertension

Current and former smokers were more likely to be hypertensive than non-smokers, even after the adjustments (Table 3).

When the analysis was stratified based on a median dTAC, current and former smokers with lower dTAC were highly likely to be hypertensive. However, this outcome changed after they were adjusted for age, BMI, academic background, physical activity, sodium, and alcohol intake. Current and former smokers with higher dTAC were highly likely to be hypertensive; however, this outcome changed after they were adjusted for BMI.

However, an opposite association was observed when coffee was excluded from the analysis. Current and former smokers who presented a lower dTAC without coffee were more likely to be hypertensive than non-smokers; even after the adjustments. However, there was no association between smoking and HTN among individuals with the highest dTAC without coffee consumption.

Discussion

Smoking has been shown to increase oxidative stress [35], which is associated with HTN due to baroreflex mitigation and nitric oxide bioactivity reduction [35]. Furthermore, smokers consume smaller amounts of antioxidant-rich food [4] than non-smokers.

Considering the above-mentioned fact, in this cross-sectional study, we hypothesized that smoking and antioxidant-rich food intake could have an antagonistic association with HTN and therefore if dTAC could influence the association.

Firstly, we compared the intake of nutrients and food groups with smoking, given the evidence that their food intake is worse than that of non-smokers, and that diets are modifiable factors capable of mitigating or exacerbating the association between smoking and NCDs [36].

Overall, smokers recorded a higher energy, alcohol, and sodium intake, as well as lower calcium intake, which are nutrients that have been associated with a high prevalence of HTN. They also recorded lower vitamin C and fruit intake, which are important contributors to dTAC. However, despite there being a significant difference in micronutrient intake between the two groups, the difference was small and may not have had a biological impact. Contrary to our hypothesis and the evidence in the literature, smokers recorded higher dTAC, even though higher values were associated with a higher prevalence of HTN. We emphasize that this association needs to be further investigated through longitudinal studies.

Furthermore, since coffee was a major contributor to dTAC in this population, and that smokers often drink high amounts of coffee and as the higher intake has been often associated with unhealthy behaviors [37], dTAC was evaluated both with and without coffee. In addition to these factors, it is necessary to exclude coffee antioxidants since the products of the Maillard reaction originated from the roasting process are the main contributors to the antioxidant

Table 2 Intake of antioxidant-rich food and nutrients, based on smoking. The Cohort of Universities of Minas Gerais (CUME Project), 2016 and 2018.

	Never Smokers (n = 3.425)		Former Smokers and Smokers (n = 878)		*p-values*[a]
Macronutrients	*mean*	*SD*[b]	*mean*	*SD*[b]	
Energy (kcal)	2363.6	923.8	2549.0	1025.1	**<0.001**
Total Fat (g/d)	91.0	22.3	91.6	23.2	0.635
Proteins (g/d)	109.7	32.5	106.0	36.0	**0.001**
Carbohydrate (g/d)	278.0	63.4	270.4	65.1	**0.001**
Total Fiber (g/d)	30.6	10.8	29.7	11.2	**0.003**
Alcohol (ml/d)	4.6	7.1	10.2	12.9	**<0.001**
Micronutrients					
Vitamin C (mg/d)	239.2	214.5	215.2	182.5	**0.001**
Vitamin E (mg/d)	9.6	3.5	9.6	4.1	0.195
Calcium (mg/d)	823.1	316.9	794.5	334.0	**0.001**
Potassium (mg/d)	3731.8	760.4	3700.5	781.5	0.471
Sodium (mg/d)	2368.5	942.5	2495.4	1164.1	**0.012**
Antioxidant sources					
Fruits (g/d)	452.4	322.3	421.8	353.9	**0.001**
Vegetables (g/d)	233.3	148.1	233.1	153.9	0.849
Dietary Total Antioxidant Capacity					
dTAC (mmol/d)	14.7	8.7	18.2	10.3	**<0.001**
dTAC[c] without coffee (mmol/d)	14.6	8.7	18.4	10.4	**<0.001**

[a] p-values recorded in the Mann–Whitney test.
[b] SD: standard deviation.
[c] dTAC: dietary total antioxidant capacity.
Intake variables were adjusted by energy intake, based on the residual method.

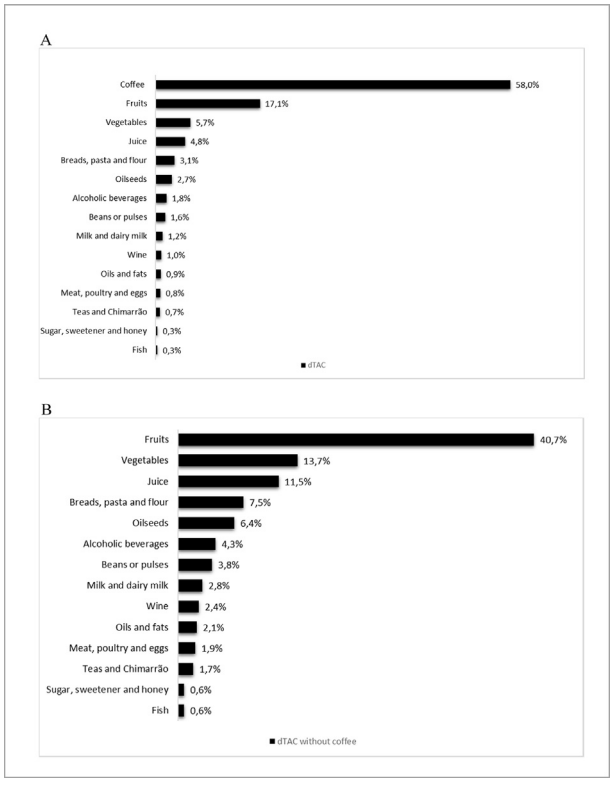

Figure 1 Groups and food items' contribution (%) to dTAC, with (1-A) or without coffee (1-B). The Cohort of Minas Gerais Universities (CUME Project), 2016 and 2018.

capacity and not the coffee itself [2]. However, the ability of the intestinal mucosa to absorb antioxidants derived from the Maillard reaction has been questioned, and the effect on endogenous defense remains unclear. Thus, coffee antioxidants may obscure the association between dTAC and study outcomes [2].

In the present study, performed among the graduate students from the different universities in Minas Gerais State, current and former smokers presented a higher likelihood of HTN. This association was in line with the results of another retrospective cohort study that confirmed the adverse effects of smoking on HTN [38] and with a cross-sectional study that reported the use of tobacco as a possible predictor of HTN [39]. Furthermore, based on the results of Atherosclerosis Risk in Communities, a longitudinal study conducted on 15,792 participants aged 45–64 years from four communities in the USA, we grouped these two variables because the risk of atherosclerotic diseases was lower among former smokers than among current smokers, but was not lower than that observed among non-smokers, since the risks associated with smoking can persist for up to 30 years [40].

According to the stratification based on dTAC, current and former smokers with higher dTAC were mostly likely to have HTN, which is contradictory, since dTAC is expected to be a protective factor. Furthermore, a longitudinal study recently found that high dTAC was associated with a reduced risk of HTN [2]. This outcome was even more significant when coffee antioxidants were excluded from the analysis. dTAC has also been associated with reduced arterial injury, another risk factor for HTN; however, this was specific for female individuals [9]. In turn, our results were independent of the major risk factors for HTN including sex, BMI, and lifestyle.

We, thus, assessed the interaction between sex and dTAC since antioxidant intake can act specifically

Table 3 Multivariate logistic regression based on the prevalence of hypertension. The Cohort of Universities of Minas Gerais (CUME Project), 2016 and 2018.

Variables	Hypertension		*P-value*
	OR	CI (95%)	
Never Smoker	1 (Ref.)	–	–
Former smoker and smoker	1.67	(1.35–2.05)	**<0.001**
Adjustment 1	1.58	(1.28–1.96)	**<0.001**
Adjustment 2	1.41	(1.13–1.74)	**0.002**
Adjustment 3	1.40	(1.12–1.74)	**0.003**
Adjustment 4	1.64	(1.32–2.04)	**<0.001**
dTAC			
<13.49 mmol/d			
Never Smoker	1 (Ref.)	–	–
Former smoker and smoker	1.54	(1.06–2.24)	**0.022**
Adjustment 1	1.46	(1.00–2.12)	**0.049**
Adjustment 2	1.33	(0.91–1.96)	0.141
Adjustment 3	1.34	(0.91–1.97)	0.133
Adjustment 4	1.57	(1.06–2.32)	0.025
≥13.49 mmol/d			
Never Smoker	1 (Ref.)	–	–
Former smoker and smoker	1.51	(1.17–1.96)	**0.002**
Adjustment 1	1.47	(1.14–1.91)	**0.003**
Adjustment 2	1.34	(1.03–1.74)	**0.030**
Adjustment 3	1.30	(0.99–1.71)	0.057
Adjustment 4	1.49	(1.14–1.94)	**0.004**
dTAC without coffee			
<13.30 mmol/d			
Never Smoker	1 (Ref.)	–	–
Former smoker and smoker	1.67	(1.34–2.08)	**0.001**
Adjustment 1	1.60	(1.28–1.99)	**<0.001**
Adjustment 2	1.42	(1.13–1.78)	**0.003**
Adjustment 3	1.40	(1.11–1.76)	**0.004**
Adjustment 4	1.63	(1.30–2.05)	**<0.001**
≥13.30 mmol/d			
Never Smoker	1 (Ref.)	–	–
Former smoker and smoker	1.49	(0.76–2.93)	0.245
Adjustment 1	1.33	(0.67–2.65)	0.419
Adjustment 2	1.30	(0.64–2.60)	0.464
Adjustment 3	1.19	(0.58–2.41)	0.638
Adjustment 4	1.43	(0.69–2.94)	0.334

Adjustment 1: Sex; Adjustment 2: Age (years); Adjustment 3: BMI (continuous); Adjustment 4: Academic background, Physical Activity, Sodium Intake (g/d), Ethanol Intake (g/d). Intake variables were adjusted based on the residual method.

depending on the sex of the individual [9]; however, no interaction was observed between them (data not shown).

However, there was an interaction between dTAC and smoking (OR = 1.90 95% CI [1.50, 2.40], $P < 0.001$) (Interaction analyses are not included in the supplementary material) supplementary material, which supported the current hypothesis that dTAC could influence the association between smoking and HTN. The imbalance between the two sexes in the investigated sample and the larger number of male smokers may also have influenced the association.

The association was stratified based on sex for clarification purposes and showed that a higher likelihood of HTN remained regardless of the participant's sex, even after adjusting for academic background, physical activity, sodium intake grams per day (g/d), and alcohol intake (g/d) (supplementary material).

The age of the participants is another factor that could have influenced these associations since HTN is more prevalent as individuals get older. Given this likely association, results were also analyzed based on age (<or ≥ than 40 years). The analysis showed a positive association between smoking and HTN in older individuals (supplementary material).

When the contribution of coffee to dTAC was excluded, current and former smokers with low dTAC were more likely to have HTN, but not those with a high dTAC. This outcome suggests that a high intake of antioxidants derived from sources other than coffee among smokers may mitigate the harmful effects of smoking on HTN.

Other studies that have shown an inverse association between dTAC and some NCDs, such as acute myocardial infarction [41], stroke [42], and type 2 diabetes [43], have excluded coffee antioxidants. Altogether, these findings corroborate the benefits of antioxidants derived from sources other than coffee.

The association between dTAC and oxidative stress levels is a matter of debate. The results of a cross-sectional study indicated an inverse association between dTAC and low-density lipoprotein oxidation, which is an oxidative stress marker used to investigate the risk of cardiovascular diseases [13].

Furthermore, a systematic review and dose–response meta-analysis of prospective studies showed a correlation between the intake of foods rich in antioxidants and the levels of nutrients in the plasma [6]. Knowing the action of antioxidants, it has been assumed that a high dTAC could stabilize free radicals and prevent cell damage. However, it is worth noting that these findings are not a suitable substitute for the non-measurement of oxidative stress.

Fruits and vegetables, which have shown the highest antioxidant contribution to the dTAC without coffee, are important sources of nutrients such as potassium, vitamins, fiber, antioxidants, and phytochemicals. Phytochemicals are one of the main antioxidant components of human diets [44,45] and hence have been consistently associated with a reduced risk of HTN [2,44,46]. This corroborates recommendations by the Dietary Approach to Stop Hypertension method, which is an interesting approach as it is balanced in nutrients that are involved in the pathophysiology of HTN, such as fatty acids, sodium, potassium, and calcium. Adherence to this diet should be recommended to help manage HTN since there is evidence of effectiveness in reducing blood pressure levels [47,48] and also in improving antioxidant capacity [49].

On the other hand, coffee is one of the most antioxidant-abundant food items; it comprises a wide range of bioactive compounds, such as caffeine, diterpenes and chlorogenic acids. Chlorogenic acids are the most abundant group of phenolic compounds observed in this beverage [50,51]. However, the effect of coffee on cardiovascular diseases, such as HTN, remains unclear [2].

Caffeine, which is an alkaloid with psychoactive properties, is the most widely investigated substance in coffee [2,51,52]. It has stimulating effects on the human sympathetic nervous system, which can lead to increased vascular resistance and high blood pressure levels [52,53]. Moreover, the harmful effects of coffee can also vary depending on the

cytochrome P4501A2 genotype (CYP1A2) [54,55]. CYP1A2 is an enzyme complex that metabolizes caffeine in the liver. Individuals can be classified as either fast (CYP1A2*1A) or slow caffeine metabolizers (CYP1A2*1F), depending on their genetic polymorphisms [56]. The adverse effects of caffeine are more significant for slow metabolizers, suggesting an increased risk of acute myocardial infarction [54] and HTN [55] in the group.

Noteworthily, a complementary analysis was performed to test the association between coffee consumption and HTN. The results showed an increased OR for HTN as the number of coffee cups consumed by participants also increased; however, this association did not remain after adjusting for age and BMI (supplementary material).

The current study had some limitations. Firstly, its cross-sectional design did not allow for assessment of the causality of the observed associations. However, studies of this nature allow the establishment of hypotheses that can be proven through longitudinal studies. Using FFQ to assess dietary intake and dTAC may lead to inaccurate outcomes due to the difficulty related in reporting the quantities, but using photo albums of serving sizes can help minimize bias. Moreover, the use of FFQ to assess dTAC has already been validated, where a strong positive correlation has been observed between them [57]. Furthermore, we did not assess plasma TAC to check bioavailability; however, there has been a positive correlation between dietary antioxidant intake and plasma TAC [58,59]. In addition, dTAC from FFQ was positively correlated with the plasma TAC in subjects with a dTAC above the median [57].

Another limitation of this study is the lack of oxidative stress measurements, but the method used to estimate dTAC was a reliable indicator for assessing the oxidative capacity of the diet and applicable for investigating the relationship between its antioxidant potential and health outcomes [12,57].

Additionally, residual confounding by some unmeasured or poorly measured factors cannot be totally ruled out. However, we adjusted for several potential confounding factors related to lifestyle and diet. Furthermore, the lack of dTAC data on Brazilian food items and knowledge about which cigarette was smoked by the participants could also be limitations to the current study. However, it is worth highlighting aspects such as sample size and participant's high schooling, which gave statistical power and good accuracy to the answers provided by them.

Overall, we investigated the effect of dTAC on the association between smoking and HTN in graduate students from different universities in the Minas Gerais State. The results provide additional information about the global intake of dietary antioxidants and their association with HTN, which is an important risk factor for cardiovascular outcomes. To the best of our knowledge, this is the first nationwide study to identify the influence of dTAC on the association between smoking and HTN. The current results highlight the importance of conducting longitudinal studies to determine causality between the analyzed variables.

In conclusion, current and former smokers, and those with high dTAC have a higher risk likelihood of having HTN, but this relationship appears to be influenced by coffee rather than other foods rich in antioxidants, such as fruits and vegetables. Therefore, the intake of fruits, vegetables, and antioxidant sources other than coffee should remain the focus of nutritional strategies for HTN, whereas moderate coffee intake should be recommended for hypertensive individuals. Although dTAC without coffee seems to attenuate the association between smoking and HTN, cessation of smoking remains an essential strategy for HTN control.

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Declaration of competing interest

The authors declare that they have no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.numecd.2021.05.025.

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