

The Correlation between Caffeine Intake and the Risk of Hypertension

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Abstract. *Background:* Hypertension is a common chronic disease. It can aggravate the risk of cardiovascular disease, stroke, kidney disease, etc., affecting people's health. Caffeine is a natural ingredient in many foods and beverages, which is more prevalent in people's daily intake. It is thought to have a possible effect on blood pressure. However, there is still controversy regarding the relationship between caffeine intake and risk of hypertension. Therefore, an in-depth study of the effects of caffeine on hypertension can help people develop sound dietary advice and strategies to prevent hypertension. *Methods:* 5153 participants from NHANES were included in the study. Measure blood pressure and identify hypertensive patients. Participants' dietary data were then collected via 24-hour food recall and food frequency questionnaires. Caffeine intake data were collected in the MEC dietary interview room. Considering covariates such as BMI, smoking status, alcohol intake and dietary salt intake. Analyzed using linear regression, non-linear regression and logistic regression. *Results:* A nonlinear relationship was shown between caffeine intake and systolic and diastolic pressure (Systolic blood pressure: p-value < 0.01; Diastolic blood pressure: p-value < 0.05). In the nonlinear relationship, a U-shaped curve and an inverted U-shaped curve were found by restrictive cubic spline models. A logistic regression also proved in this study that caffeine intake has a significant impact to the risk of hypertension (p-value < 0.01). Caffeine intake had no significant effect on blood pressure in menopausal women (p-value > 0.05). *Conclusion:* Our study shows U-shaped and inversed U-shaped association between caffeine intake and systolic and diastolic pressure. We also show that caffeine intake has positive affect the probability of getting hypertension.

Keywords: epidemiology, coffee, blood pressure.

1. Introduction

Hypertension, commonly known as high blood pressure, impact on people's health by its harmful symptoms, include heart stroke, blood vessel disease, and kidney damage [1]. According to the World

Health Organization (WHO), approximately 1.28 billion people aging from 30-79 years suffered from hypertension [1]. Based on the widespread impact of hypertension on society, establishing effective methods to prevent and treat hypertension requires more attention [2-8]. Some studies pointed out that there is a relationship between hypertension and caffeine [2,3]. Many foods or beverages containing caffeine serve as natural stimulants to provoke the neuron system and accelerate the heart rate, systolic forces, and diastolic forces, which will affect blood pressure theoretically. Discover the correlation between caffeine intake and hypertension would help us understanding the undergo mechanism of hypertension and seek insights of benefits from caffeine.

Although a lot of research has been conducted to investigate the specific relationship between caffeine intake and hypertension, debates still exist in the field of science. Some research considered that coffee intake plays a small role in increasing and developing hypertension [3,9]. On the contrary, some scientists claimed that consuming an appropriate amount of caffeine will either protect the heart and blood vessels or irrelevant with hypertension [4-5]. In these literatures, authors claimed that with more caffeine intake will benefit the prevention of hypertension. Therefore, the relationship between caffeine intake the risk of hypertension remained controversy on whether it could benefit the prevention of hypertension and thus needed more attention. Furthermore, some studies suggested that the relationship between caffeine intake and the risk of hypertension was inverse U-shaped [2,6], which gave an insight that caffeine intake could have inverse relationship to risk of hypertension depending on the amount of consumption. Others instead stated that there was no or a little non-linear relationship between the caffeine intake and hypertension [10,11]. The research mentioned above produced many controversies and differences. However, we still lack a uniform consensus on the correlation between caffeine intake and hypertension.

While previous studies have provided valuable insights, significant limitations and research gaps still exist. Notably, many prospective observational studies have been constrained by their narrow population focus, hindering the generalizability of their findings across diverse demographic groups, including gender, age, and ethnicity [3,7]. Similarly, in some studies, BMI (body mass index) [10], smoking [6], alcohol consumption [6,10], sodium intake [10], and other factors [6,10] were not included in the analysis as covariates, further limiting the comprehensiveness and depth of these studies.

This study aims to fill current research gaps and address the shortcomings of existing research through a more comprehensive research design. The primary objective of this study is to delve into the specific association between caffeine intake and hypertension risk, through detailed data analysis and model construction, reveal the underlying correlations and assist with the public health policy formulation and individual health management.

2. Methodology

2.1. Study population

The research objects of this study are from the participants of National Health and Nutrition Examination Survey (NHANES). NHANES is designed to collect data on the diet, nutritional status, health, and health behaviors of non-institutionalized US populations. The data were collected through home interviews, followed by specific inspection and medical examination and interviews.

Dietary data were collected using a combination of 24-hour food recall and food frequency questionnaires. The dataset has been filtered and will be further screened to ensure a diverse and representative sample. Further screening would facilitate the analysis of the relationship between caffeine intake and the risk of high blood pressure.

2.2. Blood Pressure and Hypertension

The outcome variable of concern in this study was the presence of hypertension. Researchers measured blood pressure in participants aged 8 years and older. Three measurements were taken. The first read was to make good preparations. The second is to maintain the correct posture. The third is to operate the blood pressure monitor (repeat the measurement at least three times at 1–2-minute intervals). The last is

to record and analyze. The purpose of the first blood pressure measurement is to obtain preliminary information about the participant's blood pressure at a given moment in time. However, pre-measurement activities and emotional state may affect the first measurement, resulting in some errors. The purpose of the second measurement is to reduce the chance of errors. The third measurement further validates the stability of the blood pressure and ensures accurate and consistent readings. In this study, a sample with diastolic blood pressure greater than 90 mmHg or systolic blood pressure greater than 140 mmHg is defined as hypertensive patients [1].

2.3. Caffeine Consumption

The main contributing factor in this study was caffeine intake. The data was collected in the mobile examination center (MEC) diet interview room. Participants would be provided with a set of measurement guidelines so that they could review what they eat. At the end of the interview, participants were given measuring cups, spoons, rulers, and a food modeling booklet, as well as 2D drawings containing guidelines for the various measurements available in the MEC. These tools were used to collect food types and quantities during telephone interviews.

2.4. Assessment of covariates

In addition to these two factors, several key covariates were considered to control for potential confounders. These include body mass index (BMI), smoking status, alcohol consumption and dietary salt intake. BMI could be calculated by measuring the height and weight of the participants. Data on smoking and alcohol use were obtained from home interview questionnaires. Dietary salt intake was estimated based on 24-hour dietary recall data. Standardized protocols were used in the process of collecting these variables, while other factors that could affect blood pressure were considered. This ensured a more comprehensive and accurate assessment of the relationship between caffeine intake and high blood pressure.

2.5. Statistical Analysis

Blood pressure was measured three times in the NHANES, and both diastolic and systolic blood pressure were measured each time. Therefore, the average of obtained blood pressure measurements was chosen as diastolic and systolic blood. Caffeine intake, alcohol intake, and sodium intake were averaged over two days (or separate values if only one day was available) to reflect a more general diet. This study also excluded samples without smoking status since many researchers have agreed that smoking has a significant impact on the effects of caffeine on blood pressure [2,7].

Since previous studies have suggested that there is a high probability of a nonlinear relationship between caffeine and blood pressure [2,4], nonlinear regression models with restrictive cubic spline were used to find the relationship between caffeine and hypertension adjusting by age, BMI, alcohol intake, sodium intake and sex. Considering that hypertension is a binary variable, logistic regression models were also used to analyze the relationship between caffeine intake and hypertension. Meanwhile, menopausal women are widely recognized to have a higher risk of high blood pressure [12-14]. A linear regression model for women over 50 years of age was used to analyze the relationship between caffeine intake and blood pressure. All analyses were done by using R version 4.4.1. All statistical tests were evaluated at an alpha level of 0.05.

3. Results

Table 1. Baseline characteristics of the study population by presence or absence of hypertension (N=5153)

	Hypertension (N=965)	No Hypertension (N=4188)	Overall (N=5153)	P- value
Diastolic: Blood pressure (mm Hg)				
Mean (SD)	86.1 (12.3)	70.1 (9.00)	73.1 (11.5)	<0.001
Median [Min, Max]	86.7 [44.0, 135]	70.0 [38.0, 90.0]	72.0 [38.0, 135]	
Systolic: Blood pressure (mm Hg)				
Mean (SD)	152 (14.8)	115 (12.0)	122 (19.1)	<0.001
Median [Min, Max]	149 [118, 219]	115 [76.3, 140]	119 [76.3, 219]	
Caffeine Intake (mg)				
Mean (SD)	134 (143)	121 (190)	124 (183)	<0.001
Median [Min, Max]	98.0 [0, 1140]	72.0 [0, 4680]	76.0 [0, 4680]	
Age (years)				
Mean (SD)	60.8 (14.4)	41.1 (20.4)	44.8 (20.9)	<0.001
Median [Min, Max]	63.0 [12.0, 80.0]	40.0 [12.0, 80.0]	46.0 [12.0, 80.0]	
BMI (kg/m**2)				
Mean (SD)	30.4 (7.13)	28.7 (7.48)	29.0 (7.44)	<0.001
Median [Min, Max]	29.2 [14.8, 64.2]	27.6 [13.2, 74.8]	27.9 [13.2, 74.8]	
Alcohol Intake (gm)				
Mean (SD)	8.29 (25.0)	5.96 (18.4)	6.40 (19.8)	0.002
Median [Min, Max]	0 [0, 388]	0 [0, 301]	0 [0, 388]	
Sodium Intake (mg)				
Mean (SD)	3250 (1590)	3310 (1550)	3300 (1560)	0.122
Median [Min, Max]	2960 [370, 12400]	3080 [86.0, 25900]	3070 [86.0, 25900]	
Smoking				
Yes	194 (20.1%)	797 (19.0%)	991 (19.2%)	0.748
No	771 (79.9%)	3391 (81.0%)	4162 (80.8%)	

There were 5153 participants including 965 people with hypertension and 4188 people without it overall in this study. Table 1 provided statistical descriptions of multiple variables for both hypertension and non-hypertension groups, including diastolic blood pressure, systolic blood pressure, caffeine intake, age, body mass index, alcohol intake, sodium intake, and whether participants smoke. Comparing the characteristic distribution of hypertensive and non-hypertensive populations, the mean and median diastolic blood pressure and systolic blood pressure of hypertensive people were significantly higher than those of non-hypertensive people. Meanwhile, the mean and median caffeine intake and alcohol

intake in the hypertensive group was also slightly higher than in the non-hypertension group, although the difference was not significant. And the mean age of the hypertensive group was significantly higher than that of the non-hypertension group, which is consistent with the theory that hypertension is usually age-related. The significant difference between the two groups was also seen in the BMI. Although studies have found a significant effect of sodium intake and smoking on hypertension, there was no significant difference between the mean and median values of sodium intake and smoking rate between the two groups.

Table 2. Restrictive cubic spline model results between blood pressure and caffeine intake

Characteristic	Systolic: Blood pressure (mm Hg)		Diastolic: Blood pressure (mm Hg)	
	Beta ¹	SE ²	Beta ¹	SE ²
Caffeine Intake (mg)				
x	-0.172***	0.063	-0.062	0.042
x ²	132***	45.9	67.6**	30.7
x ³	-138***	47.9	-70.8**	32.0
x ⁴	6.56***	2.14	3.60**	1.43
Age (years)	0.501***	0.012	0.100***	0.008
BMI (kg/m**2)	0.025	0.031	0.353***	0.021
Alcohol Intake (gm)	0.063***	0.012	0.063***	0.008
Sodium Intake (mg)	0.001***	0.000	0.000*	0.000
Smoking	-1.21**	0.596	-2.26***	0.398
Sex	0.372	0.456	0.035	0.305
No. Obs.	5,153		5,153	
Adjusted R ²	0.288		0.126	
AIC	43,307		39,148	

¹*p<0.1; **p<0.05; ***p<0.01
²SE = Standard Error
³x = Caffeine Intake (mg)

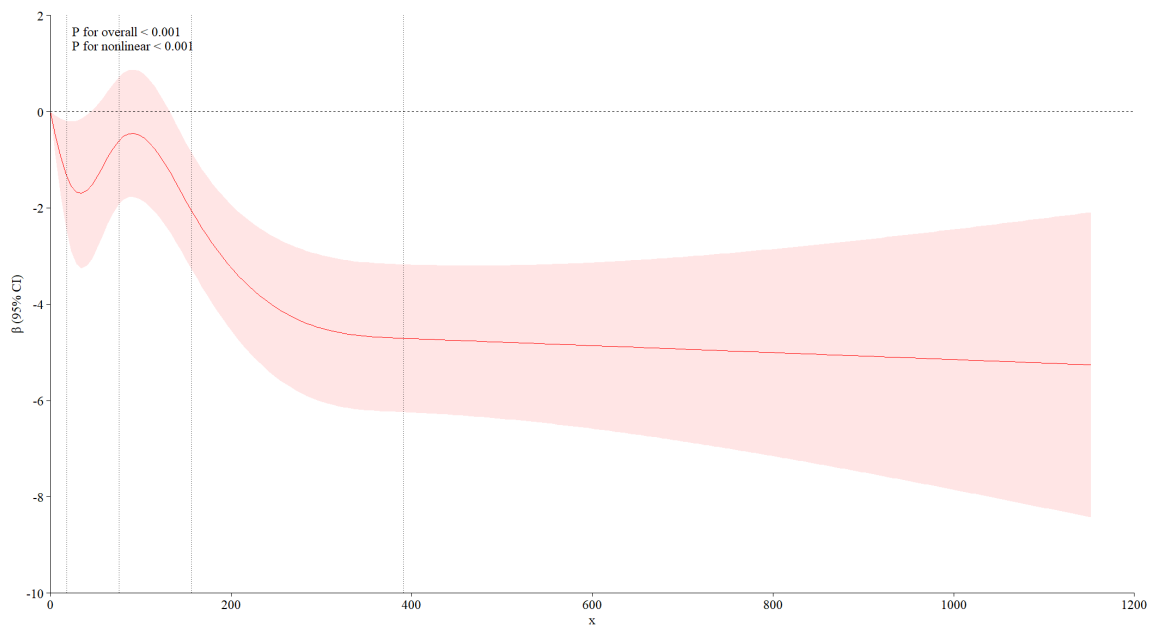


Figure 1. Coefficient of caffeine intake in systolic blood pressure

The vertical dashed lines represent the 0.05, 0.275, 0.5, 0.725, and 0.95 percentiles of caffeine intake, and their specific values are 0.0, 18.5, 76.0, 156.5, and 390.7 mg. Estimates were adjusted for age, BMI, alcohol intake, salt intake, smoking, and gender. The overall correlation p-value and nonlinear p-value were less than 0.001 for all outcomes.

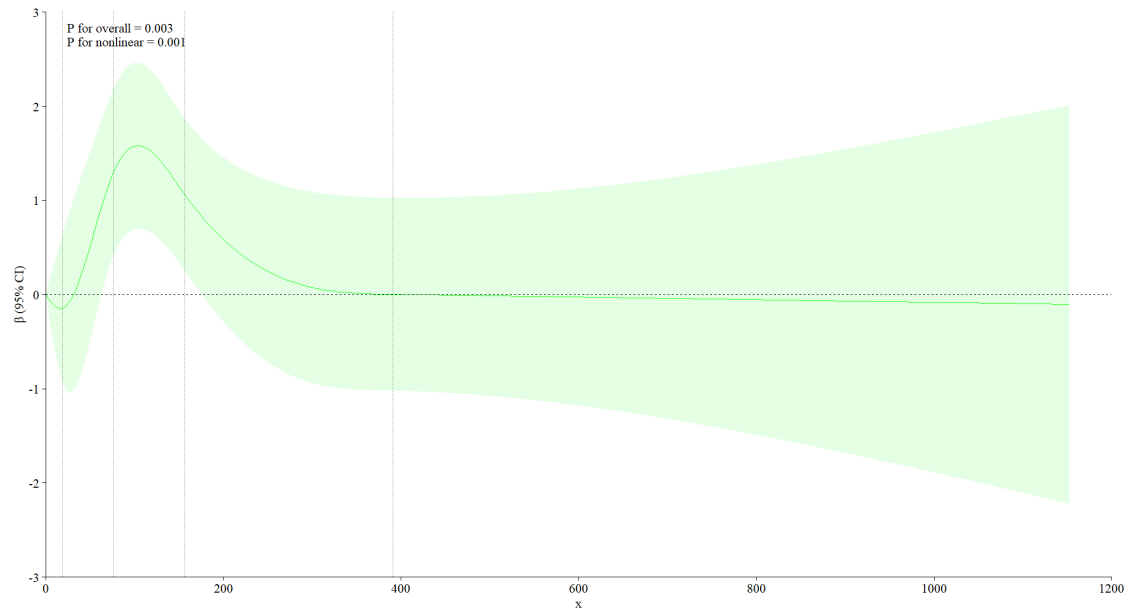


Figure 2. Coefficient of caffeine intake in diastolic blood pressure

The vertical dashed lines represent the 0.05, 0.275, 0.5, 0.725, and 0.95 percentiles of caffeine intake, and their specific values are 0.0, 18.5, 76.0, 156.5, and 390.7 mg. Estimates were adjusted for age, BMI, alcohol intake, salt intake, smoking, and gender. The overall correlation p-value was 0.003, and nonlinear p-value was 0.001.

The restrictive cubic spline model was used to observe a nonlinear relationship between caffeine intake and blood pressure. This study found that caffeine intake has a negative relationship with both systolic and diastolic blood pressure at caffeine intake below 18.5 mg, followed by a significant alternating positive and negative relationship (Figure 1, Figure 2). Although caffeine intake has the negative correlation with systolic blood pressure overall, a U-shaped relationship and an inverted U-shaped relationship also occur during the increase in caffeine intake (Figure 1). Caffeine intake was positively correlated with diastolic blood pressure over time as caffeine intake increased, although the effects fluctuated (Figure 2). This suggests that caffeine intake has a significant effect on both diastolic and systolic blood pressure, but the mechanisms of the effect are likely to be different.

Table 3. Logistic regression model results between hypertension and caffeine intake

Characteristic	Hypertension	
	OR ¹²	SE ²
Caffeine Intake (mg)	0.999***	0.000
Age (years)	1.06***	0.002
BMI (kg/m**2)	1.02***	0.005
Alcohol Intake (gm)	1.01***	0.002
Sodium Intake (mg)	1.00*	0.000
Sex	1.05	0.079
Smoking	0.736***	0.101

Table 3. (continued).

No. Obs.	5,153
AIC	4,173
BIC	4,226
¹ *p<0.1; **p<0.05; ***p<0.01	
² OR = Odds Ratio, SE = Standard Error	

The first two models are about the relationship between caffeine intake and blood pressure, which intuitively reflects the effect of caffeine on blood pressure. In order to analyze the relationship between caffeine intake and risk of hypertension, a logistic regression model was introduced for analysis. We found that for every milligram increase in caffeine intake, the chance of developing hypertension was reduced by about 0.1% (Table 3). However, the effect was statistically significant (p<0.01), although the actual magnitude was small.

Table 4. Linear regression model results between blood pressure and caffeine intake in menopausal women

Characteristic	Systolic: Blood pressure (mm Hg)		Diastolic: Blood pressure (mm Hg)	
	Beta ¹	SE ²	Beta ¹	SE ²
Caffeine Intake (mg)	-0.00081	0.002	-0.00263*	0.001
Age (years)	0.35542***	0.031	0.36870***	0.023
BMI (kg/m ²)	0.07333*	0.042	0.31918***	0.032
Alcohol Intake (gm)	0.07848***	0.019	0.06513***	0.014
Sodium Intake (mg)	0.00100***	0.000	0.00024	0.000
Smoking	-1.6238**	0.821	-1.2657**	0.623
No. Obs.	1,468		1,468	
Adjusted R ²	0.155		0.297	
AIC	11,543		10,734	
¹ *p<0.1; **p<0.05; ***p<0.01				
² SE = Standard Error				

Several studies have shown that menopausal women are at high risk of hypertension [12-14], we subset our dataset and reproduce the same analysis. Consistent with the results of previous studies by Rhee et al. [10], there was no significant relationship between caffeine intake and blood pressure in menopausal women (Table 4).

4. Discussion

This study suggests that caffeine intake has a moderating effect on blood pressure and is associated with the risk of developing hypertension. This is consistent with the finding of Zhenzhen Zhang, et al. [15] that certain components of coffee have the effect of lowering blood pressure. Gaeini et al. [5] found that coffee contains a variety of bioactive compounds such as chlorogenic acid, caffeol and cafestol. They have antioxidant, anti-inflammatory and vasodilatory effects, affect nitric oxide synthesis, lipid metabolism and endothelial function [16,17], and can lower blood pressure. Among the metabolites of chlorogenic acids, ferulic acid is able to positively affect blood pressure by increasing the bioavailability of nitric oxide and by enhancing the endothelium-dependent vasodilatory effects induced by acetylcholine [18, 19]. Other factors included in the model, such as age, BMI, alcohol and sodium intake, can also raise blood pressure. For example, blood vessel elasticity decreases with age, leading to increased blood pressure [20]. There is also the fact that people with higher BMI are usually associated with obesity and metabolic disorders leading to hypertension. Additionally, we found a tendency for

blood pressure to increase when a certain threshold was exceeded. This is related to the mechanism by which caffeine induces atherosclerosis by releasing norepinephrine and epinephrine which further cause vasoconstriction, thereby affecting vascular elasticity [21].

In order to make the final results more accurate, multiple studies have attempted large-scale data and scientific methods of analysis and incorporation of a number of confounding factors. We included age, sex, BMI, lifestyle and so on. Giuseppe et al [20] have also shown that these factors can influence blood pressure response to caffeine. Köksal et al. 's [9] study focused on age as a confounding factor, but also mentioned gender, BMI, waist circumference, smoking status and other factors that may be related to blood pressure. We recognize that the relationship between caffeine intake and hypertension is complex and can be influenced by a number of factors. In the selection of lifestyle confounding factors, we focused on smoking and alcohol consumption. Guessous et al. [22] also mention that smoking may affect the effect of coffee or caffeine on blood pressure. We analyzed it and got that caffeine has a moderating effect on blood pressure to some extent. And the results obtained by the meta of D'Elia et al. [4] are in line with ours to a certain extent. We also researched the effect of caffeine intake on systolic and diastolic blood pressure in menopausal women. Finally, it was concluded that caffeine intake in menopausal women was not associated with either blood pressure. This agrees with the findings of Rhee et al. [10].

Of course, there are many differences between us and other studies. We have some discrepancies compared to the findings of Köksal et al [9]. Our findings alternated between positive and negative correlations between caffeine intake and blood pressure values. But Köksal et al. noted positive correlation between caffeine and blood pressure. This may be due to differences in the study population and methods or other factors of the covariates considered. Our study population came from the NHANES database, whereas Chei et al. [2] chose a study population from the Singapore Chinese Health Cohort. The results may vary because the relationship between caffeine and blood pressure is influenced by different people's lifestyle, diet, genetic background and other factors. In conclusion, the assessment of caffeine intake in different studies is confounded by a number of factors. For example, blood pressure is not always measured in the same way.

There are some limitations to our study. First, there is the problem of under-representation of certain groups. The data used in our study came from NHANES. While the dataset is representative, it is not representative of the community as a whole. Moreover, we still have unconsidered covariates. Examples include individual genetic differences, dietary habits, and lifestyle. Lastly, we can't determine a causal relationship between caffeine and high blood pressure. Our study was conducted on observational data and the effect of confounding factors cannot be completely excluded. Therefore, our findings can only suggest an association between caffeine intake and hypertension. Our strength is that we used a non-linear model, which allows us to observe the relationship between caffeine intake and blood pressure values more comprehensively. We also analyzed specific populations. A subset of analyses was conducted for the high-risk group of menopausal women. This helps to provide more insight into the effect of caffeine on the risk of hypertension in different populations.

5. Conclusion

This study focused on the correlation between caffeine intake and risk of hypertension. The results present that caffeine has a modulating effect on blood pressure and is associated with the risk of developing hypertension. However, this study still has some limitations. For example, under representation of certain groups and the inability to establish a causal relationship between caffeine and hypertension. Currently, there is no basis to suggest that the adult population can prevent HPT by avoiding coffee consumption. Further research in this direction can be done in the future by incorporating more nuanced variables. It enables a better understanding of the relationship and its implications for public health and personal health management.

Author Contribution

All the authors contributed equally to this work and should be considered as co-first authors.

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