The link between dietary nutrients intake and cardiovascular diseases in cold regions

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Abstract

Background: The cold winter weather in northern China influences the dietary habits of its residents, contributing to a heightened risk of cardiovascular disorders, such as hypertension and coronary heart disease. Key factors include low vegetable consumption and high salt and fat intakes. This study aims to investigate the relationships between northern dietary nutrient intake in northern China and cardiovascular disorders during the winter season. Methods: A food frequency questionnaire tailored to the actual eating habits in northern China was designed. Retrospective data from 955 Chinese adults were collected from November to March between 2014 to 2023. Logistic regression was employed to analyze the relationship between dietary nutrients and cardiovascular diseases, with model performance assessed using receiver operating characteristic (ROC) curves. Results: Adjusted for gender, age, and body mass index (BMI), an inverse association was observed between vitamin A (OR = 0.706, 95% CI: 0.550, 0.907), nicotinic acid (OR = 0.584, 95% CI: 0.447, 0.762), phosphorus (OR = 0.777, 95% CI: 0.608, 0.994), selenium (OR = 0.719, 95% CI: 0.560, 0.923), zinc (OR = 0.683, 95% CI: 0.531, 0.880), methionine (OR = 0.730, 95% CI: 0.569, 0.936), arginine (OR = 0.753, 95% CI: 0.588, 0.964), lysine (OR = 0.758) 0.706, 95% CI: 0.550, 0.907), aspartic acid (OR = 0.730, 95% CI: 0.569, 0.936) and hypertension. Additionally, a negative association was found between niacin (OR = 0.752, 95% CI: 0.597, 0.946) and coronary heart disease. Conversely, a positive association was identified between iodine and hypertension (OR = 1.305, 95% CI: 1.020, 1.669) and coronary heart disease (OR = 1.301, 95% CI: 1.037, 1.634). Conclusion: Our study suggests that maintaining a balanced dietary intake of vitamin A, niacin, phosphorus, selenium, zinc, methionine, arginine, lysine, and aspartic acid can be beneficial in preventing hypertension. Adequate niacin intake is associated with a lower risk of coronary heart disease. However, excessive iodine intake may contribute to hypertension and coronary heart disease.

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1 Introduction

China's report on cardiovascular health and disease highlights a concerning increase in the prevalence of cardiovascular diseases (CVDs)[1]. In 2020, CVDs became the primary cause of death in urban and rural China, accounting for 48.00% in rural areas and 45.86% in urban areas. CVDs contributed to 2 out of every 5 deaths, with an estimated 330 million individuals affected, including 11.39 million with coronary heart disease and 245 million with hypertension^[2]. In 2020, risk factors for CVDs have surged among the Chinese population, with a consistent rise in factors such as dietary fat energy supply ratio[3], physical activity deficiency^[4], and obesity^[5], contributing to hypertension and coronary heart disease. Notably, salt intake remains significantly higher than recommended by dietary guidelines^[6].

In comparison to southern China, northern China experiences a more extended winter and lower average temperature^[7], drastically altering the winter eating habits of northern residents. Northern residents have lower vegetable intake and higher salt and fat intake during the winter season[8]. Sodium intake in the North averages 4,733 mg/d, substantially surpassing the 2,

491 mg/d in the South^[9]. Epidemiological studies^[10] indicate a noteworthy increase in the risk of CVDs, including hypertension, coronary heart disease, and heart failure, among the northern population compared to the south. It was found that the prevalence of hypertension varied significantly between the South and the North in A study involving 950,356 patients revealed a 4.25% increase in the North^[11]. Analyzing over 5 million people in China with World Health Organization methods and standards^[10], northern China exhibited significantly higher coronary heart disease rates and fatality rates than southern China, with the maximum difference reaching 32.9 times and 17.6 times, respectively.

The primary measures to prevent CVDs encompass both pharmaceutical interventions and lifestyle adjustment^[1]. While drug treatments benefit coronary heart disease patients, they come with higher costs and potential side effects. Lifestyle adjustments, including adopting healthy diets, engaging in regular exercise, quitting smoking, and weight management, are crucial aspects of preventive care. In-depth research has increasingly emphasized the economic, safe, and effective advantages of a healthy diet. In-depth research has increasingly emphasized the economic, safe, and effective advantages of a healthy diet. Currently, research on the effect of dietary nutrient intake on CVDs in cold regions of China predominantly focuses on excessive sodium salt intake, with limited exploration into other nutrient-centric vascular diseases.

Therefore, investigating the correlation between dietary nutrient intake and CVDs among individuals in cold regions of China holds significant practical and theoretical implications. Understanding the dietary nutrient intake and prevalence of the winter population in the north can provide valuable insights for preventive strategies and public health interventions.

2 Material and Methods

2.1 Study population

This study employed an online questionnaire to investigate the dietary nutrient intake and associated diseases in Northeast China from November to March between 2014 and 2023. A total of 1,210 subjects participated in the questionnaire and physical examination. Among them, 204 participants were excluded due to a history of smoking and heavy alcohol consumption, 25 were excluded for missing dietary intake data, and 24 were excluded due to severe underlying diseases. Consequently, 955 adults were included in the present study. T Exclusion criteria comprised individuals (1) younger than 18 years old, with unreasonable energy intake levels (> 4,200 kcal/d for male; > 4,000 kcal/d for female, < 600 kcal/d for all)^[12]; (2) with special

diseases, pregnant, smoking (defined as smoking one cigarette or more per day for over 6 months); (3) with excessive alcohol consumption (long-term drinking history of more than 5 years, equivalent to ethanol \geq 40 g/d for men and \geq 20 g/d for women, or heavy drinking history within 2 weeks, equivalent to ethanol > 80 g/d). This study was approved by the Ethics Committee of Harbin Medical University (HMUIRB2019006PRE).

2.2 Survey operations

This dietary survey was conducted online using the online dietary survey software (www.yyjy365.org/die) with a semi-quantitative food-frequency questionnaire on the types and frequency of food intake in the past three months. Information collected included gender, ethnicity, age, height, weight, waist circumference, smoking frequency, alcohol consumption, and disease history. Dietary intake data were converted online into daily intake of various nutrients.

2.3 Statistical analysis

Nutrient density (nutrients/energy) was utilized to measure the relationship between nutrients and disease. Age, body mass index (BMI), and nutrient density were described using the median and 25th and 75th percentiles for non-normally distributed data, and numbers (percentage) for categorical variables. Mann-Whitney U test or Chi-square test analyzed mean differences in age, sex, BMI, and dietary nutrient density between CVD patients and control groups. Binary logistic regression models were employed to determine odds ratios (ORs) and 95% confidence intervals (95% CIs) for association of hypertension and coronary heart disease (dependent variables) with nutrient density quartiles (independent variables). The crude model was unadjusted, while model 1 adjusted for age, sex, and BMI. Predictive abilities of the models were evaluated using ROC curve analysis, with the area under the curve (AUC) calculated. An AUC > 0.5 indicated favorable predictive values, with a higher AUC suggesting superior model performance. All analyses were conducted using SPSS 23.0 software (IBM), and significance was set at P < 0.05(two-tailed).

3 Results

3.1 Characteristics of subjects

Table 1 presents a comparison of baseline characteristics between patients and non-patients with hypertension and coronary heart disease among 955 subjects. The overall prevalence of hypertension was 5.97% and coronary heart disease was 7.33%. The coronary heart disease group

Table 1 Characteristics of variables in cardiovascular disease patients and controls

Group	Age group	Body Mass Index	Male, N (%)	Protein (g)	Fat (g)	Carbohydrate (g)
Hypertension	1					
No (N = 898)) 28.00 (26.00, 33.00)	20.79 (19.22, 23.33)	333.00 (94.07%)	90.51 (60.45, 122.12)	72.22 (45.87, 106.79)	387.04 (272.79, 509.90)
Yes (N = 57)) 28.00 (26.00, 37.50)	21.26 (19.6, 24.42)	21.00 (5.93%)	80.08 (56.27, 122.17)	64.27 (46.28, 88.20)	372.50 (285.82, 615.75)
<i>P</i> -value	0.555	0.125	< 0.001	0.388	0.197	0.419
Coronary Hea	art Disease					
No (N = 885)) 28.00 (26.00, 33.00)	20.82 (19.23, 23.39)	333.00 (94.07%)	90.42 (60.58, 122.17)	71.79 (45.66, 106.79)	388.28 (274.42, 511.81)
Yes (N = 70)) 28.00 (27.00, 40.25)	21.11 (19.31, 23.09)	21.00 (5.93%)	80.80 (53.28, 122.71)	69.33 (48.50, 87.80)	365.41 (224.89, 531.62)
<i>P</i> -value	0.023	0.858	< 0.001	0.185	0.694	0.474
Group	Riboflavin (mg)	Thiamine (mg)	Vitamin A (µg)	Vitamin B6 (mg)	Vitamin C (mg)	Vitamin E (mg)
Hypertension	1	-				
No (N = 898)) 1.41 (0.92, 2.05)	1.20 (0.82, 1.63)	925.54 (517.59, 1,710.44)	0.24 (0.14, 0.44)	120.08 (58.28, 209.39)	40.14 (24.87, 60.68)
Yes (N = 57)) 1.32 (0.82, 2.03)	1.16 (0.80, 1.89)	801.00 (284.87, 1,343.33)	0.24 (0.10, 0.53)	106.95 (61.73, 202.70)	38.23 (20.55, 64.54)
<i>P</i> -value	0.613	0.904	0.029	0.673	0.625	0.733
Coronary Hea						
•) 1.41 (0.93, 2.06)	1.20 (0.82, 1.64)	943.71 (519.69, 1705.79)	0.25 (0.13, 0.44)	121.98 (59.64, 213.96)	40.41 (24.92, 61.45)
` ') 1.22 (0.76, 1.93)	1.06 (0.74, 1.59)	735.89 (296.19, 1354.86)	0.21 (0.11, 0.46)	98.92 (48.79, 155.37)	34.64 (22.31, 56.64)
P-value	0.193	0.305	0.025	0.555	0.046	0.249
Group	Niacin (mg)	Folic acid (µg)	lodine (µg)	Calcium (mg)	Potassium (mg)	Phosphorus (mg)
Hypertension		1 c (p.g)	(1-3)	(3)		
) 20.38 (13.83, 28.73)	73.84 (41.44, 128.70)	81.86 (42.70, 125.39)	615.41 (375.11, 934.22)	2,542.93 (1,615.01, 3,642.86)	1.362.93 (919.71, 1.860.15)
) 18.00 (11.22, 29.79)	62.65 (25.54, 122.97)	104.42 (68.04, 153.63)	597.23 (340.93, 997.81)	2,482.19 (1,470.94, 4,019.28)	
P-value	0.225	0.238	0.013	0.862	0.788	0.524
Coronary Hea						
) 20.48 (13.76, 29.03)	73.97 (41.39, 127.68)	81.89 (42.21, 124.60)	618.73 (380.44, 935.29)	2.560.09 (1.637.66, 3.668.76)	1,362.79 (918.85, 1,878.76)
) 18.04 (10.95, 26.21)	59.07 (27.64, 146.35)	101.22 (68.07, 171.15)	543.73 (343.58, 939.36)		1,183.31 (782.70, 1,812.27)
P-value	0.119	0.292	0.002	0.247	0.181	0.221
Group	Magnesium (mg)	Manganese (mg)	Sodium (mg)	Iron (mg)	Copper (mg)	Selenium (µg)
Hypertension		Manganese (mg)	Socialii (ilig)	non (mg)	Copper (mg)	Seleman (µg)
• •) 440.03 (298.73, 645.32)	7.53 (5.34, 10.47)	2,568.41 (1,704.26, 3,732.52)	25.70 (17.67.36.19)	3.40 (2.33, 4.94)	63.46 (39.46, 94.65)
) 433.98 (260.22, 675.52)	7.22 (4.78, 11.47)	3,026.25 (2,014.28, 4,098.46)		3.28 (2.29, 5.05)	56.61 (37.66, 95.31)
P-value	0.806	0.790	0.111	0.887	0.741	0.387
		0.790	0.111	0.007	0.741	0.367
Coronary Hea		7.57 (5.00, 40.40)	0.500.77 (4.700.00, 0.700.07)	05.07.(47.07.00.70)	0.44 (0.05, 4.00)	00.40.(00.40.05.40)
` ') 442.46 (298.1, 647.99)	7.57 (5.33, 10.46)	2,562.77 (1,700.28, 3,728.87)	, , ,	3.41 (2.35, 4.92)	63.46 (39.40, 95.16)
) 412.58 (271.69, 595.50)	6.61 (5.13, 10.96)	2,983.25 (1,941.12, 4,107.40)	, , ,	3.23 (2.21, 5.03)	55.46 (34.62, 85.42)
P-value	0.342	0.347	0.041	0.740	0.247	0.175
Group	Zinc (mg)	Phenylalanine (mg)	Alanine (mg)	Methionine (mg)	Glycine (mg)	Glutamic (mg)
Hypertension						
) 14.37 (10.29, 20.04)		2,704.55 (1,582.74, 4,057.18)			10,006.82 (6,099.84, 14,887.29
` ') 13.36 (8.73, 19.64)		2,171.41 (1,622.00, 4,272.82)			9,515.27 (6,221.20, 15,955.90)
<i>P</i> -value	0.355	0.557	0.357	0.17	0.404	0.913
Coronary Hea	art Disease					
) 14.39 (10.30, 20.05)	2.450.90 (1.445.22, 3.531.06)	2,709.43 (1,601.39, 4,072.64)	806.53 (478.10, 1,227.53)	2,491.04 (1,447.51, 3,729.27)	10,167.11 (6,133.60, 14,999.23
No (N = 885)	, 1 1100 (10.00, 20.00)	, , . , . , . , . , . , , , , ,	, (, , , , ,			
) 12.71 (8.58, 19.92)	,	2,274.25 (1,465.48, 3,518.46)	650.94 (411.30, 1,103.53)	2,073.89 (1,408.37, 3,299.27)	8,312.50 (5,751.56, 13,982.29)

Continued

Table 1 Continued

Group	Cystine (mg)	Arginine (mg)		Lysine (mg)		Tyrosine (ı	mg)	Leucine	e (mg)	Proli	ne (mg)
Hypertension											
No (N = 898)	844.43 (494.29, 1,259.87)	3,335.42 (1,923.87, 4,9	976.38)	3,206.37 (1,909.13	3, 4,869.15)	1,819.72 (1,0	77.51, 2,674.60)	4,175.34	(2,465.20, 6,157.57)	3,051.2	24 (1,844.42, 4,506.25
Yes (N = 57)	838.53 (484.25, 1,484.28)	2,523.52 (1,886.05, 5,	025.71)	2,604.95 (1,729.35	5, 4,460.87)	1,501.33 (1,1	26.23, 2,802.08)	3,535.24	(2,626.79, 6,196.59)	3,271.	71 (1,821.18, 5,588.25
P-value	0.629	0.237		0.130		0.443		0.474		0.467	
Coronary Hea	art Disease										
No (N = 885)	854.68 (497.82, 1,290.68)	3,337.59 (1,922.76, 5,	003.71)	3,208.75 (1,916.36	6, 4,930.73)	1,819.53 (1,0	86.62, 2,684.79)	4,178.11	(2,487.75, 6,200.85)	3,117.5	56 (1,847.31, 4,557.99
Yes (N = 70)	710.08 (463.58, 1,202.81)	2,815.21 (1,882.05, 4,	812.81)	2,597.67 (1,734.08	3, 4,404.98)	1,477.30 (976	5.56, 2,359.55)	3,432.64	(2,230.87, 5,298.00)	2,633.8	35 (1,762.23, 4,403.17
P-value	0.223	0.198		0.090		0.118		0.119		0.226	
Group	Tryptophan (mg)	Serine (mg)	Thre	onine (mg)	Aspartic	(mg)	Valine (mg)		Isoleucine (mg	1)	Histidine (mg)
Hypertension											
No (N = 898)	682.79 (410.16, 998.28)	2,443.07 (1,444.74, 3,512.75)	2,174 3,169		4,910.27 (2 7,249.60)	2,923.00,	2,634.84 (1,58 3,837.36)	3.07,	2,361.87 (1,420.43 3,490.25)		1,367.87 (812.18, 2,034.38)
Yes (N = 57)	584.06 (445.65, 1006.89)	2,133.17 (1,504.37, 3,817.04)	1,809 3,271	59 (1,357.18, 83)	3,784.74 (2 7,818.86)	2,772.53,	2,303.76 (1,68 4,042.45)	1.28,	1,932.22 (1,511.23 3,764.42)		1,128.85 (852.37, 2,121.03)
P-value	0.630	0.688	0.443		0.258		0.497		0.349		0.429
Coronary Hea	art Disease										
No (N = 885)	683.64 (417.80, 1009.06)	2,443.68 (1,463.02, 3,538.73)	2,181 3,180	23 (1,303.60, 69)	4,919.08 (2 7,277.07)	2,956.43,	2,635.44 (1,60 3,873.66)	1.45,	2,362.93 (1,438.17 3,524.50)		1,367.91 (825.89, 2,039.53)
Yes (N = 70)	555.24 (373.39, 925.48)	1,950.61 (1,306.93, 3,361.83)	1,794. 2,818.	58 (1,200.29, 03)	4,018.36 (2 6,782.53)	2,743.24,	2,165.47 (1,46 3,302.72)	0.66,	1,932.71 (1,321.35 3,220.44)		1,140.37 (730.45, 1,812.08)
P-value	0.182	0.147	0.125		0.119		0.136		0.130		0.136

Data are presented as numbers (percentage) for categorical variables or 50th (25th, 75th) for continuous variables.

exhibited a higher proportion of individuals aged over 35 years than the non-coronary heart disease group, irrespective of gender. No significant differences were observed in the intake of most nutrients among those who fell ill. However, the hypertension group had higher iodine intake and lower vitamin A intake. The intake of iodine and sodium was higher in The coronary heart disease group had higher iodine and sodium intake but lower vitamin A and vitamin C intake (all *P* < 0.05)

3.2 Associations between cardiovascular disease and three major nutrients

No significant associations were found between coronary heart disease and protein, fat, and carbohydrate in both the crude and model 1 (Table 2). An inverse association was found between protein and hypertension, with *ORs* of 0.661 (95% CI: 0.512, 0.853) and 0.658 (95% CI: 0.506, 0.856) in crude and model 1, respectively. Across all models, no significant associations were found between carbohydrates and fat with hypertension.

3.3 Associations between hypertension and nutrients

Table 3 displays the *ORs* (95% CIs) of hypertension based on quartiles of nutrient density of vitamins, minerals, and amino acids. Univariate logistic regression analysis demonstrated

the intakes of various nutrients, including vitamin A (OR = 0.706, 95% CI: 0.550, 0.907), niacin (OR = 0.584, 95% CI: 0.447, 0.762), phosphorus (OR = 0.777, 95% CI: 0.608, 0.994), selenium (OR = 0.719, 95% CI: 0.560, 0.923), zinc (OR = 0.683, 95% CI: 0.531, 0.880), methionine (OR = 0.730, 95% CI: 0.569, 0.936), arginine (OR = 0.753, 95% CI: 0.588, 0.964), lysine (OR = 0.706, 95% CI: 0.550, 0.907), and aspartic (OR = 0.730, 95% CI: 0.569, 0.936), correlated with a decreased risk of hypertension. A significant positive correlation was observed between iodine intake and hypertension (OR = 1.305, 95% CI: 1.020, 1.669). These results remained consistent after adjusting for age, sex, and BMI (model 1).

3.4 Associations between coronary heart disease and nutrients

Table 4 presents the *ORs* (95% CIs) of coronary heart disease based on quartiles of nutrient density of vitamins, minerals, and amino acids. Univariate logistic regression analysis revealed that niacin (OR = 0.728, 95% CI: 0.581, 0.912), and methionine (OR = 0.797, 95% CI: 0.639, 0.996) intakes were correlated with a decreased risk of coronary heart disease, while iodine (OR = 1.336, 95% CI: 1.068, 1.672) and sodium (OR = 1.267, 95% CI: 1.014, 1.582) intakes were positively correlated with coronary heart disease. Adjusting for age, sex, and BMI (model 1) showed inverse associations between niacin intake and

Table 2 ORs and 95% CIs for hypertension and coronary heart disease according to the quartiles of nutrient density.

Nutrient density	Crude			Model 1				
	OR	95% CI	P-value	OR	95% CI	<i>P</i> -value		
Hypertension								
Protein	0.661**	0.512-0.853	0.001	0.658**	0.506-0.856	0.002		
Fat	0.949	0.747-1.206	0.669	0.962	0.756-1.224	0.755		
Carbohydrate	1.263	0.989-1.613	0.061	1.248	0.972-1.603	0.083		
Coronary heart disea	ase							
Protein	0.829	0.664-1.033	0.095	0.837	0.667-1.050	0.124		
Fat	1.236	0.991-1.543	0.060	1.231	0.985-1.537	0.067		
Carbohydrate	0.986	0.793-1.226	0.902	0.975	0.779-1.219	0.822		

CI, confidence interval; OR, odds ratio; Crude has not been adjusted by any potential factors; Model 1 has been adjusted by age, gender and body mass index; P < 0.05 or P < 0.01

coronary heart disease (OR = 0.752, 95% CI: 0.597, 0.946), and a positive association between iodine intake and coronary heart disease (OR = 1.301, 95% CI: 1.037, 1.634).

3.5 ROC analysis of hypertension

Table 5 shows the areas under the curves (AUC) for each nutrient density as a predictor factor of hypertension. The best cutoff value, sensitivity, specificity, and the maximum Youden index for each nutrient density were computed. The results showed that protein, vitamin A, niacin, phosphorus, selenium, zinc, methionine, arginine, lysine, and aspartic acid were identified as protective factors, while iodine was a risk factor for hypertension. After adjusting for age, sex, and BMI, the AUC was improved, as depicted in Fig. 1.

3.6 ROC analysis of coronary heart disease

Table 6 shows the AUC for each nutrient density as a predictor factor of coronary heart disease. Niacin was identified as a protective factor, and iodine as a risk factor for coronary heart disease. After adjusting for age, sex, and BMI, the AUC was improved, as illustrated in Fig. 2.

4 Discussion

In this study, we investigated the dietary structure of the winter population in northern China and explored its associations with CVDs. Our findings revealed an inverse association between vitamin A, niacin, phosphorus, selenium, zinc, methionine, arginine, lysine, aspartic acid, and hypertension. Similarly, niacin showed an inverse association with coronary heart disease. Conversely, iodine exhibited a positive association with hypertension and coronary heart disease.

Table 3 Associations between the quartiles of nutrient density and hypertension

Nutrient density	Crude	•		Model 1			
	OR	95% CI	P-value	OR	95% CI	<i>P</i> -value	
Vitamins							
Riboflavin	0.827	0.649-1.055	0.126	0.823	0.644-1.052	0.120	
Thiamine	0.948	0.746-1.205	0.661	0.922	0.721-1.178	0.516	
Vitamin A	0.706	0.550-0.907	0.007	0.678	0.525-0.875	0.003	
Vitamin B6	0.879	0.691–1.119	0.295	0.863	0.676-1.102	0.238	
Vitamin C	0.906	0.712-1.152	0.421	0.900	0.698-1.160	0.415	
Vitamin E	0.948	0.746-1.205	0.661	0.970	0.760-1.238	0.806	
Niacin	0.584**	0.447-0.762	< 0.001	0.588**	0.449-0.771	< 0.001	
Folic acid	0.816	0.640-1.041	0.101	0.805	0.630-1.028	0.083	
Minerals							
Lodine	1.305	1.020-1.669	0.034	1.316	1.026-1.688	0.031	
Calcium	0.920	0.723-1.169	0.495	0.920	0.716–1.182	0.514	
Potassium	0.866	0.680-1.102	0.242	0.857	0.665-1.104	0.232	
Phosphorus	0.777	0.608-0.994	0.044	0.778	0.606-0.999	0.049	
Magnesium	0.892	0.702-1.135	0.354	0.868	0.673-1.119	0.273	
Manganese	0.866	0.680-1.102	0.242	0.815	0.635-1.046	0.108	
Sodium	1.187	0.932-1.513	0.165	1.220	0.953-1.562	0.114	
Iron	0.892	0.702-1.135	0.354	0.877	0.686–1.120	0.293	
Copper	1.037	0.816-1.317	0.768	1.018	0.798-1.298	0.885	
Selenium	0.719	0.560-0.923	0.010	0.718	0.558-0.924	0.010	
Zinc	0.683**	0.531-0.880	0.003	0.672**	0.520-0.868	0.002	
Amino acids							
Phenylalanine	0.934	0.734–1.187	0.575	0.949	0.739–1.220	0.685	
Alanine	0.840	0.659-1.070	0.158	0.852	0.661–1.097	0.214	
Methionine	0.730	0.569-0.936	0.013	0.740°	0.572-0.958	0.022	
Glycine	0.892	0.702-1.135	0.354	0.907	0.706–1.166	0.447	
Glutamic	1.052	0.828-1.337	0.677	1.074	0.838-1.377	0.572	
Cystine	1.117	0.878-1.422	0.366	1.129	0.884-1.442	0.331	
Arginine	0.753	0.588-0.964	0.025	0.757 [*]	0.586-0.978	0.033	
Lysine	0.706	0.550-0.907	0.007	0.715 [°]	0.550-0.929	0.012	
Tyrosine	0.840	0.659-1.070	0.158	0.848	0.658-1.093	0.202	
Leucine	0.920	0.723-1.169	0.495	0.937	0.730-1.203	0.611	
Proline	1.117	0.878-1.422		1.141	0.890-1.463		
Tryptophan	0.920			0.940	0.732-1.206		
Serine	0.948			0.961	0.749–1.233		
Threonine	0.866	0.680-1.102		0.880	0.684–1.132		
Aspartic		0.569-0.936			0.563-0.948		
Valine	0.920			0.936	0.730–1.202		
Lsoleucine	0.853	0.670-1.086		0.859	0.668-1.104		
Histidine	0.879	0.691–1.119		0.898	0.698-1.154		

Notes: CI, confidence interval; OR, odds ratio; Crude has not been adjusted by any potential factors; Model 1 has been adjusted by age, gender and Body Mass Index; P < 0.05 or P < 0.01.

Table 4 Associations between the quartiles of nutrient density and coronary heart disease

Nutrient density	Crude)		Model 1			
	OR	95% CI	P-value	OR	95% CI	<i>P</i> -value	
Vitamins							
Riboflavin	0.882	0.709-1.098	0.262	0.856	0.685-1.070	0.172	
Thiamine	0.927	0.745-1.153	0.498	0.885	0.706-1.108	0.285	
Vitamin A	0.829	0.664-1.033	0.095	0.808	0.644-1.015	0.066	
Vitamin B6	0.951	0.764-1.182	0.648	0.929	0.745-1.158	0.510	
Vitamin C	0.871	0.700-1.085	0.218	0.813	0.644-1.026	0.081	
Vitamin E	0.905	0.727-1.125	0.368	0.906	0.726-1.131	0.383	
Niacin	0.728	0.581-0.912	0.006	0.752	0.597-0.946	0.015	
Folic acid	0.964	0.775–1.199	0.742	0.939	0.754-1.169	0.572	
Minerals							
Lodine	1.336	1.068-1.672	0.011	1.301	1.037-1.634	0.023	
Calcium	0.974	0.784-1.211	0.815	0.927	0.737-1.165	0.515	
Potassium	0.893	0.718-1.112	0.312	0.841	0.668-1.059	0.141	
Phosphorus	0.882	0.709-1.098	0.262	0.877	0.700-1.098	0.253	
Magnesium	0.905	0.727-1.125	0.368	0.846	0.672-1.067	0.157	
Manganese	0.893	0.718-1.112	0.312	0.846	0.675-1.060	0.145	
Sodium	1.267	1.014-1.582	0.037	1.253	0.997-1.576	0.053	
Iron	0.999	0.803-1.242	0.990	0.964	0.772-1.205	0.748	
Copper	0.916	0.736-1.139	0.430	0.878	0.704-1.095	0.248	
Selenium	0.851	0.683-1.060	0.149	0.839	0.672-1.049	0.124	
Zinc	0.850	0.682-1.059	0.147	0.831	0.665-1.039	0.104	
Amino acids							
Phenylalanine	0.916	0.736-1.139	0.430	0.934	0.743-1.173	0.555	
Alanine	0.850	0.682-1.059	0.147	0.864	0.686-1.088	0.213	
Methionine	0.797	0.639-0.996	0.046	0.811	0.643-1.023	0.077	
Glycine	0.871	0.700-1.085	0.218	0.891	0.708-1.121	0.324	
Glutamic	0.939	0.755-1.168	0.570	0.953	0.759-1.195	0.675	
Cystine	0.986	0.793-1.226	0.902	0.995	0.797-1.243	0.965	
Arginine	0.882	0.709-1.098	0.262	0.893	0.711-1.121	0.327	
Lysine	0.818	0.656-1.020	0.075	0.834	0.661-1.053	0.127	
Tyrosine	0.860	0.691-1.072	0.180	0.873	0.693-1.100	0.249	
Leucine	0.939	0.755–1.168	0.570	0.967	0.770-1.215	0.775	
Proline	0.974	0.784-1.211	0.815	0.990	0.790-1.240	0.929	
Tryptophan	0.939	0.755–1.168	0.570	0.960	0.765-1.206	0.728	
Serine	0.871	0.700-1.085	0.218	0.883	0.702-1.110	0.286	
Threonine	0.905	0.727-1.125	0.368	0.924	0.735–1.162	0.501	
Aspartic	0.85	0.682-1.059	0.147	0.858	0.681-1.082	0.195	
Valine	0.916	0.736-1.139	0.430	0.937	0.746-1.177	0.574	
Lsoleucine	0.905	0.727-1.125	0.368	0.918	0.732-1.153	0.462	
Histidine	0.882	0.709-1.098	0.262	0.903	0.718–1.137	0.386	

CI, confidence interval; OR, odds ratio; Crude has not been adjusted by any potential factors; Model 1 has been adjusted by age, gender and body mass index; P < 0.05 or P < 0.01.

CVDs. particularly hypertension and coronary heart disease. have been extensively studied in relation to dietary factors. The underlying mechanisms of hypertension often involve endothelial dysfunction, oxidative stress, and inflammation[13-14], while for coronary heart disease, the intricate interactions between local endothelial dysfunction, inflammatory reaction, lipid oxidation, hemostasis, and thrombosis play crucial roles[15-16]. Our study contributes to this body of knowledge by identifying specific nutrients associated with cardiovascular health. Specifically, we uncovered the relationships between the nutrient intake of various kinds and CVDs, with an inverse association between vitamin A. niacin, phosphorus. selenium, zinc, methionine, arginine, lysine, aspartic acid, and hypertension and an inverse association between Niacin and coronary heart disease. Conversely, iodine intake was positively associated with hypertension and coronary heart disease.

The inverse association between vitamin A intake and hypertension revealed in this study might be partially explained by a study documenting the participation of vitamin A in endothelial function through regulating the nitric oxide pathway^[17]. Additionally, vitamin A is known to possess antioxidative capacity against sulfur-based free radicals and anti-inflammation properties[18]. Vitamin A deficiency can be proinflammatory or promote existing inflammatory responses^[19-20]. In agreement with the inverse association between nicotinic acid and hypertension identified in this study, nicotinic acid has been reported to enhance endothelial nitric oxide production, promote vasodilation, and alleviating endothelial dysfunction[21-22]. Niacin plays a role in regulating abnormal lipid metabolism and improving endothelial function. as well as producing antioxidative and anti-inflammatory effects^[23]. Additionally, Niacin reduces endothelial oxidative stress by increasing the cellular content of nicotinamide adenine dinucleotide phosphate, and inhibiting the production of reactive oxygen species in endothelial cells^[23]. In addition, nicotinic acid can decrease the release of inflammatory markers^[24-25]. Clinical trials have also confirmed reductions in total mortality and coronary events and regression of coronary atherosclerosis after nicotinic acid treatment[26].

Excessive iodine intake, primarily through iodized salt and pickled foods, was positively associated with hypertension and coronary heart disease^[27]. Iodine is a trace element essential for the synthesis of thyroid hormones, but either excessive or insufficient iodine intake can have adverse effects on the body^[28]. Excessive iodine intake may also increase blood glucose level and blood pressure, thereby increasing the risk of hypertension and diabetes^[29]. Excessive iodine intake may lead to a decrease in serum HDL-C level and an increase

Table 5 Receiver operator characteristic analysis between nutrient density and hypertension

	AUC (95% CI)	Best cutoff	Sensitivity (%)	Specificity (%)	Maximum of Youden index
Protein					
Protein	0.549 (0.471–0.628)	0.059	63.20	50.90	0.14
Model of Protein#	0.600 (0.521-0.679)	0.075	40.40	81.10	0.22
Vitamins					
vitamin A	0.605 (0.526-0.685)	0.079	42.10	76.20	0.18
Model of vitamin A#	0.643 (0.559-0.727)	0.062	66.70	62.10	0.29
Nicotinic acid	0.657 (0.583-0.730)	0.088	49.10	76.60	0.26
Model of Nicotinic acid#	0.684 (0.612-0.756)	0.067	68.40	66.40	0.35
Minerals					
Lodine	0.582 (0.507-0.657)	0.058	61.40	50.80	0.12
Model of lodine#	0.628 (0.552-0.704)	0.060	61.40	59.20	0.21
Phosphorus	0.577 (0.501-0.654)	0.074	36.80	75.80	0.13
Model of Phosphorus#	0.619 (0.544-0.694)	0.044	89.50	30.70	0.20
Selenium	0.600 (0.528-0.673)	0.057	70.20	51.30	0.22
Model of Selenium#	0.636 (0.563-0.709)	0.054	77.20	51.00	0.28
Zinc	0.615 (0.537-0.692)	0.080	43.90	76.30	0.20
Model of Zinc#	0.657 (0.584-0.729)	0.062	64.90	61.40	0.26
Amino acids					
Methionine	0.596 (0.523-0.669)	0.057	64.90	51.00	0.16
Model of Methionine#	0.632 (0.560-0.705)	0.051	75.40	46.80	0.22
Arginine	0.587 (0.519-0.654)	0.058	64.90	51.00	0.16
Model of Arginine#	0.625 (0.552-0.699)	0.051	75.40	46.50	0.22
Lysine	0.605 (0.535–0.676)	0.057	68.40	51.20	0.20
Model of Lysine#	0.636 (0.562-0.709)	0.051	75.40	48.00	0.23
Aspartic acid	0.596 (0.527-0.665)	0.057	68.40	51.20	0.20
Model of Aspartic acid#	0.632 (0.560-0.705)	0.051	73.70	47.30	0.21

AUC, area under the curve; CI, confidence interval; Sensitivity + specificity - 1; Model has been adjusted by age, gender and body mass index.

Table 6 Receiver operator characteristic analysis between nutrient density and coronary heart disease

	AUC (95% CI)	Best cutoff	Sensitivity (%)	Specificity (%)	Maximum of Youden index*
Vitamins					
Nicotinic acid	0.597 (0.527–0.667)	0.090	40.00	76.30	0.16
Model of Nicotinic acid#	0.623 (0.553-0.693)	0.067	68.60	53.70	0.22
Minerals					
Lodine	0.589 (0.519-0.658)	0.090	38.60	76.00	0.15
Model 1 of lodine#	0.609 (0.540-0.678)	0.060	72.90	45.60	0.19

AUC, area under the curve; CI, confidence interval; Sensitivity + specificity - 1; Model has been adjusted by age, gender and body mass index.

in LDL-C level. Serum HDL-C is an anti-atherosclerosis lipoprotein, which can clear excess cholesterol in the body and prevent coronary heart disease. Serum LDL-C is involved in the transport of endogenous cholesterol and cholesterol esters, which can cause atherosclerosis^[29]. An animal study found that dietary phosphorus had significant hypertension-heightening and hypotensive effects in spontaneously hypertensive and normotensive rats^[30]. Phosphorus plays an important role in maintaining cellular structure and function

and can affect the regulation of hypertension. Phosphorus is closely involved in calcium regulation [31]. Another study [32] unveiled a close correlation between dietary phosphorus and calcium in the context of hypotension. Phosphorus may affect blood pressure by regulating hormones through calcium [33] that can stabilize cell membrane [34], and calcium load can impair vascular smooth muscle contractility [33]. A study [35] involving 710 Belgium individuals between 1985 and 1998 uncovered that hypotension in men had selenium concentrations > 20 μ g/L.

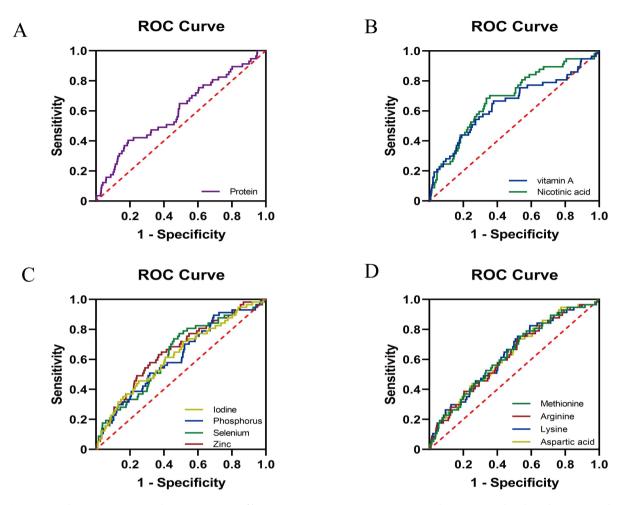


Fig. 1 Areas under receiver operating characteristic curves of hypertension. A, protein; B, Vitamins; C, Minerals; D, Amino acids (Adjusted estimation: adjusted for gender, age, and BMI).

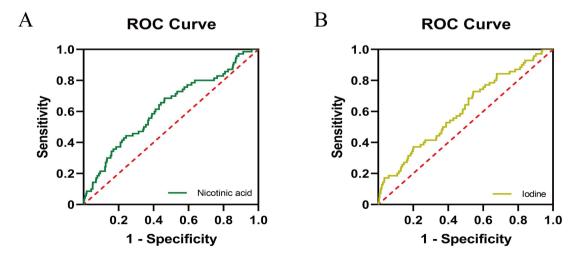


Fig. 2 Areas under receiver operating characteristic curves of coronary heart disease. A, Nicotinic acid; B, Iodine (Adjusted estimation: adjusted for gender, age, and BMI).

A study involving 2169 Inuit individuals indicate that patients with low selenium and high mercury levels were more likely to develop cardiovascular disease, suggesting that selenium may have a hypotensive effect^[36]. To date, evidence for the potential role of trace element zinc in hypertension has been rare and contradictory. A study[37] reported an inverse relationships between dietary zinc and systolic blood pressure in young obese women and no correlation between serum and urine zinc concentrations and systolic or diastolic blood pressure after adjusting for dietary intake. An animal study[38] showed that excessive zinc intake increased systemic blood pressure and reduced renal blood flow. However, an inverse correlation between blood pressure and serum zinc was also observed[39]. Another animal model study[40] suggested a link between hypertension and zinc deficiency through unknown mechanisms.

We found an inverse association between dietary protein and hypertension, consistent with the data reported by other researchers^[41]. While such phenomenon may be attributable to certain specific amino acids, limited research on the potential links between dietary amino acids and human blood pressure has been published. The inverse associations between methionine, arginine, lysine, aspartic acid, and hypertension were observed in this study. The effect of methionine on blood pressure appears to be indirectly mediated by an elevation of homocysteine levels^[42-43]. Arginine is a precursor of vasodilator nitric oxide[44] that can reduce systolic and diastolic blood pressures. Another study[45] found a link between the ratio of arginine to lysine and the incidence rate of hypertension. Markus et al.[46] found that lysine has an inhibitory effect on hypertension through metabonomic research. Aspartic acid can regulate blood pressure through altering arginine levels^[47]. Our findings imply that properly guided intake of vitamins, minerals, amino acids and iodized salt, and balanced energy metabolism should be implemented for the prevention of CVDs in Northeast China.

There were several limitations in our study. First, the subject participated the present study through the online dietary survey voluntarily and randomly, and the sample size of the population was relatively small. Compared to the full coverage data obtained by the census, our study needs to be verified in

a large number of people. Second, Dietary investigation is an observational study. In order to have a deeper understanding of the relationship between dietary intake and hypertension and coronary heart disease, dietary intervention experiments need to be performed for verifying the results.

5 Conclusion

In conclusion, our study identifies specific dietary factors associated with hypertension and coronary heart disease in the unique context of extremely cold winters in northern China. Understanding these associations can inform public health strategies to address cardiovascular disease risks related to dietary habits and contribute to promoting healthier eating attitudes among residents in northern China.

Author contributions

Feng R N and Wang C conceived the study design. Hong Q Q, Cao J J and Li J did the data acquisition. Hong Q Q, Deng L X, Wang J and Zhao Y did the statistical analysis. Hong Q Q and Wang C wrote the manuscript. All authors approved the submitted draft.

Ethics approval

This study was approved by the Ethics Committee of Harbin Medical University (HMUIRB2019006PRE).

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Conflict of interest

All authors did not have any competing interest to declare.

Data availability statement

The data are available from the corresponding author on reasonable request.

References

[1] Report on Cardiovascular Health and Diseases in China 2021: An Updated Summary. BES, 2022; 35 (7): 573-603.

[2] Report on Cardiovascular Health and Diseases in China 2022: Key points interpretation. Chin J Cardiovasc Sci, 2023; 28 (4): 297-312. (In

Chinese)

- [3] Zhai F Y, Du S F, Wang Z H, et al. Dynamics of the Chinese diet and the role of urbanicity, 1991-2011. Obes Rev, 2014; 15 Suppl 1 (1): 16-26.
- [4] Ng S W, Norton E C, Popkin B M. Why have physical activity levels declined among Chinese adults? Findings from the 1991-2006 China health and nutrition surveys. Soc Sci Med, 2009; 68 (7): 1305-1314.
- [5] Mi Y J, Zhang B, Wang H J, et al. Prevalence and secular trends in obesity among Chinese adults, 1991-2011. Am J Prev Med, 2015; 49 (5): 661-669.
- [6] Du S, Batis C, Wang H, et al. Understanding the patterns and trends of sodium intake, potassium intake, and sodium to potassium ratio and their effect on hypertension in China. Am J Clin Nutr, 2014; 99 (2): 334-343
- [7] Wang C, Zhang Z, Zhou M, *et al.* Nonlinear relationship between extreme temperature and mortality in different temperature zones: A systematic study of 122 communities across the mainland of China. Sci Total Environ, 2017; 586: 96-106.
- [8] Wang M, Huang Y, Song Y, et al. Study on environmental and lifestyle factors for the north-south differential of cardiovascular disease in China. Front Public Health, 2021; 9: 615152.
- [9] Anderson C A, Appel L J, Okuda N, *et al.* Dietary sources of sodium in China, Japan, the United Kingdom, and the United States, women and men aged 40 to 59 years: the INTERMAP study. J Am Diet Assoc, 2010; 110 (5): 736-745.
- [10] Wu Z, Yao C, Zhao D, et al. Multiprovincial monitoring of the trends and determinants of cardiovascular diseases (Sino-MONCA project)--III.Association between risk factor levels and cardiovascular disease. Lung and Blood Vessel Medical Center, 1998 (2): 5-8. (In Chinese)
- [11] PRC National Blood Pressure Survey Cooperative Group. Prevalence and development trends of hypertension in China. Chinese Journal of Hypertension, 1995 (S1): 9-15. (In Chinese)
- [12] Guo P, Zhu H, Pan H, et al. Dose-response relationships between dairy intake and chronic metabolic diseases in a Chinese population. J Diabetes, 2019; 11 (11): 846-856.
- [13] Guzik T J, Touyz R M. Oxidative stress, inflammation, and vascular aging in hypertension. Hypertension, 2017; 70 (4): 660-667.
- [14] Loperena R, Harrison D G. Oxidative stress and hypertensive diseases. Med Clin North Am, 2017; 101 (1): 169-193.
- [15] Ross R. The pathogenesis of atherosclerosis: a perspective for the 1990s. Nature, 1993; 362 (6423): 801-809.
- [16] Fuster V, Badimon L, Badimon J J, et al. The pathogenesis of coronary artery disease and the acute coronary syndromes (2). N Engl J Med, 1992; 326 (5): 310-318.
- [17] Achan V, Tran C T, Arrigoni F, et al. all-trans-Retinoic acid increases nitric oxide synthesis by endothelial cells: a role for the induction of dimethylarginine dimethylaminohydrolase. Circ Res, 2002; 90 (7): 764-769.
- [18] Jialal I, Norkus E P, Cristol L, *et al.* beta-Carotene inhibits the oxidative modification of low-density lipoprotein. Biochim Biophys Acta, 1991; 1086 (1): 134-138.
- [19] Reifen R. Vitamin A as an anti-inflammatory agent. Proc Nutr Soc, 2002; 61 (3): 397-400.
- [20] Wiedermann U, Chen X J, Enerbäck L, *et al.* Vitamin A deficiency increases inflammatory responses. Scand J Immunol, 1996; 44 (6): 578-584.

- [21] Sahebkar A. Effect of niacin on endothelial function: a systematic review and meta-analysis of randomized controlled trials. Vasc Med, 2014: 19 (1): 54-66.
- [22] Wu B J, Yan L, Charlton F, et al. Evidence that niacin inhibits acute vascular inflammation and improves endothelial dysfunction independent of changes in plasma lipids. Arterioscler Thromb Vasc Biol, 2010; 30 (5): 968-975
- [23] Zeman M, Vecka M, Perlík F, et al. Pleiotropic effects of niacin: Current possibilities for its clinical use. Acta Pharm, 2016; 66 (4): 449-469
- [24] Thoenes M, Oguchi A, Nagamia S, et al. The effects of extended-release niacin on carotid intimal media thickness, endothelial function and inflammatory markers in patients with the metabolic syndrome. Int J Clin Pract, 2007; 61 (11): 1942-1948.
- [25] Kuvin J T, Dave D M, Sliney K A, *et al.* Effects of extended-release niacin on lipoprotein particle size, distribution, and inflammatory markers in patients with coronary artery disease. Am J Cardiol, 2006; 98 (6): 743-745.
- [26] Tavintharan S, Kashyap M L. The benefits of niacin in atherosclerosis. Curr Atheroscler Rep, 2001; 3 (1): 74-82.
- [27] Rust P, Ekmekcioglu C. Impact of salt intake on the pathogenesis and treatment of hypertension. Adv Exp Med Biol, 2017; 956: 61-84.
- [28] Yadav K, Pandav C S. National iodine deficiency disorders control programme: Current status & future strategy. Indian J Med Res, 2018; 148 (5): 503-510.
- [29] Liu J, Liu L, Jia Q, et al. Effects of excessive iodine intake on blood glucose, blood pressure, and blood lipids in adults. Biol Trace Elem Res, 2019; 192 (2): 136-144.
- [30] Bindels R J, Van Den Broek L A, Hillebrand S J, et al. A high phosphate diet lowers blood pressure in spontaneously hypertensive rats. Hypertension, 1987; 9 (1): 96-102.
- [31] Felsenfeld A J, Rodriguez M. Phosphorus, regulation of plasma calcium, and secondary hyperparathyroidism: a hypothesis to integrate a historical and modern perspective. J Am Soc Nephrol, 1999; 10 (4): 878-800
- [32] Elliott P, Kesteloot H, Appel L J, *et al.* Dietary phosphorus and blood pressure: international study of macro- and micro-nutrients and blood pressure. Hypertension, 2008; 51 (3): 669-675.
- [33] Resnick L M. The role of dietary calcium in hypertension: a hierarchical overview. Am J Hypertens, 1999; 12 (1 Pt 1): 99-112.
- [34] Das U N. Nutritional factors in the pathobiology of human essential hypertension. Nutrition, 2001; 17 (4): 337-346.
- [35] Nawrot T S, Staessen J A, Roels H A, *et al.* Blood pressure and blood selenium: a cross-sectional and longitudinal population study. Eur Heart J, 2007; 28 (5): 628-633.
- [36] Hu X F, Eccles K M, Chan H M. High selenium exposure lowers the odds ratios for hypertension, stroke, and myocardial infarction associated with mercury exposure among Inuit in Canada. Environ Int, 2017; 102: 200-206.
- [37] Kim J. Dietary zinc intake is inversely associated with systolic blood pressure in young obese women. Nutr Res Pract, 2013; 7 (5): 380-384.
- [38] Kasai M, Miyazaki T, Takenaka T, et al. Excessive zinc intake increases systemic blood pressure and reduces renal blood flow via kidney angiotensin II in rats. Biol Trace Elem Res, 2012; 150 (1-3): 285-290.
- [39] Bergomi M, Rovesti S, Vinceti M, et al. Zinc and copper status and

blood pressure. J Trace Elem Med Biol, 1997; 11 (3): 166-169.

- [40] Williams C R, Mistry M, Cheriyan A M, et al. Zinc deficiency induces hypertension by promoting renal Na (+) reabsorption. Am J Physiol Renal Physiol, 2019; 316 (4): F646-F653.
- [41] Altorf-Van Der Kuil W, Engberink M F, Brink E J, *et al.* Dietary protein and blood pressure: a systematic review. PLoS One, 2010; 5 (8): e12102
- [42] Robin S, Maupoil V, Groubatch F, et al. Effect of a methionine-supplemented diet on the blood pressure of Wistar-Kyoto and spontaneously hypertensive rats. Br J Nutr, 2003; 89 (4): 539-548.
- [43] Ditscheid B, Fünfstück R, Busch M, et al. Effect of L-methionine supplementation on plasma homocysteine and other free amino acids: a placebo-controlled double-blind cross-over study. Eur J Clin Nutr, 2005;

- 59 (6): 768-775.
- [44] Raghavan S A, Dikshit M. Vascular regulation by the L-arginine metabolites, nitric oxide and agmatine. Pharmacol Res, 2004; 49 (5): 397-414.
- [45] Altorf-Van Der Kuil W, Engberink M F, De Neve M, et al. Dietary amino acids and the risk of hypertension in a Dutch older population: the Rotterdam Study. Am J Clin Nutr, 2013; 97 (2): 403-410.
- [46] Rinschen M, Palygin O, Golosova D, et al. Accelerated lysine metabolism conveys kidney protection in salt-sensitive hypertension. Nat Commun, 2022; 13 (1): 4099.
- [47] Hou E, Sun N, Zhang F, et al. Malate and Aspartate Increase L-Arginine and Nitric Oxide and Attenuate Hypertension. Cell Rep, 2017; 19 (8): 1631-1639.