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Dietary zinc intake and 10-year atherosclerotic cardiovascular disease risk in diabetes mellitus patients: evidence from NHANES database

Xiaoqiong Lyu[1*], Liping Chen[2] and Wenbin Wang[1]

Abstract

Objective Atherosclerotic cardiovascular disease (ASCVD) is the leading cause of death in diabetes mellitus (DM) patients. Oxidative stress and inflammation are important pathological mechanisms affecting the occurrence and development of ASCVD in DM patients. Dietary zinc acts a key role in anti-oxidation, anti-inflammation and blood glucose regulation. This study purposes to explore the relationship between dietary zinc intake and 10-year ASCVD in DM patients.

Methods Based on the National Health and Nutrition Examination Survey (NHANES) 2007–2018, the 10-year risk of ASCVD was assessed using the 2018 ACC/AHA guidelines & pooled cohort equations model. The total dietary zinc intake was calculated through 24-h dietary recall. Weighted univariable, multivariate logistic regression and restricted cubic splines (RCS) were performed to evaluate the association between dietary zinc intake and 10-year risk of ASCVD among patients with DM. Stratified analysis based on the history of hypertension, dyslipidemia and hypoglycemic agent's treatment were further evaluated these associations.

Results Finally, we included 3,053 DM patients, of which 1,245 (40.78%) had high risk of 10-year ASCVD. We found higher dietary zinc intake was related to lower 10-year ASCVD risk among patients with DM (OR = 0.77, 95%CI: 0.61–0.99, $P = 0.044$), especially in patients with hypertension (OR = 0.53, 95%CI: 0.36–0.80), dyslipidemia (OR = 0.74, 95%CI: 0.58–0.95, $P = 0.019$), and hypoglycemic agent's treatment (OR = 0.71, 95%CI: 0.54–0.93, $P = 0.016$).

Conclusion Sufficient dietary zinc intake has potential benefits for cardiovascular health among patients with DM. Further large-scale and well-designed prospective study are needed to further explore these associations.

Keywords Dietary zinc intakes, Diabetes mellitus, Atherosclerotic cardiovascular disease, NHANES database

*Correspondence:
Xiaoqiong Lyu
lvvxq@outlook.com
[1]Department of Endocrinology and Rheumatology Immunology, The First People's Hospital of Lin'an District, Hangzhou, 360 YiKang Street, Lin'an District, Hangzhou City 311300, Zhejiang Province, China
[2]Department of Clinical Laboratory, The First People's Hospital of Lin'an District, Hangzhou, Hangzhou City 311300, Zhejiang Province, China

Introduction

Diabetes mellitus (DM) affects approximately 500 million individuals worldwide, which becomes a global public health crisis [1]. Atherosclerotic cardiovascular disease (ASCVD), a coronary heart disease, is characterized by peripheral artery disease and ischemic stroke [2]. It is well established that compared with general population, the individuals with diabetes were at an increased risk of ASCVD. ASCVD has been shown to be the leading cause of morbidity and mortality in DM patients [3]. Identifying modifiable factors contributing to ASCVD in DM patients and good health management of DM are necessary to reduce the global disease and economic burden.

Oxidative stress and inflammation are important pathological mechanisms affecting the occurrence and development of ASCVD in DM patients [4, 5]. Not only can oxidative stress (OS) lead to inflammatory response, but inflammation itself can also induce the formation of free radicals [6]. The relationship between dietary nutrients and oxidative stress and inflammation levels in the body has attracted extensive attention from scholars, especially dietary zinc [7]. Zinc is an essential co-factor for superoxide dismutase enzyme and also promotes the reduction and neutralization of free radicals, thus playing a relevant role in the antioxidant defense of DM patients [8]. Barman et al. [9] suggested that zinc supplements can attenuate diabetes-included oxidative stress in circulation as well as in cardiac and hepatic tissues. A systematic review showed that elevated serum zinc levels were related to a lower risk of CVDs [10]. A meta-analysis conducted by Liu et al. [11] suggested zinc deficiency was associated with the incidence of myocardial infarction significantly. Although the association between zinc intake and health issue are reported by numerous analyses, the results may not necessarily indicate a consistent trend. Animal studies have shown that higher levels of dietary zinc intake may induce oxidative damage, resulting in toxic damage to organisms [12]. In addition, clinical epidemiological studies have shown that excessive zinc exposure may lead to memory loss, gastrointestinal symptoms, and anemia [13–15]. In conclusion, the association between zinc intake and health risks remains controversial.

To data, few evidences have investigated the association between dietary zinc intake and ASCVD risk in patients with DM. Hence, the present study aimed to assess the association between dietary zinc intake and 10-year risk of ASCVD in DM patients to lay a theoretical basis for the cardiovascular health of DM patients.

Materials and methods

Study design

All data of present cross-sectional study were extracted from the National Health and Nutrition Examination Survey (NHANES) database 2007–2018. NHNAES, conducted by the National Center of Health Statistics (NCHS), aims to assess the overall health and nutritional status of non-institutional population in the U.S. All data from the NHANES have been approved by the NCHS Ethics Review Board, and all participants had provided written informed consent [16]. According to the Ethics Review Board of The First People's Hospital of Lin'an District, Hangzhou, cross-sectional studies have been exempted from the ethical review.

Study participants

Totally 4,398 subjects diagnosed with DM and did not suffer from CVD in the NHANES 2007–2018 were initial extracted. Among them, 763 subjects aged < 40 years old or aged > 79 years old, 354 subjects missing dietary zinc intake, and 228 missing the complete 10-year ASCVD risk calculation information were excluded. Eventually, 3,053 eligible subjects were included for the next analysis. Participants who answered yes to "Ever told you had angina/heart failure/heart attack/coronary heart disease/stroke/congestive heart failure" were defined as having CVD.

Calculation of 10-year ASCVD risk

The American College of Cardiology/American Heart Association (ACC/AHC) pooled cohort 10-year risk of ASCVD score (%) was calculated based on age, gender, race, systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), hypertension treatment, diabetes, and smoking status [17]. ASCVD score < 20% was classified as low risk and ASCVD score ≥ 20% as high risk among DM patients [15].

Assessment of dietary zinc intake

The data of dietary zinc and supplement intake were obtained based on 24-h dietary recall interview, which were using the United States Department of Agriculture (USDA)'s Automated Multiple-Pass Method [18]. Subjects were asked to recall all food and beverages (other than regular drinking water) consumed prior to this interview, and a detailed description of the food [19]. The USDA's Food and Nutrient Database for Dietary Studies and NHANES Dietary Supplement Database were used to calculate intakes of nutrients. Total dietary zinc intake was calculated as the sum of dietary and supplement. For male, zinc intake < 11 mg/d was considered insufficient, and a zinc intake ≥ 11 mg/d was considered sufficient; for female, zinc intake < 8 mg/d was considered insufficient, and a zinc intake ≥ 8 mg/d was considered sufficient.

Potential variables

The potential covariates included age, gender, race, education level, physical activity and poverty-to-income

ratio (PIR). The physical examinations and laboratory tests comprised of body mass index (BMI), SBP, DBP, TC, HDL, glycated hemoglobin (HbA1c), albumin, creatinine (Scr), white blood cells (WBC), lymphocyte, neutrophil, platelets (PLT) and urinary albumin to creatinine Ratio (UACR). Smoking status was divided into never smoker (smoking less than 100 cigarettes in their life), current smoker (smoking less than 100 cigarettes in s/he life and still smoking when s/he answered this questionnaire), and former smoker (if the participants had smoked at least 100 cigarettes in their life, and had quit smoking when s/he answered this questionnaire) [20]. Each participant was required to answer how often s/he had drunk alcoholic drinks in the past 12 months. According to these question, the drinking status was categorized into four strata (0, < 1, 1-<8, ≥ 8 drinks per week) and classified as none, mild, moderate and heavy, respectively [21].

Diabetic retinopathy, CVD, hypertension, dyslipidemias, DM and diabetic kidney disease (DKD) were diagnosed based on laboratory tests, self-reported and medication history. Diabetic retinopathy was confirmed using self-reported item, suggesting a doctor had informed the respondent that diabetes had affected their eyes [22]. Hypertensive was defined as SBP ≥ 140 mmHg, DBP ≥ 90 mmHg, self-reported diagnosed as high blood pressure, or taking blood pressure medication [23]. Antihypertensive drug use was identified base on respondents' self-reported use of the following drugs: adrenergic blocking agents, calcium channel blocjers, diuretics, antihypertensive combinations, angiptensin II inhibitors, aldosterone receptor antagonists, renin inhibitor, angiotensin receptor blockers and neprilysin inhibitors. Dyslipidemias was defined as TC ≥ 200 mg/dL (5.2 mmol/L), triglyceride (TG) ≥ 150 mg/dL (1.7 mmol/L), low-density lipoprotein cholesterol (LDL-C) ≥ 130 mg/dL (3.4 mmol/L), HDL-C ≤ 40 mg/dL (1.0 mmol/L), self-reported hypercholesterolemia or receiving cholesterol-lowering therapy [24]. DM were defined as HbA1c ≥ 6.5%, fasting glucose ≥ 126 mg/dL, 2 h glucose tolerance test (OGTT) ≥ 200 mg/dL, or diagnosed as DM by the clinician [25]. The urine albumin/creatinine ratio was used to calculate the ACR. The eGFR scores were calculated using the Chronic Kidney Disease Epidemiology Collaboration algorithm. ACR ≥ 30 mg/g and/or eGFR < 60 mL/min/1.73m^2 were used to diagnose DKD in DM patients [26]. Hypoglycemic drug use was identified based on respondents' self-reported use of insulin or any other anti-diabetic agents. Healthy eating index (HEI-2015) is a continuous score from 0 to 100 that is used to assess whether an individual's dietary intake meets the Dietary Guidelines of American (DGA). HEI-2015 includes 13 food components that have been described in previous studies [27]. The scores of each component were summed to calculate the final HEI-2015 score, with higher scores representing better adherence to the dietary pattern recommended by the DGA.

Statistics analysis

Patients with DM were divided into high 10-year ASCVD group and low 10-year ASCVD group. Continuous variables were described as mean and standard error (S.E.), and weighted t-test was used to compare the differences between two groups. Categorical variables were presented as frequency and percentage [n (%)], and weighted χ^2 test was used to compare the differences between two groups. Multivariate imputation by chained equations (MICE) was utilized to missing data imputation, and sensitivity analysis was performed to verify sensitivity before and after imputation of missing data (Table S1). The weighted univariate and multivariate logistics regression analysis were used to explore the association between dietary zinc intake and 10-year risk of ASCVD among DM patients, with odds ratios (HRs) and 95% CIs. Model 1 was a crude model without adjusting covariates. Model 2 adjusted BMI, physical activity, DKD, Fe, WBC, uric acid (UA), PLT and HEI-2015. Subgroup analyses based on the history of hypertension, dyslipidemia and use of hypoglycemic agents were further conducted to explore the association between dietary zinc intake and 10-year ASCVD risk in DM patients. Differences were considered statistically significant when the two-sided P-value < 0.05. All statistical analyzes were performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Characteristics of DM patients

The subjects screening procedures was exhibited in Fig. 1. Finally, 3,053 eligible patients with DM were included, with the mean age of 58.32 (± 0.26) years old. Among them, 1,245 (40.78%) DM patients had high risk of developing ASCVD in 10 years. The proportion of patients with DM with sufficient dietary zinc intake in high risk of 10-year ASCVD group was significantly lower than that in the low risk of 10-year ASCVD group (60.24% vs. 65.29%). Differences were found in age, gender, race, the level of SBP, DBP, BMI, energy, protein, creatinine, eGFR, PLT, urine albumin and urinary albumin to creatinine ratio, height, smoking status, the history of antihypertension agents, DKD, hypertension, lipid lowering drugs and anticoagulant agents between two groups (P < 0.05) (Table 1).

Dietary zinc intake and the 10-year ASCVD risk

Table 2 reported the association between dietary zinc intake and the 10-year risk of ASCVD. Directed acyclic graph (DAG) diagram was used to display dependencies between outcome (10-year ASCVD risk), exposure (zinc intake), and confounding variables to determine

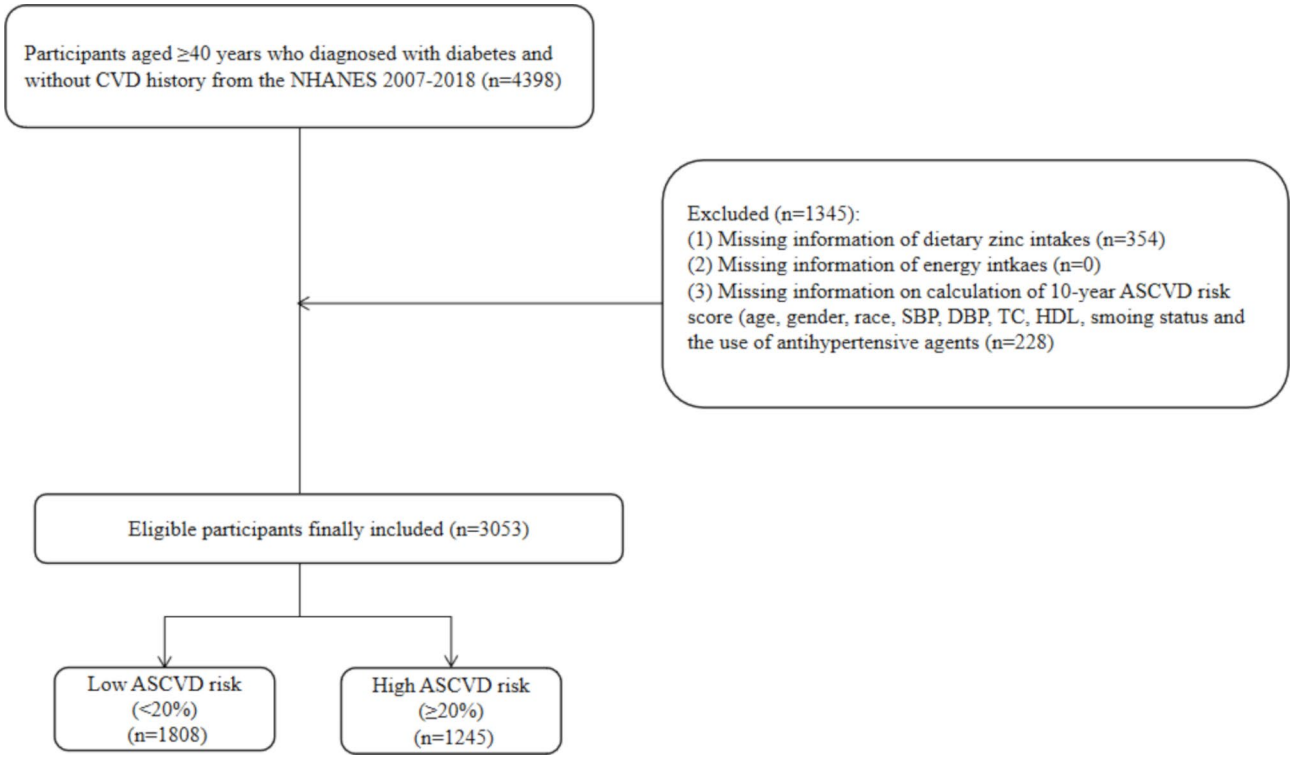

Fig. 1 The flow chart of population screening

(Fig. 2). After adjusted BMI, physical activity, DKD, Fe, UA, WBC, PLT and HEI-2015 in model 2, compared with the deficiency dietary zinc intake group, sufficient dietary zinc intake was associated with the lower risk of 10-year ASCVD among patients with DM (OR = 0.78, 95%CI: 0.61–0.99, $P = 0.044$). The restricted cubic spline (RCS) curve suggested that there was no nonlinear relationship between dietary zin intake and 10-years ASCVD risk in patients with DM (P for nonlinear = 0.085) (Fig. 3).

Dietary zinc intake and 10-year ASCVD risk among DM patients with or without hypertension, dyslipidemia and antihypertension agent's history

Figure 4 shown the association between dietary zinc intake and 10-year ASCVD risk in DM patients stratified by the history of hypertension, dyslipidemia and hypoglycemic agent's treatment. Compared with the deficiency dietary zinc intake group, sufficient dietary zinc intake was associated with the 10-year ASCVD risk among the DM patients with the history of hypertension (OR = 0.53, 95%CI: 0.35–0.81, $P = 0.004$), dyslipidemia (OR = 0.76, 95%CI: 0.59–0.97, $P = 0.026$), and hypoglycemic agent's treatment (OR = 0.71, 95%CI: 0.54–0.93, $P = 0.014$), respectively.

Discussion

In this cross-sectional study of nationally representative US adults with DM, we observed an association between dietary zinc intake and the risk of 10-year ASCVD in DM patients, especially in patients with the history of hypertension, dyslipidemia and hypoglycemic agent's treatment. High dietary zinc intake may have a potential beneficial for cardiovascular health in DM patients.

Over the past few decades, despite significant progresses in the prevention and treatment of ASCVD, ASCVD remains one of leading causes of mortality worldwide [12, 28]. DM is one of the risk factors for ASCVD. Previous study has investigated that chronic inflammatory and oxidant responses play important role in the occurrence and development of diabetes and ASCVD, as well as other deadly complications [29]. As an essential trace element, zinc can improve the production of the antioxidant metallothionein, and improve the antioxidant capacity of the body. Previous researched have investigated the associations between dietary zinc intakes and diabetes and its complications, but with inconsistent conclusions. A review on dysregulated zinc metabolism and DM emphasized that zinc supplementation may significantly contribute to its clinical application in the treatment of diabetes and related metabolic abnormalities, as well as in alleviating diabetic complications caused by oxidative stress, which is consistent with our findings [30]. Another research also demonstrated that

Table 1 Characteristics of DM patients

Variables	Total ($n=3053$)	Low risk ($n=1808$)	High risk ($n=1245$)	Statistics	*P*
Age, year, Mean (± S.E)	58.32 (0.26)	53.73 (0.28)	67.05 (0.36)	t=-31.26	< 0.001
Gender, n (%)				$\chi^2=65.059$	< 0.001
Female	1592 (51.79)	1104 (59.55)	488 (37.05)		
Male	1461 (48.21)	704 (40.45)	757 (62.95)		
Race, n (%)				$\chi^2=38.059$	< 0.001
Non-Hispanic Black	748 (13.68)	374 (12.12)	374 (16.64)		
Non-Hispanic White	910 (58.69)	498 (56.27)	412 (63.26)		
Mexican American	648 (11.18)	427 (12.85)	221 (8.01)		
Others	747 (16.46)	509 (18.75)	238 (12.09)		
SBP, mmHg, Mean (± S.E)	129.24 (0.58)	124.21 (0.60)	138.79 (1.01)	t=-12.50	< 0.001
DBP, mmHg, Mean (± S.E)	72.08 (0.36)	72.99 (0.46)	70.34 (0.61)	t = 3.45	< 0.001
TC, mg/dL, Mean (± S.E)	191.75 (1.31)	191.21 (1.59)	192.78 (2.31)	t=-0.56	0.578
HDL, mg/dL, Mean (± S.E)	47.92 (0.43)	48.99 (0.53)	45.88 (0.63)	t = 4.00	< 0.001
Smoking, n (%)				$\chi^2=25.676$	< 0.001
Never smoker	1651 (52.46)	1106 (57.24)	545 (43.39)		
Former smoker	913 (32.38)	480 (30.01)	433 (36.88)		
Current smoker	489 (15.16)	222 (12.75)	267 (19.73)		
Antihypertensive agents, n (%)				$\chi^2=38.897$	< 0.001
No	1216 (41.03)	885 (48.03)	331 (27.74)		
Yes	1837 (58.97)	923 (51.97)	914 (72.26)		
Zinc, mg, Mean (± S.E)	15.62 (± 0.45)	15.43 (± 0.48)	15.97 (± 0.84)	t = 0.587	0.558
Zinc, n (%)				$\chi^2=3.967$	0.046
Deficiency	1238 (36.45)	703 (34.71)	535 (39.76)		
Sufficient	1815 (63.55)	1105 (65.29)	710 (60.24)		
PIR, Mean (± S.E)	2.88 (0.05)	2.93 (0.07)	2.78 (0.07)	t = 1.65	0.102
Education level, n (%)				$\chi^2=1.719$	0.633
Below high school	1020 (21.69)	573 (20.73)	447 (23.49)		
High school/GED	666 (24.09)	385 (24.13)	281 (24.00)		
College and above	537 (23.59)	330 (24.27)	207 (22.31)		
Some university/AA degree	830 (30.63)	520 (30.87)	310 (30.19)		
Height, cm, Mean (± S.E)	167.25 (0.30)	166.62 (0.40)	168.46 (0.43)	t=-3.10	0.003
Weight, kg, Mean (± S.E)	91.89 (0.63)	92.51 (0.77)	90.71 (0.91)	t = 1.64	0.105
BMI, kg/m^2, Mean (± S.E)				$\chi^2=12.377$	0.002
<25	387 (11.19)	219 (11.79)	168 (10.03)		
25–30	900 (26.09)	479 (23.05)	421 (31.85)		
≥30	1766 (62.73)	1110 (65.16)	656 (58.12)		
Physical activity, MET·min/week, n (%)				$\chi^2=2.833$	0.092
Mild	2026 (64.86)	1184 (66.36)	842 (62.02)		
Moderate/Strenuous	1027 (35.14)	624 (33.64)	403 (37.98)		
Drinking, n (%)				$\chi^2=7.467$	0.113
None	899 (25.17)	537 (24.92)	362 (25.65)		
Mild	987 (36.40)	616 (36.63)	371 (35.95)		
Moderate	444 (16.76)	273 (18.32)	171 (13.79)		
Heavy	228 (8.42)	124 (7.76)	104 (9.67)		
Unknown	495 (13.26)	258 (12.37)	237 (14.95)		
Diabetic retinopathy, n (%)				$\chi^2=5.141$	0.077
No	1774 (59.55)	1036 (57.45)	738 (63.53)		
Yes	859 (29.09)	531 (30.49)	328 (26.43)		
Unknown	420 (11.36)	241 (12.06)	179 (10.03)		
DKD, n (%)				$\chi^2=40.280$	< 0.001
No	2230 (75.37)	1435 (81.20)	795 (64.32)		
Yes	823 (24.63)	373 (18.80)	450 (35.68)		
Hypertension, n (%)				$\chi^2=132.385$	< 0.001

Table 1 (continued)

Variables	Total ($n=3053$)	Low risk ($n=1808$)	High risk ($n=1245$)	Statistics	*P*
No	2179 (73.97)	1498 (84.12)	681 (54.70)		
Yes	874 (26.03)	310 (15.88)	564 (45.30)		
Dyslipidemia, n (%)				$\chi^2=1.909$	0.167
No	481 (13.89)	316 (14.78)	165 (12.21)		
Yes	2572 (86.11)	1492 (85.22)	1080 (87.79)		
CVD family history, n (%)				$\chi^2=0.119$	0.730
No	2629 (85.28)	1534 (85.00)	1095 (85.81)		
Yes	424 (14.72)	274 (15.00)	150 (14.19)		
Hypoglycemic agents, n (%)				$\chi^2=3.558$	0.059
No	1216 (41.46)	744 (43.28)	472 (38.00)		
Yes	1837 (58.54)	1064 (56.72)	773 (62.00)		
LLDs, n (%)				$\chi^2=7.155$	0.007
No	1699 (53.48)	1081 (56.19)	618 (48.33)		
Yes	1354 (46.52)	727 (43.81)	627 (51.67)		
Antiplatelet agents, n (%)				$\chi^2=0.008$	0.928
No	2950 (97.69)	1754 (97.67)	1196 (97.73)		
Yes	103 (2.31)	54 (2.33)	49 (2.27)		
Anticoagulant agents, n (%)				$\chi^2=11.530$	< 0.001
No	3007 (98.51)	1787 (99.15)	1220 (97.28)		
Yes	46 (1.49)	21 (0.85)	25 (2.72)		
Energy, kcal, Mean (± S.E)	1969.64 (26.40)	2012.14 (32.68)	1888.97 (32.75)	t = 3.00	0.003
Protein, g, Mean (± S.E)	79.92 (1.12)	81.92 (1.51)	76.14 (1.40)	t = 2.82	0.006
Fe, mg, Mean (± S.E)	18.41 (0.49)	18.23 (0.55)	18.76 (0.96)	t=-0.47	0.637
HbA1c, %, Mean (± S.E)	7.11 (0.04)	7.12 (0.06)	7.08 (0.06)	t = 0.54	0.589
Albumin, g/dL, Mean (± S.E)	4.19 (0.01)	4.19 (0.01)	4.19 (0.01)	t=-0.05	0.961
Scr, mg/dL, Mean (± S.E)	0.90 (0.01)	0.86 (0.02)	0.97 (0.02)	t=-5.45	< 0.001
eGFR, Mean (± S.E)	92.30 (0.55)	97.29 (0.66)	82.82 (0.84)	t = 14.10	< 0.001
WBC, 1000/uL, Mean (± S.E)	7.72 (0.08)	7.69 (0.09)	7.78 (0.11)	t=-0.73	0.470
Lymphocyte, 1000/uL, Mean (± S.E)	2.21 (0.03)	2.24 (0.03)	2.17 (0.05)	t = 1.28	0.205
Neutrophil, 1000/uL, Mean (± S.E)	4.65 (0.06)	4.62 (0.07)	4.72 (0.08)	t=-0.99	0.326
PLT, 1000/uL, Mean (± S.E)	243.77 (2.25)	248.94 (2.67)	233.98 (3.13)	t = 4.02	< 0.001
Urine Scr, mg/dL, Mean (± S.E)	113.29 (1.93)	114.06 (2.37)	111.85 (3.13)	t = 0.57	0.567
Urine Albumin, mg/dL, Mean (± S.E)	80.04 (9.64)	61.57 (11.44)	115.08 (18.07)	t=-2.51	0.014
UACR, mg/g, Mean (± S.E)	81.49 (9.66)	62.30 (10.80)	117.91 (15.85)	t=-3.21	0.002
Total bilirubin, Mean (± S.E)	0.63 (± 0.01)	0.62 (± 0.01)	0.64 (± 0.02)	t = 0.842	0.402
UA, Mean (± S.E)	5.65 (± 0.04)	5.51 (± 0.05)	5.93 (± 0.05)	t = 6.080	< 0.001
HEI-2015, Mean (± S.E)	51.69 (± 0.34)	51.36 (± 0.44)	52.31 (± 0.50)	t = 1.469	0.145

χ^2: chi-square test; t:t-test; S.E: standard error; ASCVD: atherosclerotic cardiovascular disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC: total cholesterol; HDL: high-density lipoprotein; PIR: poverty-to-income ratio; GED: general educational development; BMI: body mass index; DKD: diabetic kidney disease; AA: associate of arts; Fe: Ferrum; MET: metabolic equivalent task; CVD: cardiovascular disease; LLDs: lipid lowering drugs; HbA1c: glycosylated hemoglobin; Scr: creatinine; eGFR: estimate glomerular filtration rate; WBC: white blood cell; PLT: platelet; UACR: urinary albumin to creatinine ratio; UA: uric acid; HEI-2015: healthy eating index-2015

Table 2 Association between dietary zinc intake and 10-year ASCVD risk among patients with DM

Variables	Model 1		Model 2	
	OR (95%CI)	*P*	OR (95%CI)	*P*
Zinc	1.03 (0.94–1.13)	0.505	1.00 (0.89–1.13)	0.966
Zinc				
Deficiency	Ref		Ref	
Sufficient	0.81 (0.65-1.00)	0.051	0.78 (0.61–0.99)	**0.044**

Ref: reference; OR: odds ratio, CI: confidence interval; ASCVD: atherosclerotic cardiovascular disease

Model 1: crude model;

Model 2: adjusting for Fe, BMI, physical activity, DKD, WBC, PLT, UA and HEI-2015

although the specific role of zinc homeostasis in vascular dysfunction remains unclear, imbalances in intracellular zinc metabolism are related to high risk of DM and CVD [31]. An et al. [32] suggested that there was moderate to high-quality evidence that zinc supplementation reduces CVD risk factors. Not all micronutrients are likely to benefit cardiometabolic health. However, a cross-sectional analysis suggested that higher levels of zinc were associated with an increased prevalence of metabolic syndrome [33]. It was speculated excessive zinc may be actually increase the expression of pro-inflammatory cytokines

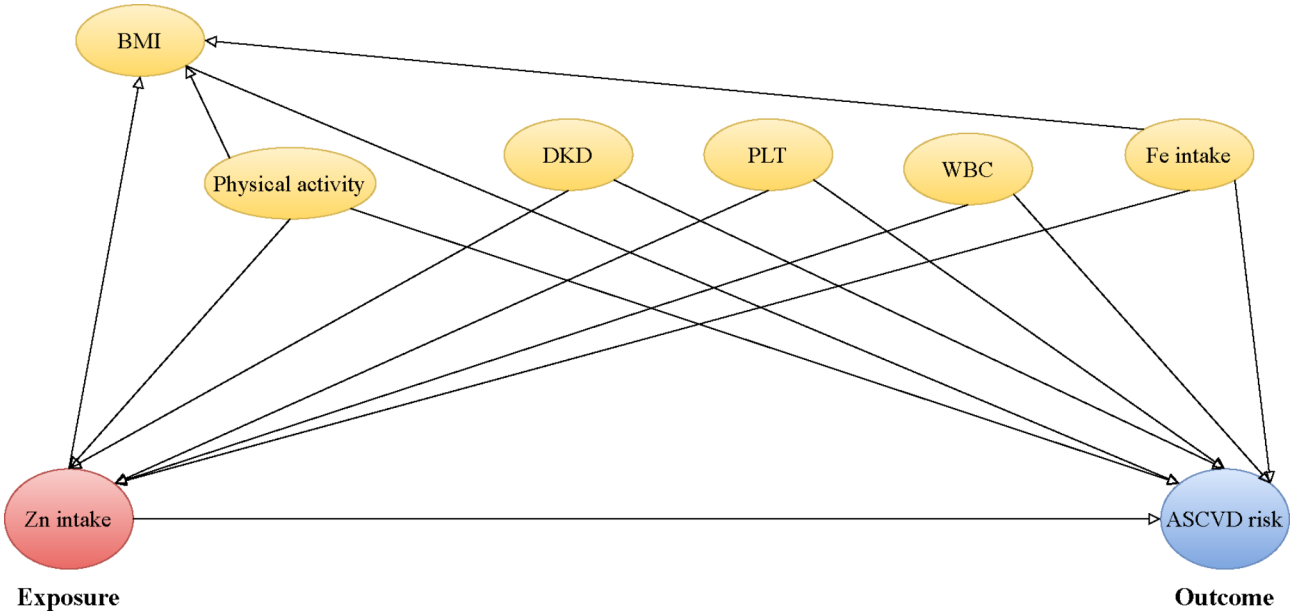

Fig. 2 Directed acyclic graph (DAG) diagram between exposure, outcome and confounding variables

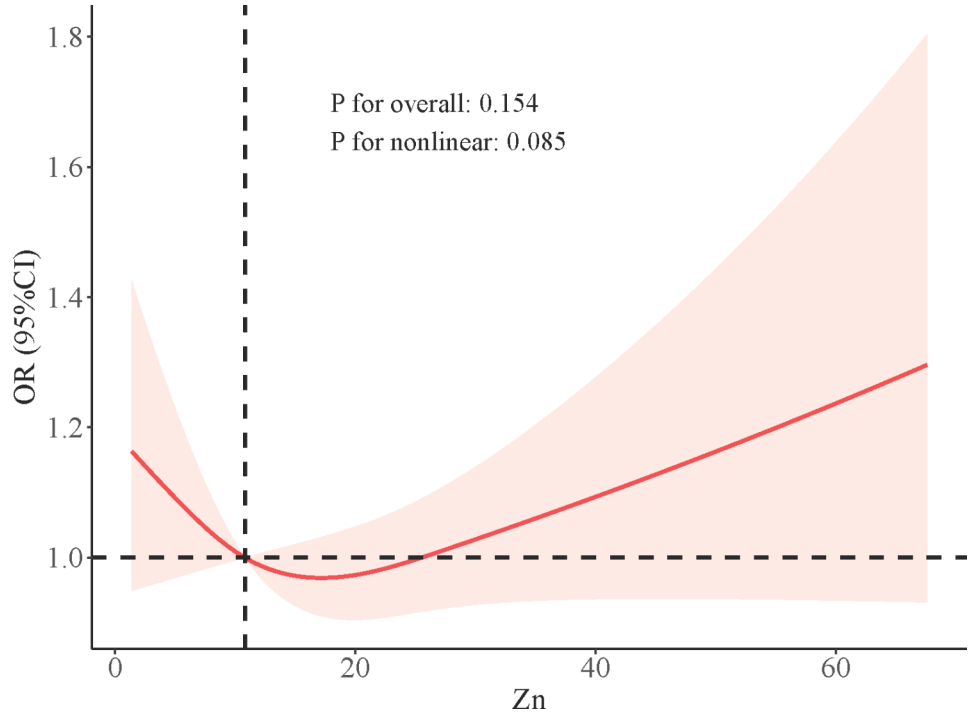

Fig. 3 The RCS curve of association of dietary zinc intake and 10-yeat ASCVD risk in DM patients
Note: RCS: restricted cubic splines; ASCVD: Atherosclerotic cardiovascular disease

[34, 35]. Excessive zinc intake may inhibit the adsorption of copper and iron, leading to copper deficiency and anemia, respectively, and may also cause adverse physiological phenomena such as nausea, vomiting, and gastrointestinal disorders [36]. Furthermore, excessive zinc intake may even lead to serious disorders in the quantity and activity of immune cells, thereby reducing the body's immunocompetence and increasing susceptibility to disease [37].

Understanding and formulating models related to a higher risk of ASCVD is vital to guide prevention efforts. In our study, ASCVD Risk Estimator Plus was used to calculate 10-year ASCVD risk based on age, sex, race, SBP, DBP, TC, HDL, LDL, smoking and whether on

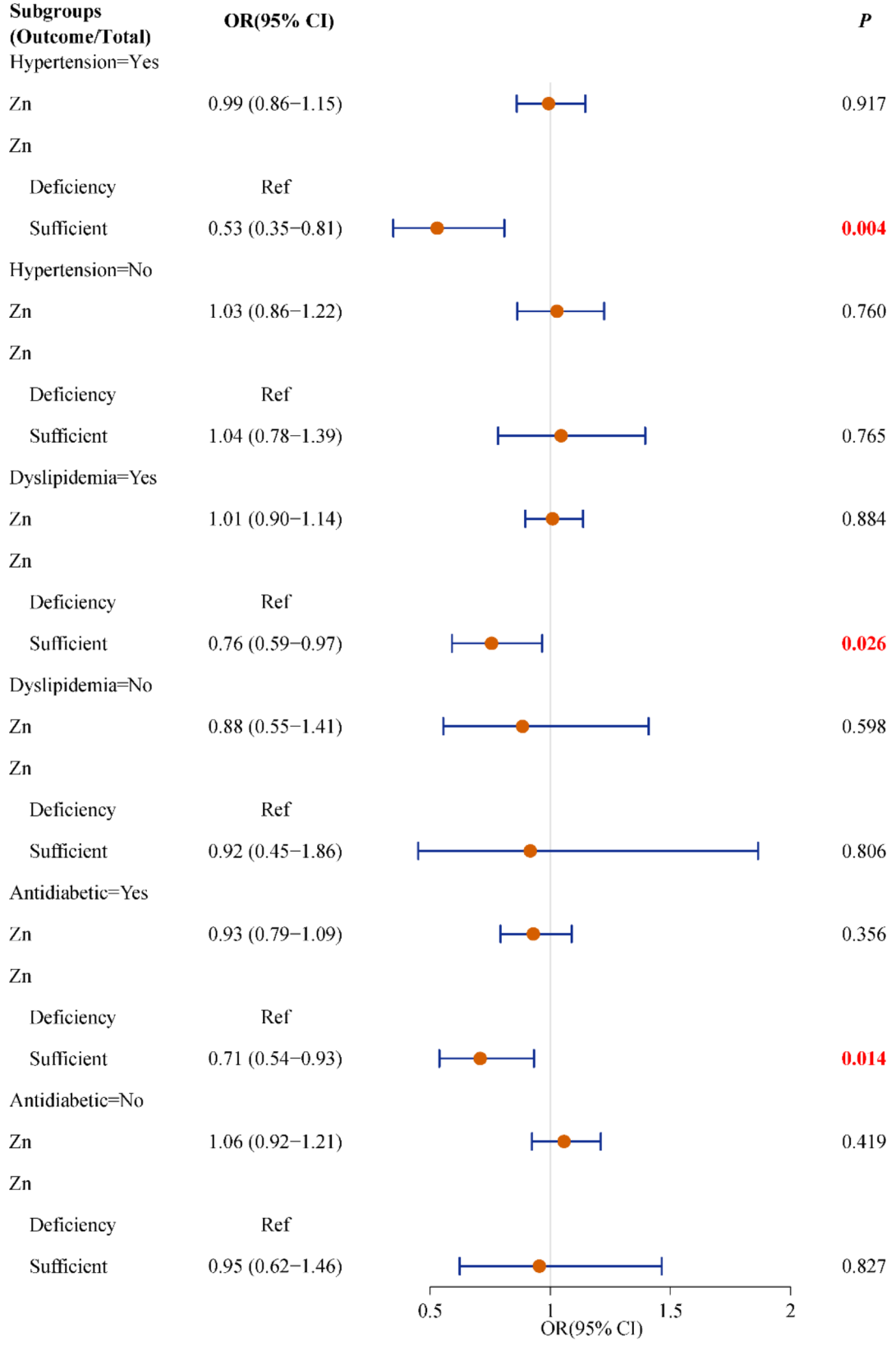

Fig. 4 Association between dietary zinc intake and 10-year ASCVD risk among DM patients with or without hypertension, dyslipidemia and hypoglycemic agent's treatment
Note: ASCVD: Atherosclerotic cardiovascular disease; DM: diabetes mellitus

antihypertensive agents [17]. A cross-sectional study based on KNHANES confirmed that dietary inflammatory index (DII) quartile was associated with 10-year ASCVD risk in Korean men; however, in women, ASCVD risk was not significantly associated with DII. The baseline in present study also shown that male (had a higher rate of 10-year ASCVD risk than female (51.81% vs. 30.65%) [38]. It was speculated that compared with females, males are more susceptible to oxidative stress than female. In addition, high risk of 10-year ASCVD was calculated as more than 7.5%, which differs from our research of more than 20%. Given the different participants included in two studies, Lee et al. observed the general population in Korea, whereas our study recruited the diabetic patients among the U.S [39]. In the subgroup analysis, we observed significant relationship between the dietary zinc intakes and the risk on 10-year of ASCVD among DM patients. These findings suggested the robustness of our results once again.

Hence, we offered reference for the management of cardiovascular health in diabetic on the association between dietary zinc intakes and the 10-year ASCVD in DM patients. A representative and high-quality NHANES database was used, and the regression models were adjusted for relevant potential variables to make the results credible and robust. For clinicians as well as patients with DM, it was necessary to be realize the benefits of dietary zinc for cardiovascular health management. Moreover, it is a beneficial move to add the zinc-enriched foods to dietary diet such as red meat, animal offal and eggs. Our study still has some limitations. First, dietary zinc intake information was obtained by 24-h dietary recall interview, which may be exist a certain recall bias. Second, the diagnosis of CVD was based on self-reporting and the results may be biased to some extent. Third, although we adjusted for as many variables related to ASCVD as possible, we still could not rule out the confounding factors that were not taken into account. Fourth, our study was a cross-sectional study and the specific causality relationship between dietary zinc intake and 10-year ASCVD risk among patients with DM cannot infer. Fifth, due to calculation of ASCVD and the availability of the NHANES database, our study focus was limited to the age of 40–79 years old, which may limit the applicability of our observations on the relationship between dietary zinc intake and 10-year ASCVD risk in patients with diabetes to the general population. Based on the findings of this study, multi-center prospective studies can be attempted in the future among children and adolescents or elderly people over 79 years old, not just limited to the NHANES database. Finally, due to data availability of NHANES, data of serum zinc were missing seriously and were therefore not included for analysis. Dietary zinc intake cannot fully characterize the level of zinc in the human body. Therefore, the association between zinc and the risk of ASCVD in patients with DM still needs to be confirmed by future large-scale, comprehensive studies evaluating the levels of dietary zinc intake and serum zinc.

Conclusion

Sufficient dietary zinc intake was related to lower 10-year ASCVD risk among DM patients, especially in individuals with the history of hypertension, dyslipidemia and hypoglycemic agent's treatment. Appropriate supplementation and zinc-rich foods intake may be beneficial for cardiovascular health among DM patients. Further researches are needed to confirm and elucidate these preliminary findings.

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Author contributions

(1), Xiaoqiong Lyu conceiving and designing the study; (2), Xiaoqiong Lyu, Liping Chen and Wenbin Wang collecting the data; (3), Xiaoqiong Lyu, Liping Chen and Wenbin Wang analyzing and interpreting the data; (4), Xiaoqiong Lyu writing the manuscript; (5), Xiaoqiong Lyu, Liping Chen and Wenbin Wang providing critical revisions that are important for the intellectual content; (6), All authors approving the final version of the manuscript.

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Data availability

The datasets used and/or analyzed during the current study are available in the NHANES database, https://www.cdc.gov/nchs/nhanes/index.htm.

Declarations

Ethics approval and consent to participate

Not applicable, because NHANES belongs to public databases, the patients involved in the database have obtained ethical approval, users can download relevant data for free for research and publish relevant articles, and our study is based on open-source data, and the The First People's Hospital of Lin'an District, Hangzhou, do not require research using publicly available data to be submitted for review to their ethics committee, so there are no ethical issues and other conflicts of interest.

Consent for publication

Not applicable, because this paper did not reveal any personal information of patients.

Competing interests

The authors declare no competing interests.

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