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### ORIGINAL RESEARCH

# Association Between Dietary Salt and Plasma Glucose, Insulin and Hemoglobin A<sub>1c</sub> Levels Among Type 2 Diabetes Patients in Eastern China

Yi Lin <sup>1</sup> Kaushik Chattopadhyay <sup>2</sup> Xi Yang <sup>3</sup> Jia-Lin Li<sup>4</sup> Yan-Shu Chen <sup>4</sup> Ye Zhou <sup>4</sup> Li Li <sup>4</sup>

<sup>1</sup>Center for Health Economics, Faculty of Humanities and Social Sciences, University of Nottingham, Ningbo, Zhejiang Province, People's Republic of China; <sup>2</sup>Division of Epidemiology and Public Health, School of Medicine, University of Nottingham, Nottingham, UK; <sup>3</sup>Department of Nutrition, Ningbo First Hospital, Ningbo, Zhejiang Province, People's Republic of China; <sup>4</sup>Department of Endocrinology and Metabolism, Ningbo First Hospital, Ningbo, Zhejiang Province, People's Republic of China

Correspondence: Li Li Department of Endocrinology and Metabolism, Ningbo First Hospital, 59, Liuting Street, Ningbo, 315010, Zhejiang Province, People's Republic of China Tel +86 13757426626 Email lilyningbo@163.com

#### Yi Lin

Center for Health Economics, Faculty of Humanities and Social Sciences, University of Nottingham, 199, Taikang East Road, University Park, Ningbo, 315100, People's Republic of China Tel +86-13916608572 Email Lily.Lin@nottingham.edu.cn **Purpose:** Type 2 diabetes (T2D) is one of the major public health concerns in China. Studies on the association between dietary salt intake and the glycemic response of T2D are lacking in China. The aim was to investigate the association between the levels of dietary salt intake and the plasma glucose, insulin and hemoglobin  $A_{1c}$  (Hb $A_{1c}$ ) levels in T2D patients. **Methods:** Patients with T2D, who accepted management and treatment by the National Standardized Metabolic Disease Management Center at Ningbo First Hospital from March 2018 to January 2020, were included in this study. Dietary salt intake was assessed through a standardized food frequency questionnaire. Anthropometry, blood pressure and biomarkers were measured by well-trained endocrinology nurses. Generalized linear models (GLMs) were used to examine the associations.

**Results:** A total of 1145 eligible T2D patients with a mean age of 51.4 years were included in the study. Fasting plasma glucose (FPG), 2-hour postprandial plasma glucose and 2-hour postprandial insulin were significantly increased across dietary salt categories. The GLMs further showed that dietary salt intake >8 g/day was positively associated with FPG and HbA<sub>1c</sub>.

**Conclusion:** Higher daily salt intake was found to be associated with FPG and  $HbA_{1c}$  in T2D patients. Lifestyle education and promotion of salt reduction should be provided to T2D patients.

**Keywords:** dietary salt, type 2 diabetes, blood glucose, insulin, glycated hemoglobin  $A_{1c}$ , China

### Introduction

Over the past four decades, the rapidly increasing prevalence of type 2 diabetes (T2D) has become a public health concern in China, due to economic development and changes in diet, lifestyle and culture influenced by westernization. The prevalence of diabetes rose from less than 1% in 1980<sup>1</sup> to 12.8% in 2017.<sup>2</sup> T2D has been the main driver for the increased prevalence of diabetes in China.<sup>3</sup> T2D patients in the tertiary hospital in Ningbo were reported to have poor glycemic control.<sup>4</sup> In addition, a study conducted by Li et al, which included 3370 T2D patients from the tertiary hospital in Ningbo, indicated that patients with T2D were at high risk of further chronic complications, including hypertension, dyslipidemia, nephropathy, retinopathy, coronary heart disease, stroke and cerebrovascular diseases.<sup>5</sup>

T2D is a lifestyle disorder and progression is highly correlated with aging, dietary and lifestyle behavior, and genetic factors.<sup>6</sup> Although dietary salt as an

essential seasoning contributes to eating pleasure and satisfaction,<sup>7</sup> many guidelines have promoted dietary salt restriction in patients with diabetes.<sup>8,9</sup> Higher intake of sodium is an established risk factor for stroke and cardio-vascular diseases.<sup>10</sup> Dietary sodium intake is evidenced to be positively associated with increased blood pressure in the general population.<sup>11,12</sup> However, the connection between dietary salt and glucose homeostasis remains elusive and has not been drawn the same attention as hypertension. The majority of dietary interventions do not focus on the relationship between dietary salt/sodium intake and the prognosis of diabetes.

To the best of our knowledge, few studies have explored the relationship between dietary salt and indicators of T2D in China, patients in particular. The objective of this study was to investigate the association between the levels of dietary salt and blood glucose, insulin and hemoglobin  $A_{1c}$  (Hb $A_{1c}$ ) in T2D patients in Ningbo, China.

## **Methods**

### Study Design and Patients

An ongoing innovation study of the management of metabolic diseases and complications is a national standardized project, implemented by the Metabolic Management Center (MMC). The National Standardized MMC called "One Center, One Stop, and One Standard Model" was established as a platform for the standardized diagnosis and treatment of metabolic diseases and their long-term follow-up.<sup>13</sup> In the MMCs, patients can receive a comprehensive series of services including registration, tests, evaluation, prescriptions and health education. Under the guidance of the MMC Experts Committee, more than 400 stringent standard operating procedures were set up for quality control of the MMC operation. The details of the national MMC are reported elsewhere.<sup>13</sup>

The present study included 2313 patients with T2D, registering in the MMC for the first time from March 2018 to January 2020, at the outpatient Department of Endocrinology, Ningbo First Hospital, Zhejiang Province, China and the National Standardized MMC. T2D was diagnosed based on the definition proposed by the World Health Organization (WHO).<sup>14</sup> Patients were excluded from this study if they met any of the following criteria: (1) age >75 years or age <18 years; (2) diagnosis with any kind of cancer; (3) positive islet autoantibodies; (4) glomerular filtration rate (eGFR) <30 mL/minute; (5) severe liver dysfunction; (6) acute infectious diseases; (7)

pregnancy or lactation; (8) incompleting standardized questionnaires on food frequency, demography and lifestyle.

The study was approved by the Research Ethics Committee of Ningbo First Hospital, China (no. 2019-R057). Written informed consent was obtained from all participants.

## **Dietary Assessment**

Dietary information was collected through a nationwide standardized food frequency questionnaire (FFQ), following the guidelines proposed by MMC and Ningbo First Hospital during outpatient visits. All of the dietary information was collected by well-trained nurses. Quantitative dietary information was collected on how many usual foods (vegetables, fruits, sova and sova products) were consumed (in grams per day), how often meat (red meat, poultry, fish and shrimps) and soft drinks were consumed per week, and how much seasoning (salt and sugar) was consumed per day. Patients were provided with a standard brochure with colorful photographs for description of the portion sizes, following the Chinese dietary guideline.<sup>15</sup> Considering the psychological responses of patients, all of the information on dietary intake was collected through multiple-choice questions.

Dietary salt was categorized into three groups:  $\leq 6, 6-8$  (excluding 6g/d) and >8 g/day, according to the Chinese dietary guideline for prevention and control of diabetes in primary care.<sup>16,17</sup> Patients with missing reports were asked to fill them in during outpatient visits, and misreported information was evaluated and corrected based on daily reasonable consumption.

## Demography and Lifestyle

All adults diagnosed with T2D who were willing to participate in the study were invited to complete the MMC standard questionnaires on their demography [education (low education: lower than college/university; and high education: college/university or above)], lifestyle [current smoking status (no and yes); current alcohol drinking status (no and yes); physical activity], medical history and medication records.

# Anthropometric Measurements and Blood Pressure

Anthropometric measurements, including height, body weight and waist circumference (WC), were measured

with the patient wearing light clothing by well-trained endocrinology nurses. Height to the nearest 0.1 cm and body weight to the nearest 0.1 kg were measured using an electronic scale (OMRON HNH-318; Dalian, Liaoning Province, China). WC was measured at the midpoint between the inferior costal margin and the iliac crest in the midaxillary line. Body mass index (BMI), defining general obesity, was calculated as weight (kg)/height (m<sup>2</sup>). Patients were classified into four BMI categories according to the China Obesity Task Force, as follows: underweight (<18.5 kg/m<sup>2</sup>), normal weight (18.5–23.9 kg/ m<sup>2</sup>), overweight (24.0–27.9 kg/m<sup>2</sup>) and obesity ( $\geq$ 28.0 kg/ m<sup>2</sup>).<sup>18</sup> Abdominal obesity was defined according to WC values: WC >90 cm in men or >85 cm in women.<sup>18</sup> Blood pressure was measured using an electronic sphygmomanometer (ORMON HBP-9020; Dalian, Liaoning Province, China) on the right or left arm after a 10-minute rest.

#### **Biomarker Measurements**

After a 10-12-hour overnight fast, blood samples were obtained in the early morning to measure the levels of biomarkers, including fasting plasma glucose (FPG), fasting insulin (FINS), HbA<sub>1c</sub>, total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), uric acid (UA) and serum creatinine (SCr). Then, the 100 g carbohydrate (steamed bread meal) test was used to assess 2-hour postprandial plasma glucose (2hPG) and 2-hour postprandial insulin (2hINS) concentrations. Lipid profiles were analyzed by enzymatic procedures. FPG and 2hPG were assessed by the glucose oxidase method and chemiluminescence immunoassay, respectively. FINS was measured by radioimmunoassay. HbA1c was determined by high-pressure liquid chromatography. UA was examined by enzymatic spectrophotometry. Biomarkers were analyzed using an auto-analyzer (Beckman Coulter AU5800; Shizuoka, Japan). Details of biomarker measurements have been reported elsewhere.<sup>19</sup>

## Statistical Analysis

The percentage of patients, mean with standard deviation (SD) and median values with interquartile range among the categories of dietary salt were presented as descriptive analyses. Continuous and categorical variables of patients' characteristics were examined by analysis of variance (ANOVA) and chi-square test, respectively. ANOVA with Bonferroni correction/Games–Howell, and the Mann–Whitney *U*-test and Kruskal–Wallis test were used to examine

mean and median values of anthropometric measurements and biomarkers within and between the categories of dietary salt.

Generalized linear models (GLMs) were used to assess the associations between salt intake and biomarkers (FPG, 2hPG, FINS, 2hINS and HbA<sub>1c</sub>) after adjusting for confounding factors (sex, age and educational levels), lifestyle factors (physical activity, smoking status and drinking status), BMI, WC, systolic blood pressure (SBP), diastolic blood pressure (DBP), UA, SCr, medication and interactions. Only significant interactions between dietary salt and confounding factors were examined in the model. Results were considered statistically significant at a two-tailed level of 0.05. Statistical analyses were conducted using IBM SPSS Statistics version 26.0.

## Results

## Study Population

In total, 1145 out of 2313 T2D patients (65.2% men) with a mean age of 51.4 years were included in the present study. They were divided into three groups according to salt intake:  $\leq 6$ , 6-8 and > 8 g/day (Table 1).

Among all patients, around 25.0% had dietary salt intake less than or equal to 6g/day. Compared to lower salt intake ( $\leq 6$  g/day), a higher prevalence of patients with overweight and central obesity was observed in the groups with higher salt intake (6–8 and > 8 g/day). Similarly, higher prevalences of hypertension, hyperlipidemia, hyperuricemia and coronary disease were seen in the groups with higher salt intake.

# Risk Factors Among Salt Intake Categories

In T2D patients, direct risk factors, including FPG, 2hPG, 2hINS and HbA<sub>1c</sub>, and indirect risk factors, including BMI, WC, VFA, SFA, TC, TG and LDL-C, were significantly different across dietary salt categories (Table 2), whereas 2hINS, SBP, DBP, HDL-C and UA were not significantly different. Within dietary salt categories, mean values of FPG, 2hPG and HbA<sub>1</sub>c were significantly higher in the group with dietary salt >8 g/day than in the groups with lower salt intake ( $\leq 6$  and 6-8 g/day).

# Associations Between Dietary Salt Intake and Blood Glucose, Insulin and HbA<sub>1c</sub>

Associations between dietary salt and plasma glucose, insulin and HbA<sub>1c</sub> among T2D patients were further investigated by GLMs (Tables 3–5). Dietary salt (6–8 and >8 g/ day) was significantly associated with all of the dependent

	Total (n=1145)	≤6 g/day (n=286)	6–8 g/day (n=443)	>8 g/day (n=416)	P*
	Mean (SD)				
Age (years)	51.4 (11.7)	50.9 (12.3)	51.8 (11.4)	51.3 (11.6)	0.596
Duration of type 2 diabetes (years)	7.5 (6.4)	7.4 (6.7)	7.8 (6.3)	7.2 (6.4)	0.409
Physical activity (minutes/week)	464.2 (1217.6)	481.3 (928.3)	481.7 (1542.3)	433.5 (979.6)	0.814
			No. (%)		
Sex					0.216
Male	746 (65.2)	178 (62.2)	284 (64.1)	284 (68.3)	
Female	399 (34.8)	108 (37.8)	159 (35.9)	132 (31.7)	
Education	· · ·				0.563
Low education	537 (46.9)	134 (46.9)	200 (45.1)	203 (48.8)	
High education	608 (53.1)	152 (53.1)	243 (54.9)	213 (51.2)	
Current smoking status	· · · ·	, ,			0.012
No	782 (68.3)	214 (74.8)	301 (67.9)	267 (64.2)	
Yes	363 (31.7)	72 (25.2)	142 (32.1)	149 (35.8)	
Current drinking status		· · · /	x- · /	(	0.001
No	654 (57.1)	189 (66.1)	247 (55.8)	218 (52.4)	
Yes	491 (42.9)	97 (33.9)	196 (44.2)	198 (47.6)	
Weight status	( )	· · · · · · · · · · · · · · · · · · ·	( )	· · · ·	0.025
Underweight	243 (21.2)	63 (22.0)	76 (17.2)	104 (25.0)	
Normal weight	414 (36.2)	109 (38.1)	177 (40.0)	128 (30.8)	
Overweight	480 (41.9)	113 (39.5)	185 (41.8)	182 (43.8)	
Obesity	8 (0.7)	I (0.3)	5 (1.1)	2 (0.5)	
Waist circumference status		()		()	<0.001
Normal	533 (46.6)	148 (51.7)	229 (51.7)	156 (37.5)	
Central obesity	612 (53.4)	138 (48.3)	214 (48.3)	260 (62.5)	
Hypertension	()	(,	(,		0.218
Yes	453 (39.6)	105 (36.7)	170 (38.4)	178 (42.8)	
Hyperlipidemia	()	,			0.933
Yes	600 (52.4)	148 (517)	231 (52.1)	221 (53.1)	
Hyperuricemia	()		( <b></b> )		0.354
Yes	202 (17.6)	45 (15.7)	75 (16.9)	82 (19.7)	
Coronary disease	(,		(. •)	()	0.509
Yes	48 (4.2)	12 (4.2)	22 (5.0)	14 (3.4)	
Stroke		( /	(0.0)	(3.1)	0.339
Yes	37 (3.2)	13 (4.5)	13 (2.9)	11 (2.6)	0.007
Medication for hypertension†				(=)	0.287
Yes	417 (36.7)	97 (33.9)	157 (35.4)	163 (39.2)	0.207
Medication for hyperlipidemia†	(30.7)	(33.7)	137 (33.1)	100 (37.2)	0.320
Yes	316 (27.6)	89 (31.1)	118 (26.6)	109 (26.2)	0.520
Medication for hyperuricemia <sup>+</sup>	510 (27.0)	07 (51.1)	110 (20.0)	107 (20.2)	0.938
Yes	30 (2.6)	8 (2.8)	12 (2.7)	10 (2.4)	0.750

Notes: \*Statistical values for continuous variables and categorical variables were obtained from analysis of variance and chi-square test, respectively. †The total sample of medication for hypertension was 1140; the total sample of medication for hyperlipidemia and medication for hyperuricemia was 1142. Abbreviation: SD, standard deviation.

variables (FPG, 2hPG, FINS, 2hINS and  $HbA_{1c}$ ) in the crude model. After further adjusting for confounding factors, lifestyle factors, BMI, WC, SBP, DBP, UA, SCr, medication and interactions, dietary salt (>8 g/day) remained statistically significant in the model and

positively associated with FPG ( $\beta$ =2.3, *P*=0.013) and HbA<sub>1c</sub> ( $\beta$ =0.67, *P*=0.032). Thus, the results showed that higher dietary salt (>8 g/day) increased FPG by 2.3 mmol/ L and HbA<sub>1c</sub> by 0.67%, compared to lower dietary salt (≤6 g/day).

Factors*	≤6 g/day (n=286)	6–8 g/day (n=443)	>8 g/day (n=416)	Р
BMI (kg/m <sup>2</sup> )	25.2 (3.8)	24.9 (3.6)	25.9 (3.8) <sup>a,d</sup>	<0.001
WC (cm)	87.6 (10.6)	87.9 (9.7)	90.4 (9.5) <sup>b,d</sup>	<0.001
VFA (cm <sup>2</sup> )	87.7 (40.1)	89.9 (40.3)	99.8 (38.7) <sup>b,d</sup>	<0.001
SFA (cm <sup>2</sup> )	175.9 (3.9)	174.0 (60.6)	189.0 (64.6) <sup>a,c</sup>	0.001
SBP (mmHg)	133.1 (17.7)	131.2 (17.7)	133.8 (18.3)	0.088
DBP (mmHg)	79.3 (11.5)	78.8 (11.0)	79.8 (10.6)	0.405
FPG (mmol/L)	8.1 (3.0)	8.7 (2.9)	8.9 (3.0) <sup>a,c</sup>	0.005
2hPG (mmol/L)	12.6 (4.7)	14.0 (5.6) <sup>b</sup>	14.2 (5.0) <sup>d</sup>	<0.001
FINS (mIU/L)	11.2 (13.8)	12.6 (42.0) <sup>a</sup>	12.2 (38.8)	0.048
2hINS (mIU/L)	38.2 (54.3)	43.0 (137.0)	44.9 (114.6)	0.194
HbA <sub>Ic</sub> (%)	7.6 (1.9)	8.2 (2.1) <sup>b</sup>	8.4 (2.0) <sup>d</sup>	<0.001
TC (mmol/L)	4.4 (1.1)	4.6 (1.2)	4.7 (1.3) <sup>b</sup>	0.002
TG (mmol/L)	1.3 (1.1)	1.4 (1.2) <sup>a</sup>	1.6 (1.2) <sup>b</sup>	0.006
LDL-C (mmol/L)	2.8 (0.851)	2.9 (0.865)	3.0 (0.910) <sup>c</sup>	0.006
HDL-C (mmol/L)	1.2 (0.303)	1.2 (0.288)	1.1 (0.272) <sup>c</sup>	0.050
Uric acid (mmol/L)	327.4 (89.8)	329.9 (89.4)	330.9 (85.6)	0.870

**Notes**: \*FINS, 2hINS and TG are presented as median values with interquartile range; the other factors are presented as mean values with standard deviation. <sup>a</sup>Significant difference from salt intake  $\leq 6$  g/day, P<0.05. <sup>b</sup>Significant difference from salt intake  $\leq 6$  g/day, P<0.05. <sup>d</sup>Significant difference from salt intake  $\leq 6$  g/day, P<0.05. <sup>d</sup>Significant difference from salt intake  $\leq 6$  g/day, P<0.05. <sup>d</sup>Significant difference from salt intake  $\leq 6$  g/day, P<0.001. <sup>c</sup>Significant difference from salt intake  $\leq 6$  g/day, P<0.001.

**Abbreviations**: BMI, body mass index; WC, waist circumference; VFA, visceral fat area; SFA, subcutaneous fat area; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; 2hPG, 2-hour postprandial plasma glucose; FINS, fasting plasma insulin, 2hINS, 2-hour postprandial plasma insulin; HbA<sub>1c</sub>, glycated hemoglobin A<sub>1c</sub>; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

## Discussion

To date, the association of dietary salt intake with the glycemic response has not been adequately investigated and understood in China, in T2D patients in particular.

The present study, using clinical data from the outpatient Department of Endocrinology and the MMC, analyzed the association between dietary salt and the glycemic response (plasma glucose, insulin and  $HbA_{1c}$ ) in T2D patients in

 Table 3 Association Between Dietary Salt Intake and Plasma
 Plasma

 Glucose
 Intake and Plasma
 Intake and Plasma

Salt Intake*	β	95% CI	Р	
	Fasting plasma glucose			
Crude model				
6–8 g/day	0.538	0.095, -0.292	0.017	
>8 g/day	0.731	0.292, 1.2	0.001	
Adjusted model <sup>a</sup>				
6–8 g/day	1.4	-0.442, 3.I	0.139	
>8 g/day	2.3	0.472, 4.1	0.013	
	2-hour postprandial plasma glucose			
Crude model				
6–8 g/day	1.4	0.625, 2.2	<0.001	
>8 g/day	1.5	0.742, 2.3	<0.001	
Adjusted model <sup>a</sup>				
6–8 g/day	2.3	-0.960, 5.6	0.166	
>8 g/day	1.5	-I.8, 4.8	0.380	

**Notes:**  $\leq 6$  g/day salt intake is the reference category in the model. <sup>a</sup>Adjusted for sex, age, education, physical activity, smoking, drinking, creatinine, uric acid, lipids, medication and interactions.

**Abbreviations**:  $\beta$ , beta-coefficient; CI, confidence interval.

 Table 4 Association Between Dietary Salt Intake and Insulin

Salt Intake*	β	95% CI	Р
	Fasting insulin		
Crude model			
6–8 g/day	20.3	7.7, 32.9	0.002
>8 g/day	7.5	-5.3, 20.2	0.251
Adjusted model <sup>a</sup>			
6–8 g/day	-22.7	-78.3, 32.8	0.422
>8 g/day	-0.274	-56.1, 55.5	0.992
	2-hour postprandial insulin		
Crude model			
6–8 g/day	47.7	19.7, 75.6	0.001
>8 g/day	22.8	-5.6, 51.1	0.116
Adjusted model <sup>a</sup>			
6–8 g/day	-73.7	-163.2, 77.6	0.229
>8 g/day	-42.8	- <b>193.6, 46.3</b>	0.486

**Notes:**  $\leq 6$  g/day salt intake is the reference category in the model. <sup>a</sup>Adjusted for sex, age, education, physical activity, smoking, drinking, creatinine, uric acid, lipids, medication and interactions.

**Abbreviations**:  $\beta$ , beta-coefficient; CI, confidence interval.

β	95% CI	Р
0.43	-0.21, 1.1	0.188
0.64	0.002, 1.3	0.049
0.44	-0.18, 1.1	0.162
0.67	0.04, 1.3	0.032
	0.64 0.44	0.43 -0.21, 1.1 0.64 0.002, 1.3 0.44 -0.18, 1.1

Table 5 Association Between Dietary Salt Intake and HbA1c

Notes: ≤6 g/day salt intake is the reference category in the model. <sup>a</sup>Adjusted for sex, age, education, physical activity, smoking, drinking, creatinine, uric acid, lipids, medication and interactions.

Abbreviations:  $\beta$ , beta-coefficient; CI, confidence interval; HbA<sub>1c</sub>, glycated hemoglobin A<sub>1c</sub>.

Ningbo. The findings indicated that higher dietary salt was positively associated with increased FPG and HbA<sub>1c</sub>.

A previous study conducted on healthy residents in Ningbo found a higher fasting blood glucose level in the group with a higher dietary salt intake ( $\geq 6$  g/day) than in the group with lower dietary salt intake ( $\leq 6$  g/day).<sup>12</sup> The results of that Chinese study are in line with our findings on FPG among Chinese patients in Ningbo, although the target populations are different. The mechanism of the association between dietary salt and the glycemic response in T2D patients is unclear. Increased dietary salt intake may suppress the activity of the renin–angiotensin–aldosterone system,<sup>20,21</sup> stimulate sympathetic activity<sup>22</sup> and cause insulin resistance.<sup>23,24</sup> Therefore, it may contribute to the development and progression of T2D complications.

In the majority of studies, the relationship between dietary salt and the glycemic response of T2D has been explored through observational studies, intervention studies and meta-analyses in healthy populations.<sup>12,25,26</sup> However, few studies have been conducted on T2D patients. Our findings showed that dietary salt was positively associated with HbA<sub>1c</sub>, which is consistent with the results from a randomized controlled trial (RCT) on salt reduction.<sup>26</sup> This observer-blind RCT, recruiting 70 patients with acute non-cardioembolic mild ischemic stroke, reported that HbA<sub>1c</sub> decreased more in the lifestyle intervention group, providing a reduction in salt intake, compared to the control group, although no significant difference was found between the two groups.<sup>26</sup> Likewise, Strazzullo et al conducted a meta-analysis including 13 studies with 177,025 participants, which indicated an association between the HbA1c level and dietary sodium in the development of cardiovascular disease.<sup>27</sup>

Higher dietary salt was found to be related to a high prevalence of overweight and obesity compared to lower

dietary salt in the present study. In addition, high blood lipid levels were significantly related to increased dietary salt intake in our study. The potential hypothesis is that high dietary salt may increase plasma glucose and postprandial plasma glucose in T2D patients through weight gain due to increased appetite and overconsumption of energy, fat and cholesterol.<sup>28</sup> Eventually, the increased fat free acid level in the blood can inhibit insulin suppression of hepatic glucose production.<sup>29</sup> Dietary salt is a key factor in increasing the feeling of thirst, resulting in greater intake of fluid drinks.<sup>30</sup> An increase in the dietary salt intake of 1 g/day was positively associated with an increase of 100 g/day total fluid and 27 g/day sugar-sweetened soft drink consumption.<sup>31</sup> In this way, it may contribute to high blood pressure/hypertension.

Several dietary guidelines recommend and advocate that patients with T2D should decrease their dietary salt intake for lowing a modest blood pressure.<sup>8,9</sup> In the present study, the results derived from descriptive analysis showed that no significant differences in SBP and DBP were found across dietary salt categories. The WHO Cardiovascular Diseases and Alimentary Comparison (WHO-CARDIAC) Study, conducted on pre- and postmenopausal women from 17 countries, reported that 24-hour sodium excretion was positively associated with blood pressure.<sup>32</sup> In T2D patients, hypertension is associated with a range of adverse outcomes for further developing cardiovascular disease and premature mortality.<sup>33</sup> The different result in our study could be attributed to the cross-sectional study design.

In this study, dietary salt was not found to be significantly associated with postprandial plasma glucose and postprandial insulin. Few studies have investigated the relationship between dietary salt and postprandial plasma glucose and insulin responses in T2D patients. An intervention study including six healthy adults, who were randomly assigned to take meals with or without added salt, suggested that moderate dietary salt intake increased postprandial plasma glucose and insulin levels.<sup>25</sup> Sodium can facilitate the absorption of glucose in the small intestine.<sup>34</sup> The potential reason for the difference between studies may be that most of our participants had been diagnosed with T2D for a certain period, so that postprandial plasma glucose and insulin responses to dietary salt were not the same as in healthy participants owing to their weak digestive system.

The relationship between dietary salt intake and hypertension is well understood in the Chinese population. In addition, there is a high level of knowledge on glycemic control through the duration and quantity of carbohydrate consumption from foods.<sup>35</sup> Patients with diabetes are recommended to restrict their total consumption of energy and carbohydrates in order to control body weight and blood glucose levels. However, more attention needs to be paid to the effect of dietary salt intake on the glycemic response in T2D patients. Therefore, hospital-based education and community-based education are required regarding the health effects of excess salt intake, food labeling and food sources.

This is the first study on the association between dietary salt intake and the glycemic response in T2D patients in Ningbo with standard national management and treatment by MMC. Nevertheless, several study limitations need to be considered. First, causality between dietary salt intake and factors of T2D cannot be assessed owing to the cross-sectional study design. Second, because of the structure of the FFQ, quantitative dietary salt intake could not be obtained, although the categories of salt intake could be collected from the patients. Therefore, it may not accurately reflect daily dietary salt intake among T2D patients. Third, total energy intake was not adjusted in the model owing to the FFQ. In addition, the reported dietary salt level could be biased towards misreporting because of the patients' psychology. Furthermore, the patients were from eastern China, so the findings may not be representative for the entire Chinese population with T2D.

### Conclusion

High dietary salt intake was found to be associated with FPG and  $HbA_{1c}$  among T2D patients. Hospital-based lifestyle education with the promotion of salt reduction should be provided to T2D patients. Future research should involve intervention studies on salt reduction to investigate the impact of the dose of dietary salt intake on the glycemic response of T2D patients.

## **Data Sharing Statement**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## **Ethics Statement**

The study was ethically approved by the Ethics Committee of Ningbo First Hospital, China (ethics approval no. 2019-R057) and followed the principles of the Declaration of Helsinki.

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## Disclosure

The authors declared no conflicts of interest for this work.

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