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Mediating effect of TyG index on the association between glucose-lipid metabolism-related dietary pattern and T2DM: a propensity score-matched analysis

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Abstract

Objective This study aimed to investigate the association of dietary patterns (DPs) with risk of T2DM, emphasizing the intermediary role of HOMA or TyG indices among a Chinese adult population.

Research design and methods Directed acyclic graphs combined with propensity score matching were used to minimize confounding, resulting in 1330 subjects for final analysis. Principal component analysis and reduced rank regression, applied to eleven food groups. Multivariable logistic regression and restricted cubic spline regression models were used to assess associations between there DPs with prevalent T2DM, as well as insulin resistance and β-cell function (HOMA-TyG). Mediation analyses were conducted to evaluate whether the HOMA-TyG index mediated the relationship between DPs and T2DM.

Results The DP1, characterized by high intakes of poultry, meat, and preserved foods, was associated with elevated body mass index, triglycerides, and hemoglobin A1c. Both PCA-DP1(OR_{Q4VsQ1} = 2.15, 95% CI: 1.53–3.03) and RRR-DP1 (OR_{Q4VsQ1} = 1.69, 95% CI: 1.82–3.58) were significantly positively correlated with T2DM. RRR-DP1 additionally demonstrated a dose-dependent relationship with HOMA-insulin resistance and TyG. Furthermore, the TyG index mediated approximately 19.51% of the relationship between RRR-DP1 and T2DM.

Conclusions These findings indicate that glucose-lipid metabolism-related dietary pattern, notably high in animal fat, exacerbates insulin resistance and heightens T2DM risk. Tailoring dietary interventions to modify this pattern may be an effective strategy for preventing and managing T2DM.

Keywords Dietary patterns, Reduced rank regression, PSM, Type 2 diabetes mellitus

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Introduction

Over the past several decades, dramatic socio-economic transitions and rapid urbanization in China have coincided with a marked rise in the prevalence of type 2 diabetes mellitus (T2DM) [1]. It is characterized by impaired insulin secretion and suboptimal peripheral tissue response to insulin, ultimately affecting energy and glucose homeostasis [2]. Research has shown that T2DM development is multifactorial, involving genetic, epigenetic, lifestyle-related, and environmental factors [1]. According to the 2019 Global Burden of Diseases, dietary factor contributed to 29.7% of the disability-adjusted life-year of diabetes [3]. Risk factors include higher intakes of unprocessed and processed meat, and low intakes of fresh fruit and vegetables [4, 5].

Emerging evidence underscores that focusing on overall dietary patterns (DPs), rather than individual foods or nutrients, may offer more practical insights for dietary interventions in the general population [6, 7]. Multiple analytical approaches have been used to identify these patterns, with a priori (dietary quality indices) and posteriori (factor analysis or principal component analysis [PCA]) methods being the most common [8]. Hybrid approaches, such as reduced-rank-regression (RRR), can further elucidate causal pathways by combining both dietary data and intermediate biomarkers [9]. While RRR has been applied to examine DPs and various metabolic pathways, including glucose homeostasis [10], inflammatory biomarkers [11], and blood lipids profiles [12], evidence linking glucose-lipid metabolism-related dietary patterns to T2DM, especially in Chinese adults, remains scarce. To bridge this gap, we used three indicators of glucose metabolism, lipid metabolism, and adiposity measures in our RRR analysis, specially selecting HbA1c and fasting C-peptide over fasting glucose and fasting insulin to better capture longer-term glycemic control and endogenous insulin secretion [13].

Insulin resistance (IR), hyperinsulinemia and islet beta cell dysfunction are crucial in T2DM onset and progression [14], and dietary factors, particularly those rich in energy and macronutrient intakes, are implicated in both hyperinsulinemia and IR [15]. Although the homeostatic model assessment (HOMA) is widely used to evaluate β-cell function and IR [16], the triglyceride glucose (TyG) index has shown superior performance for predicting IR and has been proposed as a viable alternative marker [17]. Elevated TyG levels have been associated with T2DM and may serve as an early indicator of high-risk individuals [18]. Although previous studies have linked DPs to HOMA-IR [19] and suggest that diets high in saturated fat exacerbate IR [20] while fiber intake improves glycemic control [21], investigations into the roles of DPs and TyG in T2DM are limited, and few have explored whether IR mediates the relationship between DPs and T2DM prevalence.

To address these gaps, we employed PCA and RRR to identify dietary patterns associated with glucose-lipid metabolism among Chinese adults. We then evaluated the association of these patterns with T2DM prevalence, with a particular focus on the mediating roles of HOMA and TyG indices.

Research design and methods

Inclusion and exclusion criteria

This community-based observational, cross-sectional study was conducted from June 2019 to December 2020 in Jiangsu Province, eastern China. A total of 2230 subjects, including 793 diabetes and 1437 non-diabetes were enrolled. All participants underwent a health examination, sample collection and a standardized face-to-face questionnaire including general information, self-reported medical history and the use of medications, family history of diseases (hypertension, diabetes, etc.), lifestyle (cigarette smoking, alcohol drinking, etc.), dietary behavior, and so on. All physical examinations and interviews were performed by the trained healthcare staff. This study was approved by the Institutional Review Board of Changzhou Centers for Disease Control and Prevention (Changzhou CDC Ethics [2019] 01), and all the participants signed an informed consent form before participation.

Clinical and biochemical data

T2DM was defined according to the criteria of American Diabetes Association (ADA) [2], based on at least one of the following: a self-reported physician diagnosis, current use of hypoglycemic medications or insulin, fasting blood glucose (FBG) ≥ 7.0 mmol/L or HAb1c ≥ 6.5% validated at least twice in different periods. Body mass index (BMI) was calculated by weight in kilograms divided by the square of height in meters. It was divided into three levels: normal weight (18.5 ≤ BMI < 25.0), overweight (25.0 ≤ BMI < 28.0) and obesity (BMI ≥ 28.0) [22]. The planned structured exercise was defined as engaging in (1) ≥ 20 min of strenuous exercise (e.g., running, climbing, cycling) for ≥ 3 days during the past week, (2) ≥ 30 min of regular exercise a little more challenging than usual (e.g., swimming, doubles tennis, volleyball) for ≥ 5 days during the past week, or (3) ≥ 30 min of walking faster than 5 km/h for ≥ 5 days during the past week [23]. In our study, Participants were categorized into three groups according to exercise frequency: never, activity but not sufficient (< 3 day/week of planned), sufficient (≥ 3 day/week of planned). Smoking status was defined as having smoked at least 100 cigarettes in one's lifetime. Drinking status was defined consuming alcohol at least once per month. Blood pressure was measured three

times by trained nurses using a standard mercury sphygmomanometer according to a protocol from American Heart Association (AHA) [24]. Hypertension was defined as systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg or history use of antihypertensive medications.

Plasma lipid concentrations [total cholesterol (TC), total triglycerides (TG), low-density lipoprotein cholesterol (LDLC) and high-density lipoprotein cholesterol (HDLC)] were measured using AU680 Chemistry Analyzers (Beckman-Coulter, Brea, CA, USA). High TC (≥ 6.22 mmol/L), High TG (≥ 2.26 mmol/L), low HDLC (< 1.04 mmol/L) and High LDLC (≥ 4.14 mmol/L) were defined according to the Guidelines for the Prevention and Treatment of Dyslipidemia in Chinese Adults (revised 2016) [25]. Fasting insulin and C-peptide concentrations were measured using iFlash 3000 immunoanalyzers (YHLO Biotech, Shenzhen, China). The triglyceride-glucose (TyG) index was calculated based on the formula: TyG index = log [[fasting TC (mg/dL) * fasting blood glucose (mg/dL)]/2] [26]. The homeostasis model assessment of β-cell function (HOMA-%β), HOMA of insulin resistance (HOMA-IR) was obtained [16]. HOMA-IR was calculated as [FBG (mmol/L) * fasting insulin (IU/mL)]/22.5. HOMA-%β was calculated as [20*fasting insulin (IU/mL)/[FBG (mmol/L)-3.5]] %. Glucose and triglyceride values were converted from mmol/L to mg/dL and multiplied by 18.020 and 88.545, respectively.

Selection of covariates and propensity score matching

Directed acyclic graphs (DAGs), created using the DAGitty v3.0 (http://dagitty.net/), were utilized to identify the minimal sufficient set of confounders for this study [27]. DAGs have been shown to outperform traditional variable selection methods, such as step-wise regression procedures, by explicitly modeling causal relationships [28]. For this analysis, T2DM was designated as the outcome and dietary patterns as the exposure. The minimal sufficient adjustment set included age, gender, household income, education, occupation, drinking, smoking, physical exercise, family history of diabetes, obesity, and metabolic syndrome (Figure S1). Subsequently, covariate balancing generalized propensity score were computed, and a 1:1 nearest neighbor matching algorithm with a caliper of 0.02 was used to create matched case-control pairs. Standardized mean differences (SMD) were evaluated before and after matching to ensure balance of covariates. Following propensity score matching (PSM), 1330 participants remained for subsequent analyses.

Dietary analysis

Dietary intake over the preceding 12 months was assessed using a food frequency questionnaire (FFQ) adapted from a previous study and from the National Institute for Nutrition and Health, Chinese Center for Disease Control and Prevention [29, 30]. Eleven major food items of the local area were included: rice, wheat, poultry, meat, fish, eggs, fresh vegetables, fresh fruits, soybeans, dairy products, and preserved food. Consumption frequencies were recorded as never/rarely, 1–3 days/week, 4–6 days/week, or daily, corresponding to 0, 2, 5, or 7 days/week, respectively. The estimated weekly intake for each food group was calculated as the average consumption per day multiplied by the frequency category. A subset of 197 participants completed repeat FFQs within one year, demonstrating satisfactory reproducibility.

PCA was used to derive dietary patterns based on these 11 food groups. Patterns were identified according to screen plot, eigenvalues > 1, interpretability and the amount of variance explained. Factor loading with values above 0.25 or lower than − 0.25 indicated prominent types. The RRR was performed to identify glucose-lipid metabolism-related dietary patterns, using 11 food groups as predictors and the the following biomarker responses: HbA1c, C-peptide, TC, TG, HDLC, LDLC, BMI. Absolute factor loading > 0.25 characterized each dietary pattern, and corresponding factor scores were derived from weighted combinations of standardized food group intakes. Spearman's correlation was used to relate these factors to continuous variables, while point-biserial correlation was employed for binary variables.

Statistical analysis

All statistical analyses were conducted on software Stata version 15.0 and R version 4.0.5. The *Shapiro–Wilk test* was conducted to assess the normality of continuous variables. Normally distributed data are expressed as mean ± standard deviation (SD), whereas non-normally distributed data are presented as median (25th-75th percentile). Categorical variables are expressed as percentages (%). The *chi-square test*, *Fisher's exact test*, *Mantel-Haenszel* method, and *ANOVA* were employed to compare group differences where appropriate.

Restricted cubic spline regression (RCS) models with three knots placed at the 1th, 50th and 99th percentiles were conducted to explore potential non-linear dose-response relationship between dietary patterns and adverse outcomes (insulin resistance (HOMA-IR, TyG index) or islet β cell function (HOMA-%β) or T2DM). Each dietary pattern score was also divided into quantiles, with the fourth quantile (Q4) signifying the highest consumption. Multiple logistic regression and generalized linear models were modeled to obtain effective parameters (odds ratios (OR) or beta coefficients (β) and 95% confidence intervals (CI)) and applied to assess the relationships between prevalent T2DM and dietary patterns. Three models were specified: model 1 was

crude without any covariables, model 2 was adjusted for age, gender, education, occupation, household income, physical exercise, drinking, smoking, and model 3 further adjusted for family history of diabetes, obesity, metabolic syndrome. Covariates in models were derived from the primary DAG analysis. Mediation analyses were performed to assess the indirect effects of DPs on the risk of T2DM through HOMA-IR, HOMA-%β, or TyG index, while controlling for covariates. The bootstrap method with 5000 samples was used to estimate indirect and total effects, and the mediation ratio was calculated as (indirect effect/total effect) *100. Cochran-Armitage trend tests were employed for statistical trend analyses. All reported *P*-values were two-sided and values 0.05 were considered statistically significant.

Sensitivity and subgroup analyses

Missing data were imputed using multiple imputation ("mice" package, https://cran.r-project.org/web/packages/mice/index.html). Additional models were fitted for comparison with the DAG approach, including full models containing all variables and models with another statistical variable selection method (least absolute shrinkage and selection operator (LASSO) regression) [31]. Covariates were gender, marriage status, physical activity, family history of diabetes, BMI, dyslipidemia. Subgroup analysis was further performed according to age, gender, and BMI categories.

Results

Characteristics of dietary patterns

A total of 2230 (49.98%, males) participants provided dietary data, with ages ranged from 20 to 92 years (mean 53.73 years). After propensity score matching, the balance between case and control groups improved substantially, as indicated by SMDs below 10% for characteristics including age, gender, education status, occupation, smoking, drinking and family history of diabetes (Fig. 1; Table 1).

As Fig. 2 and Table S1 depicts, three glucose-lipid metabolism-related dietary patterns were identified using PCA and RRR methods. The first dietary pattern (DP 1) was characterized by high intakes of animal fat foods (poultry, meat) and preserved foods. The second dietary pattern (DP 2) was marked by higher consumption of rice and wheat, whereas the third dietary pattern (DP 3)

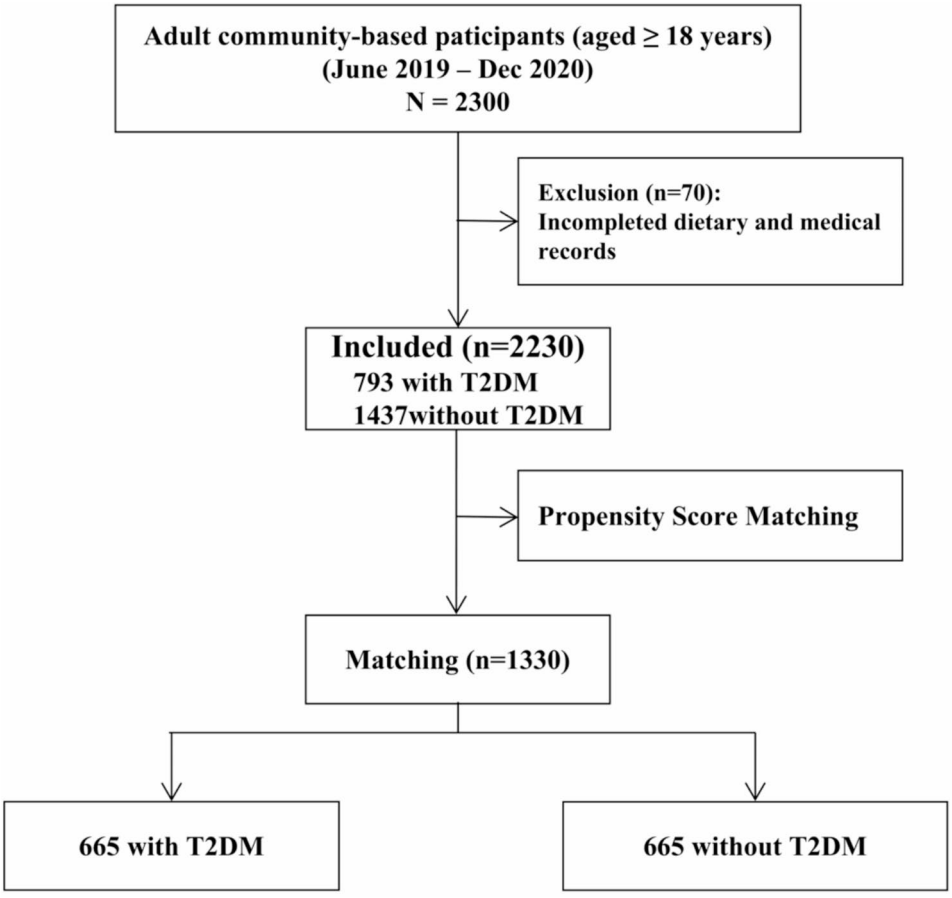

Fig. 1 Flow chart for screening subjects with inclusion and exclusion criteria

Table 1 Descriptive characters of participants in a community-based case-control study before and after matching

Characteristics	Before PSM (*N* = 2230)				After PSM (*N* = 1330)			
	Non-T2DM, *n* = 1437	T2DM, *n* = 793	*P*	SMD	Non-T2DM, *n* = 665	T2DM, *n* = 665	*P*	SMD
Age (mean ± SD, years)	49.1 ± 16.5	62.1 ± 9.59	< 0.01**	0.959	61.7 ± 11.9	61.4 ± 9.87	0.120	0.021
Gender			0.226	0.054			0.139	0.081
Male	704 (48.99%)	410 (51.70%)			324 (48.72%)	351 (52.78%)		
Female	733 (51.01%)	383 (48.30%)			341 (51.28%)	314 (47.22%)		
Marriage status			< 0.01**	0.495			0.133	0.100
Unmarried	183 (12.73%)	10 (1.26%)			11 (1.65%)	9 (1.35%)		
Married	1,214 (84.48%)	727 (91.68%)			623 (93.68%)	608 (91.43%)		
Divorced or other	40 (2.78%)	56 (7.06%)			31 (4.66%)	48 (7.22%)		
Education status			< 0.01**	0.759			0.543	0.061
Primary school or below	615 (42.80%)	555 (69.99%)			468 (70.38%)	453 (68.12%)		
Junior or senior school	300 (20.88%)	177 (22.32%)			146 (21.95%)	151 (22.71%)		
College or above	522 (36.33%)	61 (7.69%)			51 (7.67%)	61 (9.17%)		
Occupation status			< 0.01**	0.385			0.355	0.099
Managerial	618 (43.01%)	225 (28.37%)			232 (34.89%)	207 (31.13%)		
Worker	496 (34.52%)	332 (41.87%)			243 (36.54%)	261 (39.25%)		
Farmer	135 (9.39%)	51 (6.43%)			52 (7.82%)	45 (6.77%)		
Others	188 (13.08%)	185 (23.33%)			138 (20.75%)	152 (22.86%)		
Household income per year			< 0.01**	0.592			0.672	0.068
Up to ¥3000	104 (7.24%)	140 (17.65%)			96 (14.44%)	106 (15.94%)		
¥3001-¥10,000	557 (38.76%)	350 (44.14%)			307 (46.17%)	291 (43.76%)		
¥10,001-¥30,000	512 (35.63%)	104 (13.11%)			109 (16.39%)	103 (15.49%)		
More than ¥30,001	264 (18.37%)	199 (25.09%)			153 (23.01%)	165 (24.81%)		
Physical exercise			0.056	0.11			0.247	< 0.001
Never	1,106 (76.97%)	634 (79.95%)			469 (70.53%)	532 (80.00%)		
Not sufficient	275 (19.14%)	142 (17.91%)			161 (24.21%)	120 (18.05%)		
Sufficient	56 (3.90%)	17 (2.14%)			35 (5.26%)	13 (1.95%)		
BMI category, kg/m^2			< 0.01**	0.229			0.030*	0.145
Normal	679 (47.25%)	286 (36.07%)			282 (42.41%)	235 (35.34%)		
Overweight	528 (36.74%)	352 (44.39%)			263 (39.55%)	295 (44.36%)		
Obesity	230 (16.01%)	155 (19.55%)			120 (18.05%)	135 (20.30%)		
Current drinking	362 (25.33%)	191 (24.39%)	0.630	0.021	164 (24.85%)	164 (24.92%)	0.970	0.002
Current smoking	356 (24.77%)	220 (27.74%)	0.050	0.143	169 (25.41%)	185 (27.82%)	0.580	0.057
Family history of Diabetes	188 (13.08%)	291 (36.70%)	< 0.01**	0.568	137 (20.60%)	166 (24.96%)	0.058	0.104
Family history of Hypertension	542 (37.72%)	345 (43.51%)	0.008**	0.117	234 (35.19%)	261 (39.25%)	0.130	0.084
Hypertension	500 (35.51%)	500 (64.02%)	< 0.01**	0.594	294 (45.16%)	415 (63.46%)	< 0.01**	0.374
Dyslipidemia	435 (30.27%)	398 (50.19%)	< 0.01**	0.415	259 (38.95%)	336 (50.53%)	< 0.01**	0.234
Metabolic disorder	959 (83.54%)	408 (99.76%)	< 0.01**	0.613	383 (92.51%)	359 (100.00%)	< 0.01**	0.402
SBP, mmHg *	124 (114, 135)	134 (124, 144)	< 0.01**	0.531	128 (120, 140)	133 (124, 144)	< 0.01**	0.289
DBP, mmHg *	80 (73, 87)	80 (73, 87)	0.710	0.072	79 (73, 86)	80 (74, 87)	0.130	0.038
TC, mmol/L *	4.83 (4.26, 5.51)	4.92 (4.29, 5.64)	0.081	0.076	5.09 (4.43, 5.70)	4.92 (4.29, 5.66)	0.016*	0.121
TG, mmol/L *	1.30 (0.89, 1.91)	1.78 (1.24, 2.54)	< 0.01**	0.426	1.49 (1.05, 2.06)	1.83 (1.25, 2.59)	< 0.01**	0.336
LDLC, mmol/L *	2.93 (2.43, 3.49)	2.87 (2.33, 3.43)	0.031	0.094	1.33 (1.12, 1.55)	1.20 (1.02, 1.42)	< 0.01**	0.252
HDLC, mmol/L *	1.40 (1.17, 1.62)	1.20 (1.01, 1.42)	< 0.01**	0.04	3.11 (2.58, 3.60)	2.87 (2.33, 3.43)	< 0.01**	0.066
FBG, mmol/L *	5.59 (5.24, 5.99)	7.82 (6.90, 9.25)	< 0.01**	1.593	5.69 (5.31, 6.10)	7.84 (6.95, 9.30)	0.01**	1.535
HbA1c, % *	5.40 (5.10, 5.61)	6.97 (6.22, 7.88)	< 0.01**	1.687	5.47 (5.13, 5.70)	6.96 (6.25, 7.94)	< 0.01**	1.643
FIN, IU/L *	11 (8, 14)	10 (7, 15)	0.410	0.141	9.4 (7.0, 12.9)	10.5 (7.4, 15.4)	< 0.01**	0.264
C-peptide, ng/mL *	2.07 (1.63, 2.65)	2.05 (1.53, 2.76)	0.240	0.008	1.97 (1.53, 2.53)	2.10 (1.55, 2.84)	< 0.01**	0.173
Adiponectin, μg/mL*	6.87 (5.22, 9.11)	5.30 (4.21, 6.94)	< 0.01**	0.364	6.52 (4.99, 8.78)	5.28 (4.18, 6.96)	0.01**	0.282
TyG index *	4.17 (3.80, 4.59)	4.86 (4.45, 5.29)	< 0.01**	1.109	4.31 (3.97, 4.68)	4.88 (4.46, 5.31)	< 0.01**	0.957

Table 1 (continued)

Characteristics	Before PSM (*N* = 2230)				After PSM (*N* = 1330)			
	Non-T2DM, *n* = 1437	T2DM, *n* = 793	*P*	SMD	Non-T2DM, *n* = 665	T2DM, *n* = 665	*P*	SMD
HOMA-IR *	2.65 (1.90, 3.69)	3.74 (2.49, 5.57)	< 0.01**	0.353	2.41 (1.75, 3.33)	3.84 (2.51, 5.90)	< 0.01**	0.408
HOMA-%β *	103 (76, 143)	48 (31, 79)	< 0.01**	0.605	89 (64, 119)	49 (31, 81)	< 0.01**	0.376

The *Shapiro–Wilk test* was used to assess the normality data distribution. Normal data were shown as median (quartiles 25 and 75%) and compared using *Mann–Whitney U test*. Categorical data were shown as n (%) and compared using the *chi-square test* or *Fisher's exact test*. *$P < 0.05$, **$P < 0.01$

PSM, propensity score-matched analysis; T2DM, type 2 diabetes mellitus

BMI: body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, total triglycerides; LDLC, low-density lipoprotein cholesterol; HDLC, high-density lipoprotein cholesterol; FBG, fasting blood glucose; HbA1c, Hemoglobin A1c; FIN, fasting insulin; TyG index, triglyceride-glucose index; HOMA-IR, homeostasis model assessment of insulin resistance; HOMA-%β, homeostasis model assessment of β-cell function

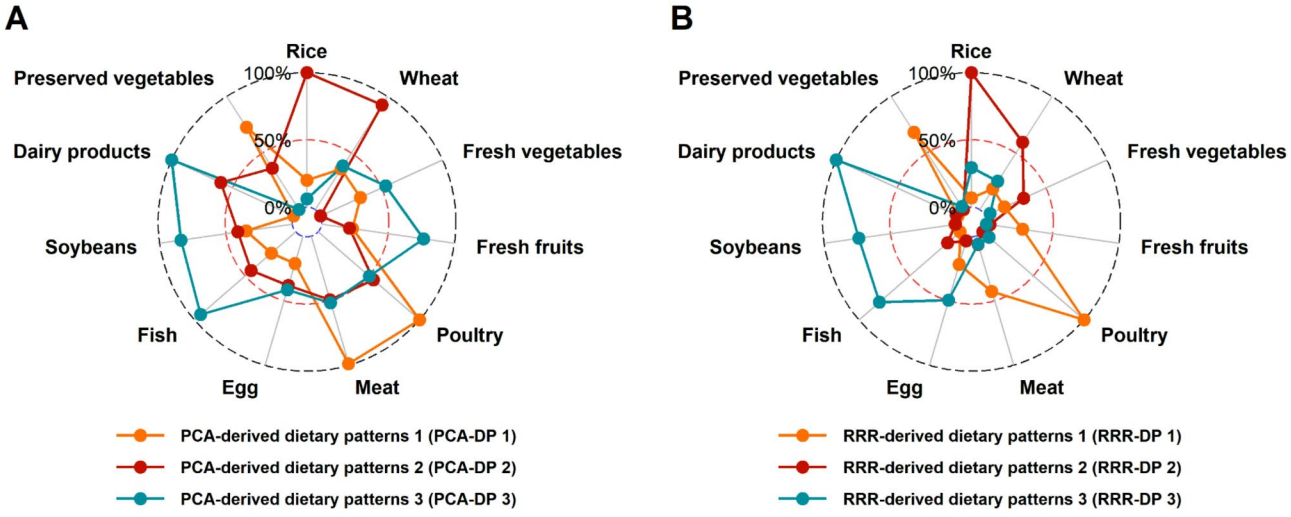

Fig. 2 Spider-web diagram of factor loadings for selected food groups for the dietary pattern identified using principal component analysis (**A**) and reduced rank regression (**B**). PCA, principal component analysis; RRR, reduced rank regression; DP, dietary pattern

featured greater intakes of fish, egg, soybeans, and dairy products. Correlations between factors and the response variables estimated, estimated via PCA and RRR, was presented in Figure S2. Notably, DP 1 showed a significant positive association with elevated TG, BMI, and HbA1c.

Relationship of different dietary patterns with T2DM risk

Restricted cubic spline regression revealed linear dose-response associations of PCA-DP1 and RRR-DP1 with risk of T2DM (Fig. 3). In the fully adjusted models, individuals in the highest quartile of these patterns had a markedly increased T2DM prevalence compared with those in the lowest quartile, whereas RRR-DP2 was negatively associated with T2DM (Table 2). Adjusting for additional confounders in model 3, DP1 continued to demonstrate a significant positive association with T2DM for both PCA [OR_{Q4VsQ1} = 2.15, 95% CI: 1.53–3.03, $P_{\_trend} < 0.01$] and RRR [OR_{Q4VsQ1} = 1.69, 95% CI: 1.82–3.58, $P_{\_trend} < 0.01$]. Conversely, RRR-DP2 maintained a significant negative association with T2DM [OR_{Q4VsQ1} = 0.65, 95% CI: 0.64–1.23, $P_{\_trend}$ = 0.021], though PCA-DP2 did not reach statistical significance [OR_{Q4VsQ1} = 0.89, 95% CI: 0.64–1.23, $P_{\_trend}$ = 0.581]. Neither PCA-DP3 nor RRR-DP3 showed significant associations with T2DM (Table 2).

Sensitivity analyses using LASSO-based confounder selection supported these results, reinforcing the robust positive association of DP1 with T2DM [PCA: OR_{Q4VsQ1} = 2.03, 95% CI: 1.47–2.83, *P-trend* < 0.001; RRR: OR_{Q4VsQ1} = 2.38, 95% CI: 1.72–3.29, *P-trend* < 0.001] (Table S2).

Relationship of dietary patterns and HOMA-TyG index

As shown in Figure S3 and Fig. 4, we also observed the dose-response association of PCA-DPs or RRR-DPs with the HOMA-TyG index. RRR-DP1 had a significant linear association with both HOMA-IR and the TyG index ($P_{HOMA-IR}$ = 0.042, $P_{TyG-index}$ = 0.001, respectively), and PCA-DP1. Each one-unit increment of RRR-DP1 score was linked to 1.12 units higher HOMA-IR (β = 1.12, *P* < 0.001, model 3) and 0.14 units higher TyG (β = 0.14, *P* < 0.001, model 3) (Table 3). Likewise, PCA-DP1 was positively associated with TyG [β_{Q4VsQ1} = 0.13, 95%CI: 0.04–0.21, $P_{\_trend}$ = 0.006]. Again, Model 2 showed similar trends, and LASSO-based sensitivity analyses corroborated the positive link of DP1 with TyG [OR_{Q4VsQ1}

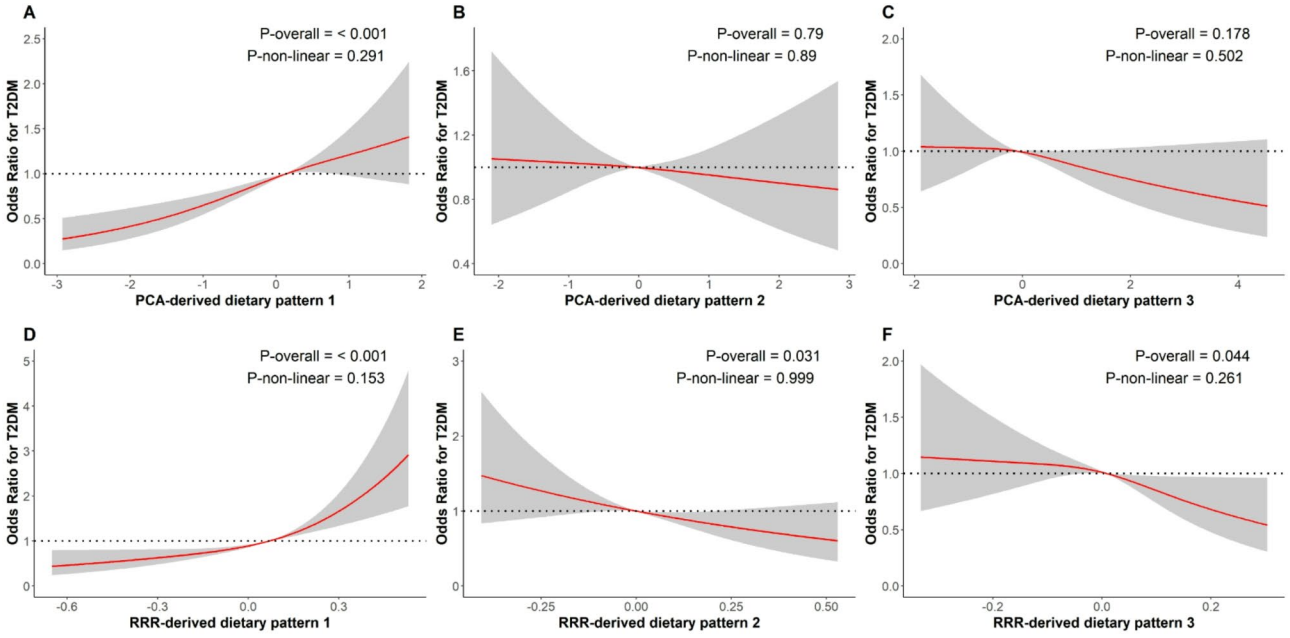

Fig. 3 Dose-response association between dietary patterns (DP) of each method (principal component analysis and reduced rank regression) and prevalent T2DM ($N = 1330$). (**A**~**C**) PCA-derived DP 1 (panel A), PCA-derived DP 2 (panel B), PCA-derived DP 3 (panel C). (**D**~**F**) RRR-derived DP 1 (panel D), RRR-derived DP 2 (panel E), RRR-derived DP 3 (panel F). T2DM, type 2 diabetes mellitus. Odds ratios (OR) and 95% confidence interval derived from restricted cubic splines regression, with knots placed at the 1th, 50th and 99th percentiles of the distribution of DP scores. Models were adjusted for age, gender, education status, household income, physical exercise, drinking, smoking, family of diabetes, obesity, metabolic disorders

= 0.12, 95% CI: 0.04–0.20, $P_{\_trend} < 0.001$] and RRR [OR_{Q4VsQ1} = 0.15, 95% CI: 0.07–0.22, $P_{\_trend} < 0.001$] (Table S2).

Subgroup analysis

To confirm the association between DP1 and prevalent T2DM, subgroup analyses by gender, age, and BMI (Fig. 5) showed younger participants, and those with higher BMI were more prone to T2DM. Among males under 60 years of age, elevated RRR-DP1 scores were positively associated with T2DM prevalence and higher TyG (Table S3, S4).

Mediation by TyG in the relationship between dietary patterns and T2DM risk

Finally, RRR-DP1 was significantly associated with T2DM after full adjustment, and mediation analysis indicated that the TyG index accounted for 19.51% of this relationship (Table 4, Tables S5, S6). Sensitivity analyses with LASSO-based models yielded comparable findings, underlining the mediating role of the TyG index in the link between dietary patterns and T2DM (Table S7).

Discussion

In this study, we applied both PCA and RRR within a propensity-score–matched case-control design to evaluate how different DPs influence T2DM risk, insulin resistance, and β-cell function. Our results reveal that a "glucose–lipid metabolism–related" DP1, distinguished by high intakes of poultry, meat, and preserved foods, is strongly associated with T2DM prevalence—an effect that appears mediated in part by elevated HOMA-IR and the TyG index.

Dietary patterns represents a complex interplay of foods and nutrients that jointly influence metabolic health [32]. By combining PCA, which aggregates food group correlations, and RRR, which integrates disease-specific biomarkers, we identified three distinct DPs. Consistent with prior epidemiological and interventional research [33–35], DP1 was characterized by significant consumption of processed or preserved meat and minimal fruit or vegetable intake—factors that have been repeatedly linked to adverse metabolic outcomes, including hypertriglyceridemia and postprandial hyperglycemia [36], contributing to IR and β-cell dysfunction [37].

Conversely, RRR-DP2—encompassing rice, wheat, and dairy—displayed an inverse association with T2DM, underscoring how biomarker-driven methods (RRR) can highlight potentially protective dietary components, such as high-fiber carbohydrates and certain dairy products [38, 39]. Although a "high-carbohydrate" diet is often viewed as a risk factor for T2DM [40], not all carbohydrate sources carry equal metabolic risks [41]. For instance, whole grains or minimally processed wheat and rice with higher fiber content can moderate postprandial hyperglycemia and reduce IR through improved glycemic

Table 2 Odds ratios (OR) and 95% confidence interval (CI) of prevalent T2DM associated with each score increase in DP

Odds Ratio (95% Confidence Interval)				
Quartile 1 (Reference, *n* = 332)	**Quartile 2 (*n* = 331)**	**Quartile 3 (*n* = 331)**	**Quartile 4 (*n* = 332)**	***P* for Trend §**
Principal component analysis				
DP 1				
Crude model (Model 1) 1.00	1.44 (1.06, 1.96) *	1.42 (1.05, 1.93) *	1.90 (1.40, 2.60) ***	< 0.001
Model 2 1.00	1.46 (1.06, 2.00) *	1.52 (1.10, 2.08) *	2.12 (1.53, 2.93) ***	< 0.001
Model 3 1.00	1.36 (0.98, 1.89)	1.42 (1.02, 1.98) *	2.15 (1.53, 3.03) ***	< 0.001
DP 2				
Crude model (Model 1) 1.00	0.91 (0.67, 1.23)	0.98 (0.72, 1.32)	0.89 (0.66, 1.21)	
Model 2 1.00	0.91 (0.67, 1,24)	1.00 (0.73, 1.35)	0.90 (0.66, 1.22)	0.639
Model 3 1.00	0.95 (0.69, 1.31)	1.01 (0.73, 1.40)	0.89 (0.64, 1.23)	0.581
DP 3				
Crude model (Model 1) 1.00	0.90 (0.66, 1.22)	0.95 (0.70, 1.29)	1.01 (0.75, 1.37)	
Model 2 1.00	0.89 (0.66, 1.22)	0.97 (0.71, 1.31)	0.96 (0.71, 1.31)	0.943
Model 3 1.00	0.84 (0.60, 1.15)	0.99 (0.71, 1.36)	1.00 (0.72, 1.38)	0.756
Reduced rank regression				
DP 1				
Crude model (Model 1) 1.00	1.22 (0.72, 2.05)	1.56 (1.19, 2.05) **	2.43 (1.78, 3.33) **	< 0.001
Model 2 1.00	1.26 (0.74, 2.13)	1.68 (1.27, 2.23) ***	2.61 (1.89, 3.61) ***	0.001
Model 3 1.00	1.33 (0.77, 2.32)	1.34 (1.26, 2.27) ***	1.69 (1.82, 3.58) ***	< 0.001
DP 2				
Crude model (Model 1) 1.00	0.83 (0.61, 1.13)	0.99 (0.73, 1.34)	0.74 (0.54, 1.00)	
Model 2 1.00	0.81 (0.60, 1.11)	0.96 (0.70, 1.32)	0.71 (0.51, 0.97) *	0.086
Model 3 1.00	0.83 (0.60, 1.15)	0.88 (0.63, 1.22)	0.65 (0.46, 0.91) *	0.021
DP 3				
Crude model (Model 1) 1.00	0.88 (0.65, 1.19)	0.90 (0.67, 1.22)	0.75 (0.55, 1.02)	
Model 2 1.00	0.88 (0.65, 1.20)	0.90 (0.66, 1.23)	0.74 (0.54, 1.01)	0.079
Model 3 1.00	0.91 (0.66, 1.25)	0.86 (0.62, 1.19)	0.73 (0.53, 1.01)	0.056

§ Trends were examined using the Cochran-Armitage trend test; *$P < 0.05$, **$P < 0.01$, **$P < 0.001$

Model 1: Unadjusted model. Model 2: Includes adjustment of age, gender, household income, education, occupation, physical exercise, drinking, smoking. Model 3: Includes adjustment of age, gender, household income, education, occupation, physical exercise, drinking, smoking, family history of diabetes, obesity, metabolic syndrome. ORs and 95% confidence interval were obtained using multiple Logistic regression. P for trend values for the medians of each quartile of scores included in the multiple generalized linear models

control and altered gut microbiota composition [42]. Moreover, cultural and regional factors—including portion sizes, cooking methods, and the combined intake of vegetables or lean protein—may collectively influence the net metabolic effect of carbohydrate-rich foods [43]. Thus, while RRR-DP2 appears high in carbohydrates, its potential protective effect may reflect the quality and context of these carbohydrates, rather than the simple quantity of total carbohydrates. Future research assessing refined versus unrefined grain intake could provide additional insights into these protective trends.

Although randomized controlled trials (RCTs) note that carbohydrate-reduced, high-protein diets improve postprandial glycemia [44], our DP3, characterized by fish, eggs, and soybeans, showed no significant correlation with T2DM. One plausible explanation is that co-consumption of refined sugars and processed meats may have dampened the inherent metabolic benefits of fish and soy [36, 45], emphasizing the importance of overall dietary context in shaping glycemic and lipid responses [46, 47].

Taken together, these patterns illustrate the multifaceted nature of diet–disease relationships. The robust linkage between DP1 and T2DM risk, in conjunction with its positive relationship to HOMA-IR and TyG, highlights IR as an early and critical driver of glucose dysregulation [48, 49]. Diets rich in saturated fats and processed foods may accelerate IR through increased circulating triglycerides, postprandial hyperglycemia, and chronic low-grade inflammation, ultimately burdening β-cell function [37]. Conversely, monounsaturated and polyunsaturated fats (MUFAs and PUFAs) could counteract IR by modifying cellular membrane composition and reducing inflammatory responses [50]. Our subgroup analyses further indicate that younger and obese individuals may be more susceptible, echoing findings in large cohort studies [9]. Coupled with evidence of TyG mediating role, these results support the hypothesis that dysregulated glucose–lipid metabolism, fostered by certain dietary behaviors, predisposes to T2DM. Interestingly, in some sensitivity models, we observed instances of a negative proportion mediated, which can occur when the indirect effect (via TyG) and direct effect of the dietary pattern move in opposite directions—a phenomenon known as competitive mediation [51, 52]. Such negative mediation proportions reflect the complexity of metabolic pathways and indicate that certain dietary components may partially mitigate or offset the diet's overall impact on T2DM. Reporting both direct and indirect effect estimates provides a clearer interpretation of these opposing forces [53].

In this context, adhering to a healthy lifestyle—including diets rich in fiber, unsaturated fats, whole grains, fruits, and vegetables—can effectively reduce the

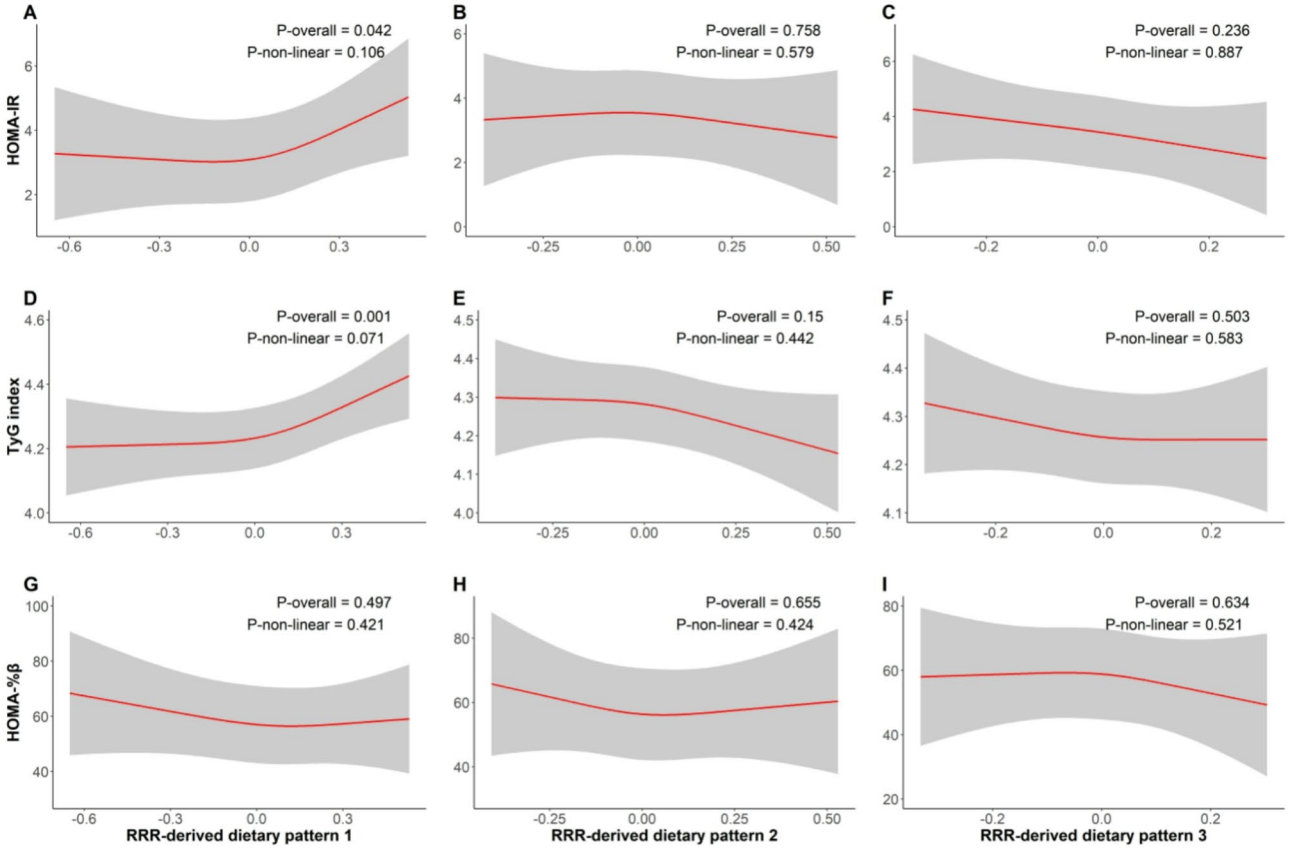

Fig. 4 Dose-response association between reduced rank regression (RRR)-derived dietary patterns (RRR-derived DP) and the homeostasis model assessment of insulin resistance (**A**∼**C**) [HOMA-IR, *n* = 1330. DP 1 (panel A), DP 2 (panel B), DP 3 (panel C)], triglyceride-glucose index (**D**∼**F**) [TyG index, *n* = 1330. DP 1 (panel D), DP 2 (panel E), DP 3 (panel F)], and homeostasis model assessment of β cell function (G∼I) [HOMA-%β, *n* = 1330. DP 1 (panel G), DP 2 (panel H), DP 3 (panel I)]

incidence and severity of metabolic syndrome [48, 54]. Plant-oriented diets appear to ameliorate IR by improving lipid profiles and attenuating systemic inflammation [55]. Although our study focused on T2DM specifically, the observed protective effect of RRR-DP2 points to broader metabolic benefits and highlights the need for integrated lifestyle interventions that target IR before hyperglycemia becomes manifest.

A major strength of this study is our comprehensive approach to confounder management. Directed acyclic graphs (DAGs) and propensity score matching (PSM) facilitated rigorous adjustments, enhancing the validity of comparisons between diabetic and non-diabetic participants. Furthermore, mediation analyses clarified the potential mechanistic role of TyG in connecting these "glucose–lipid metabolism–related" diets to T2DM risk. Nevertheless, certain limitations warrant acknowledgment. First, the cross-sectional nature of this analysis precludes causal inferences. Second, reliance on self-reported food frequency questionnaires introduces possible recall bias, and our participants from eastern China may not represent other dietary and genetic backgrounds. Additional large-scale, longitudinal, or interventional studies are needed to replicate these findings and substantiate their broader applicability.

Conclusions

In summary, our results indicate that both PCA-DP1 and RRR-DP1 are positively associated with insulin resistance (HOMA-IR, TyG index) and heightened T2DM risk in Han Chinese population, whereas RRR-DP2 demonstrates a protective association against T2DM. Furthermore, our study provides evidence that the TyG index partially mediates the link between the glucose–lipid metabolism–related RRR-DP1 and T2DM, underscoring the pivotal role of dysregulated lipid–glucose pathways in the onset of type 2 diabetes.

Table 3 Beta coefficients (β) and 95% confidence interval (CI) of HOMA-TyG index associated with each score increase in DP1

β (95% confidence interval)				
Quartile 1 (Reference, *n* = 332)	**Quartile 2 (*n* = 331)**	**Quartile 3 (*n* = 331)**	**Quartile 4 (*n* = 332)**	***P* for Trend [§]**
PCA-derived DP 1				
HOMA-%β				
Crude model (Model 1) 1.00	-7.19 (-19, 5.0)	2.27 (-9.9, 14)	0.46 (-12, 13)	0.582
Model 2 1.00	-6.04 (-18, 5.9)	2.13 (-10.0, 14)	2.80 (-9.5, 15)	0.760
Model 3 1.00	-4.03 (-16, 7.7)	3.62 (-8.2, 15)	4.49 (-7.5, 16)	0.947
HOMA-IR				
Crude model (Model 1) 1.00	0.01 (-0.07, 0.14)	0.67 (0.39, 1.70)	0.83 (0.01, 0.21)	0.066
Model 2 1.00	0.11 (-1.0, 1.2)	0.98 (-0.12, 2.10)	1.19 (0.08, 2.30) *	0.017
Model 3 1.00	0.07 (-1.0, 1.2)	0.91 (-0.18, 2.00)	1.23(0.12, 2.30) *	0.006
TyG index				
Crude model (Model 1) 1.00	-0.03 (-0.07, -0.14)	0.11 (0.01, 0.21) *	0.11 (0.01, 0.20) *	0.011
Model 2 1.00	0.04 (-0.06, 0.15)	0.13 (0.03, 0.24) *	0.13 (0.03, 0.24) *	0.005
Model 3 1.00	0.02 (-0.06, 0.09)	0.09 (0.01, 0.17) *	0.13 (0.04, 0.21) **	< 0.001
RRR-derived DP 1				
HOMA-%β				
Crude model (Model 1) 1.00	-5.33 (-18, 6.9)	-6.1 (-17, 4.7)	-7.74 (-20, 4.5)	0.222
Model 2 1.00	-1.50 (-30, 10)	-3.2 (-14, 7.4)	-1.91 (-14, 10)	0.176
Model 3 1.00	-0.62 (-29, 9.6)	-2.6 (-13, 7.8)	-2.17 (-14, 9.7)	0.154
HOMA-IR				
Crude model (Model 1) 1.00	-0.26 (-1.3, 0.81)	0.38 (-0.68, 1.40)	0.97 (-0.10, 2.0)	0.109
Model 2 1.00	-0.01 (-1.0, 1.1)	0.65 (-0.44, 1.70)	1.26 (0.16, 2.4) *	0.006
Model 3 1.00	0.04 (-1.0, 1.1)	0.54 (-0.54, 1.60)	1.08 (0.02, 2.2) *	0.027
TyG index				
Crude model (Model 1) 1.00	0.07 (-0.03, 0.17)	0.16 (0.02, 0.20)	0.21 (0.11, 0.31) *	< 0.001
Model 2 1.00	0.09 (-0.02, 0.19)	0.17 (0.07, 0.28) *	0.22 (0.12, 0.32) ***	< 0.001
Model 3 1.00	0.06 (-0.02, 0.14)	0.11 (0.03, 0.19) *	0.14 (0.06, 0.22) ***	0.002

[§]: Trends were examined using the Cochran-Armitage trend test; *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$

PCA-derived DP 1, principal component analysis-derived dietary pattern 1. RRR-derived DP 1, reduced rank regression-derived dietary pattern 1. Model 1: Unadjusted model. Model 2: Includes adjustment of age, gender, household income, education, occupation, physical exercise, drinking, smoking. Model 3: Includes adjustment of age, gender, household income, education, occupation, physical exercise, drinking, smoking, family history of diabetes, obesity, metabolic syndrome. TyG index, triglyceride-glucose index; HOMA-IR, homeostasis model assessment of insulin resistance; HOMA-%β, homeostasis model assessment of β-cell function. The β and 95% confidence interval were obtained using generalized linear models. P for trend values for the medians of each quartile of scores included in the multiple generalized linear regression models

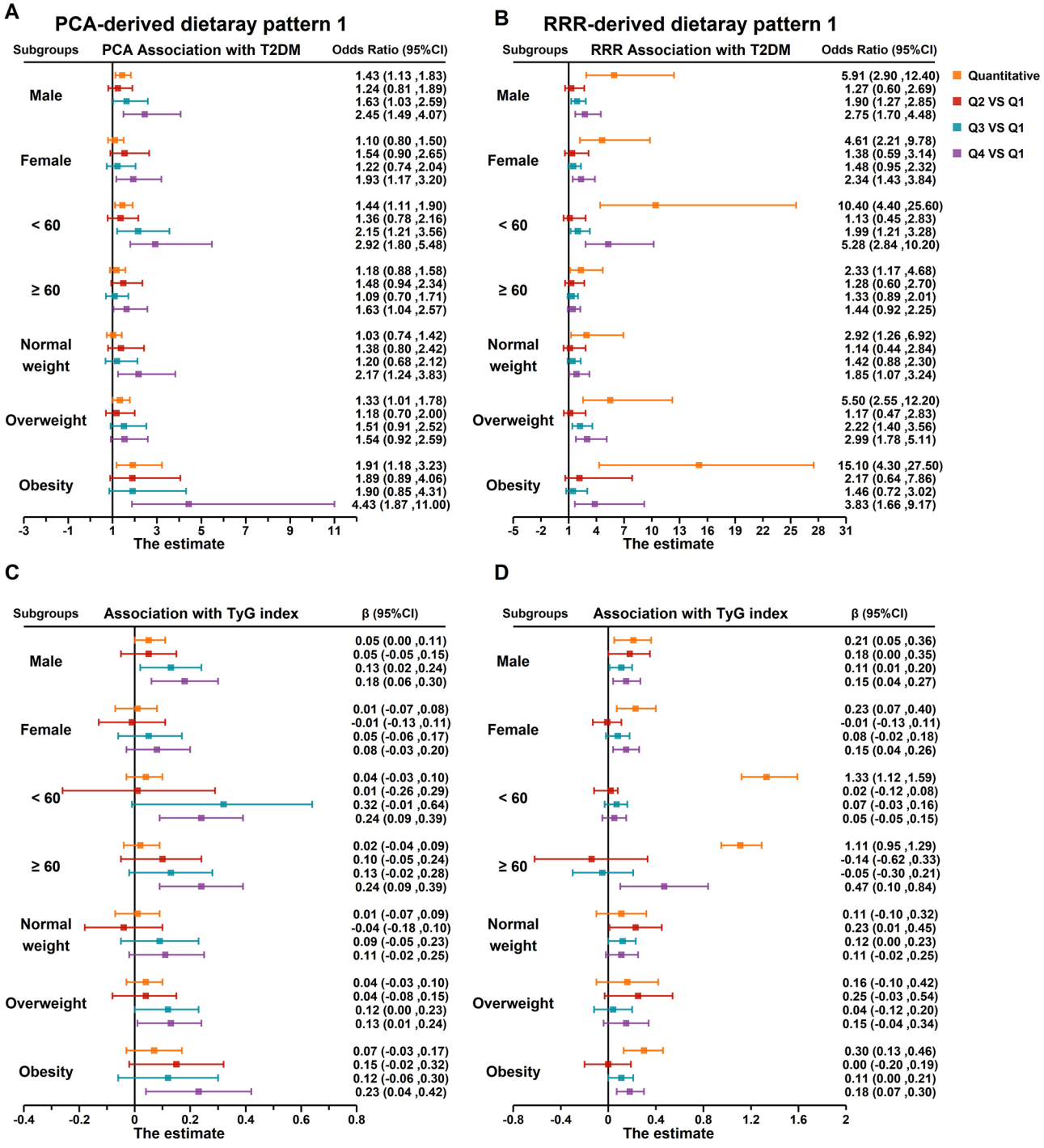

Fig. 5 The association between DPs on the risk of T2DM (**A**, **B**) and TyG index (**C**, **D**) by age, gender, and BMI category. OR, odds ratios; CI, confidence interval; β, estimated coefficients. ORs or β were adjusted for age, gender, education status, household income, physical exercise, drinking, smoking, family of diabetes, obesity, metabolic disorders. DPs, dietary patterns; T2DM, type 2 diabetes mellitus; TyG index, triglyceride-glucose index. BMI, body mass index. Normal (18.5 ≤ BMI < 25.0), overweight (25.0 ≤ BMI < 28.0) and obesity ((BMI ≥ 28.0)

Table 4 Mediation effects of TyG index on the association of DP with prevalent T2DM

Responses	Direct effects	Mediated Effect	Total Effect	Proportion Mediated (%)
Principal component analysis				
DP 1	4.21 (0.29, 7.54) *	1.02 (-0.54, 2.6)	5.23 (1.05, 8.77) **	19.51
DP 2	-0.86 (-3.34, 1.36)	-0.04 (-1.23, 1.04)	-0.90 (-3.59, 1.63)	4.81
DP 3	-1.61 (-4.31, 0.93)	-0.84 (-1.83, 0.11)	-2.45 (-5.1, 0.24)	34.22
Reduced rank regression				
DP 1	26.85 (18.39,33.23) ***	6.50 (2.61, 10.24) ***	33.35 (24.75, 39.83) ***	19.51
DP 2	-16.26 (-27.93, -2.26) *	-5.77 (-11.9, 0.46)	-22.03 (-33.44, -7.4) **	26.19
DP 3	-21.28 (-34.64, -4.12) *	-4.56 (-12.58, 5.64)	-25.84 (-39.59, -4.12) *	17.64

*$P < 0.05$, **$P < 0.01$, **$P < 0.001$

Adjusted of age, gender, household income, education, occupation, physical exercise, drinking, smoking, family history of diabetes, obesity, metabolic syndrome. TyG index, triglyceride-glucose index

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12902-025-01892-6.

Supplementary Material 1

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Author contributions

Shushu Li: Conceptualization, Software, Writing, Funding acquisition. Rong Xia: Formal analysis, Methodology, Writing. Xing Gong: Methodology, Software, Writing. Chao Wang: Data curation, Validation, Funding acquisition. Huibin Dong: Formal analysis, Investigation. Zhangyao Su: Data curation, Investigation. Yucheng Liang: Data curation, Investigation. Hechun Liu: Validation. Shoulin Wang: Conceptualization, Supervision, Funding acquisition. Tao Yang: Conceptualization, Supervision, Funding acquisition.

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Data availability

Availability of data and materialsThe datasets generated and analyzed during the current study are not publicly available due to privacy and ethical considerations but can be available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

Ethical approval was granted from the Institutional Review Board of Changzhou Centers for Disease Control and Prevention (Changzhou CDC Ethics [2019] 01).

Competing interests

The authors declare no competing interests.

Consent for publication

Not applicable.

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References

1. Wang L, Peng W, Zhao Z, Zhang M, Shi Z, Song Z, Zhang X, Li C, Huang Z, Sun X, et al. Prevalence and treatment of diabetes in China, 2013–2018. JAMA. 2021;326(24):2498–506.
2. American Diabetes A. 2. Classification and diagnosis of diabetes: standards of medical care in Diabetes-2021. Diabetes Care. 2021;44(Suppl 1):S15–33.
3. (IHME) IfHMaE. Global Burden of Disease Study 2019 (GBD 2019) Results. In.
4. Wei W, Jiang W, Han T, Tian M, Ding G, Li Y, Sun C. The future of prevention and treatment of diabetes with nutrition in China. Cell Metab. 2021;33(10):1908–10.
5. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, Navarro Rosenblatt D, Greenwood DC, Norat T. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409–19.
6. Liu Q, Wen Q, Lv J, Shi Z, Guo Y, Pei P, Du H, Yang L, Chen Y, Zhang X et al. The prospective associations of lipid Metabolism-Related dietary patterns with the risk of diabetes in Chinese adults. Nutrients 2022, 14(5).
7. Gomez-Delgado F, Katsiki N, Lopez-Miranda J, Perez-Martinez P. Dietary habits, lipoprotein metabolism and cardiovascular disease: from individual foods to dietary patterns. Crit Rev Food Sci Nutr. 2021;61(10):1651–69.
8. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. Curr Opin Lipidol. 2002;13(1):3–9.
9. Gao M, Jebb SA, Aveyard P, Ambrosini GL, Perez-Cornago A, Papier K, Carter J, Piernas C. Associations between dietary patterns and incident type 2 diabetes: prospective cohort study of 120,343 UK biobank participants. Diabetes Care. 2022;45(6):1315–25.
10. Liese AD, Weis KE, Schulz M, Tooze JA. Food intake patterns associated with incident type 2 diabetes: the insulin resistance atherosclerosis study. Diabetes Care. 2009;32(2):263–8.
11. Pajunen L, Korkalo L, Koivuniemi E, Houttu N, Pellonpera O, Mokkala K, Shivappa N, Hebert JR, Vahlberg T, Tertti K, et al. A healthy dietary pattern with a low inflammatory potential reduces the risk of gestational diabetes mellitus. Eur J Nutr. 2022;61(3):1477–90.
12. Duan MJ, Dekker LH, Carrero JJ, Navis G. Blood lipids-related dietary patterns derived from reduced rank regression are associated with incident type 2 diabetes. Clin Nutr. 2021;40(7):4712–9.
13. Watanabe RM, Bergman RN. Accurate measurement of endogenous insulin secretion does not require separate assessment of C-peptide kinetics. Diabetes. 2000;49(3):373–82.
14. Kleissl-Muir S, Rasmussen B, Owen A, Zinn C, Driscoll A. Low carbohydrate diets for diabetic cardiomyopathy: A hypothesis. Front Nutr. 2022;9:865489.

15. Hoy AJ, Nagarajan SR, Butler LM. Tumour fatty acid metabolism in the context of therapy resistance and obesity. Nat Rev Cancer. 2021;21(12):753–66.
16. Wallace TM, Levy JC, Matthews DR. Use and abuse of HOMA modeling. Diabetes Care. 2004;27(6):1487–95.
17. Khan SH, Sobia F, Niazi NK, Manzoor SM, Fazal N, Ahmad F. Metabolic clustering of risk factors: evaluation of Triglyceride-glucose index (TyG index) for evaluation of insulin resistance. Diabetol Metab Syndr. 2018;10:74.
18. da Silva A, Caldas APS, Rocha D, Bressan J. Triglyceride-glucose index predicts independently type 2 diabetes mellitus risk: A systematic review and meta-analysis of cohort studies. Prim Care Diabetes. 2020;14(6):584–93.
19. McNaughton SA, Mishra GD, Brunner EJ. Dietary patterns, insulin resistance, and incidence of type 2 diabetes in the Whitehall II study. Diabetes Care. 2008;31(7):1343–8.
20. McKeown NM, Meigs JB, Liu S, Saltzman E, Wilson PW, Jacques PF. Carbohydrate nutrition, insulin resistance, and the prevalence of the metabolic syndrome in the Framingham offspring cohort. Diabetes Care. 2004;27(2):538–46.
21. Pastorino S, Richards M, Pierce M, Ambrosini GL. A high-fat, high-glycaemic index, low-fibre dietary pattern is prospectively associated with type 2 diabetes in a British birth cohort. Br J Nutr. 2016;115(9):1632–42.
22. Consultation WHOE. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet. 2004;363(9403):157–63.
23. Gianturco V, Gianturco L, Regnoli R, Bodini BD, Turiel M, Trapani M, Bini F, De Angelis G. Healthy promotion for fighting metabolic syndrome: insights from Multi-Center HeRO-FiT cohort. Int J Environ Res Public Health 2020, 17(15).
24. Wang M, Wu T, Yu C, Gao W, Lv J, Wu Y, Qin X, Tang X, Gao P, Zhan S, et al. Association between blood pressure levels and cardiovascular deaths: a 20-year follow-up study in rural China. BMJ Open. 2020;10(2):e035190.
25. Joint committee issued Chinese guideline for the management of dyslipidemia in a. [2016 Chinese guideline for the management of dyslipidemia in adults]. Zhonghua Xin Xue Guan Bing Za Zhi. 2016;44(10):833–53.
26. Alizargar J, Bai CH, Hsieh NC, Wu SV. Use of the triglyceride-glucose index (TyG) in cardiovascular disease patients. Cardiovasc Diabetol. 2020;19(1):8.
27. Lipsky AM, Greenland S. Causal directed acyclic graphs. JAMA. 2022;327(11):1083–4.
28. Digitale JC, Martin JN, Glymour MM. Tutorial on directed acyclic graphs. J Clin Epidemiol. 2022;142:264–7.
29. Li S, Shao W, Wang C, Wang L, Xia R, Yao S, Du M, Ji X, Chu H, Zhang Z, et al. Identification of common genetic variants associated with serum concentrations of P, p'-DDE in non-occupational populations in Eastern China. Environ Int. 2021;152:106507.
30. Huang Q, Jiang H, Zhang J, Jia X, Huang F, Wang H, Zhang B, Wang L, Gu M, Huang Y, et al. Dietary patterns are associated with Multi-Dimensional cognitive functions among adults aged 55 and older in China. Front Nutr. 2022;9:806871.
31. Mahmoudian M, Venalainen MS, Klen R, Elo LL. Stable Iterative Variable Selection. *Bioinformatics* 2021.
32. Cespedes EM, Hu FB. Dietary patterns: from nutritional epidemiologic analysis to National guidelines. Am J Clin Nutr. 2015;101(5):899–900.
33. Neuenschwander M, Ballon A, Weber KS, Norat T, Aune D, Schwingshackl L, Schlesinger S. Role of diet in type 2 diabetes incidence: umbrella review of meta-analyses of prospective observational studies. BMJ. 2019;366:l2368.
34. de Koning L, Fung TT, Liao X, Chiuve SE, Rimm EB, Willett WC, Spiegelman D, Hu FB. Low-carbohydrate diet scores and risk of type 2 diabetes in men. Am J Clin Nutr. 2011;93(4):844–50.
35. Schwingshackl L, Hoffmann G, Lampousi AM, Knuppel S, Iqbal K, Schwedhelm C, Bechthold A, Schlesinger S, Boeing H. Food groups and risk of type 2 diabetes mellitus: a systematic review and meta-analysis of prospective studies. Eur J Epidemiol. 2017;32(5):363–75.
36. Parry SA, Rosqvist F, Mozes FE, Cornfield T, Hutchinson M, Piche ME, Hulsmeier AJ, Hornemann T, Dyson P, Hodson L. Intrahepatic fat and postprandial glycemia increase after consumption of a diet enriched in saturated fat compared with free sugars. Diabetes Care. 2020;43(5):1134–41.
37. Son TK, Toan NH, Thang N, Le Trong Tuong H, Tien HA, Thuy NH, Van Minh H, Valensi P. Prediabetes and insulin resistance in a population of patients with heart failure and reduced or preserved ejection fraction but without diabetes, overweight or hypertension. Cardiovasc Diabetol. 2022;21(1):75.
38. Satija A, Bhupathiraju SN, Rimm EB, Spiegelman D, Chiuve SE, Borgi L, Willett WC, Manson JE, Sun Q, Hu FB. Plant-Based dietary patterns and incidence of type 2 diabetes in US men and women: results from three prospective cohort studies. PLoS Med. 2016;13(6):e1002039.
39. Aune D, Norat T, Romundstad P, Vatten LJ. Whole grain and refined grain consumption and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis of cohort studies. Eur J Epidemiol. 2013;28(11):845–58.
40. Magkos F, Hjorth MF, Astrup A. Diet and exercise in the prevention and treatment of type 2 diabetes mellitus. Nat Rev Endocrinol. 2020;16(10):545–55.
41. Jung CH, Choi KM. Impact of High-Carbohydrate diet on metabolic parameters in patients with type 2 diabetes. Nutrients 2017, 9(4).
42. Sanders LM, Zhu Y, Wilcox ML, Koecher K, Maki KC. Whole grain intake, compared to refined grain, improves postprandial glycemia and insulinemia: a systematic review and meta-analysis of randomized controlled trials. Crit Rev Food Sci Nutr. 2023;63(21):5339–57.
43. Schulz R, Slavin J. Perspective: defining carbohydrate quality for human health and environmental sustainability. Adv Nutr. 2021;12(4):1108–21.
44. Skytte MJ, Samkani A, Petersen AD, Thomsen MN, Astrup A, Chabanova E, Frystyk J, Holst JJ, Thomsen HS, Madsbad S, et al. A carbohydrate-reduced high-protein diet improves HbA1c and liver fat content in weight stable participants with type 2 diabetes: a randomised controlled trial. Diabetologia. 2019;62(11):2066–78.
45. Osei TB, van Dijk AM, Dingerink S, Chilunga FP, Beune E, Meeks KAC, Bahendeka S, Schulze MB, Agyemang C, Nicolaou M et al. Reduced Rank Regression-Derived Dietary Patterns Related to the Fatty Liver Index and Associations with Type 2 Diabetes Mellitus among Ghanaian Populations under Transition: The RODAM Study. *Nutrients* 2021, 13(11).
46. Niu Y, Yang Z, Li X, Zhang W, Lu S, Zhang H, Chen X, Zhu L, Xing Y, Ning G, et al. Association of osteoprotegerin with impaired glucose regulation and microalbuminuria: the REACTION study. BMC Endocr Disord. 2015;15:75.
47. Santulli G, Visco V, Varzideh F, Guerra G, Kansakar U, Gasperi M, Marro A, Wilson S, Ferrante MNV, Pansini A, et al. Prediabetes increases the risk of frailty in prefrail older adults with hypertension: beneficial effects of Metformin. Hypertension. 2024;81(7):1637–43.
48. Mone P, De Gennaro S, Moriello D, Frullone S, D'Amelio R, Ferrante MNV, Marro A, Santulli G. Insulin resistance drives cognitive impairment in hypertensive pre-diabetic frail elders: the CENTENNIAL study. Eur J Prev Cardiol. 2023;30(12):1283–8.
49. Wang T, Lu J, Shi L, Chen G, Xu M, Xu Y, Su Q, Mu Y, Chen L, Hu R, et al. Association of insulin resistance and beta-cell dysfunction with incident diabetes among adults in China: a nationwide, population-based, prospective cohort study. Lancet Diabetes Endocrinol. 2020;8(2):115–24.
50. Banaszak M, Gorna I, Przyslawski J. Non-Pharmacological treatments for insulin resistance: effective intervention of Plant-Based Diets-A critical review. Nutrients 2022, 14(7).
51. MacKinnon DP, Krull JL, Lockwood CM. Equivalence of the mediation, confounding and suppression effect. Prev Sci. 2000;1(4):173–81.
52. Shrout PE, Bolger N. Mediation in experimental and nonexperimental studies: new procedures and recommendations. Psychol Methods. 2002;7(4):422–45.
53. Preacher KJ, Rucker DD, Hayes AF. Addressing moderated mediation hypotheses: theory, methods, and prescriptions. Multivar Behav Res. 2007;42(1):185–227.
54. Khalili D, Khayamzadeh M, Kohansal K, Ahanchi NS, Hasheminia M, Hadaegh F, Tohidi M, Azizi F, Habibi-Moeini AS. Are HOMA-IR and HOMA-B good predictors for diabetes and pre-diabetes subtypes? BMC Endocr Disord. 2023;23(1):39.
55. Shu Y, Wu X, Wang J, Ma X, Li H, Xiang Y. Associations of dietary inflammatory index with prediabetes and insulin resistance. Front Endocrinol (Lausanne). 2022;13:820932.

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