Original Article

Gender differences of relationship between serum lipid indices and type 2 diabetes mellitus: a cross-sectional survey in Chinese elderly adults

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Background: To investigate the gender differences of the relationships between clinical serum lipid indices and type 2 diabetes mellitus (T2DM) in Chinese elderly adults.

Methods: Between 2014 and 2016, participants selected from three communities in an urban district of Shanghai were measured for serum lipid indices of low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), total cholesterol (TC), and triglyceride (TG). Age and multivariate adjusted logistic regression models were utilized to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) of serum lipid indices on T2DM prevalence.

Results: In total, 4,023 male and 3,862 female participants were included in this study, with the T2DM prevalence proportions of 13.03% and 11.73%, respectively. In association analysis, the serum levels of LDL-c, HDL-c, TC were significant between non-T2DM individuals and T2DM patients in men, but the HDL-c and TG in women. LDL-c/HDL-c, TG/HDL-c, and TC/HDL-c ratios were associated with the T2DM prevalence only in women. In the multivariate analysis, a higher serum LDL-c level was positively associated with a reduced risk of T2DM prevalence in men with OR (95% CI) of 0.57 (0.39–0.85) (P=0.006). Higher ratios of LDL-c/HDL-c, TG/HDL-c, and TC/HDL-c were all more likely associated with the decreased risks of T2DM prevalence with the ORs ranging from 0.45 to 0.62 in men (all P<0.05), but not in women.

Conclusions: High LDL-c concentration was significantly associated with a lower T2DM prevalence in men. A gender difference of the associations between the lipid ratios and T2DM prevalence was observed for LDL-c/HDL-c and TC/HDL-c ratios, which might be validated in female T2DM prevalence in the future.

Keywords: Serum lipid indices; type 2 diabetes mellitus (T2DM); cross-sectional study; gender difference

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Introduction

Diabetes mellitus is a global health issue that describes a series of metabolic disorders characterized by high blood glucose levels. As released by the International Diabetes Federation (IDF) in 2018, 451 million people (aging 18 to 99 years old) have been estimated with diabetes worldwide in 2017 (1). However, the numbers are 108 million in 1980 (2), 171 million in 2000 (3), and 415 million in 2015 (4), which show an obvious ascending trend. Such a great number of diabetes patients burden the world with high medical care costs, increase mortality, and reduce the quality of life. These relative healthcare issues and burdens are not only caused by type 2 diabetes mellitus (T2DM) itself, but also by other organs' problems induced by high glucose, such as cardiovascular diseases (CVDs), retinopathy, kidney and brain problems (5). China has the world's largest number of diabetes patients. As estimated by a large and nationally representative survey of Chinese adults in 2013, about 109 million adults in total in mainland China suffered from diabetes (with a prevalence of 10.9%) (6).

One of the main features of T2DM is diabetic dyslipidemia, which makes effects on 72–85% of T2DM patients (7). The exact mechanisms of diabetic lipoprotein abnormalities have not been fully understood. One of the most accepted explanations is that dyslipidemia is caused by quantitative and qualitative changes (8). The quantitative change means the increase and decrease of the lipoprotein cholesterol concentrations, which has ever been explored and reviewed (9). For the qualitative alteration, it means the size and density alterations of lipoprotein cholesterol particles with the capability to attribute to lipid abnormalities. The main quantitative abnormalities of lipoprotein include the increase of triglyceride (TG) and low-density lipoprotein cholesterol (LDL-c), as well as the reduction of high-density lipoprotein cholesterol (HDL-c) (10). A Chinese cohort study published recently indicates that TG is the strongest predictor for the onset of diabetes, and besides that, one standard deviation (SD) increase of body mass index (BMI) will elevate the risk of 1.29 times compared to people who have normal glucose tolerance and prediabetes (11). Another cohort study notes that the increased serum levels of total cholesterol (TC), TG, TC/HDL-c, and TG/HDL-c ratios may increase the risk of T2DM incidence (12). Despite the quantitative alteration, researchers also suggest that the "quality" of LDL-c may exert greater influence on T2DM for the identification potential of dense LDL-c to people with higher risks of T2DM (13). The mechanisms of lipoprotein size contributing to the pathogenesis of T2DM may be attributed to the modulation of inflammatory responses that impair beta-cell function and beta-cell mass (14).

Mounting evidence of gender-specific effects on T2DM has been raised (15), and the inclusion of the gender dimension in biomedical research has been called for by many organizations (16). Differences in genetic background, life behaviors, and environmental factors contribute to the discrepancy of T2DM and its associated complications in different genders. European men are usually diagnosed with diabetes at a younger age and with a lower BMI than women (17). Sex hormone modulates glucose and lipid homeostasis in central and peripheral targets. As reported before, higher levels of androgens lead to increased body weight in women (18); relatively higher testosterone levels in women and lower levels in men are related to incident diabetes (19). Socioeconomic status, which usually assesses by educational level, income, and occupation, are also found to play different roles in men and women (20). Health behaviors, such as smoking, alcohol consumption, and tea drinking, also have gender disparities on T2DM (21-23). All the above evidence implied that gender imbalances exist in T2DM. In our study, we aim to evaluate the relationship between clinical lipid metabolism indices and T2DM prevalence in a community-based study in urban Shanghai, which is located in the east of China. From this cross-sectional study, we firstly provide the epidemiological evidence to validate the relationship between clinical lipid indices and T2DM prevalence modifying by gender. These results may then help to identify subgroups of the population who are at a high risk of T2DM. In terms of public health, it will also provide recommendations for people who have lipid metabolic abnormalities to have medical interventions as early as possible. We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/atm-20-2478).

Methods

Study populations & settings

In this study, participants who measured serum lipid indexes were selected from three communities in an urban district in Shanghai between 2014 and 2016. A total of 3,862 female and 4,023 male participants were enrolled

from two cohort studies, which started in 1997 and 2002, separately (24,25). The variables from the baseline and follow-up surveys were chosen to be exposure factors. All the questionnaire surveys and the anthropometric measurements were collected by trained interviewers who were retired and professional medical workers. The study was performed according to the guidelines of the Declaration of Helsinki 2013 (26) and approved by the Renji Hospital Ethics Committee of Shanghai Jiao Tong University School of Medicine (KY2019-196), and written informed consent was obtained from each participant before the interview.

Clinical measurements, laboratory analysis & definitions

Blood samples were collected after overnight fasting of at least 10 hours at the checkup in the community health centers. Measurements had been done while the participants were on their usual diet and took no medications. Fasting LDL-c, HDL-c, TG, and TC were measured by the standardized enzymatic colorimetric methods. All the clinical assays were done by the Shanghai Lan Wei Medical Laboratory Company Limited in the Changing District of Shanghai using Roche reagents.

The outcomes of T2DM were defined as undergoing treatment with insulin or oral hypoglycemic agents (anti-diabetes drug usage), or the concentration of fast blood glucose was ≥7.0 mmol/L, or the participant had a personal history of T2DM (27). T2DM was diagnosed by experts from the community-health centers or hospitals with rich clinical and pathological experience. Participants' ages were calculated as the check date of the clinical testing minus the date of birth. Baseline BMI was calculated as weight (kg)/height^2 (m^2) and utilized in analysis instead of follow-up BMI in order to minimize the bias of the weight change after T2DM diagnosis. Other variables, such as education (classified into four categories, primary school and below, junior high school, senior high school, and tertiary and above), occupation (three categories, classified into professional, clerical, and manual workers), menopause (only for women, yes/no), smoking (yes/no), alcohol drinking (yes/no), tea drinking (yes/no), medical history of coronary heart disease (CHD, yes/no), anti-diabetes drug usage (yes/no), and anti-hypertension drug usage (yes/no) were taken into consideration. Four clinical lipid metabolism indices were measured and categorized into normal and abnormal groups by the standard clinical concentrations. The criteria for LDL-c, TG, and TC were 3.37, 2.26, and 5.20 mmol/L, separately (28). For HDL-c, the criteria were 1.04 mmol/L for men and 1.15 mmol/L for women, respectively, which was recommended by the Shanghai Lan Wei Medical Laboratory Company Limited and the local community-based hospitals. Continuous alternations of lipid profiles were also analyzed. In terms of the ratios of LDL-c/HDL-c, TG/HDL-c, and TC/HDL-c, we further categorized them into tertiles in non-T2DM individuals with the lowest tertile serving as the reference group, the detailed cutoff values of the tertiles in each gender were shown in Table S1.

Statistical analysis

All analyses were separately performed in each gender. Continuous variables were presented as mean ± SD. Categorical variables were presented as frequency and percentage. Student's *t*-test was used for independent samples for comparisons of variables with normal distribution and the Wilcoxon test was used for comparisons of non-parametric ones. Chi-square tests (or Fisher's exact tests when appropriate) were used to compare the distributions of categorical variables. To figure out the relationships of LDL-c/HDL-c, TG/HDL-c, and TC/HDL-c ratios with T2DM prevalence, logistic regression models were carried out to obtain odds ratios (ORs) and 95% confidence intervals (CIs) by calibrating all potential confounders. The regression models could be defined as two types: (I) adjusted for age (continuous scale); (II) adjusted for multivariate including age (continuous scale), education, occupation, BMI (continuous scale), personal history of CHD, menopause (only for women), anti-diabetes drug usage, anti-hypertension drug usage, as well as lifestyle factors of smoking, alcohol drinking, and tea drinking.

Data analyses were conducted using SAS version 9.2 (SAS Institute, Cary, NC, USA), and re-verified by SPSS statistical package (version 20.0, SPSS Inc., USA). All statistical tests were two-sided, and a $P<0.05$ was considered statistically significant.

Results

Characteristics of the participants

The demographic and basic characteristics of the participants were presented in *Table 1*. In total, 524 male and 453 female participants were diagnosed with T2DM, with the prevalence proportions of 13.03% and 11.73%,

Table 1 Characteristics of study participants in the cross-sectional survey in urban Shanghai

Variables	Male			Female		
	Non-T2DM (N=3,499)	T2DM (N=524)	P	Non-T2DM (N=3,409)	T2DM (N=453)	P
Continuous variables						
Age	66.22±7.91	67.24±7.96	0.006	65.04±8.34	68.11±8.22	<0.0001
BMI	23.89±2.96	25.45±2.81	<0.0001	23.81±3.15	26.23±3.30	<0.0001
SBP	127.31±16.94	133.55±18.27	<0.0001	119.97±17.44	130.12±18.28	<0.0001
DBP	82.95±10.28	85.22±10.54	<0.0001	77.06±10.02	81.32±9.88	<0.0001
Lipid profiles						
LDL-c	3.12±0.88	2.86±0.87	<0.0001	3.47±0.87	3.51±1.05	0.534
HDL-c	1.31±0.35	1.24±0.32	0.0001	1.58±0.40	1.49±0.37	<0.0001
TG	1.57±1.28	1.74±1.72	0.033	1.55±0.89	1.86±1.47	<0.0001
TC	4.88±0.97	4.64±1.05	<0.0001	5.52±0.99	5.53±1.15	0.923
LDL-c/HDL-c	2.53±0.91	2.45±0.97	0.113	2.33±0.81	2.46±0.86	0.003
TG/HDL-c	1.44±1.79	1.69±2.10	0.034	1.12±0.94	1.45±1.81	0.001
TC/HDL-c	4.00±1.20	4.00±1.31	0.981	3.73±1.06	3.97±1.16	<0.0001
Categorical variables						
Education			0.004			<0.0001
≤ Primary school	189 (5.41)	47 (8.97)		526 (15.43)	123 (27.15)	
Junior high school	1,395 (39.95)	221 (42.18)		1,518 (44.54)	194 (42.83)	
Senior high School	1,211 (34.68)	166 (31.68)		1,022 (29.99)	91 (20.09)	
Tertiary and above	697 (19.96)	90 (17.18)		342 (10.04)	42 (9.93)	
Occupation			0.978			0.465
Professional	772 (22.10)	117 (22.33)		788 (23.12)	93 (21.53)	
Clerical	740 (21.18)	109 (20.80)		712 (20.89)	96 (21.19)	
Manual	1,982 (56.73)	298 (56.87)		1,902 (55.79)	264 (58.28)	
Ever smoking	2,364 (67.56)	359 (68.51)	0.665	55 (1.61)	15 (3.31)	0.011
Ever alcohol drinking	1,218 (34.81)	163 (31.11)	0.096	72 (2.11)	14 (3.09)	0.185
Ever tea drinking	2,280 (65.16)	362 (68.08)	0.078	1,028 (29.98)	150 (34.44)	0.053
Hypertension	1,392 (39.78)	299 (57.06)	<0.0001	1,269 (37.22)	280 (61.81)	<0.0001
Anti-hypertension drug usage	1,188 (33.95)	255 (48.66)	<0.0001	930 (27.28)	199 (43.93)	<0.0001
Coronary heart disease	126 (3.60)	35 (6.68)	0.001	186 (5.46)	62 (13.69)	<0.0001

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol; TG, Triglyceride; TC, total cholesterol; T2DM, type 2 diabetes mellitus.

respectively. The numbers of patients who had ever had anti-diabetes drug treatment were 282 (53.82%) in men and 237 (52.32%) in women. The estimated means of the time period from diagnosis to blood testing in T2DM prevalent patients were 7.74 years in men and 8.50 years in women, respectively. All participants were more than 50 years old. Compared to non-T2DM participants, T2DM patients were older, had higher BMI, systolic blood pressure

Table 2 Correlations between clinical serum lipid indices and T2DM prevalence

Lipid indices (mmol/L)	Male			Female		
	Non-T2DM	T2DM	P	Non-T2DM	T2DM	P
LDL-c			<0.0001			0.801
<3.37	1,585 (64.40)	260 (75.58)		1,345 (46.93)	180 (47.62)	
≥3.37	876 (35.60)	84 (24.42)		1,521 (53.07)	198 (52.38)	
HDL-c			0.017			0.011
<1.04† (1.15)‡	532 (21.62)	94 (27.33)		361 (12.53)	65 (17.20)	
≥1.04† (1.15)‡	1,929 (78.38)	250 (72.67)		2,512 (87.47)	313 (82.80)	
TG			0.066			<0.0001
<2.26	2,948 (84.86)	425 (81.73)		2,913 (86.11)	356 (78.76)	
≥2.26	526 (15.14)	95 (18.27)		470 (13.89)	96 (21.24)	
TC			<0.0001			0.114
<5.20	2,239 (64.45)	383 (73.65)		1,277 (37.75)	188 (41.59)	
≥5.20	1,235 (35.55)	137 (26.35)		2,106 (62.25)	264 (58.41)	
LDL-c/HDL-c			0.152			0.033
Low	821 (33.36)	127 (36.92)		955 (33.32)	103 (27.25)	
Intermediate	820 (33.32)	120 (34.88)		956 (33.36)	128 (33.86)	
High	820 (33.32)	97 (28.20)		955 (33.32)	147 (38.89)	
TG/HDL-c			0.406			<0.0001
Low	820 (33.32)	106 (30.81)		955 (33.32)	89 (23.54)	
Intermediate	820 (33.32)	111 (32.27)		956 (33.36)	122 (32.28)	
High	821 (33.36)	128 (36.92)		955 (33.32)	167 (44.18)	
TC/HDL-c			0.354			0.002
Low	822 (33.40)	128 (37.21)		956 (33.36)	95 (25.13)	
Intermediate	818 (33.24)	105 (30.52)		954 (33.29)	128 (33.86)	
High	821 (33.36)	112 (32.27)		956 (33.36)	155 (40.01)	

Data are expressed as n (%). †, the normal medical reference range for males; ‡, the normal medical reference range for females. LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol; TG, Triglyceride; TC, total cholesterol; T2DM, type 2 diabetes mellitus.

(SBP), and diastolic blood pressure (DBP) in both genders. Significant differences could be observed in education levels between T2DM patients and non-T2DM individuals in each gender. Referring to lifestyle factors (include smoking, alcohol drinking, and tea drinking habits), only smoking in women could be significantly observed between T2DM and non-T2DM individuals (P=0.011). Personal medical histories of hypertension and CHD were also significant between these two groups.

Associations between clinical lipid indices and T2DM prevalence

The associations between clinical lipid measures and T2DM prevalence stratified by gender were presented in *Table 2*. In males, LDL-c, HDL-c, and TC were significantly related to T2DM prevalence; and in females, HDL-c and TG were found to be associate with T2DM prevalence. As lots of studies pinpointed that LDL-c/HDL-c, TG/HDL-c, and TC/HDL-c ratios could be served as indicators for

T2DM incidence. We also evaluated their roles in T2DM prevalence and found no differences in males but significant meanings in females (all P<0.05). Quantitative distributions of all the clinical lipid indices between T2DM cases and non-T2DM individuals also had been explored (*Table 1*).

Logistic regression analysis between clinical lipid indices and T2DM prevalence

Table 3 presented the relations of different lipid indices and T2DM prevalence by using the logistic regression models in separate gender. When adjusting by age, significant associations of lipid indices and T2DM prevalence were observed in higher HDL-c with ORs (95% CIs) of 0.72 (0.56–0.93) (P=0.012) in men and 0.71 (0.53–0.95) (P=0.022) in women, respectively; and in higher TG concentrations with ORs (95% CIs) of 1.09 (1.03–1.15) (P=0.031) in men and 1.26 (1.16–1.37) (P=0.0002) in women, respectively. Whereas, significant associations between LDL-c and TC and T2DM prevalence were both observed in males, but not in females. After calibrating by multivariate, null associations were detected in HDL-c, TG, or TC categories with T2DM prevalence in both genders, but significance was found in higher LDL-c concentration and the decreased risk of T2DM prevalence in males with OR (95% CI) of 0.57 (0.39–0.85) (P=0.006).

We also estimated the association between the continuous change of blood lipid indices and T2DM prevalence. In the age-adjusted model, per unit alterations of lipid indices that significantly decreased T2DM prevalence were LDL-c, HDL-c, and TC in males, and it's HDL-c in females. Per unit change of TG was associated with increased risks of T2DM prevalence in both sexes with ORs (95% CIs) of 1.09 (1.03–1.15) (P=0.003) in males and 1.26 (1.16–1.37) (P<0.0001) in females, respectively. When adjusting by multivariate factors, a unit change of LDL-c and TC were significantly associated with T2DM prevalence in males with ORs (95% CIs) of 0.71 (0.58–0.87) (P=0.001) and 0.85 (0.73–0.98) (P=0.021), respectively; no significance was found in females.

Referring to the lipid ratio indices, diverse results were detected in different genders. As shown in *Table 4*, all the highest levels of lipid ratios (include LDL-c/HDL-c, TG/HDL-c, and TC/HDL-c ratios) were positively associated with higher T2DM prevalence only in females with the ORs ranging from 1.44 to 1.70 (P<0.01), but null associations were detected in males by using the age-adjusted model. Nevertheless, in multivariate models, the results shifted, meaningful associations for all higher lipid ratios with the decreased risks of T2DM prevalence were observed in men with the ORs ranging from 0.45 to 0.62 (all P<0.05), but not in women. When estimating their relationships by analyzing the continuous alterations of lipid ratio indices in the multivariate model, one unit changes of LDL-c/HDL-c and TC/HDL-c were positively associated with the reduced risks of T2DM prevalence.

Discussion

In our cross-sectional study, the prevalence proportions of T2DM were 13.03% in men and 11.73% in women, respectively, which were a bit higher than the estimated prevalence from a national survey with 9.9% in men and 11.6% in women (29). This discrepancy might be attributed to multiple reasons. Firstly, it might be partly caused by the region factor. All participants in this study were recruited from an urban district of Shanghai City. As previous studies indicated, the prevalence rate of T2DM in urban areas was significantly higher than that in rural areas in China (29-31), which was consistent with our results. Secondly, significant differences in T2DM prevalence in different age groups of each gender were detected in our study. As some studies pointed out that age was a certified risk factor for T2DM (31,32). Age variability between our study (≥50 years) and the meta-analysis (20–75 years) (29) could also explain the reason for the relatively higher T2DM prevalence in our population. Besides, age might not be the only factor associated with high T2DM prevalence, synergistic effects contributed by other factors might also play important roles. As *Table 1* presented, the education distributions of T2DM patients among participants were meaningful in both genders (*Table 1*, all P<0.004), which suggested education was an important variable that related to T2DM prevalence in urban Shanghai. We also found that T2DM patients had higher BMI levels than healthy participants in both genders, which were consistent with previous researches (33,34). When exploring the relationships between lifestyle factors (including smoking, alcohol drinking, and tea drinking habits) and T2DM prevalence in men, no significance was detected, which was different from the meta-analyses conducting in Japan (35). In women, significant associations were detected in non-smokers and ever-smokers. As validated by a Chinese population-based study, environmental tobacco exposure increased T2DM risks with a dose-response relationship (36), which also verified our results laterally.

Table 3 Logistic regression analysis between serum lipid indices and T2DM prevalence

Lipid indices (mmol/L)	Age-adjusted model		Multivariate model	
	OR (95% CI)	P	OR (95% CI)	P
Male				
LDL-c				
<3.37	1	–	1	–
≥3.37	0.60 (0.46–0.77)	<0.0001	0.57 (0.39–0.85)	0.006
Continuous	0.72 (0.62–0.82)	<0.0001	0.71 (0.58–0.87)	0.001
HDL-c				
<1.04	1	–	1	–
≥1.04	0.72 (0.56–0.93)	0.012	0.98 (0.65–1.47)	0.912
Continuous	0.51 (0.35–0.73)	<0.0001	1.31 (0.80–2.14)	0.286
TG				
<2.26	1	–	1	–
≥2.26	1.31 (1.03–1.67)	0.031	0.66 (0.43–1.01)	0.057
Continuous	1.09 (1.03–1.15)	0.003	0.94 (0.82–1.08)	0.367
TC				
<5.20	1	–	1	–
≥5.20	0.67 (0.54–0.82)	<0.0001	0.78 (0.58–1.04)	0.094
Continuous	0.78 (0.71–0.86)	<0.0001	0.85 (0.73–0.98)	0.021
Female				
LDL-c				
<3.37	1	–	1	–
≥3.37	1.01 (0.81–1.25)	0.933	1.05 (0.77–1.44)	0.758
Continuous	1.07 (0.95–1.20)	0.285	1.08 (0.91–1.29)	0.369
HDL-c				
<1.15	1	–	1	–
≥1.15	0.71 (0.53–0.95)	0.022	1.12 (0.70–1.78)	0.647
Continuous	0.57 (0.43–0.76)	<0.0001	1.04 (0.69–1.57)	0.850
TG				
<2.26	1	–	1	–
≥2.26	1.59 (1.24–2.04)	0.0002	0.99 (0.68–1.45)	0.956
Continuous	1.26 (1.16–1.37)	<0.0001	1.03 (0.89–1.18)	0.728
TC				
<5.20	1	–	1	–
≥5.20	0.91 (0.74–1.11)	0.340	0.96 (0.72–1.28)	0.782
Continuous	1.04 (0.94–1.14)	0.452	1.07 (0.93–1.22)	0.364

LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol; TG, Triglyceride; TC, total cholesterol; OR, odds ratio; CI, confidence interval. Age-adjusted model: adjusted by age; Multivariate model: adjusted by age (continuous), BMI (continuous), education, occupation, menopause (yes/no, only for women), smoking (yes/no), alcohol drinking (yes/no), tea drinking (yes/no), anti-diabetes and anti-hypertension drug usages, and coronary heart disease (yes/no).

Table 4 Logistic regression analysis between LDL-c/HDL-c, TG/HDL-c, TC/HDL-c ratios and T2DM prevalence

Lipid ratio indices	Age-adjusted model			Multivariate model		
	OR (95% CI)	P	P_{trend}	OR (95% CI)	P	P_{trend}
Male						
LDL-c/HDL-c			0.109			0.0002
Low	1	–		1	–	
Intermediate	0.96 (0.74–1.26)	0.784		0.62 (0.42–0.92)	0.017	
High	0.80 (0.60–1.07)	0.129		0.45 (0.29–0.70)	0.0004	
Continuous	0.92 (0.81–1.04)	0.186		0.69 (0.56–0.85)	0.0004	
TG/HDL-c			0.138			0.009
Low	1	–		1	–	
Intermediate	1.07 (0.81–1.43)	0.630		0.58 (0.38–0.88)	0.011	
High	1.25 (0.95–1.65)	0.118		0.57 (0.37–0.88)	0.012	
Continuous	1.06 (1.01–1.11)	0.016		0.92 (0.80–1.07)	0.274	
TC/HDL-c			0.436			0.001
Low	1	–		1	–	
Intermediate	0.84 (0.64–1.11)	0.227		0.55 (0.36–0.83)	0.004	
High	0.92 (0.70–1.21)	0.545		0.51 (0.33–0.79)	0.003	
Continuous	1.01 (0.92–1.11)	0.783		0.76 (0.65–0.90)	0.002	
Female						
LDL-c/HDL-c			0.008			0.639
Low	1	–		1	–	
Intermediate	1.23 (0.93–1.63)	0.139		1.20 (0.81–1.79)	0.362	
High	1.44 (1.10–1.88)	0.008		1.12 (0.75–1.67)	0.583	
Continuous	1.22 (1.07–1.39)	0.003		1.05 (0.86–1.27)	0.637	
TG/HDL-c			0.0001			0.773
Low	1	–		1	–	
Intermediate	1.27 (0.95–1.70)	0.110		1.00 (0.66–1.51)	0.993	
High	1.70 (1.29–2.25)	0.0002		0.98 (0.64–1.49)	0.913	
Continuous	1.22 (1.12–1.33)	<0.0001		0.99 (0.84–1.16)	0.871	
TC/HDL-c			0.001			0.887
Low	1	–		1	–	
Intermediate	1.34 (1.01–1.78)	0.043		1.22 (0.82–1.81)	0.339	
High	1.61 (1.22–2.11)	0.0007		1.02 (0.68–1.53)	0.924	
Continuous	1.22 (1.11–1.35)	<0.0001		1.03 (0.89–1.19)	0.697	

Age-adjusted model: adjusted by age; Multivariate model: adjusted by age (continuous), BMI (continuous), education, occupation, menopause (yes/no, only for women), smoking (yes/no), alcohol drinking (yes/no), tea drinking (yes/no), anti-diabetes and anti-hypertension drug usages, and coronary heart disease (yes/no). LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol; TG, Triglyceride; TC, total cholesterol; OR, odds ratio; CI, confidence interval.

Higher HDL-c and lower TG levels were associated with lower risks of T2DM prevalence in both genders in our research (*Table 2*), which were consistent with other studies (37,38). A nationwide population-based study in Korea enrolling 5,114,735 adults with a median follow-up period of 5.1 years had found that lower means of HDL-C were associated with higher risks of diabetes incidence in a stepwise manner (39). Genetic studies were also conducted to explore the relationship between HDL-c and T2DM. As indicated by a large data set with 34,840 T2DM cases and 114,982 control subjects using 140 lipid-associated genetic variants to assess the relationship between lipid profiles and T2DM, genetically determined lower HDL-c concentrations were associated with T2DM prevalence (40). Otherwise, lipid genotype scores of well-established single nucleotide polymorphism in 95 loci showed that low HDL-c or high TG levels were related to elevated risks of T2DM prevalence (41). From the above previously published studies, it could be concluded that high HDL-c levels were good for health and positively associated with the reduced risks of diabetes incidence or prevalence.

However, the roles of LDL-c and TC on diabetes prevalence had not been consistently verified in our study. In the multivariate logistic model within our research (*Table 3*), a higher LDL-c concentration was associated with a lower risk of diabetes prevalence in males with OR (95% CI) of 0.57 (0.39–0.85) (P=0.006), but null associations were detected in females. The positive effects of LDL-c to T2DM in our study were similar to the results obtained from the Framingham Heart Study when adjusting by multivariate including sex, as it concluded that a higher LDL-c concentration was associated with a lower risk of diabetes with OR (95% CI) of 0.81 (0.70–0.93) (P=0.004) (42). Another large community-based cross-sectional study in the Netherlands also suggested that T2DM prevalence among patients with familial hypercholesterolemia who suffering from more severe LDL mutations was significantly lower than among unaffected relatives, which also agreed with our results (43). However, contrary conclusions of higher LDL-c concentrations associated with higher risks of T2DM incidence had also been demonstrated in other studies (44). This discrepancy might be introduced by race and ethnicity, which had been recommended to be taken into consideration in clinical care (45). Interestingly, in another community-based cross-sectional study without gender-specific analysis in North China, per-SD increases of LDL-c, TG, TC, TG/HDL-c, and TC/HDL-c were all meaningfully associated with increased T2DM prevalence in the multivariate logistic model (all ORs >1.50) (46), which were totally different from ours. These disparities also suggested that race and ethnicity might not be the major influencing factor. A Mendelian random analysis (47) reported that LDL-c played a causal role in T2DM with the elevated LDL-c significantly increased the risk of T2DM, which made the effects of LDL-c on T2DM confusing compared to our results.

After exploring the effects of LDL-c/HDL-c, TG/HDL-c, and TC/HDL-c ratios on T2DM prevalence, we found that they all had negative associations in males but positive relations in females when adjusting by age. However, their roles shifted when adjusting for multiple confounding factors in the multivariate logistic model (as shown in *Table 4*, higher LDL-c/HDL-c, TG/HDL-c, and TC/HDL-c ratios were associated with T2DM prevalence in males, but null associations were detected in females). This disparity might be caused by several reasons. Firstly, the variations in specific gender might be attributed to the different characteristics of two studied groups, such as their education levels, smoking habit, BMI, anti-DM drug usage, and anti-hypertension drug usage, etc., the disparities of those factors might lighten their relevance with T2DM. On the other hand, these results also implied that the strong relationships of personal characters and T2DM in separate gender (17,19-23). More importantly, the inconsistent influences of high LDL-c/HDL-c, TG/HDL-c, and TC/HDL-c ratios in each gender neither adjusting with age nor multivariate suggested the gender-specific roles of clinical lipid indices on T2DM. Although limited gender-specific results of T2MD prevalence from other studies had been explored currently, the gender-specific effects of LDL-c on T2DM risks had been estimated. In the Bogalusa Heart Study, higher LDL-c placed girls at a disproportionally higher risk of T2DM as women (48), which suggested that LDL-c in women posed more risk effects on T2DM and implied the positive role of men, which was quite consistent with our results. As indicated by the CCMR-3B Study, the inability of women to achieve LDL-c goals was greater than men, which also implied the existence of gender imbalances in lipid metabolism (49). And another study examining lipid management also pointed out that disparities existed in lipid control in different genders (50).

In summary, no consistent conclusions could be drawn and the disparities of diverse viewpoints presented in different studies implied the necessity of further verification. Moreover, some limitations could be addressed in our study. For this study is a cross-sectional design, the relationships

between clinical lipid indices and T2DM prevalence might be biased by other residual confounders, such as BMI. After diagnosing with T2DM, people might introduce some healthy diet habits into their lives, which would result in a decrease of BMI; and the decreased BMI would also affect T2DM in turn. Furthermore, selection bias might exist in the study, which was the drawback of all cross-sectional studies. To minimize it, age balanced between our study and its original cohorts. The validations in larger population-based case-control or cohort studies with more demographic and clinical or treatment information should be recommended in the future.

Conclusions

Our study provided more information for Chinese community-based cross-sectional studies. Summarily, we enrolled 7,885 participants in total, and primarily evaluated the gender-specific relationship between serum clinical lipid indexes and T2DM in Chinese elderly adults. As similar to the results reported by other studies, low TG and high HDL-c levels were associated with decreased T2DM prevalence in both genders in our study. However, different conclusions could be drawn between other studies and ours when taking account of the roles of LDL-c and TC, which might need further explorations. Besides that, we also did a secondary analysis of the primary data and found that LDL-c/HDL-c, TG/HDL-c, and TC/HDL-c ratios had gender-specific differences between T2DM patients and non-T2DM subjects, which had rarely been done by other studies before.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Renji Hospital Ethics Committee of Shanghai Jiao Tong University School of Medicine (KY2019-196) and written informed consent was obtained from each participant before the interview.

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Supplementary

Table S1 Cutting off values of the tertiles of LDL-c/HDL-c, TG/HDL-c, TC/HDL-c ratios in the cross-sectional survey in Shanghai

Cutting off value	Male			Female		
	LDL-c/HDL-c ratio	TG/HDL-c ratio	TC/HDL-c ratio	LDL-c/HDL-c ratio	TG/HDL-c ratio	TC/HDL-c ratio
1st tertile	2.05	0.79	3.41	1.89	0.66	3.15
2nd tertile	2.88	1.39	4.38	2.62	1.15	4.07

LDL-c, low-density lipoprotein cholesterol; TG, Triglyceride; HDL-c, high-density lipoprotein cholesterol; TC, total cholesterol.

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