

# Association of Triglyceride-Glucose Index with the Risk of Hyperhomocysteinemia Among Chinese Male Bus Drivers: A Longitudinal Study

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**Background:** Insulin resistance (IR) and hyperhomocysteinemia (HHcy) are significant risk factors for cardiovascular disease (CVD). As an important marker for IR, Triglyceride-Glucose (TyG) index maybe a significant predictor for HHcy progression, reflecting cardiovascular risk. However, the relationship between TyG index and HHcy has been unknown, especially for the high-risk occupation group of male bus drivers. This longitudinal study was initially conducted to explore the outcome of TyG index in predicting HHcy among male bus drivers.

**Methods:** In total, 1018 Chinese male bus drivers with Hcy data and regular follow-up from 2017 to 2021 were screened, and 523 non-HHcy subjects at baseline were included in the longitudinal cohort. A restricted cubic spline (RCS) was performed to investigate the possible non-linear relationship between TyG index and the progression of HHcy. A multivariate logistic regression model was used to explore the association between TyG index and developing HHcy via assessing the value of odds ratio (OR) and 95% confidence interval (CI).

**Results:** After the median follow up time of 2.12 years, approximately 27.7% of male bus drivers (mean age: 48.1 years) was identified as new incidents HHcy. Multivariate logistic regression found that the higher level of TyG was associated with an increased risk of new onset HHcy (OR = 1.47; 95% CI: 1.11–1.94); and the association seemed to be strong among male bus drivers with elevated low-density lipoprotein cholesterol (LDL-C) ( $P$  for interaction < 0.05).

**Conclusion:** As a higher risk occupation group for HHcy, male bus drivers should cause much more attentions from policy makers, employers, and health professionals in China. Identifying male bus drivers with HHcy is of significance at an earlier stage in the primary care setting. Being a significant predictive factor for HHcy, TyG index could be used to monitor and prevent Chinese male bus drivers from HHcy, especially for individuals with elevated LDL-C.

**Keywords:** hyperhomocysteinemia, insulin resistance, triglyceride-glucose index, longitudinal study, male bus drivers, HHcy, IR, TyG

## Introduction

Cardiovascular disease (CVD) has been identified as one of the most significant leading causes of mortality and morbidity globally,<sup>1</sup> as well the top cause of death in China.<sup>2</sup> Owing to the sensitive and stressful occupation characteristics, bus drivers were reported to have a higher risk of CVD.<sup>3</sup> Homocysteine (Hcy) is a sulfhydryl-containing amino acid presenting in plasma and an important in-process product in the metabolism of cysteine and methionine.<sup>1,4,5</sup> Recent research has proved that hyperhomocysteinemia (HHcy) was an independent predictor for CVD,<sup>4–6</sup> defined as the level of serum Hcy greater than 15.0  $\mu\text{mol/L}$ .<sup>7</sup> In addition, HHcy was verified to be associated with carcinoma, Alzheimer's disease, vascular dementia, Parkinson's disease, and diabetic kidney disease.<sup>8–11</sup> It is worth noting that the prevalence of HHcy in China is significantly higher than in other countries,<sup>12–16</sup> and its incidence is much higher in men than in women.<sup>1,16–18</sup>

Numerous studies had conducted to explore HHcy being a CVD risk factor, whereas relatively few studies had focused on factors related with HHcy in healthy population,<sup>1</sup> especially for the special occupation group of bus drivers. Moreover, there is an undisputed obvious sex ratio gap in this occupation, and the majority of bus drivers were male.<sup>19</sup> Therefore, as a possible high risk of occupational group, it is warranted to explore the prevalence of HHcy and its predictors for male bus drivers.

In addition to HHcy, insulin resistance (IR) was likewise found as one of the main contributors to CVD,<sup>20</sup> which is regarded as an insulin-regulated defect in tissue glucose metabolism control.<sup>21,22</sup> The “gold standard method” for IR assessing is hyperinsulinemic-euglycemic clamp,<sup>23–25</sup> and its alternative method was Homeostatic Model Assessment (HOMA-IR) by calculating insulin and glucose levels to determine IR.<sup>26</sup> However, these tests are so expensive and complex to detrimentally restrict their wide use.<sup>23,24,27</sup> As a low cost, easily accessible biochemistry test,<sup>28</sup> Triglyceride-glucose (TyG) index calculated via fasting serum glucose (GLU) and triglyceride values, has been reported as an appropriate surrogate indicator of IR.<sup>29,30</sup> Previous research found that TyG Index was positively related with IR that was measured via the glucose clamp<sup>23</sup> and HOMA-IR.<sup>31</sup> Furthermore, recent research reported that TyG index was a reliable diagnostic tool for IR; and in some cases, it may even better than HOMA-IR,<sup>32–34</sup> being suitable for large population research and clinical settings.<sup>23</sup> Therefore, TyG index was chosen as an IR biomarker in the present study.

As discussed above, HHcy and IR are significant risk factors for CVD.<sup>5,6,20</sup> As an important marker for IR, TyG index maybe a predictor for HHcy progression, reflecting cardiovascular risk. However, the relationship of TyG index and HHcy has been not explored in the existing literature, especially for the possible high-risk occupation group of male bus drivers for HHcy. Thus, this longitudinal study firstly investigate the association between TyG level and the development of HHcy for Chinese male bus drivers as well as to provide the effective evidence for protecting these bus drivers from HHcy.

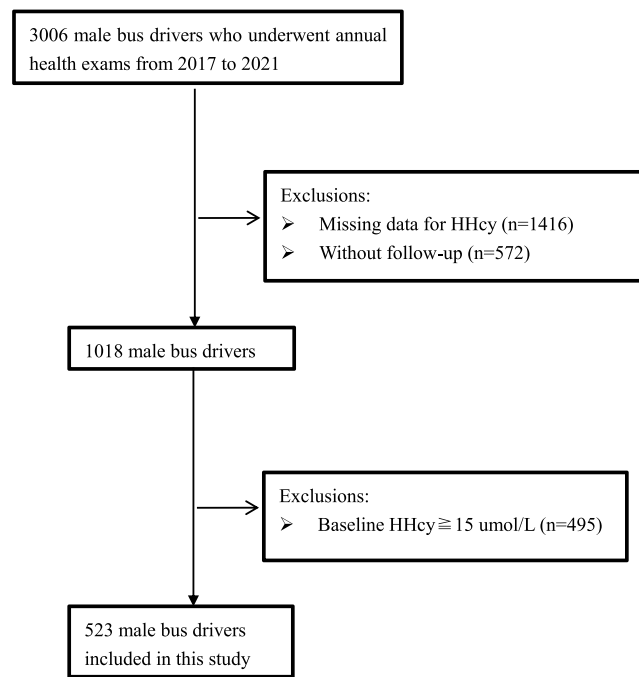
## Methods

### Research Design

In the current longitudinal research, study subjects included 523 male bus drivers, as one part of an annual health examination program at Shenzhen People's Hospital in Shenzhen City, China, from 2017 to 2021. Initially, 3006 male bus drivers who had worked for more than two years and underwent the annual physical examinations at this period were recruited. After screening, individual with missing data on Hcy ( $n = 1416$ ), without follow-up ( $n = 572$ ) were excluded; and 1018 male bus drivers were enrolled in the longitudinal cohort. Excluded ones with HHcy ( $\text{Hcy} \geq 15.0 \mu\text{mol/L}$ ) at baseline checkup ( $n = 495$ ), at final 523 subjects were included in data analysis and their median follow up period was 2.12 years. The study flow chart was illustrated in [Figure 1](#). The current research was undertaken in accordance with the Declaration of Helsinki, and was approved by the institutional ethics committee of Shenzhen People's Hospital. Prior to participation, all subjects offered their signed consent form.

### Anthropometric Measurement and Laboratory Assessment

During the process of annual health examination, study subjects' age and sex were recorded, and their weight, height, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were obtained by experienced professional health workers. The data of comorbidities comprised whether these bus drivers were diagnosed as dyslipidemia, hypertension, diabetes, or hyperuricemia. Fasting blood samples were collected by venipuncture in the morning and analyzed in a core laboratory. Serum Hcy level was measured by enzyme cycling method. The information about laboratory assessment included total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyl transpeptidase  $\gamma$  (GGTP), serum uric acid (SUA), creatinine (Cr), blood urea nitrogen (BUN), GLU, hemoglobin (HGB), homocysteine (Hcy), urine pondus hydrogenii (UPH), urine proteinuria (PRO), and estimated glomerular filtration rate (eGFR).



**Figure 1** Flow chart of our study population selection.

**Abbreviation:** HHcy, hyperhomocysteinemia.

## Study Definitions

In our study, the calculation formula of TyG was:  $\text{Ln}[\text{fasting triglycerides (mg/dl)} \times \text{fasting glucose (mg/dl)} / 2]$ .<sup>35,36</sup> HHcy was regarded as the serum Hcy  $\geq 15.0 \mu\text{mol/L}$ .<sup>7</sup> Body mass index (BMI) calculation divided an individual's weight in kilograms by the height in meters squared.<sup>37</sup> In regarding to the new guideline for hyperuricemia diagnosis and management in China,<sup>38</sup>  $\text{SUA} \geq 420 \mu\text{mol/L}$  (7mg/dl) was defined as hyperuricemia for male bus drivers. According to the guideline of dyslipidaemia management for Chinese adults,  $\text{TC} \geq 6.2 \text{ mmol/L}$ ,  $\text{LDL-C} \geq 4.1 \text{ mmol/L}$ ,  $\text{HDL-C} < 1.0 \text{ mmol/L}$ ,  $\text{TG} \geq 2.3 \text{ mmol/L}$  were defined as elevated TC, elevated LDL-C, lower HDL-C, and elevated TG, respectively;<sup>39</sup> and  $\text{TC} \geq 6.2 \text{ mmol/L}$ ,  $\text{TG} \geq 2.3 \text{ mmol/L}$ ,  $\text{HDL-C} < 1.0 \text{ mmol/L}$  and/or  $\text{LDL-C} \geq 4.1 \text{ mmol/L}$ , or currently conducting pharmacological treatment, were regarded as dyslipidaemia.<sup>40</sup> PRO was recorded as negative (–) and positive (+).

## Data Analysis

The descriptive statistics of categorical variables and continuous variables were presented by numbers, percentages (%), and mean, standard deviation (SD), respectively. The comparison of socio-demographic and clinical characteristics among two groups according to the diagnosis of HHcy was conducted via Student's *t*-test and one-way ANOVA (analysis of variance) in terms of continuous data, and  $\chi^2$  (chi-square) tests in terms of categorical data. A restricted cubic spline (RCS) was used with knots placed at the 5th, 35th, 50th, 65th, and 95th percentiles to explore the possible non-linear relationship between TyG index and the risk of HHcy after adjusting for confounders of age, Cr, SBP, and DBP. The univariate and multivariate logistic regression models were undertaken to investigate the relationship between the TyG index and the progression of HHcy via assessing the value of odds ratio (OR) and 95% confidence interval (CI). Three multivariate logistic regression models were constructed in our study and these models comprised known potential confounders between TyG index and HHcy, as well as significant covariates in univariate analysis ( $P < 0.05$ ). Model 1 was not adjusted; model 2 was adjusted for age, Cr and SUA; and model 3 was adjusted for age, Cr, SUA, SBP, and DBP. Moreover, subgroup analysis was performed to explore the potential factors to modify the relationship. R 4.1.3 software (R Foundation, Vienna, Austria) performed all statistical analysis and the  $P$ -value  $< 0.05$  (two-tailed) was regarded as statistically significant.

## Results

### Baseline Characteristics of Male Bus Drivers

To assess the outcome of TyG Index in predicting incident HHcy, 523 male bus drivers without HHcy at baseline were included in our longitudinal cohort, and the mean age of these participants was 48.1 (2.88) years. After a median follow up period of 2.12 years, approximately 27.7% (145/523) of male bus drivers suffered from HHcy. Table 1 described the comparisons of baseline characteristics between subjects classified with and without HHcy in the longitudinal cohort. Individuals with developing HHcy were more likely to have higher values of SBP, DBP, BMI, TG, Cr, GLU, HGB, TyG index; to have higher incidences of hypertension, obesity, elevated TC, and positive PRO; and have a lower level of eGFR compared with ones without developing HHcy.

**Table 1** Baseline Characteristics Among Male Bus Drivers Classified by with and without HHcy

	All Subjects N = 523*	Non-HHcy (-) N = 378	HHcy (+) N = 145	P value
<b>Age (year)</b>	48.1 (2.88)	48.0 (2.87)	48.5 (2.88)	0.097
<b>Age group</b>				0.058
40–49 years	386 (73.8%)	288 (76.2%)	98 (67.6%)	
50–59 years	137 (26.2%)	90 (23.8%)	47 (32.4%)	
SBP (mmHg)	129 (17.0)	128 (16.3)	132 (18.5)	0.027
DBP (mmHg)	81.2 (11.7)	80.1 (11.1)	84.0 (12.8)	0.001
<b>Comorbidities</b>				
Dyslipidemia	302 (57.7%)	210 (55.6%)	92 (63.4%)	0.124
Diabetes	47 (8.99%)	30 (7.94%)	17 (11.7%)	0.236
Hypertension	168 (32.1%)	111 (29.4%)	57 (39.3%)	0.038
Hyperuricemia	146 (27.9%)	102 (27.0%)	44 (30.3%)	0.510
<b>Obesity-related index</b>				
BMI (kg/m <sup>2</sup> )	25.5 (3.12)	25.2 (3.02)	26.1 (3.30)	0.010
<b>BMI group</b>				0.038
<24 kg/m <sup>2</sup>	167 (31.9%)	130 (34.4%)	37 (25.5%)	
24–28 kg/m <sup>2</sup>	258 (49.3%)	186 (49.2%)	72 (49.7%)	
≥28 kg/m <sup>2</sup>	98 (18.7%)	62 (16.4%)	36 (24.8%)	
<b>Laboratory parameters</b>				
TC (mg/dL)	5.27 (1.05)	5.24 (0.95)	5.35 (1.27)	0.353
<b>TC group</b>				
Elevated TC	83 (15.9%)	52 (13.8%)	31 (21.4%)	0.045
TG (mg/dL)	2.06 (1.78)	1.94 (1.61)	2.35 (2.13)	0.037
<b>TG group</b>				0.202
Elevated TG	150 (28.7%)	102 (27.0%)	48 (33.1%)	
HDL-C (mg/dL)	1.18 (0.25)	1.19 (0.25)	1.15 (0.25)	0.137
<b>HDL-C group</b>				0.380
Lower HDL-C	160 (30.6%)	111 (29.4%)	49 (33.8%)	
LDL-C (mg/dL)	3.47 (0.74)	3.45 (0.71)	3.53 (0.81)	0.304
<b>LDL-C group</b>				0.097
Elevated LDL-C	97 (18.5%)	63 (16.7%)	34 (23.4%)	
ALT (U/L)	30.4 (22.8)	31.1 (24.9)	28.8 (15.7)	0.211
AST (U/L)	25.3 (12.4)	25.6 (13.5)	24.5 (8.79)	0.290
γ-GGT (U/L)	42.4 (37.6)	41.4 (35.4)	44.9 (42.8)	0.382
SUA (mg/dL)	6.41 (1.38)	6.37 (1.35)	6.52 (1.44)	0.277
Cr (μmol/L)	79.1 (11.2)	78.1 (10.0)	81.9 (13.4)	0.002
BUN (mmol/L)	12.9 (3.12)	13.0 (3.22)	12.8 (2.87)	0.425
GLU (mol/L)	5.71 (1.82)	5.57 (1.39)	6.06 (2.62)	0.032
HGB (g/L)	157 (11.0)	157 (11.3)	159 (9.87)	0.018

(Continued)

**Table 1** (Continued).

	All Subjects N = 523*	Non-HHcy (-) N = 378	HHcy (+) N = 145	P value
Hcy ( $\mu\text{mol/L}$ )	12.1 (1.89)	11.7 (1.91)	13.1 (1.39)	<0.001
TyG index	8.92 (0.68)	8.86 (0.63)	9.05 (0.78)	0.012
UPH				0.581
6 $\leq$ UPH $\leq$ 7	253 (48.4%)	188 (49.7%)	65 (44.8%)	
UPH < 6	264 (50.5%)	186 (49.2%)	78 (53.8%)	
UPH > 7	6 (1.15%)	4 (1.06%)	2 (1.38%)	
PRO(+)	14 (2.68%)	6 (1.59%)	8 (5.52%)	0.028
eGFR ( $\text{mL/min/1.73m}^2$ )	98.6 (15.7)	99.9 (14.5)	95.5 (18.2)	0.010

Note: \*Mean (SD), n/N (%).

**Abbreviations:** SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGTP, gamma glutamyl transpeptidase  $\gamma$ ; SUA, serum uric acid; BUN, blood urea nitrogen; Cr, creatinine; GLU, glucose; HGB, hemoglobin; Hcy, homocysteine; UPH, urine pondus hydrogenii; PRO, urine proteinuria; eGFR, estimated glomerular filtration rate.

## Dose-Response Relationship Between TyG Index and HHcy

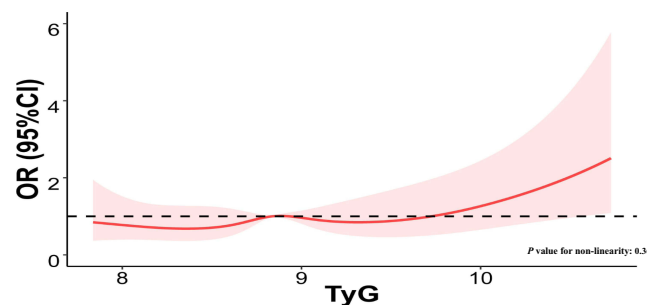
Figure 2 illustrated a RCS model with five knots (the 5th, 35th, 50th, 65th, and 95th percentiles) to investigate the possible non-linear relationship between TyG index and the progression of HHcy after adjusting for confounders. The findings indicated that no significant non-linear relationship was observed between TyG index and HHcy ( $P$  value for non-linearity: 0.36).

## The Relationship of TyG Index with Developing HHcy

The multivariate-adjusted logistic regression results were shown in Table 2 to explore the association between TyG index and developing HHcy. It indicated that TyG index was positively related with HHcy. To be more specific, with 1 unit increment in TyG index, all male bus drivers' risk of developing HHcy was 1.47 times higher (OR = 1.47; 95% CI: 1.11–1.94). This relationship remained statistically significant after adjustment for other confounding factors, such as age, Cr, SUA, SBP, and DBP (OR = 1.47; 95% CI: 1.11–1.94).

## Subgroup Analysis on Relationship of TyG Index with Developing HHcy by Different Groups

Stratification analysis likewise was conducted to reveal the association between TyG index and developing HHcy by different groups. Table 3 shown that there were no significant interactions in these subgroups, including BMI group (<24 vs. 24–28 vs.  $\geq 28 \text{ kg/m}^2$ ), diabetes (no vs. yes), hypertension (no vs. yes), hyperuricemia (no vs. yes), age group (40–49 years vs. 50–59 years), elevated TC group (no vs. yes), lower HDL-C group (no vs. yes), and elevated TG group (no vs. yes) ( $P$  value for interaction > 0.05); while the significant interaction was found in the elevated LDL-C group (no vs. yes) ( $P$  value for interaction < 0.05). It



**Figure 2** The RCS for the possible non-linear relationship between TyG index and HHcy in male bus drivers.

**Notes:** splines with knots = c(5,35,50,65,95); all adjusted for age, Cr, SUA, SBP, and DBP.

**Abbreviations:** OR, odds ratio; HHcy, hyperhomocysteinemia; TyG, triglyceride-Glucose index.

**Table 2** Relationship of TyG Index with Developing HHcy Among Male Bus Drivers

All Subjects (N = 523)	Odds Ratio (95% CI)		
	Model 1	Model 2	Model 3
TyG index	1.47 (1.11, 1.94)**	1.54 (1.16, 2.07)**	1.46 (1.09, 1.97)*
Age		1.06 (0.99, 1.13)	1.07 (0.99, 1.14)
Cr		1.03 (1.01, 1.05) ***	1.03 (1.01, 1.05) ***
UA		1 (1.00, 1.00)	1.00 (1.00, 1.00)
SBP			0.98 (0.96, 1.01)
DBP			1.05 (1.01, 1.08)**

**Notes:** \*0.01<P value <0.05; \*\* 0.001<P value <0.01; \*\*\* P value <0.001; Model 1 was unadjusted; model 2 was adjusted for age, Cr and SUA; and model 3 was adjusted for age, Cr, SUA, SBP, and DBP.

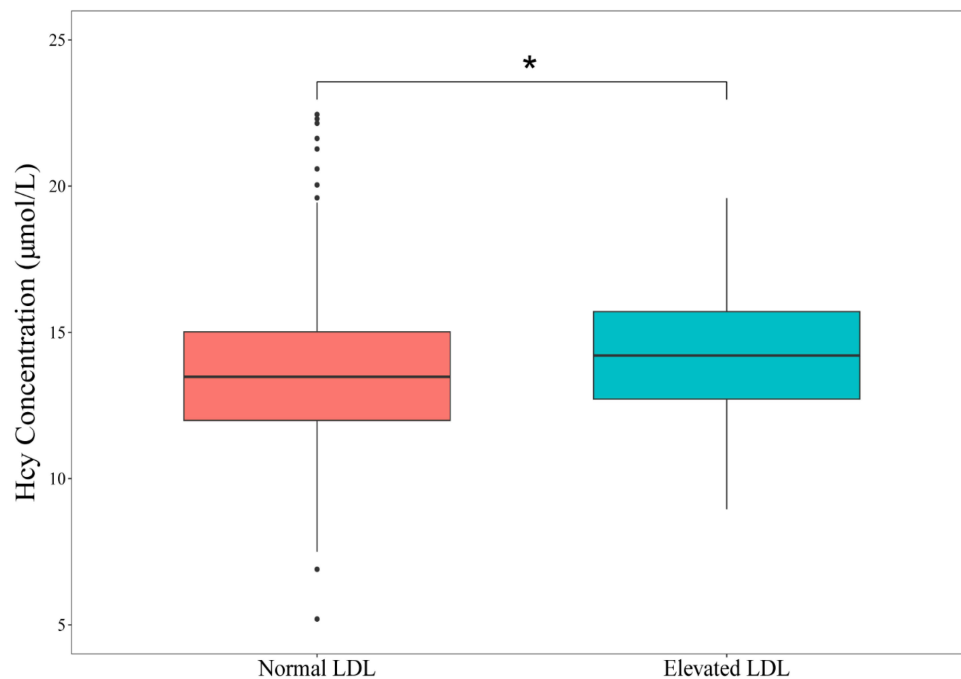
**Abbreviations:** CI, Confidence interval; Cr, creatinine; SUA, serum uric acid; SBP, systolic blood pressure, DBP, diastolic blood pressure.

**Table 3** Subgroup Analysis for the Association Between TyG Index and Developing HHcy

All Subjects (N = 523)	Odds Ratio (95% CI)			
Subgroups	Model 1	Model 2	Model 3	P for Interaction
BMI group				0.596
<24 kg/m <sup>2</sup>	2.13(1.14, 4.06)*	2.06(1.05, 4.07)*	2.11(1.06, 4.24)*	
24–28 kg/m <sup>2</sup>	1.35(0.92, 1.97)	1.49(1.00, 2.23)*	1.41(0.93, 2.14)	
≥28 kg/m <sup>2</sup>	1.15(0.61, 2.16)	1.32(0.68, 2.59)	1.36(0.69, 2.73)	
Diabetes				0.389
No	1.35(0.96, 1.91)	1.36(0.93, 1.98)	1.27(0.86, 1.86)	
Yes	1.91(0.97, 4.21)	1.64(0.79, 3.66)	1.53(0.72, 3.50)	
Hypertension				0.883
No	1.41(0.97, 2.03)	1.54(1.05, 2.27)*	1.51(1.02, 2.24)*	
Yes	1.47(0.96, 2.30)	1.48(0.95, 2.36)	1.41(0.89, 2.30)	
Hyperuricemia				0.699
No	1.41(1.03, 1.95)*	1.53(1.10, 2.14)*	1.49(1.06, 2.11)*	
Yes	1.61(0.90, 2.92)	1.73(0.92, 3.31)	1.61(0.84, 3.14)	
Age group				0.367
40–49 years	1.37(0.99, 1.89)	1.41(1.01, 1.96)*	1.32(0.94, 1.86)	
50–60 years	1.84(1.07, 3.26)*	2.14(1.15, 4.21)*	2.14(1.13, 4.28)*	
Increased TC				0.184
No	1.21(0.84, 1.72)	1.32(0.90, 1.93)	1.24(0.84, 1.83)	
Yes	1.86(1.10, 3.37)*	1.85(1.09, 3.29)*	1.76(1.01, 3.23)*	
Increased LDL-C				0.032
No	1.26(0.93, 1.71)	1.35(0.98, 1.87)	1.24(0.88, 1.73)	
Yes	3.13(1.44, 7.72)**	3.06(1.37, 7.92)*	3.24(1.43, 8.42)**	
Decreased HDL-C				0.546
No	1.56(1.08, 2.26)*	1.46(1.00, 2.16)	1.38(0.93, 2.06)	
Yes	1.30(0.81, 2.08)	1.48(0.89, 2.49)	1.39(0.82, 2.37)	
Increased TG				0.740
No	1.57(0.88, 2.80)	1.8(0.98, 3.32)	1.7(0.92, 3.18)	
Yes	1.8(1.02, 3.29)*	1.93(1.08, 3.57)*	1.85(1.02, 3.49)*	

**Notes:** \*0.01<P value <0.05; \*\*P value <0.01.

**Abbreviations:** CI, Confidence interval; BMI, body mass index; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride.



**Figure 3** The comparison of Hcy concentration between normal LDL-C group and elevated LDL-C group.

**Note:** \*0.01 <  $P$  value < 0.05.

**Abbreviations:** Hcy, homocysteinemia; LDL-C, low-density lipoprotein cholesterol.

indicated that the association between TyG index and HHcy seemed to be strong among these male bus drivers with elevated LDL-C. Figure 3 likewise illustrated that a significant difference existed in the mean serum Hcy level between normal LDL-C group (13.7  $\mu\text{mol/L}$ ) and elevated LDL-C group (14.2  $\mu\text{mol/L}$ ) ( $P < 0.05$ ).

## Discussion

Sound evidence have proved that both HHcy and IR were the significantly independent risk factors for CVD,<sup>4–6,20</sup> which was regarded as one of the most common leading causes of mortality and morbidity globally.<sup>1</sup> As an important marker of IR, TyG index could be monitored to predict HHcy progression. However, the relationship between TyG index and HHcy has been unknown in the existing literature, especially for the possible high-risk occupation group of male bus drivers. Thereby, the longitudinal study was initially conducted to demonstrate the outcome of TyG index in predicting incident HHcy among male bus drivers to fill the research gap.

First of all, we observed that these male bus drivers had a higher prevalence of the development of HHcy. For instance, approximately 27.7% of male bus drivers (mean age: 48.1 years) was identified as new incidents HHcy after a median follow up time of 2.12 years in the current research, which was higher than the corresponding incidents among other working population reported in the previous studies. For example, the other longitudinal study found that followed by the median years of 2.98, about 23.5% of community residents (mean age: 57.5) from Shanghai, China, developed to encounter new HHcy.<sup>2</sup> Another retrospective cross-sectional study found that only 8.2% of relatively healthy Taiwanese working population had HHcy, and their mean age of was 57.4 years.<sup>1</sup> The recent systematic review summarized the incidence of HHcy in China, and reported that the pooled prevalence of HHcy was 22.7% and 17.9% among Chinese population aged from 45–65 years and <45 years, respectively.<sup>16</sup>

A meta-analysis reviewing 92 studies estimated that decreasing Hcy by only 3  $\mu\text{mol/L}$  could diminish the risk of stroke by 24% and ischaemic heart disease by 16%.<sup>15</sup> HHcy has been proved to pose a heavy metabolic burden,<sup>41</sup> and higher level of Hcy could negatively influence multiple organs via forming species of active oxygen and promoting dysfunction of endothelial smooth muscle cell, which resulted in varied diseases.<sup>42</sup> Thereby, as a higher risk occupation group for HHcy, male bus drivers should cause much more attentions from policy makers, employers, and health



professionals. Our research findings indicate that it is urgent to develop effective prevention and intervention to reduce this preventable disorder for male bus drivers. Moreover, identifying male bus drivers with HHcy is of significance at an earlier stage in the primary care setting, so that timely treatment might be conducted for the control and prevention of HHcy progression and its consequences.

The other significant finding in the current research was that TyG index could independently predict the progression of HHcy for male bus drivers. To be more specific, our multivariate analysis found that the higher level of plasma TyG was related with an increased risk of new HHcy (OR = 1.46; 95% CI: 1.09–1.97) among male bus drivers, independently of other known risk factors for HHcy; and the relationship of TyG index with HHcy seemed to be strong among these subjects with elevated LDL-C (*P* value for interaction < 0.05). Even though the mechanism behind the correlation is not well understood, some factors maybe contribute to it. First of all, IR has been shown to cause substrate metabolism change and inefficient energy metabolism,<sup>43</sup> thus might detrimentally affecting the renal excretory function for Hcy. Moreover, IR has been proved to induce inappropriate activation of the renin–angiotensin–aldosterone system and the sympathetic nervous system,<sup>44</sup> which could negatively influence kidney function. Furthermore, relating with hyperglycemia and free fatty acid elevation, IR could cause the various local and systematic inflammation.<sup>45</sup>

To our knowledge, this is the first study investigating the association between TyG index and HHcy for Chinese male bus drivers in the literature. Our findings indicated that measurement of TyG Index could be beneficial in the early screening of HHcy for male bus drivers. It needs to be noted that TyG index has the advantage for clinical applications as TG and glucose concentrations are tested routinely. For instance, all of 3006 Chinese male bus drivers recruited in the study measured the level of TG and glucose; while only 1560 of them measured the serum Hcy. Therefore, being a significant predictive factor for HHcy, TyG index can be used to monitor and prevent male bus drivers from HHcy.

The strength of the current research was that it is the first to explore the association between TyG index and HHcy for Chinese male bus drivers, so that it has significant implications for the prevention and control of HHcy for Chinese male bus drivers especially in the primary care setting. Another is the longitudinal research design that could diminish the reverse causation effect. By contrast, several limitations related to the research need to be reported. First, our research subjects of male bus drivers were from single city of Shenzhen, Southeast area of China, which would limit the generalizability of our research findings. Second, the sample size was relatively small in the present longitude study as almost half of male bus drivers did not choose to test their serum Hcy level and about one fifth of our subjects were lost during the follow up period. Thus, the basis of data could not be avoided. We recommend that the HHcy test would be a required item in the annual physical examination for male bus drivers. Third, some covariates about the lifestyle of male bus drivers that potentially influence their Hcy levels were not included in the research, such as dietary habits, smoking and alcohol habit, and supplement of B vitamins and folate, which should be considered in the further research.

## Conclusion

As a higher risk occupation group for HHcy, male bus drivers should cause much more attentions from policy makers, employers, and health professionals in China. Identifying male bus drivers with HHcy is of significance at an earlier stage in the primary care setting, so that timely intervention and treatment can be conducted for the prevention of HHcy progression and its consequences. Higher TyG index was proved to be significantly associated with a higher prevalence of new HHcy for male bus drivers. Being a significant predictive factor for HHcy, TyG index can be used to monitor and prevent Chinese male bus drivers from HHcy that are much more meaningful in clinical practice, especially for subjects with elevated LDL-C.

## Data Sharing Statement

The data presented in this study are available on request from the corresponding author. The data are not publicly available due to privacy restrictions.

## Ethics Approval

The present study was undertaken in accordance with the Declaration of Helsinki, and was approved by the institutional ethics committee of Shenzhen People's Hospital (Ethical approval number: LL-KY-202224).



## Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

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## Disclosure

The authors declare no conflicts of interest.

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