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The association of triglyceride and glucose index, and triglyceride to high-density lipoprotein cholesterol ratio with prehypertension and hypertension in normoglycemic subjects: A large cross-sectional population study

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Abstract

Insulin resistance (IR) plays an important role in the development of hypertension. Triglyceride and glucose index (TyG index), and triglyceride to high-density lipoprotein cholesterol ratio (TG/HDL-c) as effective IR surrogate indexes have been verified in numerous studies. Therefore, the authors conducted a large cross-sectional study to explore the association of TyG index and TG/HDL-c with prehypertension and hypertension in the same normoglycemic subjects from Tianjin, China. A total of 32 124 adults were eligible for this study. According to the level of blood pressure, the enrolled individuals were divided into three groups, which were normotension, prehypertension, and hypertension. In multiple logistic regression analysis, there was associated with prehypertension and hypertension when comparing the highest TyG index to the lowest TyG index and corresponding ORs were 1.795 (1.638, 1.968) and 2.439 (2.205, 2.698), respectively. For TG/HDL-c, the corresponding ORs were 1.514 (1.382, 1.658) and 1.934 (1.751, 2.137), respectively. Furthermore, when comparing the fourth quartile to the first quartile of TyG index and TG/HDL-c, respectively, both corresponding ORs of hypertension were higher than prehypertension. Elevated TyG index and TG/ HDL-c levels were associated with prehypertension and hypertension in normoglycemic individuals. Moreover, the TyG index was more significant than TG/HDL-c in distinguishing hypertension. They have the potential to become cost-effective monitors in the hierarchical management of prehypertension and hypertension.

1 | INTRODUCTION

Essential hypertension is usually clustered with other cardiovascular risk factors, such as aging, obesity, insulin resistance, diabetes, and hyperlipidemia.¹⁻³ A large number of clinical and epidemiological evidence show that insulin resistance is closely related to hypertension.^{4,5} The coexistence of insulin resistance and hypertension can lead to a significant increase in the risk of cardiovascular disease and type 2 diabetes mellitus (DM2).⁶

Although the hyperinsulinemic-euglycemic clamp (HIEC) technique is the gold standard of insulin resistance (IR), it is complicated, painful, and unachievable.⁷ Homeostasis model assessment for IR

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(HOMA-IR) index is an indirect method, which needs to measure insulin, so it is difficult to repeat the same results.⁸⁻¹⁰ Therefore, a new index of insulin resistance is needed. At present, many studies evidenced that some simple routine biochemical indexes, such as the product of fasting triglyceride and glucose index (TYG), and the ratio of triglyceride to high-density lipoprotein cholesterol (TG/HDL-c), can be calculated as non-insulin resistance indicators and are more accurate and practical.^{11,12}

Luis E. Simental-Mendía et al proved that elevated TyG index was significantly associated with the presence of prehypertension and hypertension in children and adolescents. ¹³ Hyungseon Yeom et al suggested that a high TG/HDL-c ratio in adolescents was associated with hypertension in early adulthood.¹⁴ However, few of these studies have large samples to evaluate the relationship between non-insulin resistance indicators and hypertension, as well as prehypertension in the same population.^{10,13-23} Therefore, we conducted a large cross-sectional study to explore the association of TyG index, TG/HDL-c ratio with prehypertension and hypertension in the same normoglycemic subjects from Tianjin, China.

2 | PATIENTS AND METHODS

2.1 | Subjects

The data were collected from the early screening population of the Ministry of Finance and the National Health and Family Planning Commission in 2018. Screening objects were permanent residents in the jurisdictions aged 35–75. Of the 43 298 adults with initial data, individuals taking hypoglycemic drugs, lipid-lowering drugs, fasting blood glucose ≥7.0 mmol/L, and information incomplete were excluded. Finally, 32 124 adults remained eligible for this study. According to the level of blood pressure, the enrolled individuals were divided into three groups, which were normotension, prehypertension, and hypertension. This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments and approved by the ethics committee of Tianjin Chest Hospital. All participants provided written informed consent to participate in the study.

2.2 | Clinical measurements

The questionnaire was used to survey the general characteristics including age, sex, smoking history, drinking history, marital status, family history, and medication. According to the routine protocol, a complete physical examination, including measurement of the patients' height, weight, and blood pressure, was carried out. Weight (kg) and height (m) were measured with patients wearing only underwear. The body mass index (BMI) was calculated. The systolic blood pressure (SBP) and diastolic blood pressure (DBP) and heart rate (HR) were measured twice with an electronic sphygmomanometer

after 5 minutes of rest, two blood pressure measurements were recorded at 5-min intervals, and the means were used for the data analysis.

The blood samples of individuals were collected after at least 8 hours of overnight fasting. Serum levels of triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), highdensity lipoprotein cholesterol (HDL-c), and fasting plasma glucose (FPG) were measured by a biochemical auto-analyzer.

2.3 | Definition

Normotension was defined as systolic BP (SBP) <120 mm Hg and diastolic BP (DBP) <80 mm Hg. Prehypertension was defined as $120 \le SBP < 140$ mm Hg and/or $80 \le DBP <90$ mm Hg. Hypertension was defined as SBP ≥140 mm Hg and/or DBP ≥ 90 mm Hg, or use antihypertensive medications currently.²⁴ TG/HDL-c ratio was calculated as TG (mg/dl)/HDL-c (mg/dl). TyG index was calculated as the Ln[TG (mg/dl) ×FPG (mg/dl)/2].^{25,26} BMI was calculated as weight (kg)/height² (m).

2.4 | Statistical analysis

The data were analyzed by using SPSS version 25.0 for windows. The Kolmogorov-Smirnov normality test was performed to determine whether the data were distributed normally or not. The continuous variables of non-normal distribution were expressed as medians [interquartile range (IQR)], and the categorical variables were expressed as frequencies [percentages (%)]. Continuous variables were compared using the Kruskal-Wallis H test, and categorical variables among groups were compared using the chi-squared test.

Spearman's correlation analysis was used to determine the correlation between TyG index, TG/HDL-c, and their related parameters. Univariate logistic analysis was used to evaluate the association of each parameters with prehypertension and hypertension. Multiple logistic regression analyses were applied to explore the association of TyG indexes and TG/HDL-c with prehypertension and hypertension. According to the relationship between the TyG index and the TG/HDL-c as continuous variables and presence of prehypertension and hypertension were nonlinear relation in logistic regression analysis, TyG index and TG/ HDL-c were divided into four guartiles and the lowest guartile was used as a reference, and age, sex, smoking, drinking, marital status, BMI were adjusted as Model 1. The classifications of TyG index and TG/HDL-c were as follows: quartile 1 (Q1) (≤8.48), quartile 2 (Q2) (8.49-8.76), quartile 3 (Q3) (8.77-9.12), and quartile 4 (Q4) (≥9.13) for TyG; and quartile 1 (Q1) (≤1.74), quartile 2 (Q2) (1.75-2.49), guartile 3 (Q3) (2.50-3.63), and guartile 4 (Q4) (≥ 3.64) for TG/HDL-c. The area under the receiver operating characteristic (ROC) curves was calculated to distinguish hypertension by TyG index and TG/HDL-c. For a statistical inference, all *p* values are bilateral, and a *p*-value of less than .05 was considered statistically significant.

3 | RESULTS

3.1 | Descriptive statistics

Based on the status of their blood pressure, eligible study participants (n = 32 124) were classified into three groups: normotension (n = 7248), prehypertension (n = 13 343), and hypertension (n = 11 533). Baseline characteristics of three groups with blood pressure are shown in Table 1. Significant differences in age, sex, marital status, smoking, drinking, HR, BMI, SBP, DBP, TC, TG, HDL-c, LDL-c, and GLU between the groups were observed (*p* <.001). The age of prehypertension (56.6) was higher than normotension (52.1) and hypertension (51.5). Individuals with hypertension showed significantly higher levels of SBP and DBP than prehypertension and normotension. With the increasing trend of

 TABLE 1
 The clinical characteristics

 of normotension, prehypertension, and
 hypertension

blood pressure in normotension, prehypertension, and hypertension, the percentages or medians of smoking, drinking, HR, BMI, TC, TG, LDL-c, and GLU were rising, while the median of HDL-c was descending.

3.2 | Correlation analysis

As shown in Table 2, the association between TyG index, TG/HDL-c and age, HR, BMI, SBP, DBP, TC, TG, LDL-c and GLU were positive correlation, while HDL-c was negative correlation in Spearman correlation analysis (*p* <.001).

3.3 | Univariate logistic analysis

Table 3 describes age, sex, marital status, smoking, drinking, BMI, TyG, and TG/HDL-c were significantly related to prehypertension and hypertension in univariate logistic analysis. Meanwhile, TyG index and TG/HDL-c were calculated as continuous variables.

Variables	Normotension (n = 7248)	Prehypertension (n = 13 343)	Hypertension (n = 11 533)	p-value
Age	52.1 (44.8, 61.7)	56.6 (47.9, 65.5)	51.5 (43.3, 61.9)	<.001
Sex (men)	2045 (28.2%)	5578 (41.8%)	4751 (41.2%)	<.001
Marital status				<.001
Not married	108 (1.5%)	120 (0.9%)	115 (1.0%)	
Married	6928 (95.6%)	12 879 (96.5%)	10 743 (93.2%)	
Divorced	78 (1.1%)	85 (0.6%)	97 (0.8%)	
Widowed	134 (1.8%)	259 (1.9%)	578 (5.0%)	
Smoking	890 (12.3%)	1785 (13.4%)	2440 (21.2%)	<.001
Drinking	1101 (15.2%)	2237 (16.8%)	3113 (27.0%)	<.001
HR (bpm)	72.5 (68.0, 78.5)	73.0 (70.0, 78.5)	75.0 (69.0, 82.0)	<.001
BMI (kg/m ²)	23.6 (22.0, 25.6)	24.6 (22.9, 26.7)	26.3 (24.1, 28.7)	<.001
SBP (mm Hg)	112.5 (107.0, 116.5)	127.0 (122.0, 131.0)	147.5 (139.0, 160.0)	<.001
DBP (mm Hg)	70.5 (65.5, 74.00)	79.0 (73.5, 82.0)	85.0 (78.0, 92.0)	<.001
TC (mg/dl)	163.32 (139.83, 190.47)	171.39 (145.33, 192.31)	176.16 (147.17, 209.19)	<.001
TG (mg/dl)	119.48 (93.81, 147.80)	129.21 (98.24, 177.89)	140.72 (103.55, 198.24)	<.001
HDL-c (mg/dl)	53.41 (46.44, 65.02)	53.02 (45.66, 65.79)	51.47 (43.34, 61.92)	<.001
LDL-c (mg/dl)	96.75 (76.63, 115.33)	104.49 (81.27, 116.87)	107.50 (82.04, 130.03)	<.001
GLU (mg/dl)	97.20 (90.00, 104.40)	97.20 (91.80, 104.40)	102.60 (95.40, 109.80)	<.001
TyG	8.65 (8.41, 8.90)	8.75 (8.46, 9.10)	8.88 (8.56, 9.24)	<.001
TG/HDL-c	2.23 (1.61, 2.96)	2.47 (1.74, 3.54)	2.78 (2.86, 4.14)	<.001

Note: HR, BMI, SBP, DBP, TC, TG, HDL-c, LDL-c, and GLU were described as medians [interquartile range (IQR)]; and sex, marital status, smoking, and drinking as frequencies [percentages (%)]. Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; GLU, fasting glucose; HDL-c, high-density lipoprotein cholesterol; HR, heart rate Age; LDL-c, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides.

TABLE 2Spearman correlation between TG/HDL-c ratio, TyGindex, and clinical/laboratory parameters

	TyG		TG/HDL-c	
Parameters	r	p value	r	p value
Age	0.078	<.001	0.027	<.001
SBP	0.184	<.001	0.15	<.001
DBP	0.15	<.001	0.166	<.001
ТС	0.155	<.001	0.105	<.001
TG	0.969	<.001	0.848	<.001
HDL-c	-0.148	<.001	-0.592	<.001
LDL-c	0.155	<.001	0.105	<.001
GLU	0.350	<.001	0.157	<.001
BMI	0.226	<.001	0.249	<.001
HR	0.098	<.001	0.067	<.001

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; GLU, fasting glucose; HDL-c, high-density lipoprotein cholesterol; HR, heart rate; LDL-c, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; TG/HDLc, triglyceride to high-density lipoprotein cholesterol; TyG, fasting triglyceride and glucose.

 TABLE 3
 Clinical/laboratory parameters Univariate logistic

 analysis with the risk of prehypertension and hypertension

	Prehypertension		Hypertension	
Variables	OR (95% CI)	p values	OR (95% CI)	p values
Age	1.031 (1.028, 1.034)	<.001	1.094 (1.091, 1.098)	<.001
Sex (men)	1.828 (1.718, 1.944)	<.001	1.782 (1.673, 1.899)	<.001
Marital status	5			
Married	1.673 (1.288, 2.173)	<.001	1.456 (1.118, 1.897)	.005
Divorced	0.981 (0.656, 1.467)	.925	1.168 (0.785, 1.738)	.444
Widowed	1.740 (1.247, 2.428)	.001	4.051 (2.933, 5.595)	<.001
Smoking	1.103 (1.012, 1.202)	<.001	1.917 (1.764, 2.083)	<.001
Drinking	1.125 (1.040, 1.217)	.003	2.064 (1.913, 2.228)	<.001
BMI	1.121 (1.110, 1.132)	<.001	1.300 (1.287, 1.314)	<.001
TyG	1.710 (1.605, 1.822)	<.001	2.873 (2.691, 3.068)	<.001
TG/HDL-c	1.152 (1.130, 1.174)	<.001	1.293 (1.268, 1.318)	<.001

Note: Abbreviations: BMI, body mass index; TG/HDL-c, triglyceride to high-density lipoprotein cholesterol; TyG, fasting triglyceride and glucose.

3.4 | Multiple logistic regression analyses

Multiple logistic regression analyses were applied to explore the association of TyG index and TG/HDL-c with prehypertension and

hypertension. TG/HDL-c and TyG index were divided into four quartiles, and the lowest quartile was used as a reference; age, sex, smoking, drinking, marital status, and body mass index were adjusted as Model 1. The Model 1 analysis of Table 4 showed that the presence of prehypertension was 1.795 times higher in those in the fourth quartile at baseline (95% CI: 1.638–1.968) and 1.091 times in those in the third quartile (95% CI: 1.006-1.183), while there is no significant difference in the second quartile. Besides, the presence of hypertension was 2.439 times higher in those in the fourth quartile at baseline (95% CI: 2.205-2.698) and 1.289 times in those in the third quartile (95% CI: 1.175–1.415), while there is no significant difference in the second quartile. And we can see that in Figure 1, the ORs of corresponding TyG index quartiles in hypertension were higher than prehypertension.

The Model 1 analysis of Table 5 showed that the presence of prehypertension was 1.891 times higher in those in the fourth quartile at baseline (95% CI: 1.734–2.063), while it is no significant difference in the third and second quartiles. Moreover, the presence of hypertension was 1.934 times higher in those in the fourth quartile at baseline (95% CI: 1.751–2.137), while it is no significant difference in the third and second quartiles. And we can see that in Figure 2, the ORs of corresponding TG/HDL-c quartiles in hypertension were higher than prehypertension. These findings indicated that a higher TyG index and TG/HDL-c were associated with hypertension.

$3.5~\mid~$ The area under the ROC curve with its 95% CI for distinguishing hypertension by TyG index and TG/ HDL-c

According to Table 6 and Figure 3, the area under the ROC curve (AUC) with its 95% CI for distinguishing hypertension by TyG and TG/HDL-c was 0.596 (0.591,0.601) and 0.577 (0.572,0.583), respectively. And TyG index was greater than TG/HDL-c in association with hypertension (P =.0001) using DeLong et al methods.²⁷

4 | DISCUSSION

As far as we all know, this is the first large cross-sectional study to investigate the relationships between different TYG index, TG/HDL-c quartiles, and prehypertension and hypertension in participants without diabetes mellitus from Tianjin, China. The current investigation showed that elevated TyG index and TG/HDL-c levels were associated with prehypertension and hypertension, independently of other known risk factors such as age, sex, smoking, drinking, marital status, and body mass index in this study. Furthermore, the association between TyG index, TG/HDL-c and age, HR, BMI, SBP, DBP, TC, TG, LDL-c and GLU were positive correlation, while HDL-c was negative correlation in Spearman correlation analysis. Moreover, multiple logistic regression analysis suggested both fourth and third quartiles of the TyG index were associated with prehypertension and hypertension. There was an association with prehypertension

TABLE 4 Association between the TyG index quartiles and risk of incident prehypertension and hypertension

Variables	Quartile 1	Quartile 2	Quartile 3	Quartile 4	p for trend
Prehypertension					
Unadjusted	1.000 (ref)	1.017 (0.943, 1.096)	1.229 (1.136, 1.328) [*]	2.136 (1.956, 2.333) [*]	<.001
Model 1	1.000 (ref)	0.955 (0.884, 1.032)	1.113 (1.027, 1.207) [*]	1.876 (1.713, 2.055) [*]	<.001
Hypertension					
Unadjusted	1.000 (ref)	1.157 (1.066-1.256) [*]	1.845 (1.699-2.003)*	3.889 (3.551-4.258)*	<.001
Model 1	1.000 (ref)	0.973 (0.889, 1.066)	1.377 (1.257, 1.510) [*]	2.701 (2.445, 2.983)*	<.001

Note: Model1 was adjusted for age, sex, smoking, drinking, marital status, and body mass index. *Means *p* <.001.

FIGURE 1 The OR between the TYG index quartiles and presence of prehypertension and hypertension



Variables	Quartile 1	Quartile 2	Quartile 3	Quartile 4	p for trend
Prehypertension					
Unadjusted	1.000 (ref)	1.091 (1.011-1.178) [*]	1.201 (1.111-1.298) [*]	1.891 (1.734-2.063)*	<.001
Model 1	1.000 (ref)	0.989 (0.914, 1.070)	1.051 (0.969, 1.139)	1.575 (1.439, 1.724) [*]	<.001
Hypertension					
Unadjusted	1.000 (ref)	1.134 (1.045-1.230)*	1.393 (1.283-1.512) [*]	3.085 (2.824-3.371)*	<.001
Model 1	1.000 (ref)	0.952 (0.869, 1.043)	1.069 (0.975, 1.172)	2.103 (1.907, 2.320)*	<.001

Note: Model 1 was adjusted for age, sex, smoking, drinking, marital status, and body mass index. *Means *p* <.001.

and hypertension when comparing the highest TyG index (the fourth quartile) to the lowest TyG index (the first quartile) and corresponding ORs were 1.795 (1.638,1.968) and 2.439 (2.205,2.698), respectively. However, for TG/HDL-c, multiple logistic regression analysis suggested only the fourth quartile of TG/HDL-c was associated with prehypertension and hypertension. The highest quartile to the lowest quartile of prehypertension and hypertension and corresponding ORs were 1.514 (1.382,1.658) and 1.934 (1.751,2.137), respectively. Furthermore, when comparing the fourth quartile to the first quartile of TyG index and TG/HDL-c, respectively, both corresponding ORs of hypertension were higher than prehypertension. And TyG index was greater than TG/HDL-c in association with hypertension (p =.0001).

Many studies demonstrated insulin resistance is associated with diabetes, obesity, coronary artery disease, coronary artery

calcification, hypertension, and metabolic disorders, because of hyperinsulinemia. ²⁸⁻³⁵ Some people think that the relevant reasons between insulin resistance and hypertension were as follows: First, with the insulin increasing, the sympathetic nervous system and the renin-angiotensin-aldosterone system were activated and the corresponding systolic blood pressure and diastolic blood pressure were elevated.^{28,36} Second, when insulin resistance induces hyperinsulinemia, the sodium reabsorption from renal tubules is increased and leads to high blood pressure.^{5,30,37} Third, hyperglycemia makes the extracellular osmotic pressure higher than the intracellular osmotic pressure, in order to make a relative balance between extracellular and extracellular osmotic pressure, the water flows into the blood vessels, which increases the circulating blood volume and blood pressure in the blood vessels,³⁷ but no guideline suggests the certain association between IR surrogate index and hypertension.



Variable	AUC	95% CI	Z statistics	p values
TYG	0.596	(0.591, 0.601)	22.946	<.0001
TG/HDL-c	0.577	(0.572, 0.583)	29.074	<.0001
TyG vs TG/HDL-c			9.997	.0001

TABLE 6 The AUC with its 95% CI for distinguishing hypertension by TyG and TG/HDL-c

FIGURE 2 The OR between the

prehypertension and hypertension

TG/HDL-c guartiles and presence of

Abbreviation: AUC, area under the curve and TyG vs TG/HDL-c: using DeLong et al to compare the areas under two correlated receiver operating characteristic curves.



FIGURE 3 Receiver operative characteristic curves for distinguishing hypertension by TyG index and TG/HDL-c

In a 9-year longitudinal population-based study, the TyG index has been reported as a good indicator for incident hypertension, and Cox regression analyses indicated that a higher TyG index was associated with an increased risk of subsequent incident hypertension.¹⁶ In one prospective cohort study, during the 20-year follow-up, high TG/HDL-c ratio in adolescents was associated with hypertension in early adulthood.¹⁴ However, Jie Fan, MB et al showed that MET-IR was significantly associated with prehypertension in subjects with normoglycemia, while TyG index and TG/HDL-c were not statistically significant.¹⁰ In the present study, the logistic regression analysis showed that TyG index and TG/HDL-c were closely related to prehypertension and hypertension, and we also found that the distinguishing ability of TyG index was better than TG/HDL-c in hypertension. In future, we will explore whether elevated TYG and TG/ HDL-c can predict the major adverse cardiovascular events in hypertension individuals.

The disadvantage of this study is that we cannot show a certain causality association between prehypertension and hypertension, and TyG index and TG/HDL-c. Another limitation is that we were not able to directly conduct the hyperinsulinemic-euglycemic clamp (HIEC) technique of the insulin resistance in our study population and to further compare the surrogate indexes with direct markers of insulin resistance. Moreover, the study population from Tianjin, China, might limit the generalizability of TyG index and TG/HDL-c to other ethnic groups. In addition, diuretics and β -blocker may change lipid profile, 38,39 but the proportion of diuretics and $\beta\text{-blocker}$ in antihypertensive drugs is relatively low in this study,⁴⁰ which may be not enough to affect the overall experimental results, and this needs to be conducted further explorations in future. Finally, less similar research about the relationship between prehypertension and hypertension with TyG index and TG/HDL-c in normoglycemic subjects results in a limited possible comparison of results. Therefore, further prospective and randomized studies will be required to confirm our findings.

5 | CONCLUSIONS

The current investigation evidenced that elevated TyG index and TG/HDL-c levels were associated with the presence of prehypertension and hypertension, independently of other known risk factors such as age, sex, smoking, drinking, marital status, and body mass index in this study. Moreover, the TyG index was more significant than TG/HDL-c in distinguishing hypertension. Therefore, they have the potential to become cost-effective monitors in the hierarchical management of prehypertension and hypertension.

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CONFLICT OF INTEREST

The authors report no conflicts of interest.

AUTHOR CONTRIBUTIONS

(I) Conception and design: H Cong, F Zhang, Y Zhang; (II) Administrative support: H Cong, Z Guo; (III) Provision of study materials or patients: Y Zhang, H Cong; (IV) Collection and assembly of data: H Cong, Y Zhang, X Xing; (V) Data analysis and interpretation: F Zhang, M Ren, Hua Yang; (VI) Manuscript writing: F Zhang; (VII) Final approval of manuscript: All authors.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments and approved by the ethics committee of Tianjin Chest Hospital. All participants provided written informed consent to participate in the study.

DATA AVAILABILITY STATEMENT

The data for the research were obtained from an existing database containing details held by the Early Screening and Comprehensive Intervention Program for High-Risk Population of Cardiovascular Disease. The authors elect to not share data.

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