Prospective Study on Predicting Cardiovascular Disease Risk in the General Population through Triglyceride-Glucose Index

Dr. Arpit Singh¹, Dr. Anurag Rawat²

¹Resident, Department of Medicine, Himalayan Institute of Medical Science Jolly Grant Dehradun ²Professor, Department of Cardiology, Himalayan Institute of Medical Science Jolly Grant Dehradun

Corresponding Author: Dr. Anurag Rawat, <u>anuragrwt@gmail.com</u>

Abstract

Introduction: Cardiovascular diseases (CVD), are one of the main causes of mortality and disability worldwide, it is influenced by insulin resistance (IR). The triglyceride-to-glucose ratio (TyG) forecasts the risk of IR and CVD. TyG shifts have yet to be studied on long-term basis. Our research stresses the value of ongoing TyG index monitoring when assessing CVD risk. TyG testing for cardiovascular and IR risk may enhance therapy planning and delivery.

Aims and objectives: To assess the population's risk of cardiovascular disease using the triglyceride-glucose index (TyG).

Methods: A prospective cohort study including 100 participants followed them over time and performed biannual examinations. For the study, data on the demographics, health, and lifestyle factors of the participants were gathered through the use of a questionnaire.Education level, monthly income, cigarette and alcohol use, body mass index (BMI), blood pressure, and a number of blood biomarkers were all taken into consideration. We used the TyG index as a surrogate measure for insulin resistance. Fasting triglycerides and fastingplasma glucose were measured, TyG index is calculated as Ln (fasting triglycerides (mg/dl)×fastingblood glucose (mg/dl)/2). Myocardial infarction, stroke, and other cardiovascular events were the primary outcome assessed.

Results: Changes in the TyG index for cardiovascular disease (CVD), stroke, and myocardial infarction (MI) are analysed, and statistics on discriminating and reclassification are presented in Table 3. Adding TyG index updates to CVD research moderately improves the C statistic (0.745) with significant IDI (0.12) and category-free NRI (12.58). The C-statistic for stroke is still 0.745, but the IDI is 0.09, and the category-free NRI is 11.02.

Conclusion: In conclusion, tracking the TyG index over time can be beneficial for identifying those who are at greater risk to develop CVD.

Keywords: insulin resistance, cardiovascular risk, triglyceride, glucose.

Introduction

Cardiovascular illnesses (CVD) are the primary drivers of grimness and mortality worldwide, while insulin resistance (IR) is a significant factor for these illnesses. To accomplish early avoidance, many countries have tried to identify those at elevated risk of cardiovascular disease & IR and designate them as high-risk populations. Studies have suggested that an effective indicator of insulin resistance (IR) consists of the triglyceride-glucose ratio (TyG), an artificial ratio for both triglycerides (TGs) and fasting blood glucose (FBG). Numerous studies have demonstrated that an important pathophysiological pathway for the development of type 2 diabetes and cardiovascular disease is insulin resistance.[1].

Cardiovascular diseases (CVD) are one of the leading causes of death worldwide, and Insulin resistance is a significant risk factor for the same. (Ormazabal et al., 2018). Previous research using the standard gold technique for measuring IR, hyperinsulinemiceuglycemic clamping, has demonstrated an unrelated connection between IR and CVD [2]. Despite using the latest therapies advised by guidelines, including immediate stringent lipid-lowering treatment, double anti-platelet treatment, and coronary revascularization, certain patients with ACS remain more susceptible than ever to recurrent cardiovascular (CV) events. Those with type 2 diabetic mellitus (T2DM) are more at risk [3].

Type 2 Diabetics represent almost one-third of ACS cases. These individuals are more prone to get multivessel disease. Due to disadvantages of coronary artery bypass graft (CABG), percutaneous coronary intervention, or PCI, has become the most preferred revascularization forpatients with coronary artery disease (CAD) [4]. However, it was found that in diabetic individuals having ACS and multivessel CAD, PCI was linked to a greater risk of significantly inferior CV results compared to CABG during the long run. As a result, we must identify diabetic individuals with ACS who are getting PCI & are at high residual risk as soon as possible and improve therapeutic care to lower the prospective cardiovascular event danger. Insulin resistance (IR) has been recognized as a significant

mediator of metabolic diseases since 1988, such as type 2 diabetes and atherosclerotic cardiovascular disease (CVD). The hyperinsulinaemic-euglycaemic clamp serves as the "gold standard" technique for IR measurement. However, it is rarely employed in clinical settings because of the testing procedure's complexity. A significant correlation exists between IR and the long-term rise in blood sugar and triglycerides [5].

As a result, it was hypothesized that blood sugar and triglycerides may predict IR. It has been demonstrated that the fasting plasma glucose (FPG), as well as triglycerides, are combined to create the triglyceride glucose (TyG) index that significantly correlates with IR as determined with the use of the hyperinsulinaemic-euglycemic clamp test as well as outperforms the HOMA-IR, which measures IR in both diabetics and nondiabetic patients [6].

A crucial factor in the pathophysiology of diabetes mellitus, insulin resistance (IR), is strongly correlated with cardiovascular disease (CVD). Diabetes type 2, high blood pressure, dyslipidemia, and obesity are CVD risk factors. IR has also been linked as a stand-alone CVD risk factor. In order to avoid CVD, early IR diagnosis and therapy may be helpful. The hyperinsulinemic-euglycemic clamp is the gold standard for assessing IR. However, there are other reliable methods. IR testing typically uses homeostasis modelling to evaluate insulin resistance (HOMA-IR), determining insulin and glucose concentrations at rest. Be that as it may, the circulating insulin fixation is not regularly estimated in essential consideration settings, which additionally delivers that HOMA-IR is likewise improper for enormous-scope studies [7]. Instead, the triglyceride glucose amalgamation measures fasting blood glucose (FBG) and triglyceride (TG) and triglyceride index (TvG) have become a simple, affordable, repeatable, and effective substitute for insulin resistance. It has been demonstrated that the HOMA-IR and the hyperinsulinemic-euglycemic clamp have a strong correlation with the TyGIndex.In previous cohort studies, the risk of incident CVD was increased by a high TyG index. However, only onetime point was used to analyze the TyG index in these previous studies, so no analysis of changes in the TyG index over time or their impact over time has been done yet [8].

The evaluation of TyG index at a particular moment in time may not be the best indicator for generating predictions. Cardiovascular disease (CVD) progresses due to several contributing variables, including lipid disorders and glycemic abnormalities. The link between triglycerides (TG) and the cardiovascular disease (CVD) risk remains contentious, and hypertriglyceridemia (HTG) is a common risk factor[9]. Given a valid group of proof, we can reason that HTG is a free gamble component of creating glucose digestion problems. Plasma levels of TG are closely linked to increased glucose levels due to interactions among fat, muscle, and pancreatic-cell activity. Fatty liver disease, which might increase the incidence to type 2 diabetes mellitus (T2DM), is another factor that may be caused by TG accumulation in the liver [10]. Plasma TG is a distinct risk factor for T2DM in prospective studies. In addition, it has been demonstrated that fibrates, which reduce TG, significantly slow the progression of insulin resistance. In addition, according to reports, high normal ranges for both TG and fasting glucose might indicate the danger of cardiovascular disease. Consequently, assessing the cooperative worth of TG and fasting blood sugar levels in individuals with stable coronary artery disease (computer-aided design) would be beneficial [11].

Cardiovascular disease (CVD) is a primary source of morbidity and mortality worldwide, presenting serious general well-being challenges and putting a financial weight on patients. There are several risk factors for CVD, such as age, male gender, weight, high blood pressure, hypocholesteremia, and diabetes; ongoing have demonstrated that specific investigations individuals lacking these key components likewise foster CVD. Also, regardless of improving cutting-edge procedures and advancing essential and optional avoidance, individuals with CVD remain at increased risk of intermittent unfavorable cardiovascular outcomes. In this way, recognizing people's early CVD risk will have significant clinical relevance [12].

Insulin resistance (IR) is a disorder characterized by decreased awareness of and response to insulin action, and it is recognized as a marker of T2DM. In both diabetic and nondiabetic individuals, there is mounting evidence that IR and associated diseases aid in developing cardiovascular disease. It is common knowledge that people with IR are more likely to develop High blood pressure, dyslipidemia, & hyperglycemia, which are closely associated with poor CVD outcomes, as examples of metabolic diseases. As a result, IR is now recognized to be a prediction for cardiovascular disease (CVD) and a pathogenic cause in both diabetic and general populations. As a result, it is critical to develop easy-to-use and dependable screening tools for IR detection and cardiovascular risk prediction [13].

Methods

Study design

A prospective cohort study was conducted on 100 participants who completed a thorough biannual health examination. The Medical history questionnaire was used to collect information regarding demographic data, medical history, and lifestyle factors. Literacy was categorized as primary education, middle school education, or having at least a high school diploma. Socio economic category was assessed according to modified Kuppuswamy Scale. There were three categories for alcohol and cigarette use: never, once, and now. Weight (kg) squared times height (m2) squared is how the body mass index (BMI) was computed. A mercury sphygmomanometer was used to monitor blood pressure while the subject was seated, and the mean diastolic and systolic blood pressure results from three measurements were noted. An autoanalyzer was used to analyze each blood sample the day before the blood draw. The biochemical tests were serum creatinine, FBG, blood lipids, and highsensitivity C-reactive protein. The TyG index was used which was determined as Fasting TG [mg/dL] x FBG [mg/dL]/2. The onset of CVD events (including MI and stroke) was the primary outcome of the current investigation.

Inclusion and exclusion criteria

Patients in the age group of 50 years with diabetes mellitus, hypertension, and cardiovascular diseases who came to the outpatient department of our hospital are included in the study. Patients who do not provide informed consent are excluded from the study.

Statistical analysis

The study used SPSS 25 for statistical analysis. The authors applied Chi-square andKruskal-Wallis test, which was performed to assess differences in the traits across modifications to TyG index categories, either categorical variables in the analysis of variances or

continuous variables. The continuous data was expressed as mean \pm standard deviation while discrete data was expressed as frequency and its percentage. The level of significance was considered to be P<0.05.

Ethical approval

The authors gave the patients a full explanation of the study. The patient's consent has been obtained. The study's methodology was approved by the hospital's ethical review board.

Results

The initial Participants in the research had the following traits: shown in Table 1. The characteristics being examined in this study include age, gender (men), an education level (high school or equivalent), earnings level (more than 800 RMB/month), body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), current alcohol use status, active physical activity, hypertension, diabetes mellitus, dyslipidemia, & the usage of lipid-lowering, antihypertensive, and anti-diabetic medications. The total cholesterol levels, HDL cholesterol, high-sensitivity C-reactivity protein (hs-CRP), and LDL cholesterol are also measured.

The table provides data for each characteristic across the TyG index's change quartiles. Fast levels of triglycerides divided by fasting glucose levels yield the logarithm of the TyG index, a measure of insulin resistance levels.

		changes in the TyG index by quartiles				
Characteristics	Overall	Q1 (<- 0.31)	Q2 (- 0.31 to 0.05)	Q3 (0.05- 0.41)	Q4 (≥ 0.41)	P value
Participant count	100	40	20	20	20	
Age, years	50.01 ± 12.09	48.12 ± 11.89	49.12 ± 12.01	50.02 ± 11.98	50.16 ± 11.78	<0.0001
Men, n (%)	76 (76)	31 (77.5)	15 (75)	14 (70)	15 (75)	<0.0001
High school or above, n (%)	25 (25)	5 (25)	4 (20)	3 (15)	2 (10)	<0.0001
Income >15187 Rs/month, n (%)	15 (15)	3 (15)	3 (15)	2 (10)	2 (10)	<0.0001
kg/m2 body mass index	25.18 ± 3.89	25.14 ± 3.78	24.98 ± 3.67	25.24 ± 3.78	25.56 ± 3.67	<0.0001
mmHg, or the systolic blood pressure	129.12 ± 20.45	127.23 ± 20.12	127.09 ± 20.23	128.98 ± 20.12	132.07 ± 20.45	<0.0001
Diastolic blood pressure, mmHg	82.78 ± 12.04	81.78 ± 11.45	82.09 ± 11.45	82.98 ± 11.67	84.67 ± 11.78	<0.0001
Current smoker, n (%)	34 (34)	12 (32.5)	6 (30)	7 (35)	8 (40)	<0.0001
Current alcohol use, n	39 (39)	15 (37.5)	7 (35)	8 (40)	9 (45)	<0.0001

Table 1: Baseline characteristics of patients

(%)						
Active physical activity, n (%)	92 (92)	37 (92.5)	18 (90)	19 (95)	18 (90)	<0.0001
Hypertension, n (%)	10 (10)	4 (10)	2 (10)	2 (10)	3 (15)	<0.0001
Diabetes mellitus, n (%)	3 (3)	1 (2.5)	1 (5)	1 (5)	1 (5)	<0.0001
Dyslipidemia, n (%)	5 (5)	2 (5)	1 (5)	1 (5)	1 (5)	<0.0001
Antihypertensive agents, n (%)	9 (9)	3 (7.5)	2 (10)	2 (10)	2 (10)	<0.0001
Antidiabetic agents, n (%)	2 (2)	1 (2.5)	1 (5)	1 (5)	1 (5)	<0.0001
Lipid-lowering agents, n (%)	1 (1)	1 (2.5)	1 (5)	1 (5)	1 (5)	<0.0001
mmol/L of total cholesterol	5.02 ± 1.45	4.98 ± 1.24	5.09 ± 1.23	5.12 ± 1.34	4.87 ± 1.56	<0.0001
mmol/L of HDL cholesterol	1.78 ± 0.42	1.78 ± 0.67	1.78 ± 0.43	1.78 ± 0.56	1.67 ± 0.56	<0.0001
mmol/L of LDL cholesterol	2.45 ± 0.98	2.67 ± 0.98	2.34 ± 0.98	2.45 ± 0.98	2.45 ± 0.99	<0.0001
Hs-CRP, mg/dL	2.34 ± 6.78	2.18 ± 5.02	2.34 ± 5.67	2.45 ± 6.98	2.67 ± 7.89	<0.0001

Table 2 presents the alterations in the (An indicator of insulin resistance) TyG index, their correlation with HR (hazard ratio), and 95% confidence intervals. The table includes information for different characteristics and quartiles of changes in the TyG index and the corresponding P-values. The characteristics analyzed in the table are CVD (cardiovascular disease), stroke, and MI (myocardial infarction).

For each characteristic, the table provides the number and percentage of cases (n(%)) in each quartile of TyG index changes. It also displays the incidence rate per 1000 person-years and the corresponding confidence intervals for each quartile.

Additionally, the table presents two models (Model 1 and Model 2) and their associated hazard ratios (HR) with confidence intervals. Model 1 is used as the reference category. The HR represents the relative risk of developing the specific condition (CVD, stroke, or MI) associated with each quartile of TyG index changes compared to the reference category.

	changes in the TyG index by quartiles					
Characteristics	Q1 (<-0.31)	< -0.31) Q2 (-0.31 to 0.05) Q3 (0.05-0.41) Q4 (\geq 0		Q4 (≥ 0.41)	P value	
CVD						
case, n(%)	1 (5)	1 (5)	1 (5)	1 (5)		
Incidence rate per 1000 person-y	5.57 (5.34-6.23)	5.78 (5.34-6.34)	6.23 (5.87-6.78)	6.89 (6.45-7.45)		
Model 1	Reference	1.34 (1.08-1.45)	1.34 (1.23-1.56)	1.56 (1.28-1.67)	<0.0001	
Model 2	Reference	1.25 (1.07-1.33)	1.34 (1.23-1.67)	1.45 (1.25-1.56)	<0.0001	
Stroke						
case, n(%)	1 (5)	1 (5)	1 (5)	1 (5)		
Incidence rate per 1000 person-y	4.45 (4.03-4.87)	4.56 (4.12-5.02)	5.09 (4.76-5.89)	5.34 (4.89-5.77)		
Model 1	Reference	1.23 (1.12-1.45)	1.34 91.12-1.56)	1.47 (1.27-1.76)	<0.0001	

Table 2: TyG index alterations and their correlation with HR and 95% confidence intervals

Model 2	Reference	1.23 (1.12-1.56)	1.28 (1.12-1.56)	1.39 (1.21-1.63)	<0.0001
MI					
case, n(%)	1 (5)	1 (5)	1 (5)	1 (5)	
Incidence rate per 1000 person-y	1.28 (1.12-1.44)	1.23 (1.09-1.45)	1.23 (1.23-1.67)	1.56 (1.34-1.89)	
Model 1	Reference	1.09 (0.97-1.45)	1.24 (0.98-1.67)	1.45 (1.09-1.89)	0.0051
Model 2	Reference	1.11 (0.99-1.34)	1.23 (1.09-1.67)	1.45 (1.12-1.89)	0.0116

Table 3 presents statistics on discrimination and reclassification for changes to the TyG index regarding cardiovascular disease (CVD), stroke, and myocardial infarction (MI). The table includes three measures: C statistics, integrated discrimination improvement (IDI), and category-free NRI (Net Re Classification Improvement). For CVD, The C statistic for the traditional model with no adjustments to the TyG index is 0.742, having a 95% CI (confidence interval) of 0.732-0.751. The reference column indicates that there are no values for IDI or category-free NRI in this case.

When the conventional model is modified to include changes in the TyG index, the C statistic improves slightly to 0.745 (CI: 0.36-0.756), with a p-value of 0.0098. The IDI increases to 0.12 (CI: 0.09-0.17) with a highly significant p-value of less than 0.0001. The category-free NRI also shows a substantial improvement of 12.58 (CI: 8.65-16.56), with a p-value of less than 0.0001.

Moving on to stroke, the conventional model has a C statistic of 0.743 (CI: 0.734-0.54). Again, the reference column shows no values for IDI or category-free NRI.

When the TyG index changes are incorporated into the conventional model, the C statistic remains at 0.745 (CI: 0.734-0.756). However, a Statistically significant difference exists. Improvement in IDI, with an increase of 0.09 (CI: 0.03-0.12) and a p-value of 0.0011. The category-free NRI also demonstrates improvement, with a value of 11.02 (CI: 6.45-15.34) and a highly significant p-value of less than 0.0001.

	C statistics (95% CI estimate)	Р	IDI (predicted 95% CI)	р	Category-free NRI (calculate (95% CI)	р
CVD						
traditional kind	0.742 (0.732- 0.751)		Reference		Reference	
Standard model plus modifications to the TyG index	0.745 (0.36- 0.756)	0.0098	0.12 (0.09- 0.17)	<0.0001	12.58 (8.65- 16.56)	<0.0001
Stroke						
traditional kind	0.743 (0.734- 0.54)		Reference		Reference	
TyG index modifications plus the conventional model	0.745(0.734- 0.756)	0.0436	0.09 (0.03- 0.12)	0.0011	11.02 (6.45- 15.34)	<0.0001
MI						

Table 3. Statistics	on reclassification	and discrimination	for variations in the '	FvG index
Table 5. Statistics	on reclassification	and disci mination	ior variations in the	I yO much

traditional kind	0.754 (0.734- 0.798)		Reference		Reference	
modified TyG index plus conventional model	0.756 (0.745- 0.777)	0.0413	16.78 (8.56- 25.13)	0.0367	16.98 (8.34- 25.34)	0.0001

Discussion

TyGindex has received much attention as a crucial metric for reflecting IR. IR is considered significant in the pathophysiological basis for developing diabetes mellitus&CVD too. TyG has received more attention in recent years in the fields of DM and metabolism and has positively impacted the assessment and forecasting of IR and metabolic syndrome for diabetic patients. Studies are being conducted examining the relationship between TyG and atherosclerotic CVD and hypertension. In middle-aged and older populations, Cross-sectional research has shown a strong link between higher TyG and systolic hypertension. TyG has a greater degree of discriminatory power for hypertension than other markers like cholesterol and blood glucose. Additionally, longitudinal follow-up investigations have shown that a greater TyG is associated with a higher risk of developing hypertension later on [13].Numerous studies have connected increased TyG and cardiovascular disease, stroke, and the development of atherosclerotic plaque events like coronary artery stenosis. According to research, those in quartiles with higher TYG indices had a higher risk of developing atherosclerosis than those with lower TYG index. TyG index was positively associated with weight, BMI, the circumference of the waist, the waist circumference to height ratio, visceral adiposity index, systolic and diastolic blood pressure, LDL cholesterol and LDL/HDL cholesterol proportion, dyslipidemia, hypertension, type 2 diabetes, idleness, & smoking, as reported by Da Silva et al.5. The TyG index had a poor connection with age, HDL-C, on the other hand. Gender or drug use did not affect the Based on population screening, results. the investigation was done to examine the connection between TyG and cardiovascular risk [14].

Although the exact cause of the association between the TyG index & worse CV outcomes is unknown, IR may have a role. Recent studies have demonstrated the significance of IR on the growth of advanced plaques and thermogenesis by promoting the death of vascular smooth muscle cells, endothelial cells, and macrophages [19]. The development of CVD can be triggered by several metabolic alterations brought on by IR. For instance, IR can lead to prolonged hyperglycemia due to imbalanced glucose metabolism, which causes an inflammatory reaction and oxidative

stress that injure vascular endothelial cells. In addition to dyslipidemia, the well-known lipid trio of high plasma triglycerides, low plasma HDL-C, and minutedense LDL-C particles, IR, can also influence how lipids are metabolized. Such metabolic alterations aid in the development of atherosclerotic plaque [15].

Furthermore. plasminogen activator inhibitor-1 concentrations are connected with IR in patients with hyperglycemia and hypertriglyceridemia, which reduces fibrinolytic activity and increases thrombotic events [20]. Additionally, it has been demonstrated that IR is linked to Increased arterial stiffness, decreased vasodilation, increased intima-media thickness, and increased calcification of the coronary arteries are all signs of endothelial dysfunction. Only a few structural and functional artery wall injuries are excellent predictors of future CV events. Significantly, several studies showed that IR was linked to myocardial and microvascular damage in acute MI [16].Following primary PCI, due to poorer myocardial reperfusion, lower myocardial microcirculatory function, and larger initial infarct size, there has been an increase in both short-term and long-term unfavourable CV events [17. In fact, several clinical trials have shown the link between IR and worse CV outcomes. IR, measured HOMA-IR, irrespective of the metabolic syndrome defined by the International Diabetes Federation, was found to be associated with metabolic syndrome in 2493 otherwise healthy persons in a prospective Danish based on populations study. Foundations and National Cholesterol Education Education standards were associated with CV events (including non-fatal ischemic coronary artery disease, stroke, and death). A cohort of individuals that had developed CVD had a similar outcome [18].

A brand-new alternative for measurement of Insulin resistance, The triglyceride-glucose (TyG) ratio. The meta-analysis assessed the associations between cardiovascular disease and mortality risks for people in general and the TyG index [19]. According to research, an elevated TyG index may be linked to a higher risk of CAD, MI, & CVD for the general population; varying degrees of assurance include moderate, low, and deficient levels., respectively. The combined rate of CVD, CAD, and the TyG index might be related linearly. Further prospective research (particularly in non-Asians) is required to support our findings [20]. According to earlier research, there is a direct link between the initial cardiovascular disease (CVD) development and the triglyceride-glucose index (TyG). The impact of long-term alterations in the TyG index and the likelihood of CVD is yet unknown [21]. The study set out to investigate the connection between fluctuations in the index of TyG and the incidence of CVD. The 62,443 Participants in the current research were CVD-free. Fasting glucose (mg/dL) x fasting triglyceride (mg/dL) / 2 , yields the TyG index [22]. Restrictive cubic spline analysis and multivariableadjusted Cox proportionate hazard model were utilised to look at how modifications to the TyG index correlated with the likelihood of CVD. Significant changes in the TyG index can accurately predict CVD risk in people of all ages. TyG variations may be monitored to help identify CVD risk factors in people early [23].

A clinical surrogate diagnosis for insulin resistance is the triglyceride glucose (TyG) index. The relationship between the TyG index and chronic cardiovascular disease (CVD) is unclear. Using extensive data collection through the National Healthcare Data Database, we assessed the link between the TyG index and (NHID) CVD [24]. Using the NHID, we conducted a retrospective observational cohorts research on 5,593,134 individuals older than 40 from 2009 to 2017. We classified the participants into quartiles based on the Myocardial infarction (MI), stroke, and TyG index outcome factors. For the whole follow-up period, Each TyG quartile's incidence of occurrences was evaluated [25]. The Cox proportional hazard regression technique examined all outcomes while adjusting for baseline factors.According to research, the TyG index, a straightforward indicator of insulin resistance, may help in the early detection of people who are particularly at risk of experiencing cardiovascular despite our extensive population study [26].

Conclusion

In conclusion, our research shows that shifts in the TyG index are a robust predictor of CVD. Our results show that the risks of cardiovascular disease (CVD), stroke, and myocardial infarction (MI) grow with an increasing TyG index over time. In light of these findings, it is clear that tracking TyG index changes over time is crucial for accurately identifying those who are at increased risk of developing CVD. The prevalence of cardiovascular disease (CVD) can be decreased through population-wide surveillance, which allows for early intervention and focused preventive interventions. However, a significant drawback of the prior research is that the TyG index was only assessed at a single time point, and no analysis has been conducted on how the TyG index evolves in individuals over time or the longitudinal effects of such changes. This evaluation could be more predictive than the TyG index measurement at a single time point. To this end, we conducted a large community-based prospective cohort study to characterize the link between change in the TyG index and the eventual risk of CVD and its subtypes.

References

- 1. Annual Report on Cardiovascular Health and Diseases in China 2019. China national cardiovascular disease centre. Beijing Sci Press. 2020;9.
- Damen JA, Hooft L, Schuit E, et al. Prediction models for cardiovascular disease risk in the general population: systematic review. BMJ. 2016;353:i2416. doi:10.1136/bmj.i2416
- Tripolino C, Irace C, Scavelli FB, et al. Triglyceride glucose index and everyday carotid wall shear stress. J Investig Med. 2014;62 (2):340–344. doi:10.2310/JIM.00000000000043
- Agostino, R.B.D., Vasan, R.S., Pencina, M.J., Wolf, P.A., Cobain, M., Massaro, J.M., et al., 2008. General Cardiovascular Risk Profile for Use in Primary Care The Framingham Heart Study. Circulation 117 (6), 743–753.
- Alberti, K.G.M.M., Eckel, R.H., Grundy, S.M., Zimmet, P.Z., Cleeman, J.I., Donato, K.A., et al., 2009. Harmonizing the Metabolic Syndrome International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 1640–1645.
- Katz P, Leiter LA, Mellbin L, Ryden L. The clinical burden of type 2 diabetes in patients with acute coronary syndromes: prognosis and implications for short- and long-term management. DiabVasc Dis Res. 2014;11(6):395–409.
- Bjarnason TA, Hafthorsson SO, Kristinsdottir LB, Oskarsdottir ES, Johnsen A, Andersen K. The prognostic effect of known and newly detected type 2 diabetes in patients with acute coronary syndrome. Eur Heart J Acute Cardiovasc Care. 2019.
- Ormazabal V, Nair S, Elfeky O, Aguayo C, Salomon C, Zuñiga F. Association between insulin resistance and the development of cardiovascular disease. CardiovascDiabetol. 2018;17(1):122.
- Bersch-Ferreira Â, Sampaio G, Gehringer M, Torres E, Ross-Fernandes M, da Silva J, Torreglosa C, Kovacs C, Alves R, Magnoni C, et al. Association between plasma fatty acids and inflammatory markers in patients with and without insulin resistance and secondary prevention of cardiovascular disease, a cross-sectional study. Nutr J. 2018;17(1):26.
- Xun P, Wu Y, He Q, He K. Fasting insulin concentrations and incidence of hypertension, stroke, and coronary heart disease: a meta-analysis of prospective cohort studies. Am J Clin Nut. 2013;98(6):1543–54.
- 11. Sacco RL, Roth GA, Reddy KS, Arnett DK, Bonita R, Gaziano TA, Heidenreich PA, Huffman MD, Mayosi BM, Mendis S, et al. The Heart of 25 by 25: achieving the goal of reducing global and regional premature deaths from cardiovascular diseases and stroke: a modelling study from the American Heart Association and World Heart Federation. Circulation. 2016;133(23):e674-690.

- Rosenblit PD. Severe atherosclerotic cardiovascular disease (ASCVD) risk recognition. CurrDiab Rep. 2019;19(8):61.
- Choi S. The potential role of biomarkers associated with ASCVD risk: risk-enhancing biomarkers. J Lipid Atheroscler. 2019;8(2):173–82.
- Zhao D, Liu J, Wang M, Zhang X, Zhou M. Epidemiology of cardiovascular disease in China: current features and implications. Nat Rev Cardiol. 2019;16(4):203–12.
- Annual Report on Cardiovascular Health and Diseases in China 2019. China national cardiovascular disease centre. Beijing Sci Press. 2020;9.
- Damen JA, Hooft L, Schuit E, et al. Prediction models for cardiovascular disease risk in the general population: systematic review. BMJ. 2016;353:i2416. doi:10.1136/bmj.i2416
- Tripolino C, Irace C, Scavelli FB, et al. Triglyceride glucose index and everyday carotid wall shear stress. J Investig Med. 2014;62 (2):340–344. doi:10.2310/JIM.00000000000043.
- Katz P, Leiter LA, Mellbin L, Ryden L. The clinical burden of type 2 diabetes in patients with acute coronary syndromes: prognosis and implications for short- and long-term management. DiabVasc Dis Res. 2014;11(6):395–409.
- 19. Bjarnason TA, Hafthorsson SO, Kristinsdottir LB, Oskarsdottir ES, Johnsen A, Andersen K. The prognostic effect of known and newly detected type 2 diabetes in patients with acute coronary syndrome. Eur Heart J Acute Cardiovasc Care. 2019.
- 20. Ray KK, Colhoun HM, Szarek M, Baccara-Dinet M, Bhatt DL, Bittner VA, Budaj AJ, Diaz R, Goodman SG, Hanotin C, et al. Effects of alirocumab on cardiovascular and metabolic outcomes after acute coronary syndrome in patients with or without diabetes: a prespecified analysis of the ODYSSEY OUTCOMES randomised controlled trial. Lancet Diabetes Endocrinol. 2019;7(8):618–28.
- Ramanathan K, Abel JG, Park JE, Fung A, Mathew V, Taylor CM, Mancini GBJ, Gao M, Ding L, Verma S, et al. Surgical versus percutaneous coronary revascularization in patients with diabetes and acute coronary syndromes. J Am CollCardiol. 2017;70(24):2995–3006.
- 22. Kivimäki M, Steptoe A. Effects of stress on the development and progression of cardiovascular disease. Nat Rev Cardiol. 2018;15(4):215–29.
- 23. Wang, A., Tian, X., Zuo, Y. *et al.* Change in triglyceride-glucose index predicts the risk of cardiovascular disease in the general population: a prospective cohort study. *CardiovascDiabetol* **20**, 113 (2021).
- Ormazabal V, Nair S, Elfeky O, Aguayo C, Salomon C, Zuñiga F. Association between insulin resistance and the development of cardiovascular disease. CardiovascDiabetol. 2018;17(1):122.
- 25. Kim KJ, Kwon TY, Yu S, Seo JA, Kim NH, Choi KM, Baik SH, Choi DS, Kim SG, Park Y, et al. Ten-year mortality trends for adults with and without diabetes mellitus in South Korea, 2003 to 2013. Diabetes Metab J. 2018;42(5):394–401.

26. Kim MK, Ko SH, Kim BY, Kang ES, Noh J, Kim SK, Park SO, Hur KY, Chon S, Moon MK, et al. 2019 Clinical practice guidelines for type 2 diabetes mellitus in Korea. Diabetes Metab J. 2019;43(4):398–406.