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Original Research Articles

Is the Triglyceride-Glycated Hemoglobin Index Superior to Triglyceride-Glucose Index in Predicting Metabolic Syndrome in an American Adult Population

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Abstract: The triglyceride-glucose index (TyG index) is a validated measure of insulin resistance that reliably predicts Metabolic Syndrome (MetS) type 2 diabetes (T2DM) and premature atherosclerotic cardiovascular diseases (ASCVD). It includes measures of carbohydrate and lipid metabolism. We postulated that glycated hemoglobin (HbA1c), which in contrast to fasting glucose, reflects glycemic status over 2–3 months and not at a single time of day, may serve as a superior biomarker of MetS when combined with plasma triglycerides as the Ty-HbA1c index. Using data from a large cohort of American adults (n = 5039) in the National Health and Nutrition Examination Survey (NHANES) study, we compared the Ty- HbA1c and TyG index in predicting prevalent MetS, a harbinger of both T2DM and ASCVD. In this cohort, 22% of patients had MetS and the TyG and Ty- HbA1c indices were significantly increased in patients with MetS. Although both indices showed very good prediction performance on the prevalent of MetS, the TyG index had a significantly superior prediction as indicated by the Receiver Operating Characteristic (ROC) Area under the curve (AUC). Moreover, this significance was consistent across the 3 race groups. In the prediabetes subgroup, the ROC-AUC for TyG index was significantly higher than the Ty-HbA1c index. In conclusion, this cross-sectional study shows that the Ty-HbA1c index is not superior to the well-accepted TyG index in predicting MetS, a proxy of cardio-metabolic disorders in this large study of American adults. Furthermore, given that the TyG index is based on only fasting TG and glucose levels, it is more cost-effective.

Keywords: triglyceride-glucose index; glycated hemoglobin; metabolic syndrome; insulin resistance; prediabetes

1. Introduction

Non-enzymatic glycation of hemoglobin results in the formation of HbA1c, is a reliable indicator of glycemia within a period of 2–3 months [1–3]. It is a standardized common clinical laboratory test that is available universally. The method should be certified by the National Glycohemoglobin Standardized Program traceable to the Diabetes Control and Complications Trial reference assay [1–3].

Large prospective clinical trials have shown, in both type 1 and type 2 diabetic patients, that therapies that lower HbA1c delayed or prevented complications [4,5]. HbA1c has been accepted universally as a target to forestall especially microvascular complications of diabetes.

In addition, it is a useful biomarker for diagnosing diabetes, prediabetes, and cardiovascular risk [1–3].

Terminal products of non-enzymatic glycation, Advanced glycation end-products (AGEs) also appear to play a role in vascular complications, including atherosclerosis cardiovascular disease (ASCVD) [6,7].

The triglyceride-glucose index (TyG index) is a validated measure of insulin resistance that reliably predicts Metabolic Syndrome (MetS) type 2 diabetes (T2DM) and ASCVD [8–11]. It includes measures of both glucose and lipid metabolism.

We postulated that HbA1c, which in contrast to fasting glucose, reflects glycemic status over a period of 2–3 months [2,3] and not at a single time of day, may serve as a superior biomarker of MetS when combined with plasma triglycerides as an index.

Using data from a large cohort of American adults, we compared the performance of Ty- HbA1c and TyG indices in predicting prevalent MetS, a harbinger of both T2DM and ASCVD [12,13].

2. Methods

Data from the National Health and Nutrition Examination Survey (NHANES) cycles from 2005 to 2018 were used (https://www.cdc.gov/nchs/nhanes/index.htm (accessed on 15 April 2025)) as detailed by previous reports from the (CDC) Centers of Disease Control and Prevention [14–16]. NHANES was approved by the National Center for Health Statistics institutional review board, and written consent was obtained from all participants. To minimize confounding factors, the data set was restricted to non-Hispanic whites (NHW) and non-Hispanic African-American (AA) and Hispanic American (HA) participants of either sex aged 20–80 years. To be more comparable to our previously published studies in nascent MetS, we excluded current smokers, participants with diabetes, or CRP > 10mg/L [17]. Participants were defined as having MetS if they had three or more cardio-metabolic features of MetS. Controls needed to have 2 or fewer of MetS factors and not be on blood pressure medications. A total of n = 5039 individuals (3948 Controls and 1091 MetS) were studied.

Fasting blood samples were collected from participants after histories and physical examinations. Laboratory tests were assayed by standardized techniques as described previously. Moreover, CRP was assayed by the highly sensitive assay. The details of the different assays have been reported previously [14–16]. The triglyceride-glucose (TyG) index was calculated as reported previously [8]:

$$\text{Ln [fasting triglycerides (mg/dl)} \times \text{fasting plasma glucose (mg/dl)/2]}$$

The HbA1c-glucose (Ty-HbA1c) index was calculated as:

$$\text{Ln [HbA1c ((mmol/mol))} \times \text{fasting plasma glucose (mmol/L)/2].}$$

SAS version 9.4 (SAS Institute, Cary, NC) was used for statistical analysis and significance was defined as a two-sided p-value < 0.05. Results are expressed as median and interquartile range. The Wilcoxon Rank Sum test was used to compare age and metabolic characteristics between controls and MetS participants. Differences between controls and MetS group were also compared with adjusted linear covariance models controlling for age, waist circumference, sex, and race. After combining the control and MetS groups, Spearman rank correlation coefficients were determined to assess the association between the two indices and relevant variables. Logistic regression models were used to calculate the AUC of ROC. The areas under the correlated ROC curves were compared and the 95% Confidence Intervals (CI) were determined. Confounding variables, such as sex, age, and waist circumference were adjusted for in the logistic regression and with general linear models comparing controls and MetS groups.

3. Results

Table 1 depicts the salient cardio-metabolic features of patients with MetS (21.7%) and controls. Notably, age was not significantly different between the 2 groups. As expected, waist circumference (WC), blood pressure, glucose and triglyceride levels were significantly increased, although high density lipoprotein-cholesterol (HDL-C) levels were significantly lower. In addition, hsCRP, HOMA-IR, non-HDL-C and HbA1c levels were higher in the MetS group.

All subsequent analyses were adjusted for covariates.

Both the TyG index and Ty-HbA1c index were significantly increased in patients with MetS.

Table 1. Salient Clinical Characteristics of Controls and MetS groups.

	Control	MetS	*p* (Control vs. MetS)
n	3948	1091	
Female/Male, n (%)	2128/1820 54/46	556/535 51/49	0.09
Race& ethnicity AA/Hispanic/Non-Hispanic White, n (%)	751/1381/1816 (19/35/46)	120/351/620 (11/32/57)	<0.0001
Age, y	41 (29–56)	58 (43–69)	<0.0001
BMI, kg/m^2	26.6 (23.6–30.1)	31.5 (28.4–35.4)	<0.0001
Waist circumference, cm	93 (85–102)	107 (101–116)	<0.0001
Systolic BP, mmHg	115 (107–125)	129 (117–142)	<0.0001
Diastolic BP, mmHg	69 (62–75)	73 (64–81)	<0.0001
Glucose, mg/dL	97 (91–102)	109 (100–115)	<0.0001
Triglycerides, mg/dL	86 (61–121)	175 (128–225)	<0.0001
HDL cholesterol, mg/dL	56 (47–67)	43 (37–50)	<0.0001
Non-HDL cholesterol, mg/dL	132 (107–159)	154 (129–183)	<0.0001
CRP, mg/L	1.4 (0.6–2.9)	2.5 (1.2–4.5)	<0.0001
HOMAIR	1.9 (1.3–3.0)	4.1 (2.8–6.0)	<0.0001
HbA1c, %	5.3 (5.1–5.6)	5.6 (5.3–509)	<0.0001
Ty-HbA1c index	2.8 (2.5–3.2)	3.6 (3.3–3.9)	<0.0001
TyG index	8.3 (8.0–8.7)	9.1 (8.8–9.4)	<0.0001

Results are median (25th–75th percentile). *p*-value from Wilcoxon Rank Sum test for continuous variables.

As shown in Figure 1, the TyG and Ty-HbA1c indices showed very good prediction on the prevalent of MetS in the entire group (n = 5039), with an ROC-AUC of 0.86 (CI) ranging from 0.85–0.87) and ROC-AUC of 0.85 (CI ranging from 0.84 to 0.86). Importantly, the differences between the 2 indices as shown in Figure 1, were significantly in favor of the TyG index contrary to our hypothesis. Comparisons of the 3 race groups confirmed the superiority of the TyG index compared to the Ty-HbA1c index in all 3 races (Table 2). Both the TyG and Ty-HbA1c indices were significantly lower in the AA group compared to the HA group.

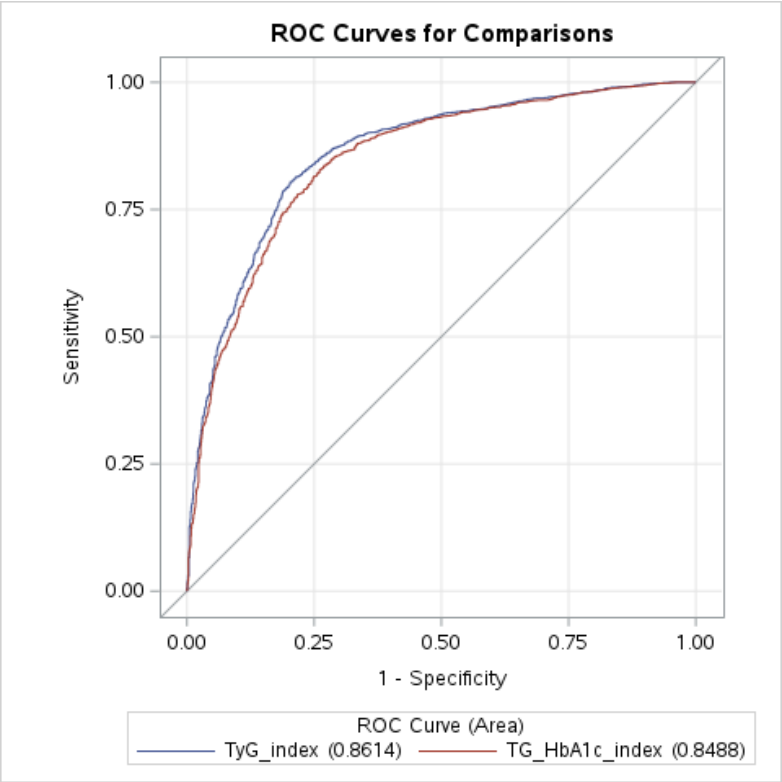

Figure 1. Comparison of ROC-AUC for TyG index and Ty-HbA1c in predicting prevalent Metabolic Syndrome. ROC-AUC for TyG index was significantly higher than Ty-HbA1c; 0.86 (CI of 0.85–0.87) vs. 0.85 (CI of 0.84–0.86), delta of 0.01, $p < 0.00001$.

Table 2. ROC Area Under the Curve by race/ethnic group.

	AA	**HA**	**NHW**		
	n = 871	**n = 1732**	**n = 2436**	***Race/Ethnicity Comparison***	***p-Value***
Ty-HbA1c index	0.81 (0.77, 0.85)	0.86 (0.84, 0.89)	0.85 (0.83, 0.87)	*AA vs. HA* *AA vs. NHW* *HA vs. NHW*	***0.02*** *0.09* *0.29*
TyG index	0.82 (0.78, 0.86)	0.87 (0.86, 0.89)	0.86 (0.85, 0.88)	*AA vs. HA* *AA vs. NHW* *HA vs. NHW*	***0.02*** *0.05* *0.41*
TyG-Ty-HbA1c, (95%CI)	0.01 (0.000, 0.02) $p = 0.049$	0.01 (0.005, 0.02) $p = 0.0001$	0.01 (0.01, 0.02) $p < 0.0001$		

ROC Receiver Operating Characteristic; AA African-American; HA Hispanic American; NHW non-Hispanic White.

We also examined the ability of both indices to predict MetS in individuals with prediabetes (n = 2653) defined by ADA criteria of a plasma glucose of 110–125 mg/dl and or a HbA1c of 5.7–6.4% [1]. The results confirmed that the TyG index had superior prediction performance with an ROC-AUC of 0.83 (CI of 0.81 to 0.84) vs ROC-AUC of 0.81 (CI of 0.79–0.83) for Ty-HbA1c index with a delta of 0.016, p < 0.0001

As shown in Table 3, both indices were significantly correlated with age and the 5 features of MetS. In addition, they showed significant correlation with hsCRP, HOMA-IR, and non-HDL-C. Also, there was a strong correlation between TyG index and Ty-HbA1c index of 0.98. These significant correlations were consistent across the subgroup analyses by race.

Table 3. Association of Triglyceride-HbA1c index and TyG index with MetS and related components.

	All n = 5039		**AA n = 731**		**HA n = 1732**		**NHW n = 2436**	
	Ty-HbA1c Index	**TyG Index**	**Ty-HbA1c Index**	**TyG Index**	**Ty-HbA1c Index**	**TyG Index**	**Ty-HbA1c Index**	**TyG Index**
Age	0.27	0.25	0.26	0.24	0.26	0.24	0.26	0.23
BMI	0.34	0.35	0.34	0.33	0.34	0.33	0.40	0.41
Waist Circumference	0.41	0.42	0.39	0.39	0.39	0.39	0.45	0.47
Systolic BP	0.26	0.27	0.26	0.27	0.26	0.27	0.30	0.30
Diastolic BP	0.15	0.15	0.17	0.18	0.17	0.18	0.16	0.17
Glucose	0.30	0.38	0.30	0.38	0.30	0.38	0.28	0.36
TG	0.98	0.99	0.98	0.99	0.98	0.99	0.98	0.98
HDL-cholesterol	−0.46	−0.49	−0.46	−0.48	−0.46	−0.48	−0.48	−0.51
Non-HDL-C	0.58	0.57	0.59	0.59	0.59	0.59	0.56	0.56
CRP	0.29	0.28	0.23	0.22	0.23	0.22	0.34	0.33
HOMA-IR	0.47	0.49	0.48	0.51	0.48	0.51	0.48	0.52
HbA1c	0.34	0.22	0.39	0.28	0.39	0.28	0.36	0.24
Ty-HbA1c index	-	0.98	-	0.98	-	0.98	-	0.98
TyG_index	0.98	-	0.98	-	0.98	-	0.98	-

Results are Spearman rho correlations, all $p < 0.0001$. Correlations with TyG index in bold. AA African-American; HA Hispanic American; NHW non-Hispanic White.

4. Discussion

In this report, we chose MetS as our end point since it confers at least a 5-fold increase in the risk of T2DM and at least a 2-fold increase in the risk of ASCVD and, is thus a good proxy of cardio-metabolic disorders [12,13]. In addition, we used the NHANES data set since it reflects the general US population and provides a large sample size of 5039 individuals. Our data suggests that despite the compelling scientific basis for HbA1c being a measure of long-term glycaemia, the Ty-HbA1c Index although significantly increased in patients with MetS, was not superior to the well-validated TyG index in predicting prevalent MetS in a US population. Moreover, this was reflected in the subgroup analyses by race for AA, NHW and HA. Both the TyG and Ty-HbA1c indices were significantly lower in AA than in HA. This could be explained by the lower TG levels in AA persons [18].

We further analyzed the prediction of the TyG index on persons with prediabetes. The results indicated that the TyG index was significantly superior to Ty-HbA1c in predicting MetS.

The 2 indices were significantly correlated with cardio-metabolic features, hsCRP, HOMA-IR and non-HDL-C, suggesting that both are related to insulin resistance, inflammation, and the atherogenic dyslipidemia. This further provided further evident for the high prediction value of these indices in the subgroup analyses by race. Since both indices are based on lipid and carbohydrate metabolism, the strong correlation between them is expected.

Data comparing the Ty-HbA1c and TyG indices are relatively limited. In a study comparing the TyG index and HbA1c in the diagnosis of prediabetes, it was found that both biomarkers had comparable diagnostic accuracy [19]. In a large study (n = 99,336) of patients with hypertension, a synergistic effect was observed between the TyG index and HbA1c in predicting poor blood pressure control [20].

In conclusion, we show that the Ty-HbA1c index is not superior to the well-accepted TyG index in predicting MetS, a proxy of cardio-metabolic disorders in American adults. Furthermore, since the TyG index is calculated based on fasting TG and glucose levels, it presents a more cost-effective tool [8,10]. Finally, the TyG index is a validated measure of insulin resistance, unlike the Ty-HbA1c index [10].

Ethics approval and consent to participate

The NHANES study was approved by the National Center for Health Statistics (NCHS) Research Ethics Review Board.

Author Contributions

IJ generated the idea for this publication. BAH undertook the statistical analyses. Both generated the original version and edited multiple iterations. Both approved the final version for submission.

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Informed Consent Statement

All volunteers provided written informed consent.

Data Availability Statement

The data is available from the senior author for review on reasonable request.

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Conflicts of Interest

No conflicts of interest, financial or otherwise, are declared by any of the authors. The Guest Editor who handled this manuscript to avoid any conflict of interest was Dr. Anand Singh.

Use of AI and AI-Assisted Technologies

No AI tools were utilized for this paper.

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