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Letter to the Editor

Triglyceride-glucose-uric acid (TyG-UA) index as a superior novel parameter in predicting metabolic syndrome among adult subjects

Dear Editor,

Metabolic syndrome (MS) is a condition that can cause cardiometabolic disorders, with its incidence increasing in recent decades. It is estimated that a quarter to a third of people worldwide have MS, particularly in developed countries[1]. Obesity, insulin resistance, hypertension, and dyslipidemia are common components of the metabolic syndrome[2]. Several reports have shown a close relationship between hyperuricemia and MS in adolescents, adults, and the elderly[3–5]. Elevated levels of blood uric acid are linked to oxidative stress, endothelial dysfunction, hypertension, micro-inflammatory processes, and impaired insulin action, all of which can lead to atherosclerosis, diabetes, insulin resistance, hepatic steatosis, and MS[6–9]. High triglyceride levels are also associated with inflammatory conditions including hypertension, cardiovascular disease, and diabetes[10–11]. Several research reports have shown the triglyceride-glucose (TyG) index's superiority over the homeostasis model assessment of insulin resistance (HOMA-IR) in assessing the risk of MS[12–13]. Uric acid is a laboratory biomarker routinely examined and has been proven to be significant in the occurrence of MS. However, uric acid is still rarely used in various formulas for determining MS, so we propose a novel parameter that incorporates serum uric acid levels into the TyG index formula, called the triglyceride-glucose-uric acid (TyG-UA) index, for determining the occurrence of MS.

The present cross-sectional study was conducted from December 2024 to January 2025 at Hasanuddin University Hospital, Makassar, Indonesia. One hundred seventy-four adult volunteers over 18 years old without diabetes mellitus (DM) history were recruited. Participants with inflammatory or infectious conditions, as well as those on medications that affect lipids and uric acid, were excluded. Informed consent was obtained from all participants before their involvement. This study was approved by the Institutional Review Board of Faculty of Medicine, Hasanuddin University (Approval Nos. 1097/UN 4.6.4.5.31/PP36/2024 and UH24110978).

Fasting blood samples were collected from the participants' veins, followed by serum separation. Abx Pentra 400 (Horiba) was used to measure the glucose, uric acid, triglycerides, and lipid profiles, while insulin was assessed using a Cobas e411 (Roche). HOMA-IR and TyG index were calculated as previously described[12]. The TyG-UA index was calculated using the formula: ln [glucose (mg/dL) × triglycerides (mg/dL) × uric acid (mg/dL)/3]. The International Diabetes Federation (IDF) criteria were employed to ascertain the MS state as previously described[1].

Data on continuous variables was examined for normalcy using the Kolmogorov-Smirnov test. The Chi-Square test was used to assess the difference in categorical data. The Independent T test (for normally distributed data) or the Mann-Whitney test (for non-normally distributed data) were used to examine the differences in numerical data. The area under the curve (AUC) from the receiver operating characteristic (ROC) analysis was employed to evaluate the ability of the HOMA-IR, TyG index, and TyG-UA index to detect the occurrence of MS. Cut-off values were determined by combining the most significant accumulated sensitivity and specificity values. The statistical analysis was carried out using version 21.0 of Statistical Package for the Social

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Sciences (SPSS) software.

The characteristics of both MS and non-MS subjects are shown in ***Table 1***. The TyG-UA index showed significant correlations with body mass index (BMI), waist circumference (WC), systolic blood pressure, diastolic blood pressure, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride, fasting plasma glucose (FPG), insulin, and HOMA-IR with correlation coefficients (r) of 0.324, 0.497, 0.360, 0.161, 0.486, −0.449, 0.754, 0.288, 0.364, and 0.406, respectively (all $P<0.05$). The results of the ROC curve analysis for determining the ability of HOMA-IR, TyG index, and TyG-UA index to detect the occurrence of MS are shown in ***Fig. 1***. The TyG-UA index (AUC = 0.842, 95% confidence interval [CI], 0.766–0.918, cut-off = 9.816 3, sensitivity = 75%, specificity = 83.10%) outperformed the HOMA-IR (AUC = 0.739, 95% CI, 0.709–0.875, cut-off = 2.650 4, sensitivity = 68.80%, specificity = 76.10%) and TyG index (AUC = 0.792, 95% CI 0.646–0.832, cut-off = 8.371 7, sensitivity = 75%, specificity = 70.40%) in detecting the occurrence of MS.

In the present investigation, the TyG index was modified by incorporating the uric acid parameter to create a new index termed the TyG-UA index. One of the reasons for including the uric acid parameter in the index is the presence of various studies and reviews that demonstrate correlations between high levels of plasma uric acid and various cardiometabolic disorders, including MS[14–16]. According to Maloberti *et al.*, MS risk increased by 1.6 times for each 1 mg/dL elevation in blood uric acid level[14]. A study conducted in a Taiwanese population over 50 years old reported a 2.48-fold higher MS risk in subjects with high plasma uric acid levels than those with low levels[5].

In the current study, we demonstrated that the TyG-UA index had better performance than the TyG index and HOMA-IR in determining the occurrence of MS. This finding suggests that incorporating the uric acid parameter into the TyG index enhances the index's ability to establish the condition of MS. The application of the TyG-UA index combines three parameters: triglycerides, blood glucose, and uric acid, all of which are associated with pro-inflammatory conditions. This is an effort to upgrade the ability of the TyG index, which only combines two pro-

Table 1 **Basic profile of subjects characteristics**

Variables	All (n = 174)	Non-MS (n = 142)	MS (n = 32)	P
Sex, male [n (%)]	86 (49.50)	66 (46.50)	20 (62.50)	0.102
Age (years)	30.50 (20.00–40.00)	30.00 (20.00–39.00)	31.50 (22.00–40.00)	0.545#
Body Weight (kg)	69.91±15.05	66.64±12.67	84.45±16.33	<0.001*
Height (m)	1.62±0.08	1.61±0.08	1.65±0.09	0.037*
BMI (kg/m^2)	25.51 (16.98–47.61)	24.30 (16.98–40.43)	29.94 (22.64–47.61)	<0.001#
WC (cm)	85.93±11.91	83.10±10.45	98.50±9.76	<0.001*
SBP (mmHg)	120 (80–150)	120 (80–150)	130 (110–150)	<0.001#
DBP (mmHg)	80 (50–100)	80 (50–100)	80 (70–100)	0.001#
Total Cholesterol (mg/dL)	192.98±36.51	188.58±33.58	218.50±39.46	<0.001*
LDL (mg/dL)	115.60 (46.30–185.00)	111.47 (46.30–181.00)	143.50 (65.00–185.00)	<0.001#
HDL (mg/dL)	44.00 (21.83–76.00)	45.00 (21.83–76.00)	37.00 (26.00–49.30)	<0.001#
Triglyceride (mg/dL)	108.44±38.33	99.97±31.99	146.03±41.90	<0.001*
FPG (mg/dL)	80.75 (56.50–119.80)	80.75 (56.50–112.80)	80.35 (60.00–119.80)	0.575#
Insulin (mIU/L)	10.88 (2.59–62.77)	9.87 (2.59–62.77)	16.40 (6.13–35.59)	<0.001#
UA (mg/dL)	5.07 (2.04–10.86)	4.96 (2.04–10.86)	6.16 (3.56–9.70)	<0.001#
HOMA-IR (Unit)	2.09 (0.39–16.77)	1.85 (0.39–16.77)	3.48 (0.91–8.84)	<0.001#
TyG Index (Unit)	8.28±0.39	8.20±0.35	8.62±0.38	<0.001*
TyG-UA Index (Unit)	9.48±0.56	9.36±0.50	10.06±0.47	<0.001*

Normally distributed variables are presented as mean ± standard deviation. Non-normally distributed variables are presented as median (minimum-maximum). Category variable is tested with Chi-Square test; #Mann-Whitney Test; *Independent T-Test.
Abbreviations: MS, metabolic syndrome; BMI, body mass index; WC, waist circumference; ABP, systolic blood pressure; DBP, diastolic blood pressure; LDL, low density lipoprotein; HDL, high density lipoprotein; FPG, fasting plasma glucose; UA, uric acid; HOMA-IR, homeostasis model assessment of insulin resistance; TyG index, triglyceride-glucose index; TyG-UA index, triglyceride-glucose-uric acid index.

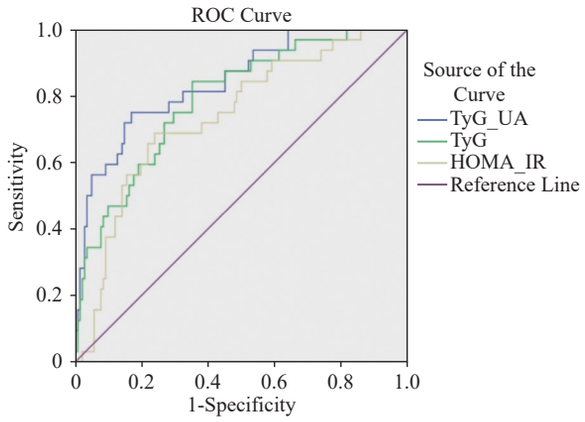

Fig. 1 **Receiver operating curve (ROC) of triglyceride-glucose-uric acid (TyG-UA) index and others as determinant of metabolic syndrome (MS).** The TyG-UA index has the greatest AUC compared to homeostasis model assessment of insulin resistance (HOMA-IR) and triglyceride-glucose (TyG) index.

inflammatory parameters. The pathophysiological explanation of uric acid's role (concerning MS components) in determining the occurrence of MS is described below.

Adipose tissue is one of the tissues proven to play an active role in producing uric acid. Research in mice shows that adipose tissue expresses xanthine oxidoreductase, essential for converting purines into uric acid, thereby enhancing uric acid production in obese mice[17]. Uric acid, can cause oxidative stress in pancreatic islet cells, leading to impaired insulin secretory function, and in hepatocyte cells, leading to hepatic insulin resistance[18]. Oxidative stress due to uric acid can also cause reactive oxygen species (ROS) formation, which can interfere with insulin signaling in target organs, resulting in insulin resistance[19]. Increased uric acid levels cause a decrease in nitric oxide (NO) and trigger renin-angiotensin system (RAS) activity, which leads to vasoconstriction. These processes will cause blood vessel remodeling and an increase in blood pressure[20]. Experiments using hepatocyte cell cultures showed that uric acid can trigger hepatocyte lipogenesis and lead to increased triglyceride production[21].

To the best of our knowledge, this is the first instance where uric acid parameters have been combined with triglycerides and glucose into one index termed the TyG-UA index. This index is more effective than the HOMA-IR and TyG index in identifying the occurrence of MS. As a cross-sectional study, it has the the inherent inability to elucidate the causal relationships between variables. Since this was a single-center study, further research in diverse populations is required to confirm these findings. In conclusion, the TyG-UA index is a novel parameter that is superior in determining MS compared with the HOMA-IR and TyG index.

Yours sincerely,

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