Fasting triglycerides and glucose index is more suitable for the identification of metabolically unhealthy individuals in the Chinese adult population: A nationwide study

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ABSTRACT

Aims/Introduction: Metabolic unhealth can be defined by the components of metabolic syndrome, which is closely connected to insulin resistance. We aimed to determine a simple index to identify metabolic unhealth in the Chinese adult population.

Materials and Methods: A total of 30,291 individuals were screened from the China National Diabetes and Metabolic Disorders Study carried out from June 2007 to May 2008. Metabolic unhealth was defined using components of the metabolic syndrome, except waist circumference. We compared the three surrogate indices of insulin resistance: the product of fasting triglycerides and glucose (TyG), triglycerides divided by high-density lipoprotein cholesterol and the metabolic score for insulin resistance for the evaluation of metabolic status.

Results: All indices had high sensitivity and specificity for the identification of metabolic unhealth, especially the TyG index with an area under the curve of 0.863 for men and 0.867 for women. Participants were divided into subgroups for further analysis. The TyG index also showed high diagnostic values, especially for younger individuals and men with normal waist circumference. Sex-specific cut-offs for three indices were also used to define metabolic unhealth. The TyG index showed the highest agreement with \( \kappa \) values of 0.603 and 0.605 for men and women between the components of metabolic syndrome and three indices.

Conclusions: We propose that the TyG index, just read in one blood laboratory test report, is simpler and more suitable for the identification of metabolically unhealthy individuals as well as who have high risk of cardiometabolic diseases of the Chinese adult population.

INTRODUCTION

Obesity is a strong risk factor for a series of cardiometabolic diseases worldwide, such as diabetes, hypertension and metabolic syndrome (MetS).1 Body mass index (BMI) is the most widely used indicator of obesity, although it might not accurately evaluate the degree of fat accumulation.2 Interestingly, not all obese individuals show the aggregation of metabolic and cardiovascular risk factors. In addition, not all lean individuals present with a healthy metabolic and disease-free phenotype.3 Therefore, two subgroups of obesity have received increasing interest in recent years: metabolically unhealthy normal weight individuals and metabolically healthy obese individuals. The former present with insulin resistance (IR) and/or hyperinsulinemia, hypertriglyceridemia or hypertension, and have a high risk of cardiovascular disease and type 2 diabetes mellitus.4-9 The latter group shows high insulin sensitivity, a lower level of fat accumulation associated with metabolic abnormalities, and a low prevalence of hypertension, hyperlipidemia and hyperglycemia.3,10-12 However,
there is a lack of a consensus on the definition of metabolic unhealth. The components of MetS are used to define metabolic abnormalities in most studies,13–17 and it is reported that metabolically healthy and metabolically unhealthy phenotypes can be present in any individual independent of BMI.18 MetS appears to be caused by a complex array of cross-connected mechanisms, and IR seems to play an important role.19,20 Direct estimation of individual IR demands diagnostic tests that have considerably high costs and low availability for epidemiological use.21 Therefore, it is necessary to determine a simple diagnostic criterion to identify individuals in the early stages of metabolic abnormality and with a high risk of cardiometabolic diseases to intervene as early as possible. Because of this connection, we hypothesize that metabolic abnormalities can be assessed based on the degree of IR.

The homeostasis model assessment for insulin resistance (HOMA-IR) index is the most widely used to evaluate the degree of IR.22 Because insulin testing is expensive, the product (HOMA-IR) index is the most widely used to evaluate the intervention as early as possible. Because of this connection, we hypothesize that metabolic abnormalities can be assessed based on the degree of IR.

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subjected to the steamed bread meal test for safety reasons that
contained approximately 80 g of complex carbohydrates.
Plasma glucose, TG, HDL-C, low-density lipoprotein
cholesterol, total cholesterol and uric acid were analyzed
enzymatically using an automated biochemical analyzer (MOD-
ULAR-000GS; Roche, Basel, Switzerland). All laboratory
measurements complied with the requirements of a standardization
and certification program.34

Definitions
All participants were divided into three groups using BMI for
Chinese men and women as the criteria38: normal weight (BMI
18.5–23.9 kg/m²), overweight (BMI 24.0–27.9 kg/m²) and obese
(BMI ≥28.0 kg/m²). According to the Chinese criterion of cen-
tral obesity, we defined increased WC as >90 cm in men and
>85 cm in women.

Participants were diagnosed with MetS based on the presence
of more than three of the following criteria defined by the har-
monized International Diabetes Federation7: (i) hyperglycemia
(fasting blood glucose levels ≥100 mg/dL [5.60 mmol/L] or
drugs for diabetes); (ii) hypertension (systolic blood pressure
≥130 mmHg and/or diastolic blood pressure ≥85 mmHg and/or
treatment to reduce blood pressure); (iii) hypertriglyceridemia
(fasting plasma triglyceride levels ≥1.69 mmol/L [150 mg/dL]
or treatment); (iv) HDL-C <40 mg/dL (1.04 mmol/L) for men
and 50 mg/dL (1.30 mmol/L) for women; and (v) central
obesity (or visceral obesity, WC >85 cm in men and >80 cm
in women).

Participants were classified according to metabolic status
based on the four metabolic parameters,13,15,39 also used in
other studies: elevated blood pressure, impaired fasting glucose
or diabetes, low HDL-C concentration and hypertriglyc-
eridemia. The metabolically healthy state was defined as the
presence of none or one of the metabolic factors, whereas the
metabolically unhealthy state was defined as the presence of
two or more metabolic factors.

The TyG was calculated as Ln [fasting triglycerides (mg/
dL) × fasting glucose (mg/dL) / 2].25,40 The TG/HDL was
defined as TG divided by HDL-C.34 The METS-IR was defined
as Ln [(2 × fasting glucose) + TG] × BMI] / (Ln[HDL-C]).26

Statistical Analysis
All data were analyzed using SPSS 20.0 (SPSS Inc., Chicago, IL,
USA). Quantitative data were expressed as the mean ± standard
deviation. Two-sample comparisons were carried out using t-
tests for normally distributed measurement data, whereas non-
normal distributed continuous variables were compared using
the Mann–Whitney U-test. Categorical variables were expressed
as the number of total cases (n) and percentages (%), and com-
pared using the χ²-test. Receiver operating characteristic (ROC)
curves were used to analyze the diagnostic value of IR surrogate
indices for metabolically healthy or unhealthy status, and to
determine the optimal cut-offs. The diagnostic value of all
indices was compared by the Z-test. The highest Youden’s Index
was used to determine the optimal diagnostic cut-off. All analy-
thesis of ROC curves was carried out using MedCalc Statistical
Software version 15.8 (MedCalc Software bvba, Ostend, Bel-
gium). Diagnostic concordance between the components of
MetS (except WC) and the TyG index was estimated using κ
values. P < 0.05 was considered to show statistical significance.

RESULTS
In total, 30,291 participants (11,984 men and 18,307 women)
were enrolled in the present study, with a mean age of
43.26 ± 13.66 years (range 20–99 years). The demographic and
clinical characteristics of the study participants are shown in
Table 1.

The ROC curve analyses confirmed the value of TyG,
METS-IR and TG/HDL in identifying metabolic unhealth. As
shown in Figure 1 and Table 2, all of the indices had high sen-
sitivity and specificity for the identification of metabolic
unhealth, with an area under the curve (AUC) for TyG (men
0.863, 95% confidence interval [CI] 0.857–0.869; women 0.867,
95% CI 0.862–0.872), METS-IR (men 0.810, 95% CI 0.803–
0.817; women 0.805, 95% CI 0.799–0.810) and TG/HDL (men
0.841, 95% CI 0.834–0.848; women 0.857, 95% CI 0.852–0.862).
The TyG index had the best diagnostic value of those indices
for metabolically unhealthy individuals.

Based on our preliminary findings, we selected the TyG
index for further analysis. Participants were separated into two
or three subgroups according to BMI (normal weight, over-
weight and obesity) and WC (normal and increased). The
AUCs (95% CIs) showed no significant difference in BMI sub-
groups both men and women in any of the groups (Figure 2
and Figure 3). The same results have been observed in WC
subgroups of women. For men, however, the AUCs of individ-
uals with normal WC (0.857, 95% CI 0.849–0.864) were higher
than those with increased WC (0.839, 95% CI 0.826–0.851; Fig-
ure 2). Furthermore, participants were divided into five age
groups (participants aged 20–30, 31–40, 41–50, 51–60 and
>60 years). We found that the AUCs (95% CIs) of age groups
20–30 years and 31–40 years outperformed other age groups
for both men and women (Figures 2,3). Furthermore, the cut-
offs of TyG index for all groups varied from 8.72 to 8.84.

Therefore, the sex-specific thresholds for the TyG index
(men 8.81, women 8.73), METS-IR (men 37.67, women 34.99)
and TG/HDL (men 1.32, women 1.09; Table 2) were used to
classify participants as metabolically healthy or metabolically
unhealthy. Kappa statistics for the agreement of metabolically
unhealthy individuals between the components of MetS (except
WC) and all indices are shown in Table 3. The κ values of
men and women were 0.603 and 0.605 with the highest agree-
ment among three indices.

DISCUSSION
The present study was a nationwide survey carried out in China
with a large sample size to ensure that the results are representa-
tive of this population. In this cross-sectional study, we directly
Table 1 | Demographic and clinical characteristics of participants

| Variable                        | Overall (n = 30291) | Men (n = 11984) | Women (n = 18307) | P-value |
|---------------------------------|---------------------|----------------|------------------|---------|
| Age (years)                     | 43.26 ± 13.66       | 43.39 ± 12.44  | 43.34 ± 12.94    | 0.399   |
| Age 1, n (%)                    | 5460 (18.0)         | 2451 (20.5)    | 3009 (16.4)      |         |
| Age 2, n (%)                    | 7889 (26.0)         | 2934 (24.5)    | 4955 (27.1)      |         |
| Age 3, n (%)                    | 8159 (26.9)         | 2996 (25.0)    | 5163 (28.2)      |         |
| Age 4, n (%)                    | 5581 (18.4)         | 2149 (17.9)    | 3432 (18.7)      |         |
| Age 5, n (%)                    | 3202 (10.6)         | 1454 (12.1)    | 1748 (9.5)       |         |
| WC, cm                          | 85.28 ± 10.2        | 79.15 ± 9.58   | 81.58 ± 10.28    | <0.0001 |
| Increased WC, n (%)             | 7938 (26.2)         | 3483 (29.1)    | 4455 (24.3)      | <0.0001 |
| Body mass index, kg/m²          | 24.48 ± 3.45        | 23.87 ± 3.35   | 24.11 ± 3.4      | <0.0001 |
| Normal weight, n (%)            | 15937 (52.6)        | 5657 (47.2)    | 10280 (56.2)     |         |
| Overweight, n (%)               | 10243 (33.8)        | 4422 (36.9)    | 5821 (31.8)      |         |
| Obese, n (%)                    | 4111 (13.6)         | 1905 (15.9)    | 2206 (12.1)      |         |
| FPG, mmol/L                     | 5.28 ± 1.2          | 5.19 ± 1.08    | 5.23 ± 1.13      | <0.0001 |
| 2-h PG, mmol/L                  | 6.5 ± 2.8           | 6.54 ± 2.53    | 6.52 ± 2.64      | 0.293   |
| Fasting plasma insulin (mU/L)   | 8.53 ± 6.35         | 8.34 ± 5.94    | 8.41 ± 6.11      | 0.009   |
| Cholesterol (mmol/L)            | 4.69 ± 0.96         | 4.66 ± 0.98    | 4.67 ± 0.97      | 0.011   |
| Triglyceride (mmol/L)           | 1.7 ± 1.24          | 1.37 ± 0.92    | 1.5 ± 1.07       | <0.0001 |
| HDL-C (mmol/L)                  | 1.27 ± 0.33         | 1.37 ± 0.33    | 1.33 ± 0.34      | <0.0001 |
| LDL-C (mmol/L)                  | 2.76 ± 0.83         | 2.71 ± 0.83    | 2.73 ± 0.83      | <0.0001 |
| Systolic blood pressure (mmHg)  | 123.08 ± 17.06      | 117.71 ± 17.39 | 119.84 ± 17.45   | <0.0001 |
| Diastolic blood pressure (mmHg) | 79.73 ± 10.86       | 75.79 ± 10.18  | 77.35 ± 10.63    | <0.0001 |
| TyG                             | 8.68 ± 0.63         | 8.48 ± 0.58    | 8.56 ± 0.61      | <0.0001 |
| METS-IR                         | 36.96 ± 7.08        | 34.73 ± 6.31   | 35.61 ± 6.71     | <0.0001 |
| TG/HDL                          | 1.5 ± 1.41          | 1.11 ± 0.96    | 1.26 ± 1.18      | <0.0001 |
| Alcohol drinking, n (%)         | 6158 (20.3)         | 5337 (44.5)    | 821 (45)         | <0.0001 |
| Cigarette smoking, n (%)        | 6276 (20.7)         | 5750 (48.0)    | 526 (2.9)        | <0.0001 |
| Physical activity, n (%)        | 10042 (33.2)        | 4021 (33.6)    | 6021 (32.9)      | 0.235   |
| Metabolically unhealthy, n (%)   | 10148 (33.5)        | 4435 (37.0)    | 5713 (11.5)      | <0.0001 |
| Elevated blood pressure, n (%)  | 8344 (27.5)         | 4100 (34.2)    | 4244 (23.2)      | <0.0001 |
| Impaired fasting glucose , n (%) | 7520 (24.8)         | 3280 (27.4)    | 4240 (23.2)      | <0.0001 |
| Low HDL-C, n (%)                | 10814 (35.7)        | 2999 (25.0)    | 7815 (42.7)      | <0.0001 |
| Hypertriglyceridemia, n (%)     | 8496 (28.0)         | 4309 (36.0)    | 4187 (22.9)      | <0.0001 |

Data are expressed as mean ± standard deviation, median (interquartile range) or n (%). Student’s t-test for continuous variables, Mann–Whitney U-test for abnormally distributed data, and χ²-test for categorical variables. Age 1, 2, 3, 4 and 5: participants aged 20–30, 31–40, 41–50, 51–60 and >60 years. 2-h PG, 2-h postprandial plasma glucose; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; WC, waist circumference.

compared three surrogate indices of IR (TyG, TG/HDL and METS-IR) on their diagnostic accuracy of metabolically unhealthy individuals. Overall, we found that the TyG index outperformed other indices with the highest sensitivity and specificity and the largest AUCs (95% CIs) for the identification of metabolic unhealth. In a subgroup analysis, the TyG index also showed high AUCs and diagnostic values, especially for younger individuals and men with normal WC. Therefore, the clinical application of the TyG index is suitable for all people.

Currently, there is still no universal consensus on the definition of metabolic status. The components of MetS are used to define metabolic disorders in many studies or are combined with HOMA-IR and C-reactive protein. Multiple versions of diagnostic criteria for MetS have been proposed during its evolution, such as the criteria from the American Heart Association/National Heart, Lung and Blood Institute (revised Adult Treatment Panel III), International Diabetes Federation and Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention. The Adult Treatment Panel III and International Diabetes Federation criteria have the same cut-offs of WC (90 cm for Chinese men and 80 cm for Chinese women) for central obesity, but the Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention criterion meets Chinese cut-offs for central obesity with WC >85 cm for men and >80 cm for women. All criteria, however, have the same values and conditions for other components of MetS. Furthermore, the components of MetS (except WC) are widely utilized in clinical settings. To ensure that the present findings were applicable to more populations, participants were classified according to metabolic status based on the four widely utilized metabolic parameters.
In addition, IR is a hallmark of obesity, diabetes and cardiovascular diseases, and leads to many of the abnormalities associated with MetS.19,20 Because testing for insulin sensitivity is expensive, the use of surrogate markers to assess insulin resistance might help to maximize medical resources, while minimizing costs and inconvenient side-effects for both clinical practice and epidemiological purposes. Thus, one of the notable advantages of the current study is that we compared the diagnostic capacity of the IR surrogates, TyG, TG/HDL and METS-IR, for identifying metabolically unhealthy individuals. The elements of all indices are significant components or highly correlated with the definition of metabolic unhealth in the present study. Although the TyG index is determined on the basis of just two parameters of easily obtained routine clinical laboratory data, it had the highest value for the identification of metabolically unhealthy individuals. Interestingly, although MetS-IR is determined on the basis of four parameters connected closely with metabolic disorders for Mexican individuals, the value of this index for the identification of metabolic unhealth was unremarkable, possibly because of racial and population differences, such as BMI and WC. Furthermore, in Figure 1, the curve of the TyG index was similar to the TG/HDL, except for the area nearing the cut-off. In Table 2, however, the AUCs (95% CIs) of the TyG index was significantly larger than the TG/HDL ($P < 0.0001$).

The TyG index was first reported as a surrogate of HOMA-IR for identifying IR in apparently healthy individuals in 2008.23 Subsequently, Fernando et al. compared the TyG index with the euglycemic-hyperinsulinemic clamp test, and suggested that TyG could be useful for the identification of individuals with decreased insulin sensitivity in 2010.40 A series of cohort and cross-sectional studies confirmed a strong correlation between the TyG index and IR,43 type 2 diabetes mellitus,30,44–46 MetS,47 hypertension,48 cardiovascular events49 and fatty liver50–52 both in China and elsewhere. Published studies have shown that the TyG index is helpful for the prediction and early identification of individuals at high risk of cardiometabolic diseases.

A Korean study by Lee et al.29 published in 2014 was the first to show that the TyG index is a useful marker for the identification of individuals with distinct metabolic characteristics within similar BMI ranges. In that study, "metabolic obesity" was defined as those individuals falling into the highest HOMA-IR quartile, and they selected non-diabetic participants for further analysis. Another study28 also showed that TyG is a simple diagnostic criterion for the identification of individuals with a higher risk of metabolic diseases in non-diabetic and normal weight individuals. That study used ROC analysis to determine the cut-off value of the TyG index (8.82 for men and 8.73 for women) for the identification of metabolically

![Figure 1](http://wileyonlinelibrary.wiley.com/journal/jdi)

**Figure 1** | Receiver operating characteristic curves of the product of fasting triglycerides and glucose (TyG), the metabolic score for insulin resistance (METS-IR) and the triglycerides divided by high-density lipoprotein cholesterol (TG/HDL) index for predicting metabolic unhealth of (a) men and (b) women. [Colour figure can be viewed at wileyonlinelibrary.com]

| Comparison of receiver operating characteristic curves for predicting metabolic unhealth of men and women |

| Men | | Women | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| | Cutoff | Sensitivity | Specificity | AUC | 95% CI | P-value | Cutoff | Sensitivity | Specificity | AUC | 95% CI | P-value |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| TyG | 8.81 | 77.47 | 83.55 | 0.863 | 0.857–0.869 | 0.0001 | 8.73 | 71.49 | 88.57 | 0.867 | 0.862–0.872 | <0.0001 |
| METS-IR | 37.67 | 70.76 | 76.00 | 0.810 | 0.803–0.817 | 0.0001 | 34.99 | 73.39 | 72.08 | 0.805 | 0.799–0.810 | <0.0001 |
| TG/HDL | 1.32 | 75.63 | 79.84 | 0.841 | 0.834–0.848 | <0.0001 | 1.09 | 73.22 | 82.44 | 0.857 | 0.852–0.862 | <0.0001 |

P-value, in comparison with the reference index (the product of fasting triglycerides and glucose [TyG]), AUC, the area under the curve values; METS-IR, the metabolic score for insulin resistance index; TG/HDL, the triglycerides divided by high-density lipoprotein cholesterol index.
obese individuals defined by MetS. The resultant cut-off was almost equal to the one determined in our current study (men 8.81; women 8.73; Table 2). Furthermore, Lee et al.52 suggested that the predictive value of the TyG index for diabetes was comparable with the predictive value of metabolic health, which was defined by the components of MetS and HOMA-IR (>90th percentile). The main difference in these studies was the definition of metabolic unhealth, which we defined according to the components of MetS (except WC).13,15,39 Although the risk and prevalence of metabolically unhealthy individuals varies considerably according to the criteria used,15,16 both metabolically healthy and unhealthy obese patients carried an elevated risk of mortality. These findings show that BMI still plays an important role in metabolically unhealthy individuals, especially in populations with higher BMI. A difference also exists, however, in population selection, and we considered only participants not taking medication for hyperglycemia, hypertension or hyperlipidemia, and a BMI ≥18.5. In fact, there were 3,775 (10.1% of 37,122 total participants) participants with diabetes, but just 1,278 (33.9% of participants with diabetes)
admitted that they had diabetes and received treatment (data not shown). It was noteworthy that nearly two-thirds of the participants were unaware of their abnormal metabolism for glucose, and these individuals attracted our attention.

The current study was a well-designed population-based survey with a large number of participants representing the general Chinese population. Nevertheless, some limitations should be acknowledged. First, we did not establish the causal relationship or clinical outcomes associated with the TyG index and metabolic status to determine whether or not the TyG index is a suitable predictive marker of cardiometabolic diseases. Second, the menopausal status of women was not determined in the survey. We were, therefore, unable to analyze the differences between pre- and post-menopausal populations. Third, misclassification of participants was possible, because we used just four components of MetS to define previously confirmed metabolically unhealthy status.13,15,39 Finally, because all participants in the present study were Chinese men and women, the applicability of our findings to other ethnic groups is uncertain.

In conclusion, by comparing common surrogate indices of IR, we provide evidence supporting the use of the TyG index to identify metabolically unhealthy individuals. Therefore, we propose that the TyG index is simpler and more suitable for the identification of metabolically unhealthy individuals and those who have a high risk of cardiometabolic diseases in the Chinese adult population.

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DISCLOSURE

The authors declare no conflict of interest.

Table 3 | Agreement (κ value) between the components of metabolic syndrome (except waist circumference) and the cut-offs of indices for the diagnosis of metabolic unhealthy individuals

| TyG | TG/HDL | METS-IR |
|-----|--------|---------|
| Men ( >8.81), n | Women ( >8.73), n | Men ( >1.32), n | Women ( >1.09), n | Men ( >37.67), n | Women ( >34.99), n |
| – | + | Total | – | + | Total | – | + | Total | – | + | Total | – | + | Total |
| MU (n) | | | | | | | | | | | | | | |
| 6318 | 1231 | 7549 | 11131 | 1463 | 12594 | 6036 | 1513 | 7549 | 10347 | 2247 | 12594 | 5737 | 1812 | 7549 | 9073 | 3521 | 12594 |
| – | + | Total | – | + | Total | – | + | Total | – | + | Total | – | + | Total | – | + | Total |
| 1011 | 3424 | 4435 | 1621 | 4092 | 5713 | 7131 | 4835 | 18307 | 1297 | 3138 | 4435 | 1519 | 4194 | 5713 | 1297 | 3138 | 4435 | 1519 | 4194 | 5713 |
| Total | 7329 | 4655 | 11984 | 12752 | 5555 | 18307 | 7131 | 4853 | 11984 | 11863 | 6444 | 18307 | 7034 | 4950 | 11984 | 10592 | 7715 | 18307 |
| k value | 0.603 | 0.605 | 0.542 | 0.537 | 0.457 | 0.415 |
| P-value | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |

MU, metabolically unhealthy.

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