Assessment of preferred methods to measure insulin resistance in Asian patients with hypertension

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Abstract

Insulin resistance (IR), a metabolic risk factor, is linked to the pathogenetic mechanism of primary hypertension. Detecting IR in the patients with hypertension will help to predict and stratify the added cardiovascular risk, institute appropriate IR management, and manage hypertension optimally. There are many methods for assessing IR, each with distinct advantages and disadvantages. The euglycemic insulin clamp and intravenous glucose tolerance test, gold standards for measuring IR, are used in research but not in clinical practice. Homeostatic model assessment (HOMA-IR), a method for assessing β-cell function and IR, is frequently applied presently, particularly in Asia. Besides, the triglyceride–glucose index (TyG) first published by South American authors showed a good correlation with the insulin clamp technique and...
Hypertension causes serious complications such as stroke, heart failure, coronary heart failure, and kidney failure. It is also associated with several other metabolic disorders such as hyperglycemia and dyslipidemia. Moreover, obesity and insulin resistance (IR) are now common in the patients with primary hypertension, leading to a further increase in cardiovascular (CV) morbidity and mortality. IR is associated with a decrease in the sensitivity of muscle and adipose tissue to insulin, a reduction in the ability to produce glucose, and an increase in fat production in the liver. Due to the importance of IR, early IR identification is of great value in stratifying CV risk, future development of cardiovascular disease, and prognosis.

Currently, there are many methods to assess IR: the most commonly used being the Homeostatic model assessment (HOMA-IR). Recently, several studies in the world have shown a relationship between triglyceride and glucose, hence, indices such as triglyceride-glucose index (TyG), triglyceride-body mass index (TyG-BMI), and triglyceride-waist circumference index (TyG-WC) have been used to assess IR. It can be easily used to screen for IR in high-risk individuals with hypertension prone to develop diabetes. It is also suitable in clinical practice as an alternative IR marker.

**1 | INSULIN RESISTANCE**

Insulin resistance is a condition in which insulin produces worse biological response than usual. In 1960, Yalow and Berson, with the introduction of radioimmunoassay, stated that "Insulin resistance is a common increase in the dose of insulin to maintain a normal response." In 1923, Kylin combined hypertension, hyperglycemia, and gout into a syndrome and over time, this syndrome changed to being called metabolic syndrome, IR syndrome, or polymetabolic syndrome. In 1988, Gerald Reaven named the syndrome X and considered it a background factor in CV disease. In 1998, the World Health Organization (WHO) gave a unified definition as "Considered insulin resistance when the HOMA index is greater than the highest quartile in the control group".

**1.1 | Pathogenesis of insulin resistance**

IR pathogenesis is broadly divided into two types: genetic or acquired IR:

- Genetic IR where there is an alteration in insulin receptors, signal changes after combination, altered β3-Adrenergic receptors. It includes genetic or primary target cell defects, autoantibodies to insulin, and accelerated insulin degradation. Mitochondrial dysfunction may also play an important role in the development of IR and associated complications.
- Acquired IR is when there is an increase in the levels of anti- regulation, drug-induced hormones, glucose intoxication, glutamine enzyme, glucose transporter defect (GLUT-4), lipid toxicity (cytokines and hormones from fat cells), decrease in insulin secretion rate, and hormone activity in tissue. Acquired IR is usually a result of obesity, inactivity, aging, and certain medical conditions or medications that counteract insulin activity. Also, secondary IR is observed in hyperthyroidism, Cushing's syndrome, acromegaly, trauma, burns, and stress. The role of infection and inflammation is currently of interest because the inflammatory mechanism can impair insulin activity and may explain the IR that can occur in non-obese individuals.

**1.2 | Methods for assessing insulin resistance**

Currently, there is no specific method to accurately assess IR. Several different methods and indicators are used for IR evaluation, some of which are frequently used in Asia for IR assessment (Table 1).

**1.2.1 | Endogenous methods or indirect measures**

These are the methods of assessing endogenous insulin activity in combination with the introduction of glucose into the body.

- Baseline fasting insulin measurement: A simple and widely used method for determining IR where fasting insulin concentration is measured and quantified. In epidemiological studies, fasting insulin concentration is commonly used as a surrogate IR marker. In normoglycemic subjects, fasting insulin correlated well with whole-body glucose uptake as measured by the "gold standard" euglycemic hyperinsulinemic clamp method, although the correlation was less in individuals with impaired glucose tolerance or type 2 diabetes mellitus.
- Oral glucose tolerance test (OGTT): The tolerance test quantifies fasting plasma glucose and glucose level after an oral glucose load. Briefly, after an overnight fast, the fasting plasma glucose level is measured, followed by remeasuring the plasma glucose level after drinking a 75 g glucose solution. The OGTT
| Method                          | Formula                                      | Normal level | Advantage                                                                 | Disadvantage                                                                                     | Correlation coefficient with HIEC                                                                 |
|--------------------------------|----------------------------------------------|--------------|---------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|
| Hyperinsulnemic euglycemic glucose clamp | ISI HEc = MCR/I mean MCR = Mmean/ (Gmean × 0.18) |              | Direct measurement of insulin under steady-state condition; Large epidemiological studies | Laborious, time-consuming, expensive, involved, experienced operator, intravenous insulin infusion, frequent blood sampling | Gold standard method                                                                            |
| HOMA-IR                        | (Io × Go)/22.5                               | <2.5         | Simple, minimally invasive, predicts fasting steady-state glucose and insulin levels | Insulin sensitivity in subjects treated with insulin needs further validation. In patients with severely impaired or absent beta cell function, HOMA-IR may not give appropriate results | Normal glucose tolerance (0.65; p < .0001), impaired glucose tolerance (0.56, p < .0001) and with type 2 diabetes melitus (0.51, p < .0001) |
| QUICKI                         | 1/[log (lµU/ml)] + log [log (Gmg/dl)]         |              | Minimally invasive surrogate for glucose clamp-derived measurements of insulin sensitivity | Complex, invasive, and costly for use in large observational epidemiological studies. Normal range to be established for each laboratory | Correlation coefficient 0.78; p < 2 × 10⁻¹²                                               |
| Matsuda index                  | 10 000/√ (fasting G × fasting I) (mean G × mean I) | <4.3 predict IR | Represent both hepatic and peripheral tissue sensitivity to insulin | Its correlation with Diabetes mellitus is very weak | 0.73 (p < .0001) in normal glucose tolerance, 0.66 (p < .0001) in impaired glucose tolerance, 0.60 (p < .0005) in nondiabetic, and 0.54 (p < .0001) in type 2 diabetes melitus |

Abbreviations: Go, plasma glucose during fasting; HEC, hyperinsulnemic euglycemic clamp; HIEC, hyperinsulnemic euglycemic clamp; HOMA-IR, homeostasis model assessment – insulin resistance; Io, plasma insulin during fasting; IR, Insulin resistance; ISI, insulin sensitivity index; MCR, Metabolic Clearance Rate; QUICKI, quantitative insulin sensitivity check index.
is a relatively crude measure of glucose tolerance and does not measure the components of insulin sensitivity and insulin secretion.3,5,7,8

- Minimal model analysis of frequently sampled intravenous glucose tolerance test (FSIVGTT) is a method developed by Bergman et al (1979) based on the glucose and insulin levels measured during a frequently sampled IV glucose tolerance test. Recently, a modified FSIVGTT used insulin infusion in conjunction with intravenous glucose.3,5,7,8

### 1.2.2 Exogenous methods or direct measures

This is a method for assessing the blood glucose response to a given amount of externally administered insulin.

- Hyperinsulinemia euglycemic clamp (HIEC): The technique of “insulin clamp” was first introduced by De Fronzo in 1979 and till date, remains the “gold standard” to assess IR. After an overnight fast, 5-120 mU/m²/min insulin is infused intravenously at a constant rate (hyperinsulinemic) and the blood glucose level is monitored at 5-10 minutes interval, while 20% dextrose is given IV at a variable rate in order to “clamp” blood glucose concentration in the normal range (euglycemic). After several hours of constant insulin infusion, steady-state conditions can be achieved for plasma insulin, blood glucose, and the glucose infusion rate.3 The glucose infusion rate for the last 30 minutes of the test, known as “steady-state,” will determine IR. This is an intrusive technique and quite complex. The main limitations of the HIEC are that it is time-consuming, labor-intensive, expensive, and requires an experienced operator to manage the technical difficulties. Moreover, the clamp utilizes steady-state insulin levels that may be supraphysiological. This results in a reversal of the normal portal to the peripheral insulin gradient. Thus, the glucose clamp may not accurately reflect insulin action and glucose dynamics under physiological conditions that a dynamic test, such as an oral meal or oral glucose load may determine.3,5,7

- Insulin tolerance test (ITT): Bonara developed this method with some improvements to overcome the disadvantages of HIEC. The procedure takes only 15 minutes and blood glucose is measured. Insulin is injected intravenously and the blood glucose is measured and quantified. The advantages of the ITT include its simplicity, speed, and the use of a bolus injection of insulin, which mimics the physiological pulsatile release of insulin, instead of a continuous infusion. Moreover, postprandial glucose tolerance is dependent on insulin sensitivity and the postprandial insulin sensitivity measurement is consistent with physiological phenomena. Some disadvantages of this method include the excess physiological insulin used and that the test does not distinguish between peripheral IR and IR in the liver. This method is simple but has the potential to cause hypoglycemia, so it is rarely used currently.3,5,7,8

- Insulin suppression test (IST): This direct method of measuring IR, introduced by Shen et al (1970), was modified by Harano et al (1978). In this method, the patients receive somatostatin simultaneously with insulin and glucose. It is less labor-intensive and less technically demanding than HIEC. However, this method is rarely used in large epidemiological studies or in the clinical care setting because IST causes side effects similar to those described for HIEC.3,5,7,8

- Rapid insulin sensitivity test (RIST): This method for quantifying insulin sensitivity was first described by Patarrao et al (2014).5 The RIST is a euglycemic test carried out after establishing the glycemic baseline, which is done by measuring the postprandial blood glucose level of arterialized venous blood samples at 5 minutes intervals until three consecutive measurements are stable. The RIST index, the insulin sensitivity parameter, is simply the amount of glucose that was administered to maintain euglycemia after the bolus administration of insulin to mimic pulsatile insulin release for avoiding hypoglycemia. The RIST is a quick method, reproducible in the same subject and on the same day, and can be performed in the fed or fasting state.

### 1.2.3 Indicators or surrogate markers for assessing insulin resistance

- Glucose/insulin ratio (G/I): Insulin and glucose are present in the blood certain proportions. High insulin levels in a person with normal blood glucose levels indicate insulin resistance. High insulin levels have a prognostic value for the risk of type 2 diabetes. The fasting glucose/insulin ratio is used in some studies as a tool to diagnose IR but this ratio is an imperfect indicator to assess insulin sensitivity.3,5

- Homeostasis model assessment of IR index (HOMA-IR index) is calculated by the formula HOMA-IR = [glucose (mmol/L) × insulin (µU/L)]/22.5.23 HOMA or log (HOMA) is extensively used in large epidemiological studies, prospective clinical trials, and research. In research settings where assessing insulin sensitivity/resistance is of secondary interest or when feasibility issues preclude the use of direct measurement by HIEC, it may be appropriate to use log (HOMA).3,8

- Beta-cell function evaluation index (HOMA-beta): This is used to assess the insulin secretory capacity of pancreatic beta cells. HOMA1-% beta index is calculated using the formula 20 × fasting plasma insulin (µU/ml)/ fasting plasma glucose (mmol/l) - 3.5. HOMA-beta is a marker to diagnose the activity of the insulin secreted from the pancreatic beta cells.8 Another related HOMA beta cells index that is HOMA β cell index with the help of HOMA model correlated equally with HIEC method. It is calculated by the equation: 20 × fasting plasma insulin (µU/ml)/ fasting plasma glucose (mmol/l) - 3.3,8

- Quantitative insulin sensitivity check index (QUICKI index): This index is intended to assess particular insulin sensitivity in obese patients. The properties that are similar to HOMA-IR are QUICKI index = 1/ [Log Insulin(µU/ml) + Log Glucose (mg/dl)], the cut-off limit being the highest quartile of the control group.4,6,8
## TABLE 2  Insulin resistance and hypertension in Asia

| Country     | Method of assessment | Number of participants | Aims                                                                 | Results                                                                 | Conclusion                                                                 |
|-------------|----------------------|------------------------|----------------------------------------------------------------------|--------------------------------------------------------------------------|---------------------------------------------------------------------------|
| Egypt       | Fasting Insulin, BMI, WC, dyslipidemia | 60 euglycemic (30 patients with hypertension, 30 healthy controls) | Explore the pathogenic role of hyperinsulinemia in essential hypertension | Significant increase of fasting insulin level, BMI, WC, dyslipidemia than those in the control, highly significant increase of insulin with HTN severity | A possible pathogenic role of hyperinsulinemia on the onset of hypertension |
| Thailand    | HOMA-IR              | 227 men and 990 women | Estimate the prevalence of IR and related CVD risks                  | 25.1% men, 21.5% women have IR.                                           | IR positively associated with selected CVD risk factors in Thai adults     |
| Japan       | IFG, HOMA-IR         | 19 166 participants with different stages of impaired glucose metabolism | The relationship of IR and hypertension                              | The rate of HTN increase from 36.3% in normal glucose, to 50.1%, 50.8%, 58.3%, and 63/8% in isolated IFG, isolated impaired glucose tolerance, IFG and impaired glucose tolerance, & DM, respectively | Hyperglycemia and hyperinsulinemia are significant contributors to the presence of hypertension |
| Japan KEIO Study | HOMA-IR            | 310 subjects, 30-58 years divided in 3 groups according HOMA-IR | Study the prediction the IR of hypertension (from 1993 to 2000)       | Hypertension found in 11.7%, 15.4%, and 29.1% (highest HOMA-IR), BP correlated with HOMA | Important role of IR in predicting HTN in middle-aged Japanese men.       |
| Japan       | HOMA-IR, ABPM, ANP, BNP, LVH | 103 patients with hypertension divided in 2 groups: dipper and nondipper | Study the relation of IR with etiology of nondipper HTN               | Fasting glucose, insulin and HOMA index were higher in nondippers         | Diminished nocturnal BP fall closely related to LVH, BNP and IR may play a key role in these process |
| Japan       | IRI (M-value), HIEC  | 1996 subjects (475 men, 521 women in T; 469 men, 531 women in S), aged 40-64 | Reveal the state of IR in Japanese HTN                               | IR was 45.4% in essential HTN and 16.3% in normotensive HTN               | IR exist among Japanese essential HTN                                     |
| Taiwan      | HOMA-IR              | 893 patients with hypertension, 889 control(Stanford Asian Pacific Program in HTN & IR sibling study) | Clustering and heritability of IR in Chinese & Japanese hypertensive families | IR is familial in nature & heritable in Chinese & Japanese HTN families |                                                                              |
| Bangladesh  | HOMA-IR              | 150 male subjects, 75 male patients with hypertension          | To observe the IR in adult males with HTN                            | Essential positive and significant relationship with IR                  | IR is higher in essential HTN                                             |
| Vietnam     | Insulin dosage, glucose before & after OGTT | 108 patients with hypertension and 36 control persons, age > 40 years | To observe the IR in Vietnamese adults with HTN                      | Plasma insulin at fasting and 2 hours after OGTT were high in the patients with hypertension | There was a state of IR in hypertensive pts despite under nutrition       |

Abbreviations: ABPM, 24 hour ambulatory blood pressure monitoring; ANP, atrial natriuretic peptide; BMI, body mass index; BNP, brain natriuretic peptide; HIEC, hyperinsulinemic euglycemic clamp; HOMA-IR, homeostasis model assessment – insulin resistance; HTN, hypertension; IFG, impaired fasting glucose; IR, insulin resistance; LVH, left ventricular hypertrophy; OGTT, oral glucose tolerance test; WC, waist circumference.
| Country            | Method of assessment | Number of participants | Aims                                                                 | Results                                                                 | Conclusion                                                                                           |
|--------------------|----------------------|------------------------|----------------------------------------------------------------------|------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|
| China              | TyG index            | 6078 persons > 60 years | Development of CVD                                                      | 22.01/1000 persons-year having CVD after 6 years FU                     | TyG index might predict CVD events                                                                   |
| China              | TyGs: TyG index, TyG-BMI, TyG-WC, TyG-WHtR | 105,070 lean adults without HTN | Investigate the association of TyGs with pre-hypertension      | TyGs higher than normotensive individuals, but only TyG-BMI, TyG-WC more significantly. | TyG-BMI might be accessible in non-obese preHTN pts                                                   |
| China              | TyG                  | 3,745 CAD patients, FU | Evaluate the prognosis value of TyG index                           | TyG associated with CV events (HR: 1.34, 95% CI: 1.100-1.691, p = .005) | TyG maybe predicting outcomes in CAD patients                                                        |
| China              | TyG                  | 4,686 subjects, 9 years FU | To investigate the incident hypertension                            | high TyG associated with increased risk of HTN incidence               | TyG can predict the incident HTN                                                                   |
| Iran               | TyG index, HOMA-IR   | 61 obese persons       | Compare TyG with HOMA-IR                                             | IR: 34%, TyG: 61%, there was a relationship between HOMA-IR and TyG, r = .004, p < .001 | TyG useful, accessible for assess IR                                                                |
| Korean National Health and Nutrition Examination | 4 parameters TyG, HOMA-IR | 11,149 subjects (4777 men) on Survey 2007-2010 | Compare TyG index and related parameters | ORs of quartile 4 compare with quartile 1: 7.6 (6.52-8.87) for TyG, 12.82 (10.89-15.10) for TyG-BMI, 16.29 (13.70-19.38) for TyG-WC, and 14.86 (12.53-17.62) for TyG-WHtR. | TyG-BMI was superior to other parameters for IR prediction in clinical settings                        |
| Korea              | TyG index, baPWV     | 2,560 persons without a history of CAD | Evaluate the relationship with arterial stiffness                     | TyG index correlate with baPWV r = .224, p < .001                   | TyG associated with aterial stiffness                                                                |
| Vietnam            | TyG, HOMA-IR, CT Angiography | 166 type 2 diabetic pts | Investigate the association between TyG and CV risk factors         | TyG correlated with HOMA-IR (p < .001). The patients with coronary syndrome had higher TyG. | TyG may be an IR marker and identify high risk of coronary stenoses                                   |
| Vietnam            | TyGs, HOMA-IR        | 69 metabolic syndrome pts, 64.9 ± 14 years | Evaluate the TyGs indices in IR                                     | TyGs correlated with HOMA-IR (r = .488, p < .001), OR: 3.362 (CI 95%, 1.21-9.30). | TyGs can be used to defining IR in the patients with MS                                              |

Abbreviations: baPWV, brachial-ankle pulse wave velocity; CT, computerized tomography; CV, cardiovascular; CVD, cardiovascular disease; FU, follow-up; HOMA-IR, homeostasis model assessment - insulin resistance; HTN, hypertension; MS, metabolic syndrome; TG-WHtR, triglyceride-waist to height ratio; TyG, triglyceride glucose index; TyG-BMI, triglyceride glucose index · body mass index; TyGs, triglyceride glucose indices; TyG-WC, triglyceride glucose index · waist circumference.
Since IR is a highly generalized concept, its definition is not universally agreed upon and has many variations. Although there are many methods to assess IR, in general HOMA-IR is used as it has high reliability in determining IR. The major advantage of both the QUICKI and HOMA models is that they both require blood to be drawn only once from a fasted patient. Thus, they do not require extensive technical expertise and have a much lower cost per subject than the HIEC, making the QUICKI and HOMA models practical for use in large-scale epidemiological studies, and clinical situations. However, both of these methods fail to provide information about the stimulated glucose and insulin systems.

Specific indices, including the Matsuda index, Stumvoll index, Avignon index, oral glucose insulin sensitivity index, Gutt index, and Belfiore index use particular sampling protocols during the OGTT. These indices of whole-body insulin sensitivity derived from plasma glucose and insulin concentrations during OGTT reflect both muscle and liver sensitivity.8

- Matsuda–De Fronzo index: This is an insulin sensitivity index that reflects a composite estimate of hepatic and muscle insulin sensitivity. This index is calculated from plasma glucose (mg/dl) and insulin (mIU/l) concentrations in fasting state and during OGTT.4–6,8

2 | INSULIN RESISTANCE AND HYPERTENSION

Insulin resistance and hypertension are the components of the metabolic syndrome and often coexist. Clinical studies have shown that a high proportion of individuals with hypertension have hyperinsulinemia or glucose intolerance.11

2.1 | Pathophysiological mechanisms

Insulin enhances the adrenergic system, increasing the activity of the sympathetic nervous system, thus increasing blood pressure. It also inhibits the stimulating effect of adrenergic agonists producing prostacyclin adipose tissue, which can in turn increase peripheral vascular resistance and hypertension. Insulin modulates intracellular cation regulation by reducing the activity of the sodium/potassium ATPase (Na+/K+ ATPase) enzymes and increasing the Na+/K+ pump of vascular smooth muscle cells, increasing their sensitivity to catecholamines and angiotensin II, and finally increasing peripheral resistance, causing hypertension. In addition, IR factors, including non-esterified fatty acids, cytokines, and adiponectin, are released from excess adipose tissue. These factors increase the ability of the vascular endothelium to affect the elasticity of blood vessels, causing hypertension. Besides its metabolic effects, insulin induces vasorelaxation by stimulating nitric oxide production in the endothelium and regulates sodium homeostasis by enhancing sodium reabsorption in the kidney; thereby, contributing to blood pressure regulation.

Hence, the patients with hypertension or before the manifestation of hypertension are at risk of developing IR, which is a risk factor for increased CV risk. Recent studies have demonstrated that IR can develop in not only the classic insulin-responsive tissues, but also CV tissues where insulin participates in the development of CV diseases and hypertension.7–11

Conversely, hypertension can cause IR by altering the delivery of insulin and glucose to skeletal muscle cells, resulting in impaired glucose uptake. Hypertension and IR can be viewed as a non-causal association, according to the following hypotheses: 1) they may represent two independent consequences of the same metabolic disorder (intracellular free calcium accumulation), or 2) IR is a genetic marker and/or a pathogenetic mechanism of multiple metabolic abnormalities frequently associated with hypertension.11

2.2 | Insulin resistance in Asian patients with hypertension

There are only a few studies investigating the relationship between hyperinsulinemia and the incidence of hypertension in Asians. Most studies have applied HOMA-IR, IRI (Insulin resistance Index), or insulin measurements to assess IR. Several studies on Japanese patients with glucose tolerance disorders13 or hypertension14 have shown that hyperinsulinemia plays a significant role in the presence of hypertension. In addition, other studies from Egypt,21 Thailand,12 Taiwan,17 Bangladesh,18 Vietnam19 have identified the role of IR in primary hypertension. Although the number of patients in these studies was small (Table 2).

3 | TRIGLYCERIDE-GLUCOSE INDICES AND INSULIN RESISTANCE

The TyG index is calculated by the formula: Ln [TG (mg/dl) × glucose (mg/dl)/2]. TyG-BMI is calculated by the formula TyG index × BMI. TyG-WC index is calculated by the formula TyG index × WC.22–24 The role of fasting triglycerides and blood glucose in IR has been mentioned in many studies. This is explained by the metabolic products produced from triglyceride adipose tissue that affect the insulin sensitivity of other adipose and muscle tissue, related to glucose production in the liver (Table 3).

Although the first use of the TyG index in evaluating IR is not yet known, it is known to be introduced by South American experts.21,26,28,40 Since 2008, Simental-Mendia et al have applied the TyG index in community screening; and Guerro-Romero et al (2010) have compared TyG index with HIEC, the IR gold standard.28 Vasques et al (2011) have also showed that the TyG index is more valuable than the HOMA-IR index in assessing IR in Brazil.25 Er et al (2016) concluded that the triglyceride-glucose-body mass index is a simple and effective method for early assessment of IR.23 The Triglyceride-Glucose Indices (TyGs) have been shown to replace HOMA-IR in IR diagnosis by many studies.24,26,33,35,36 Since then,
many authors around the world, particularly in Europe and Asia, have conducted extensive research with TyG indicators combined with anthropometric indicators in predicting CV risks such as hypertension, diabetes, and atherosclerosis.\textsuperscript{31,32,34}

The determination of obesity and visceral adipose tissue is important in the evaluation of IR via the measurement of BMI (Body Mass Index) and WC (Waist Circumference). BMI and WC are easy to measure, but cannot provide a comprehensive assessment of visceral adipose tissue or metabolic products of fat tissue. The combination of TyG and obesity evaluation using BMI and WC increases the strength of early IR diagnosis. TyG is an important marker in IR evaluation, and BMI and WC are two simple and inexpensive parameters to assess obesity and other CV risks. This combination is expressed through two indicators TyG-BMI and TyG-WC and has been recognized as a simple, effective, and clinically useful marker for IR diagnosis.\textsuperscript{23} Based on scientific and previous research findings, TyG, TyG-BMI, and TyG-WC indicators will comprehensively assess blood triglycerides, blood glucose, visceral fat, and IR, as a correlation exists between these indices and other IR indices like the HOMA-IR and QUICKI.\textsuperscript{23,24,26} The superiority of TyG, TyG-BMI, and TyG-WC compared with HOMA-IR and QUICKI in clinical IR diagnosis has been reported in several studies.\textsuperscript{22,24,30}

The TyG index is a non-insulin-based index, accessible with a single test. It is advantageous in clinical and epidemiological studies as it is a routine test performed in the primary care settings. However, it has some limitations due to the marked heterogeneity in cut-off values and IR definitions among studies.

### 3.1 Why TyG indices can be selected for screening for insulin resistance screening in Asian hypertensive population

In addition to the pioneering studies of South American authors, many studies in China and South Korea have concentrated on the value of the TyG index for evaluating IR in a large number of cases.\textsuperscript{27,29,32,34,36,37} In Rongjiong Zheng, Yushan Mao studied the TyG index of 4686 people for 9 years, showing the significance of it has some limitations due to the marked heterogeneity in cut-off values and IR definitions among studies.

4. **CONCLUSION**

There is an important relationship between IR and primary hypertension. Identifying IR in the patients with hypertension will help to manage hypertension not only in Western, but also Asian patients. There are many methods to identify insulin resistance, including the popular HOMA-IR index, the gold standard of insulin clamping technique. However, each method has certain advantages and disadvantages. Hence, the TyG indices should be further evaluated. The TyG indices can be considered as a simple parameter, suitable for screening IR in essential hypertension, particularly in developing countries in Asia.

### CONFLICT OF INTEREST

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### AUTHOR CONTRIBUTIONS

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