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Association of Triglyceride–Glucose-Based Indices with the Risk of Elevated Blood Pressure and Hypertension in a Brazilian Population

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Abstract

Insulin resistance (IR) is a central mechanism in hypertension (HTN) development, but its direct assessment is unfeasible in population studies. This cross-sectional study evaluated the association of surrogate IR indices – Triglyceride Glucose Index (TyG), Triglyceride Glucose-Body Mass Index (TyG-BMI), Triglyceride Glucose-Waist Circumference (TyG-WC), Triglyceride Glucose-Waist to Height Ratio (TyG-WHtR), Metabolic Score for Insulin Resistance (METS-IR), and Cardiometabolic Index (CMI) – with blood pressure (BP) stages: normal, elevated, and HTN. Using data from a population-based survey conducted between 2004 and 2005, including 1,365 Brazilian adults, clinical, anthropometric, and biochemical variables were analyzed through multivariable logistic regression models. TyG, TyG-BMI, TyG-WC, and TyG-WHtR were

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associated with higher BP categories. METS-IR showed inconsistent findings across analyses, whereas CMI demonstrated a positive correlation with systolic and diastolic BP. Most surrogate IR indices remained significantly associated with hypertension after adjustment for demographic, behavioral, anthropometric, clinical, and lipid-related variables, supporting an independent association with blood pressure status in this population. In fully adjusted models, TyG, TyG-BMI, TyG-WHtR, METS-IR and CMI remained significantly associated with hypertension, while the association with TyG-WC was attenuated. These findings suggest that surrogate insulin resistance indices may provide complementary information for identifying individuals at increased risk of hypertension in this Brazilian urban population. Although valuable as a historical record, the 2004–2005 context and the modest discriminatory performance of these indices highlight the need for contemporary longitudinal validation.

Keywords: insulin resistance; blood pressure; triglyceride-glucose index; hypertension; elevated blood pressure; population epidemiology.

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Summary Table

What is already known on this topic
Insulin resistance (IR) is a central pathophysiological mechanism in the development of hypertension (HTN).
Direct assessment of IR is complex for population studies, leading to the use of simple and low-cost surrogate indices, such as those based on triglycerides and glucose (TyG).
Recent studies demonstrate consistent associations between surrogate IR indices and cardiometabolic risk, including HTN, in various populations.
What this study adds

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This study showed that several surrogate insulin resistance indices were associated with elevated blood pressure and hypertension in an urban Brazilian population.
These markers, due to their simplicity and low cost, may provide complementary information for population screening and cardiometabolic risk stratification, particularly in primary healthcare and resource-limited settings.
Several associations remained significant after adjustment for demographic, clinical, anthropometric, and lipid-related variables. However, the magnitude of these associations suggests complex interactions among insulin resistance, adiposity, and other metabolic risk factors.

Introduction

Systemic arterial hypertension (HTN) represents a constant challenge for global public health. It is a multifactorial condition that causes approximately 8.5 million deaths per year and is associated with several chronic diseases, including cardiovascular disease (CVD). Also, it is a cause of organ dysfunction in the brain and kidneys, among other conditions [1,2]. Understanding the historical trends and associations of these factors in specific populations is crucial for monitoring the evolution of public health. Therefore, this study offers a historical perspective on these relationships by utilizing a population-based dataset from 2004–2005. This establishes a valuable historical baseline that characterizes the metabolic and cardiovascular profile of a Brazilian urban population prior to major subsequent shifts in lifestyle and therapeutic guidelines, thereby enabling future studies to assess temporal trends and long-term changes in these associations over the past two decades.

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Subclinical elevation of blood pressure (BP) precedes the development of HTN and the occurrence of cardiovascular events [3]. This problem is relevant in low- and middle-income countries (such as Brazil) where the prevalence of HTN has been increasing more sharply in urban areas than in rural ones [4]. Early identification of factors associated with progressive increases in BP is essential to prevent the transition to more severe conditions, contributing to risk stratification and the adoption of effective preventive measures [5, 6].

Insulin resistance (IR) is a central pathophysiological mechanism in the development of HTN. The hyperinsulinemic-euglycemic clamp is considered the gold standard for IR measurement [7]. However, this direct method is difficult to apply in epidemiological contexts due to its high cost and operational complexity [8]. In this context, surrogate indices of IR, such as the Triglyceride Glucose Index (TyG index) have been shown to be a useful tool [9]. Some variations of TyG, combined with anthropometric measures, have proven to be viable and promising alternatives for estimating IR in an indirect, practical, and cost-effective manner as well [10-12].

Recent studies demonstrate consistent associations between these surrogate IR indices and cardiometabolic risk [13-19]. However, there is still a scarcity of studies that comparatively evaluate the performance of these tools in discriminating the stages of increased BP [20-22].

Thus, this study aimed to evaluate the association between various surrogate IR indices and BP stages (normal BP, elevated BP, and HTN), as well as to estimate the predictive power of these indices for an urban population in southeastern Brazil.

Materials and Methods

1. Study Population

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This is a cross-sectional, population-based study, with a retrospective analysis of data collected between 2004 and 2005 in a medium-sized urban city located in southeastern Brazil. The sampling was probabilistic and stratified by clusters, with random selection of households in five urban regions proportional to population size. For each region, streets, households, and a single resident adult who had lived in the household for more than six months were randomly selected. When the chosen individual did not agree to participate, a neighbor in the next house was selected in the same way, totaling 1,365 participants. Trained health professionals conducted structured interviews, physical examinations, and fasting blood collection at home or in health units.

Participants were selected based on the following criteria: (1) inclusion criteria: individuals aged 18 years or older with complete data on the biochemical and clinical parameters evaluated; (2) exclusion criteria: pregnancy, severe psychiatric illness or mental disability, and being bedridden or presenting with physical limitations that prevented blood pressure and anthropometric measurements. Patients with serious terminal illnesses (such as advanced neoplasms) were also excluded to maintain population homogeneity and control for major metabolic confounders.

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2. Characteristics and Measurement

The sample size was calculated to enable reliable estimates of the prevalence of elevated BP and HTN, adopting a maximum sampling error of 3% and a 95% confidence interval (CI) (as demonstrated in a previous publication) [23]. Demographic and clinical variables included age, sex, smoking, alcohol consumption, and history of CVD. Smoking status was categorized as current, former, or non-smoker, and alcohol consumption as 'yes' or 'no', based on self-reported responses collected through a structured questionnaire.

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Weight and height were measured with participants wearing light clothing and no shoes. Body mass index (BMI) was calculated by the formula: weight (kg)/height² (m^2). Waist circumference (WC) was measured between the last rib and the iliac crest. BP was measured three times with a calibrated aneroid sphygmomanometer, after 5 to 10 minutes of rest, with the participant seated and in a controlled environment. No alcohol, caffeine, or tobacco intake was allowed in the preceding 30 minutes, which is a standardized interval widely adopted in major epidemiological studies and recommended by national and international hypertension guidelines active at the time of data collection (such as the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure) to minimize the acute pressor effects of these substances while ensuring study feasibility in large-scale home-based screenings. The average of the three measurements was used for the analysis of systolic blood pressure (SBP) and diastolic blood pressure (DBP).

Blood collection was performed after a 12-hour fast. Glucose levels were determined by an automated colorimetric method (Dimension RXL platform; Dade Behring). In applicable cases, the diagnosis of diabetes mellitus was based on fasting glucose (≥126 mg/dL) or reported use of antidiabetic medication. Creatinine clearance was calculated using 12-hour urine samples and serum creatinine, adjusted for body surface area. For descriptive purposes in Table 1, creatinine values are presented in mg/dL. Total cholesterol (TC), triglycerides (TG), HDL-C, and LDL-C were also measured using automated biochemical analyzers.

3. Definitions

BP classification was categorized according to American guideline 2017 [5]: Normal BP (SBP < 120 mmHg and DBP <80 mmHg), elevated BP (SBP 120–129 mmHg and DBP <80

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mmHg) and HTN (SBP ≥130 mmHg or DBP ≥80 mmHg), with stages 1 and 2 grouped for this study.

We used the following formulas to calculate the Surrogate IR Indices:

- TyG index = Ln [TG (mg/dL) × FPG (mg/dL)/2], where TG: fasting triglycerides and FPG: fasting plasma glucose [12];
- TyG-WC (Triglyceride Glucose-Waist Circumference) = TyG × WC (cm) [12] ;
- TyG-BMI (Triglyceride Glucose-Body Mass Index) = TyG × BMI (kg/m²) [12] ;
- TyG-WHtR (Triglyceride Glucose-Waist to Height Ratio) = TyG × [WC (cm)/ Height (cm)] [12] ;
- METS-IR (Metabolic Score for Insulin Resistance) = Ln [(2 × FPG (mg/dL)) + TG (mg/dL)] × BMI (kg/m^2)/(Ln[HDL-C (mg/dL)]), where HDL-c: high-density lipoprotein cholesterol [12] ;
- CMI (Cardiometabolic Index) = [WC (cm)/ height (cm)]×[TG (mmol/L)/HDL-C (mmol/L)] [24] .

To ensure consistency with the established literature and comparability with validated cut-off points for these IR indices, the biochemical variables (TG, FPG and HDL-C) and anthropometric variables (WC and Height) were maintained in their original units (mg/dL and cm, respectively, except CMI which uses TG and HDL-C in mmol/L, as per its original definition) within their respective formulas, as defined by their establishing references. We emphasize that other biochemical variables presented in the study adhere to the International System of Units (SI), in accordance with the journal's guidelines.

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4. Statistical Analysis

Sample size estimation was performed in the original study to ensure reliable prevalence estimates of elevated BP and hypertension, assuming a 3% margin of error and a 95% confidence interval, as previously described.

Statistical analyses were conducted using SPSS software, version 22.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using the Kolmogorov-Smirnov test ($p < 0.05$). Continuous variables with a normal distribution were described as means and standard deviations, while categorical variables were presented as absolute and relative frequencies (percentages), according to the BP groups (Normal BP, Elevated BP, and Hypertension). For the comparison of means between groups, analysis of variance (ANOVA) was employed, and the chi-squared test was used for comparisons between categorical variables. The novel IR markers were classified into quartiles (Q1 to Q4) to enable analysis with non-normal distribution data, as well as to investigate potential associations with BP levels. The means and standard deviations of SBP and DBP were calculated for each quartile. The Kruskal-Wallis test was used for variables with an asymmetric distribution. Correlations between IR parameters and blood pressure levels were explored using Spearman's correlation test. To assess the association between the indicators and the presence of elevated blood pressure, logistic regression analysis was performed.

Additionally, two separate Receiver Operating Characteristic (ROC) curve analyses were used to estimate the predictive performance of the parameters in relation to BP: one comparing Elevated BP versus Normal BP and another comparing HTN versus Normal BP. For each analysis, the AUC, sensitivity, specificity, and optimal cutoff values were estimated. A p-value < 0.05 was considered statistically significant. Before multivariate modeling, multicollinearity among

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independent variables was assessed using variance inflation factors (VIFs). TC showed evidence of collinearity with other lipid variables and was therefore excluded from the fully adjusted model. All remaining variables presented VIF values below 2.5, indicating no evidence of problematic multicollinearity was observed.

All surrogate IR indices were evaluated for their association with increasing BP levels using multivariate logistic regression. Logistic regression analyses were performed to investigate the association between surrogate insulin resistance indices and hypertension, defined as hypertension versus the combined normal BP and elevated BP categories. The normal BP and elevated BP groups were combined because the elevated BP category comprised a relatively small number of participants (n = 98) compared with the normotensive and hypertensive groups, thereby improving statistical power and model stability. Three sequentially adjusted models were constructed. Model I was adjusted for age and sex. Model II was additionally adjusted for smoking status, alcohol consumption, central obesity, diabetes mellitus, CVD and BMI. Model III included all covariates from Model II and was further adjusted for LDL-C and HDL-C. This sequential adjustment strategy was used to evaluate the stability and independence of the associations between surrogate IR indices and elevated BP after controlling for potential demographic, behavioral, anthropometric, clinical, and metabolic confounders. A sensitivity analysis excluding participants with diabetes was performed to assess the robustness of the regression results.

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Results

1. Basic Demographic Characteristics in Different Blood Pressure Categories

Of the total sample of 1,365 adult individuals, 414 (30.3%) had normal BP, 98 (7.2%) had elevated BP, and 853 (62.5%) had HTN. 668 (48.9%) were men with a mean age of 56.0 ± 14.9

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years, and 699 (51.1%) were women with a mean age of 56.1 ± 14.2 years. The overall mean age was 56.0 ± 14.5 years. Only the age variable showed an asymmetric distribution; however, all continuous variables were described by means and standard deviations, considering the sample size and comparability with other studies. Basic demographic and clinical characteristics for each BP group are detailed in Table 1. Overall, groups with higher BP showed greater proportions of men, alcoholism, obesity, diabetes, and CVD ($p < 0.05$). These groups also exhibited higher mean values for age, WC, BMI, TC, TG, LDL-C, FPG, creatinine, the TyG index and its variations (TyG-WC, TyG-BMI, TyG-WHtR), and CMI ($p < 0.05$), while HDL-C did not differ significantly ($p > 0.05$). METS-IR showed less pronounced differences across BP categories than the other surrogate IR indices.

2. The BP Levels and Proportion of BP Categories According to the Quartiles of Surrogate IR Indices

The distribution of BP categories across quartiles of surrogate IR markers is presented in Figure 1. Both SBP and DBP generally increased with higher quartiles of TyG, TyG-WC, TyG-BMI, TyG-WHtR, and CMI ($p < 0.001$), with METS-IR exhibiting minimal variation. Furthermore, Figure 1 illustrates a gradual increase in the proportion of individuals with HTN as the TyG, TyG-BMI, TyG-WC, TyG-WHtR, and CMI indices progressed from Q1 to Q4. The TyG-WC and TyG-WHtR indices were particularly notable ($p < 0.05$), showing a more pronounced increase. Significant increases in HTN prevalence were observed in Q4 for most surrogate IR markers, excluding METS-IR.

3. Correlations Between Surrogate IR Indicators and BP

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Correlation analysis, summarized in Figure 2, indicated significant associations between SBP and DBP with various IR indicators ($p \leq 0.05$ for most correlations). The intensity of these correlations is represented by a color gradient: darker shades indicate more robust associations (both positive and negative), while lighter shades denote weaker correlations. Positive correlations with SBP were observed for TyG-WC, TyG-BMI, TyG-WHtR, and CMI (all $p<0.001$). A similar positive trend was found for DBP, which also positively correlated with the TyG index ($p<0.001$). METS-IR, however, did not show a significant correlation with SBP or DBP.

4. Logistic Regression Analyses of Surrogate IR Indexes with BP Categories

Logistic regression analyses were performed to evaluate the relationship between surrogate IR indices and the risk of elevated BP (defined as combined elevated BP and HTN categories versus Normal BP). Three models were employed: In Model I, the regression was adjusted for age and sex. To control for confounding, Model II was additionally adjusted for smoking status, alcohol consumption, central obesity, diabetes, CVD, and BMI. Model III was adjusted for the covariates of Model II plus LDL-C and HDL-C. The logistic regression analyses, which revealed distinct patterns across the sequential adjustment models, are summarized in Table 2.

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In Model I, all surrogate IR indices were significantly associated with hypertension. After additional adjustment for demographic, behavioral, anthropometric, and clinical variables (Model II), most associations remained statistically significant. In the fully adjusted model (Model III), TyG, TyG-BMI, TyG-WHtR, METS-IR, and CMI remained significantly associated with hypertension, whereas the association for TyG-WC was attenuated and no longer reached statistical significance. Overall, these findings indicate that several surrogate IR indices remained independently associated with hypertension even after adjustment for conventional metabolic risk factors. Most surrogate IR indices remained significantly associated with hypertension even after

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full adjustment, including lipid-related variables, suggesting that these associations are not fully explained by conventional metabolic risk factors. Model III included lipid variables to evaluate whether the associations remained independent of lipid profile. However, because some surrogate insulin resistance indices incorporate triglyceride-related components, the possibility of overadjustment cannot be excluded.

Sensitivity analyses excluding participants with diabetes yielded results that were largely consistent with those observed in the primary analyses. Overall, the direction and magnitude of the associations remained similar after excluding diabetic participants, indicating that the observed associations were not driven by the inclusion of individuals with diabetes.

5. The Predictive Ability of Surrogate IR Indices on BP

The predictive ability of surrogate IR indices for BP levels was evaluated using ROC curve analysis, as detailed in Figure 3. To distinguish between Normal BP and Elevated BP (Figure 3A), the TyG-WC and TyG-WHtR indices demonstrated the highest discriminatory performance, followed by TyG-BMI and the TyG index, with METS-IR showing limited capability. Similarly, in identifying Normal BP versus HTN (Figure 3B), TyG-WHtR and TyG-WC showed the highest discriminatory ability, followed by TyG-BMI and the TyG index. METS-IR again exhibited limited discriminatory ability in this distinction, while the TyG index and CMI maintained similar and reasonable efficacy in both scenarios.

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Discussion

In this population-based study, several surrogate IR indices were associated with BP categories, with progressively higher values observed across increasing BP levels. These findings support the relationship between insulin resistance-related markers and blood pressure status in

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this population. These findings suggest that surrogate insulin resistance indices may contribute to cardiometabolic risk assessment in clinical and epidemiological settings, but their utility should be interpreted with caution given the modest discriminatory ability observed in the ROC analyses and the possibility of residual confounding.

The NHANES study, which evaluated nearly 5 000 American adults, showed that higher levels of TyG, TyG-BMI, TyG-WHtR, and TyG-WC increase the likelihood of HTN [25]. The analyses were stratified by sex, heart failure, coronary artery disease, stroke, diabetes, alcohol consumption, and smoking, confirming the consistency of associations between surrogate IR indices and HTN. Furthermore, both the TyG index and CMI exhibited similar predictive performance in the ROC curve analysis, surpassing METS-IR and approaching the other surrogate indices, although still inferior to TyG-WHtR and TyG-WC.

Moreover, the study suggested that the sensitivity and specificity of these indices of IR may vary according to the demographic and clinical profile of the investigated population. The Cardiometabolic Index proposed by Wakabayashi et al. in 2015 [24], was relevant in characterizing risk across different BP levels in the Japanese population. Recognized as an indirect marker of IR, the validity of CMI is supported by recent evidence, including the study by Wu and Xu (2024) [7], which demonstrated a direct association between CMI and IR. In our analysis, CMI values increased progressively with rising BP, showing adequate discriminatory capacity between elevated BP and HTN. However, in the logistic regression models, the magnitude of the association was attenuated after adjustment for metabolic variables, particularly lipid profile, suggesting that part of the relationship between CMI and BP may be influenced by other metabolic factors. Nevertheless, CMI remained significantly associated with hypertension across all models. Most surrogate IR indices also remained significantly associated with hypertension in the fully adjusted

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model (Model III), even after inclusion of total cholesterol, LDL-C, and HDL-C. These findings suggest that the observed associations are not fully explained by the lipid profile and support an independent relationship between several surrogate IR indices and hypertension in this population.

Interestingly, HDL-C levels did not differ significantly across BP categories, whereas TC and LDL-C showed significant differences. This finding may suggest that BP elevation in this population was more closely associated with atherogenic lipid alterations than with HDL-C concentrations. However, HDL-C levels are influenced by multiple genetic, behavioral, and environmental factors, which may reduce their ability to discriminate BP categories.

In contrast to the other surrogate insulin resistance indices, METS-IR showed an inverse association with hypertension after multivariable adjustment. Because BMI and HDL-C are components of the METS-IR formula and were also included as covariates in the adjusted models, overadjustment may have influenced the direction and magnitude of the observed association. Therefore, this finding should be interpreted with caution and is unlikely to represent a true protective effect of higher insulin resistance against hypertension.

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These findings highlight the multifactorial nature of HTN and the interdependence of the metabolic disturbances involved, indicating that HTN detection may require the evaluation of a broader set of biomarkers, since insulin-resistance–based indices may present limited predictive power when additional metabolic factors are considered or are already present as risk determinants. Therefore, in clinical settings where a comprehensive metabolic assessment is performed, the incremental value of these specific IR indices for BP prediction may be limited. This nuance highlights the complex, multifactorial nature of hypertension and the intricate interrelations among different metabolic dysfunctions, rather than suggesting a lack of importance of IR itself.

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Furthermore, the age of the data must be considered. Although the results are valid for the analysed period (2004–2005), substantial changes in the epidemiological profile and lifestyle patterns of the Brazilian population over the last two decades may limit the direct applicability of these conclusions to the current context. However, the clinical relevance of the association between IR and elevated BP has been well defined in different population contexts [5, 26]. The large-scale cross-sectional study by Zhang et al., showed that both the TyG index and the triglyceride/HDL-cholesterol ratio (TG/HDL-C) correlate significantly with elevated BP and HTN in normoglycemic individuals, highlighting the importance of early identification of IR via surrogate indices, including TyG and its anthropometric variations, to prevent BP progression and related comorbidities [27-29].

The underlying pathophysiology appears to involve the complex interaction between IR, visceral obesity, and endothelial dysfunction, mechanisms that contribute to hemodynamic and inflammatory changes associated with increased BP [30]. In this sense, incorporating central adiposity measures into TyG-derived indices may better reflect this integrated cardiovascular risk.

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This may partly explain the favorable performance of TyG-WC and TyG-WHtR in the ROC and quartile analyses observed in the present study. By incorporating measures of central adiposity, these indices may better reflect the contribution of visceral fat to blood pressure elevation. In contrast, METS-IR showed less consistent performance across the analyses, suggesting a weaker association with BP alterations in this population.

The strong association observed between TyG-derived indices and the increase in BP levels reflects the complex [31], pathophysiological mechanisms of insulin resistance in the genesis of HTN. Insulin resistance is characterized by a reduced tissue response to insulin, leading to compensatory hyperinsulinemia. This hyperinsulinemia, in turn, can trigger a series of events that

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contribute to elevated BP, including activation of the sympathetic nervous system, increased renal sodium reabsorption, and promotion of endothelial dysfunction, factors that culminate in increased peripheral vascular resistance and arterial stiffness. Previous studies have consistently demonstrated the relationship between elevated insulin levels or insulin resistance and the development of hypertension in various populations, corroborating the central role of this metabolic imbalance in CVD [32, 33].

The relevance of our findings is heightened by the Brazilian epidemiological context, characterized by high rates of obesity, physical inactivity, and restricted access to advanced laboratory methods for determining IR [34, 35]. The use of surrogate IR indices can facilitate early screening and the implementation of more targeted primary prevention strategies, especially in groups of greater socioeconomic vulnerability.

This study has some limitations, including its cross-sectional design, which precludes causal inference, and the lack of plasma insulin, HbA1c, oral glucose tolerance test (OGTT), and direct measures of insulin sensitivity, limiting a more comprehensive assessment of glycaemic status and insulin resistance. Additionally, data collection preceded the 2020 Brazilian hypertension guidelines, which may limit comparisons with more recent studies. Nevertheless, the use of contemporary BP classification criteria allowed a standardized assessment of BP categories across the study population, facilitating comparison with more recent epidemiological investigations. Nonetheless, methodological standardization, a large sample size, and the use of multiple validated indices strengthen the reliability of the findings. These results should be viewed as a basis for understanding the historical risk profile of this specific Brazilian population, rather than as recommendations directly applicable to the current context.

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Longitudinal studies using contemporary data and, ideally, direct measures of insulin sensitivity are warranted to confirm the predictive value of these indices and to evaluate their potential incorporation into updated clinical protocols for cardiovascular risk prevention.

It is important to note that the discriminatory performance of the evaluated surrogate IR indices was modest, with AUC values below 0.75. According to conventional criteria, these findings indicate low-to-moderate discrimination and do not support the use of these markers as standalone diagnostic tools for elevated BP or hypertension. However, these indices are inexpensive, non-invasive, and easily obtainable from routinely collected anthropometric and biochemical measurements. Therefore, they may still provide useful complementary information for population screening and risk stratification, particularly in resource-limited settings where more comprehensive cardiovascular risk assessments may not be readily available.

In addition, no universally accepted cutoff values currently exist for surrogate insulin resistance indices, and reported thresholds may vary across populations. Although establishing reference ranges for the Brazilian population was not an objective of the present study, the lack of standardized cutoffs may limit direct comparisons between studies and populations.

Because several surrogate IR indices incorporate triglyceride-related components, adjustment for lipid variables in Model III may have partially attenuated the observed associations through overadjustment. In addition, several indices share common anthropometric and metabolic components (e.g., BMI and waist circumference), which should be considered when interpreting differences in predictive performance among indices. Nevertheless, multicollinearity diagnostics indicated acceptable levels of collinearity among the variables included in the final regression models (all VIF values < 2.5), suggesting that multicollinearity was unlikely to substantially influence the stability of the estimated associations.

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The relatively small number of participants in the Elevated BP category compared with the hypertension group may have reduced the statistical power of analyses specifically aimed at distinguishing Normal BP from Elevated BP.

Conclusion

In this population-based study of Brazilian adults, several triglyceride–glucose-derived indices, particularly TyG, TyG-BMI, TyG-WHtR, and CMI, were independently associated with elevated blood pressure and hypertension after adjustment for demographic, clinical, anthropometric, and lipid-related variables, supporting the relationship between surrogate insulin resistance markers and blood pressure status. Although their discriminatory performance was modest and insufficient for standalone diagnostic use, these indices are inexpensive, simple, and easily obtainable from routine clinical measurements and may provide complementary information for cardiovascular risk stratification. These findings also provide a historical baseline for understanding cardiometabolic risk in a Brazilian population. Future longitudinal studies using contemporary data are needed to confirm their predictive value and potential clinical applicability.

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Data Availability Statement

The datasets generated and/or analyzed during the current study are not publicly available due to the confidential nature of the participant data and containing personally identifiable patient information, but are available from the corresponding author on reasonable request and with ethics committee approval.

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Author Contributions

Jessica Rodrigues Roma Uyemura: Conceptualization, Formal Analysis, Data Curation, Writing – Original Draft Preparation, Writing – Review & Editing, Visualization, Project Administration.

Patricio Lopez-Jaramillo: Conceptualization, Methodology, Supervision, Writing – Review & Editing.

José Fernando Vilela-Martin: Conceptualization, Resources, Supervision, Writing – Review & Editing.

Luciana Neves Cosenso-Martin: Data Curation, Writing – Review & Editing.

Valquiria da Silva Lopes: Writing – Review & Editing.

Tatiana Palotta Minari: Writing – Review & Editing.

Ellen de Cássia Dutra Pozzetti Gouvea: Writing – Review & Editing.

Marco Antonio Vieira-da-Silva: Writing – Review & Editing.

Kleber Aparecido de Oliveira: Writing – Review & Editing.

José Paulo Cipullo: Data Curation.

Ethical Approval

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The original study, whose data were collected between 2004 and 2005, was approved by the Research Ethics Committee on Human Subjects of FAMERP (CEP-FAMERP), under CAAE number 2087/2004 (Approval 057/2004). All participants provided written informed consent at the time of data collection.

The secondary analysis, conducted in 2018 using previously collected and anonymized data, received new approval from the Research Ethics Committee on Human Subjects of FAMERP (CEP-FAMERP), in accordance with Resolution No. 466/2012 of the Brazilian National Health Council (CAAE 84121518.1.0000.5415). Due to the retrospective nature of the study, the Research Ethics Committee on Human Subjects of FAMERP (CEP-FAMERP) waived the need of obtaining informed consent for this stage.

All methods were performed in accordance with the relevant guidelines and regulations.

Conflicts of Interest

The authors declare no conflicts of interest.

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Figure Captions

Figure 1. Proportion of BP categories according to IR quartiles. There is a gradual increase in the proportion of individuals classified with HTN as the TyG, TyG-BMI, TyG-WC, TyG-WHtR, and CMI indices advance from the first (Q1) to the fourth (Q4) quartile. The TyG-WC and TyG-WHtR indices are particularly notable, with the frequency of HTN increasing from 18.1% (Q1) to 31.1% (Q4) and from 17.8% (Q1) to 31.0% (Q4), respectively.

Figure 2. Correlation of IR parameters and other risk factors with BP levels. The heatmap presents Spearman's correlation coefficients between clinical, anthropometric, and biochemical variables, including surrogate IR indices, SBP, and DBP. SBP and DBP demonstrated significant correlations with most IR indicators ($p \leq 0.05$). The TyG-WC, TyG-BMI, TyG-WHtR, and CMI indices showed a positive correlation with SBP (r values of 0.304, 0.246, 0.331, and 0.214, respectively, $p<0.001$). For DBP, a positive correlation was also observed with the TyG index ($r=0.251$, $p<0.001$). Darker shades indicate more robust associations, while lighter shades denote weaker correlations.

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Figure 3. Receiver Operating Characteristic (ROC) analysis of insulin resistance indices for predicting BP levels. (A) ROC curves to distinguish between Normal BP and Elevated BP; and (B) ROC curves to identify Normal BP and HTN. The AUCs and their respective 95% confidence intervals are presented for each indicator. For the discrimination between Normal BP and Elevated BP, TyG-WC (AUC = 0.704) and TyG-WHtR (AUC = 0.703) showed the highest discriminatory ability among the evaluated indices, although their performance remained within the moderate range. TyG-BMI (AUC = 0.657) and the TyG Index (AUC = 0.630) demonstrated modest discriminatory capacity, whereas METS-IR (AUC = 0.498) showed no relevant discriminatory ability (Figure 3A). Similarly, for the discrimination between Normal BP and HTN, TyG-WHtR

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(AUC = 0.715) and TyG-WC (AUC = 0.710) achieved the highest AUC values, while TyG-BMI (AUC = 0.686) and the TyG Index (AUC = 0.657) exhibited modest discriminatory performance (Figure 3B). Overall, the observed AUC values indicate low-to-moderate discriminatory ability, suggesting that these indices may serve as complementary markers for population-based risk assessment rather than standalone diagnostic tools.

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Tables

Table 1 Comparisons of basic demographic characteristics and surrogate markers for IR in different BP categories.

Variables	Normal BP (n=414)	Elevated BP (n=98)	HTN (n=853)	p
Gender [n(%)]				
Male	174 (42.0%)	47 (48.0%)	445 (52.2%)	0.003
Female	240 (58.0%)	51 (52.0%)	408 (47.8%)	
Smoking status [n(%)]				
Current Smoker	99 (23.9%)	22 (22.4%)	200 (23.5%)	
Former Smoker	96 (23.2%)	27 (27.6%)	257 (30.1%)	0.119
Non-Smoker	219 (52.9%)	49 (50.0%)	396 (46.4%)	
Alcohol drinking [n(%)]				
Yes	116 (28.0%)	29 (29.6%)	274 (32.1%)	0.332
No	298 (72.0%)	69 (70.4%)	579 (67.9%)	
Age (years)	48.92±14.28	59.06±13.83	59.13±13.56	<0.001
WC (cm)				
Male	81.1±7.6	95.5±3.5	110.9±8.7	<0.001
Female	72.3±6.1	83.6±2.3	99.4±8.9	
BMI (kg/m²)	25.34±4.98	26.72±4.73	27.66±5.69	<0.001
SBP (mmHg)	107.57±10.45	122.13±2.81	139.16±18.87	<0.001
DBP (mmHg)	72.46±8.46	72.33±5.75	86.64±9.93	<0.001
TC (mmol/l)	186.06±41.40	190.66±35.98	200.31±41.71	<0.001
TG (mmol/l)	119.37±76.48	143.63±123.00	148.78±93.32	<0.001
HDL-C (mmol/l)	46.78±14.01	45.22±13.06	46.74±15.23	0.614
LDL-C (mmol/l)	116.19±33.09	117.74±30.50	124.81±33.36	<0.001
FPG (mg/dL)	78.61±20.37	87.60±28.22	87.96±32.11	<0.001
Creatinine (mg/dL)	0.91±0.23	0.96±0.24	0.99±0.29	<0.001
Index TyG	8.38±0.67	8.51±0.67	8.67±0.67	<0.001
TyG-WC	760.94±144.34	808.35±149.13	849.27±159.19	<0.001
TyG-BMI	218.76±50.51	231.69±50.26	247.45±60.90	<0.001
TyG-WHtR	467.19±88.75	493.93±89.21	527.16±95.05	<0.001
METS-IR	41.47±9.52	42.42±11.83	40.23±10.98	0.042
Obesity [n(%)]				
Yes	69 (16.7%)	22 (22.4%)	226 (26.5%)	<0.001
No	345 (83.3%)	76 (77.5%)	627 (73.5%)	
Diabetes [n(%)]				
Yes	18 (5.0%)	12 (14.1%)	111 (14.4%)	<0.001
No	343 (95.0%)	73 (85.9%)	659 (85.6%)	
CVD [n(%)]				
Yes	25 (6.0%)	8 (8.2%)	111 (13.0%)	<0.001
No	389 (94.0%)	90 (91.8%)	742 (87.0%)	
CMI	0.88±0.37	1.07±0.58	1.08±0.46	<0.001

Abbreviations: WC, waist circumference; BMI, body mass index; SBP, systolic blood pressures; DBP, diastolic blood pressures; TC, total cholesterol; TG, triglycerides; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; FPG, Fasting Plasma

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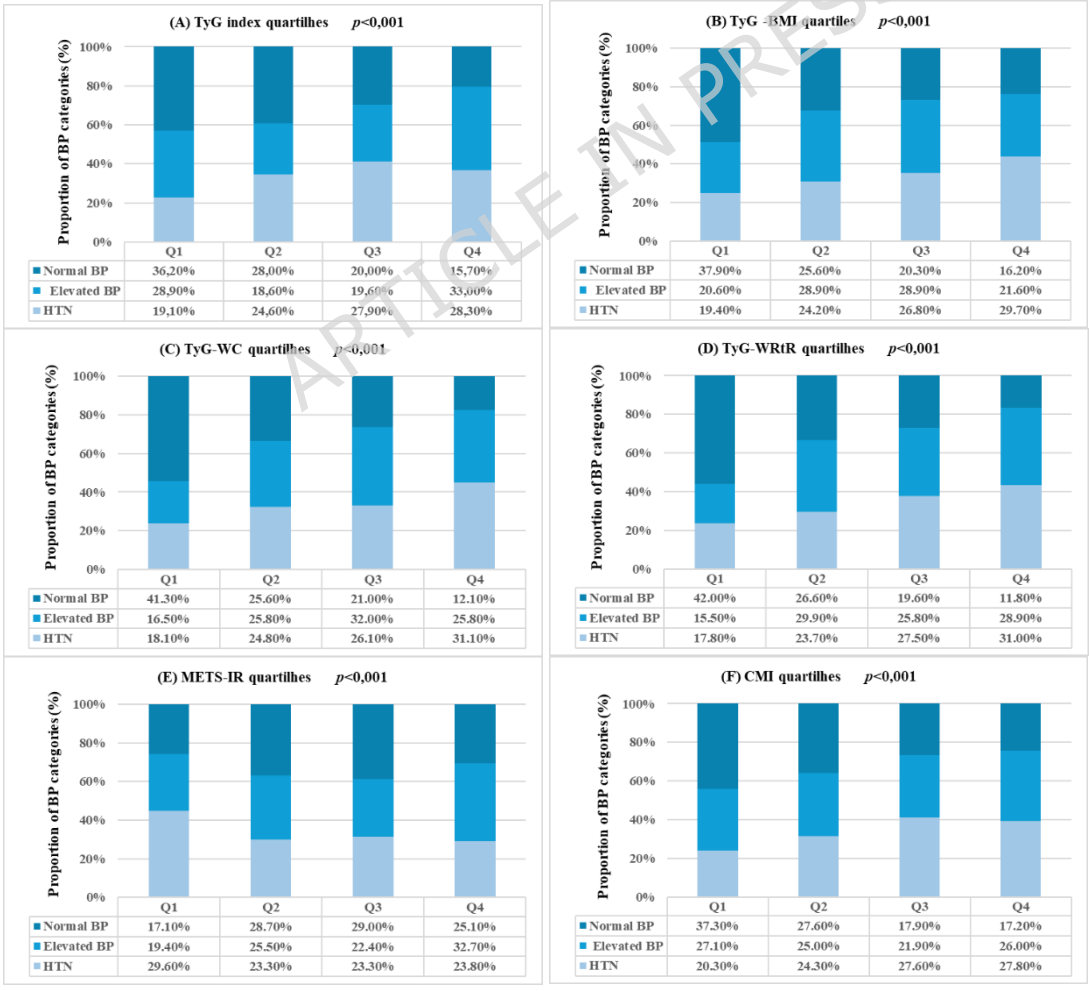
Glucose; TyG index, triglyceride glucose index, TyG-WC, triglyceride glucose-waist circumference; TyG-BMI, triglyceride glucose-body mass index; TyG-WHtR, triglyceride glucose-waist to height ratio; METS-IR, metabolic score for insulin resistance; CVD, cardiovascular diseases; CMI, cardiometabolic index.

Table 2 Binary Logistic Regression Analysis: Association between IR Indices and BP Categories.

Variables	Model I		Model II		Model III	
	OR (95%CI)	P value	OR (95%CI)	P value	OR (95%CI)	P value
TyG Index	1.859(1.530-2.257)	<0.001	1.575(1.259-1.970)	<0.001	1.722(1.332-2.226)	<0.001
TyG BMI	1.011(1.009-1.014)	<0.001	1.018(1.009-1.027)	<0.001	1.021(1.011-1.031)	<0.001
TyG WC	1.003(1.002-1.004)	<0.001	1.001(1.000-1.003)	0.038	1.001(1.000-1.003)	0.052
TyG WHtR	1.005(1.004-1.007)	<0.001	1.003(1.001-1.005)	0.012	1.003(1.000-1.005)	0.018
METS-IR	0.982(0.971-0.993)	<0.001	0.982(0.970-0.994)	0.004	0.983(0.970-0.995)	0.006
CMI	2.488(1.801-3.437)	<0.001	1.524(1.036-2.240)	0.032	2.769(1.585-4.837)	<0.001

Abbreviations: TyG index, triglyceride glucose index; TyG-BMI, triglyceride glucose-body mass index; TyG-WC, triglyceride glucose-waist circumference; TyG-WHtR, triglyceride glucose-waist to height ratio; METS-IR, metabolic score for insulin resistance; CMI, cardiometabolic index.

Figures



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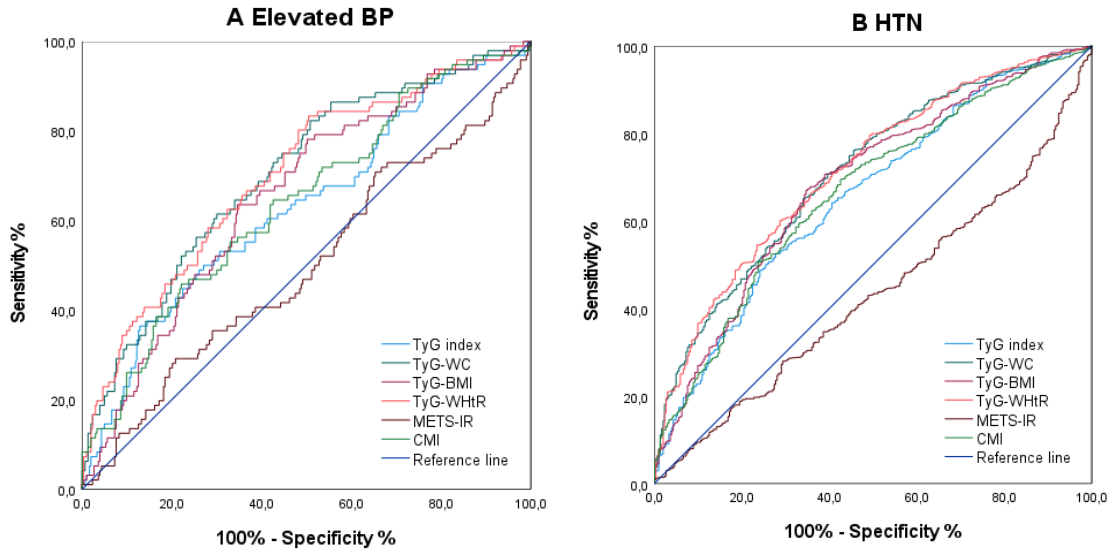
Figure 1: Proportion of BP categories according to quartiles of surrogate IR indices **(A)** TyG Index Quartiles, **(B)** TyG-BMI Quartiles, **(C)** TyG-WC Quartiles, **(D)** TyG-WHtR Quartiles, **(E)** METS-IR Quartiles, **(F)** CMI Quartiles.

	Age	SBP	DBP	WC	BMI		CT	TG	LDL	HDL	Glycemia		TyG Index	TyG-WC	TyG-BMI	TyG-WHtR		METS-IR	Creatinine
Age	1.000	0.395	0.119	0.153	-0.022		0.123	0.046	0.133	0.031	0.118		0.078	0.143	0.005	0.219		-0.015	0.2
SBP	0.395	1.000	0.711	0.289	0.215		0.163	0.172	0.123	0.023	0.215		0.213	0.304	0.246	0.331		-0.093	0.1
DBP	0.119	0.711	1.000	0.275	0.263		0.134	0.222	0.087	-0.027	0.218		0.251	0.314	0.304	0.310		-0.103	0.1
WC	0.153	0.289	0.275	1.000	0.790		0.104	0.309	0.117	-0.263	0.257		0.347	0.908	0.778	0.846		-0.049	0.2
BMI	-0.022	0.215	0.263	0.790	1.000		0.134	0.280	0.127	-0.159	0.224		0.308	0.716	0.937	0.744		-0.040	-0.0
TC	0.123	0.163	0.134	0.104	0.134		1.000	0.440	0.904	0.311	0.148		0.418	0.250	0.247	0.293		0.010	0.0
TG	0.046	0.172	0.222	0.309	0.280		0.440	1.000	0.281	-0.315	0.311		0.940	0.619	0.548	0.606		-0.040	0.1
LDL	0.133	0.123	0.087	0.117	0.127		0.904	0.281	1.000	0.097	0.062		0.265	0.194	0.188	0.227		0.022	0.0
HDL	0.031	0.023	-0.027	-0.263	-0.159		0.311	-0.315	0.139	1.000	-0.097		-0.288	-0.319	-0.238	-0.247		0.000	-0.2
FPG	0.118	0.215	0.218	0.257	0.224		0.148	0.311	0.105	-0.097	1.000		0.579	0.442	0.387	0.451		-0.074	0.0
TyG	0.078	0.213	0.251	0.347	0.308		0.418	0.940	0.269	-0.288	0.579		1.000	0.675	0.593	0.667		-0.058	0.1
TyG-WC	0.143	0.304	0.314	0.908	0.716		0.250	0.619	0.194	-0.319	0.442		0.675	1.000	0.839	0.947		-0.060	0.2
TyG-BMI	-0.005	0.246	0.304	0.778	0.937		0.247	0.548	0.188	-0.238	0.387		0.593	0.839	1.000	0.860		-0.050	0.0
TyG-WHtR	0.219	0.331	0.310	0.846	0.744		0.293	0.606	0.227	-0.247	0.451		0.667	0.947	0.860	1.000		-0.056	0.1
METS-IR	-0.015	-0.093	-0.103	-0.049	-0.040		0.010	-0.040	0.022	0.000	-0.074		-0.058	-0.060	-0.050	-0.056		1.000	-0.0
Creatinine	0.209	0.121	0.134	0.231	-0.009		0.024	0.000	0.005	-0.207	0.097		0.191	0.257	0.069	-0.132		-0.003	1.0
CMI	0.105	0.214	0.255	0.614	0.523		0.232	0.856	0.193	-0.606	0.327		0.824	0.825	0.724	0.814		-0.035	0.2

Figure 2 Correlation of IR parameters and other risk factors with BP levels.

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Test outcome variable(s)	AUC	95%CI		P value
		Lower limit	Upper limit	
TyG index	0.630	0.564	0.696	0.000
TyG-WC	0.704	0.644	0.764	0.000
TyG-BMI	0.657	0.595	0.718	0.000
TyG-WHtR	0.703	0.642	0.764	0.000
METS-IR	0.498	0.429	0.567	0.948
CMI	0.640	0.576	0.704	0.000

Test outcome variable(s)	AUC	95%CI		P value
		Lower limit	Upper limit	
TyG index	0.657	0.622	0.692	0.000
TyG-WC	0.710	0.678	0.743	0.000
TyG-BMI	0.686	0.652	0.720	0.000
TyG-WHtR	0.715	0.683	0.747	0.000
METS-IR	0.432	0.397	0.467	0.000
CMI	0.667	0.633	0.701	0.000

Figure 3. ROC curves analysis of insulin resistance indexes for predicting blood pressure levels. AUC and 95% CI of each indicator were listed below. (A) Elevated BP, (B) HTN.

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