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Original Article

Association between triglyceride-glucose index and hypertension: A systematic review and meta-analysis

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Abstract

The triglyceride-glucose (TyG) index is a simple and reliable indicator of insulin resistance, which is an important contributor to the development of hypertension. The aim of this meta-analysis was to determine the dose-response association between the TyG index and the incidence of hypertension. An extensive search was conducted through several databases, including PubMed, EMBASE, ScienceDirect, and Scopus, until June 1, 2024. The TyG index was used as the exposure, and the incidence of hypertension was measured throughout the TyG index intervals. The effect estimates were presented as odds ratios (OR) in both the unadjusted and adjusted models. Adjusted OR were carried out from all included studies to eliminate the possibility of confounding factors being involved in the incidence of hypertension. A total of 108.936 participants (mean age: 48.2 years old, male: 47%, mean body mass index: 23.9 kg/m^2) from 14 observational studies were included. The TyG index in the most eminent category was related to a higher risk of hypertension in both unadjusted (OR: 2.59, 95%CI: 2.03–3.31, p<0.001; I^2: 97.1%, p<0.001) and adjusted model (OR: 1.74, 95%CI: 1.39–2.19, p<0.001; I^2: 92.2%, p<0.001). The dose-response meta-analysis for the adjusted OR showed that the linear association analysis was not significant per 0.1 increase in the TyG index. The dose-response curve became increasingly steeper at the TyG index above 8.5. In conclusion, the TyG index was shown to be strongly linked with hypertension in a non-linear dose-response manner.

Keywords: Blood pressure, triglyceride-glucose index, hypertension, lipid, insulin resistance

Introduction

Hypertension affects more than one-third of people and is one of the leading causes of cardiovascular illness and death worldwide [1]. Several modifiable and non-modifiable risk factors have been linked to hypertension. Parameters obtained from metabolic-based laboratory and physical exams indicate prehypertension in slim individuals [2], demonstrating the possibility of a more specific risk prediction. Identifying the population at risk for hypertension is critical for timely and focused intervention.

Insulin resistance and hypertension are shown to be closely related [3]. However, measuring insulin resistance using other approaches, such as the hyperinsulinemic-euglycemic clamp, was impracticable. One of the most credible stand-in measures of insulin resistance is the triglyceride-glucose (TyG) index [4]. Triglycerides and glucose are simple and affordable

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parameters commonly measured during medical examinations in patients with chronic diseases, people who appear to be healthy without known disease, and healthy individuals. As a result, TyG index assessment will not significantly increase cost-effectiveness [5]. The TyG index was shown to be associated with prehypertension and hypertension [2,6]. Nevertheless, the dose-response relationship between the TyG index and hypertension remains obscure. Furthermore, there has been no meta-analysis of the dose-response relationship between the TyG index and hypertension currently at the time of writing. The aim of this systematic review and meta-analysis was to assess the dose-response relationship between the TyG index and the incidence of hypertension.

Methods

This meta-analysis was written in accordance with guidelines stipulated by the Meta-analysis of Observational Studies in Epidemiology/Preferred Reporting Items for Systematic Reviews and Meta-Analyses (MOOSE/PRISMA protocol). This meta-analysis was registered in the International Prospective Register of Systematic Reviews (PROSPERO), CRD42021235595.

Eligibility criteria

The inclusion criteria were studies that meet all of the following criteria: (1) prospective or retrospective observational studies and (2) reported high versus low TyG index in a comparative manner in association with the aforementioned variable. No language restrictions were imposed. Abstracts, preprints, reviews, commentaries, editorials, viewpoints, and letters were excluded.

Search strategy and study selection

An extensive literature search was performed using PubMed, Embase, Scopus, and ScienceDirect with search phrases ("triglyceride-glucose" OR "TyG" AND "Hypertension" (MeSH term)) from the inception of the database to June 1, 2024. Duplicates were eliminated after compiling the initial records. Two authors independently evaluate the articles by screening the titles and abstracts for eligibility. The entire set of papers of possibly suitable articles were evaluated using the predetermined eligibility criteria.

Data collection

Data collection to summarize data from multiple studies was conducted surreptitiously. Two authors working independently conducted the data extraction, focusing on the first author's name, study design, year, age, gender, smoking status, diabetes mellitus, body mass index, exposure, and the outcome of interest. These variables were selected due to their potential relationship with the exposure and the outcome of interest.

The exposure variable was the TyG index, computed using the formula: ln (natural logarithm) of fasting triglycerides multiplied by fasting plasma glucose divided by two [7]. The incidence of hypertension was premeditated at various TyG index intervals. The impact was estimated using odds ratios (ORs). The Newcastle-Ottawa Scale (NOS) was implemented by the authors to independently assess the possibility of bias in each study. A study with a total score of seven or above was deemed bias-free. Research with a total score of six or less was considered to be biased and thus excluded from the research [8]. The authors sorted out any disagreements through discussion.

Statistical analysis

Odds ratios (OR) were combined to examine the association between the highest category and the lowest category of the TyG index with the incidence of hypertension. If OR was unavailable, dichotomous data were converted into ORs. The DerSimonian and Laird method, which used random-effects model meta-analysis, was conducted irrespective of heterogeneity. A p-value of less than 0.05 indicated statistical significance for the effect estimate. Heterogeneity among the studies was assessed using the I^2 statistic and the Cochran Q test, with an I^2 of more than 50% or a *p*-value less than 0.15, indicating inter-study heterogeneity. A dose-response meta-analysis was performed on studies that provided at least three quantitative classifications for the TyG index. A random effects analysis was carried out based on generalized least squares regression trend estimation using log ORs spanning TyG index intervals.

Adjusted effect estimates in all included studies were derived using limited cubic splines with three knots per 0.5 increase in the TyG index. The Wald-type test was employed to assess nonlinearity by comparing the regression coefficient of the second spline to zero, resulting in a *p*-value of <0.05, indicating a deviation from linearity. Furthermore, the funnel plot and Egger test were utilized to quantify the publication bias. The meta-analysis was conducted using STATA 17.0 (StataCorp LLC, United States).

Results

Baseline characteristics

There were 108.396 participants from 14 observational studies included (**Figure 1**) [6,9-21]. The baseline characteristics of the incorporated studies are displayed in **Table 1**.

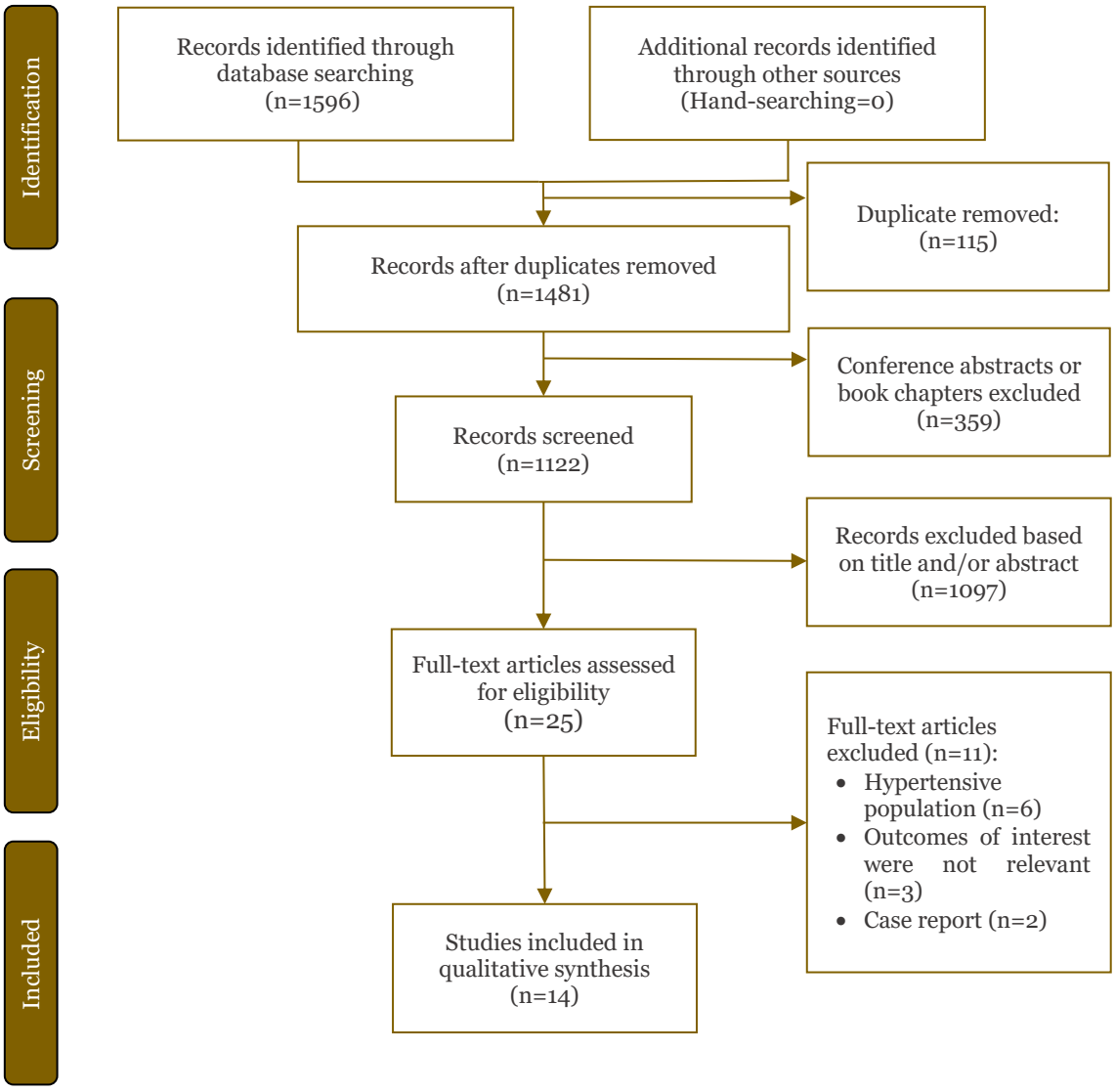

Figure 1. PRISMA flowchart.

Triglyceride-glucose index and hypertension

The highest category for the TyG index is linked to an increased hypertension risk in both unadjusted (OR: 2.59, 95%CI: 2.03–3.31, $p<0.001$; I^2: 97.1%, $p<0.001$) (**Figure 2A**) and adjusted model (OR: 1.74, 95%CI: 1.39–2.19, $p<0.001$; I^2: 92.2%, $p<0.001$) (**Figure 2B**). Dose-response meta-analysis showed a non-linear relationship between the TyG index and hypertension ($p<0.001$) (**Figure 3**). Using TyG index 7.0 as a reference value, the adjusted OR for TyG 7.5, 8.0, 8.5, and 9.0 (OR: 1.21, 95%CI: 1.12–1.30; OR: 1.42, 95%CI: 1.24–1.60; OR: 1.62, 95%CI: 1.37–1.87; OR: 1.80, 95%CI: 1.53–2.07), respectively.

Table 1. The baseline characteristics of the included studies

Author, year	Study design	Country	Samples	Mean age (years)	Male (%)	BMI (kg/m²)	DM (%)	Hypertension (%)	NOS
Bala *et al.* 2019 [9]	Cross-sectional	Romania	2,124	41.3	44.7	26.4	NA	0	7
Gao *et al.* 2023 [10]	Prospective cohort	China	4,600	48.1	44.7	22.9	NA	0	8
Jian *et al.* 2017 [16]	Cross-sectional	China	1,777	60.8	44.5	24.8	NA	0	7
Khoo *et al.* 2023 [11]	Retrospective cohort	Singapore	3,183	55.9	32.5	23.0	NA	0	7
Lee *et al.* 2022 [12]	Cross-sectional	South Korea	15,721	44.4	36.3	22.8	NA	0	8
Liu *et al.* 2023 [17]	Prospective cohort	China	4,755	57.5	52.6	NA	NA	0	7
Sanchez-Inigo *et al.* 2016 [6]	Prospective cohort	Spain	3,637	52.0	60.3	26.3	3.1	0	7
Tsai *et al.* 2024 [18]	Prospective cohort	Taiwan	2,448	28.15	88	24.3	NA	0	8
Wang *et al.* 2020 [15]	Cross-sectional	China	2,076	Stratified	39.9	25.2	NA	0	7
Wang *et al.* 2024 [19]	Retrospective cohort	China	3,413	46.2	41.5	22.5	1.2	0	8
Yuan *et al.* 2022 [20]	Prospective cohort	China	2,399	46	41.5	22.6	1	0	9
Zhao *et al.* 2022 [21]	Prospective cohort	China	10,309	48.0	39.5	22.98	2.35	0	8
Zheng *et al.* 2017 [14]	Prospective cohort	China	4,686	40.5	67.8	22.5	NA	0	7
Zhu *et al.* 2020 [13]	Cross-sectional	China	47,808	57.7	27.4	24.2	NA	4.95	7

BMI: body mass index; DM: diabetes mellitus; NA: not available; NOS: Newcastle-Ottawa scale

Publication bias

The funnel plot exhibited asymmetry for both unadjusted and adjusted models. However, Egger's test showed the absence of small-study effects for either the unadjusted or adjusted models (p>0.05).

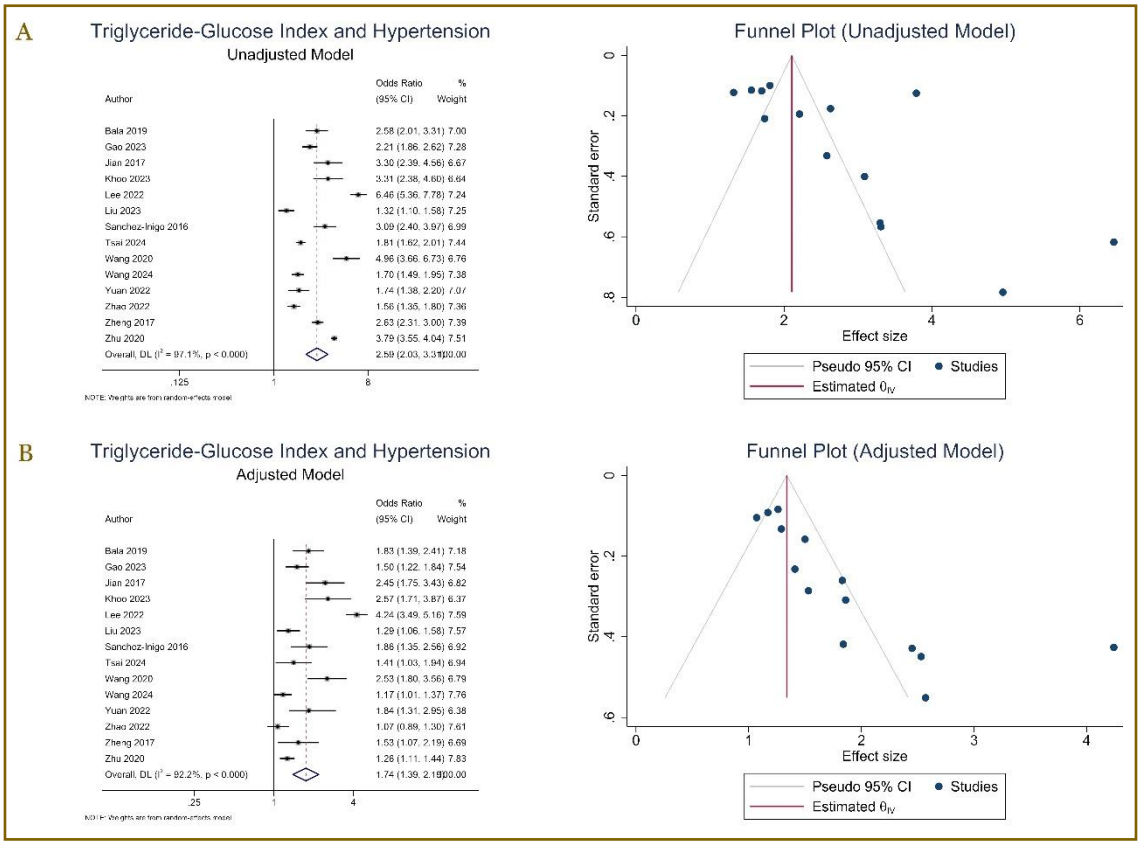

Figure 2. The triglyceride-glucose index and hypertension, with highest vs lowest categories in unadjusted model (A) and adjusted model (B).

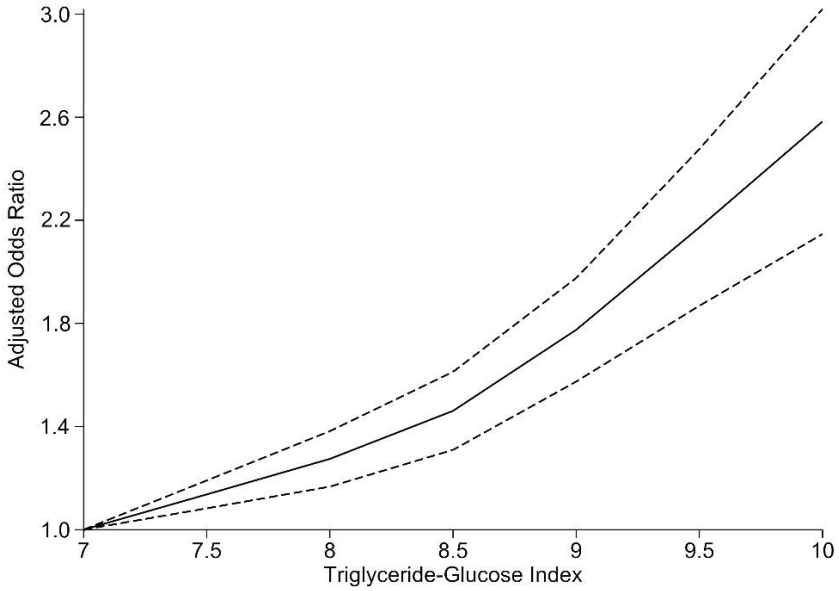

Figure 3. A dose-response meta-analysis of the triglyceride-glucose (TyG) index and the incidence of hypertension. The TyG index is associated with a higher risk of hypertension, as indicated by an adjusted odds ratio (AOR) (solid line) and a 95% confidence interval (long dashed lines).

Discussion

This meta-analysis demonstrates the association between the TyG index and hypertension. The dose-response relationship between the association was non-linear. Thus, aggressive preventive intervention is necessary in the presence of a high TyG index. A high TyG index signifies insulin resistance [7,22]. Insulin resistance alters glucose metabolism, leading to prolonged hyperglycemia, which can foster increased oxidative stress and inflammation. This cascade contributes to systemic inflammation, endothelial dysfunction, and unfavorable vascular remodeling [23,24]. Hyperinsulinemia may elevate the activity of the renin-angiotensin-aldosterone system and sympathetic nervous system, potentially increasing total vascular resistance and hypertension [25]. Moreover, neuro-hormonal system stimulation can prompt sodium and water retention [26]. The TyG index was associated with pre-hypertension in lean individuals [2] and with both pre-hypertension and hypertension in children and adolescents [27].

A high TyG index was associated with arterial stiffness [28] and unfavorable cardiovascular events in both seemingly healthy persons and those with stable coronary artery disease [29-34]. Xie *et al*. observed a temporal, reciprocal association between BMI and the TyG index, both of which were associated with hypertension incidence [35].

All the included studies reported that the group with a high TyG index was associated with a greater hypertension risk than those with a lower TyG index. Zheng *et al*., in a cohort of 4,686 participants, suggested a dose-dependent relationship between the TyG index and incident hypertension [14]. However, they did not report the linearity of this relationship. This meta-analysis supports their findings and provides evidence of a non-linear relationship, with the curve becoming steeper as the TyG index increases.

The majority of the included research offered cross-sectional data, limiting the inference of a temporal relationship between the TyG index and the incidence of hypertension. Nevertheless, the TyG index could still be considered a promising marker to predict the incidence of hypertension, as suggested by two prospective cohort studies included in this analysis [6,14].

The calculation utilized to determine the TyG index appeared to be uniformly different from the original method [7,22]. This discrepancy has raised concerns and was addressed by Vieira-Ribeiro *et al*., who were also authors using this modified formula [36]. Although seemingly minor, this alteration should not be overlooked, as it could lead to confusion in scientific research and its clinical application. A standardized calculation for this index should be promptly established.

Most of the studies included were cross-sectional. The number of available studies precludes a sufficiently powered meta-regression analysis to investigate heterogeneity. The optimal cut-off value for prognosis remains undetermined; further research is necessary to derive this value from prospective cohorts.

Conclusion

The TyG index was associated with hypertension in a non-linear dose-dependent manner. Measurement of the TyG index was simple and inexpensive and thus may be of value during medical checkups in patients with chronic diseases, apparently healthy, and healthy individuals. Determining the TyG index cut-off point will be useful for risk stratification. A high TyG index beyond a specific cut-off point may indicate a high risk of developing hypertension in the future. Thus, a more aggressive lifestyle intervention and more frequent blood pressure measurements are needed for this population. Further studies are needed to determine whether pharmacological interventions are necessary in patients with high TyG index.

Ethics approval

Not required.

Acknowledgments

We have no acknowledgments to declare.

Competing interests

All the authors declare that there are no conflicts of interest.

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Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

How to cite

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