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Triglyceride glucose waist circumference and non alcoholic fatty liver disease: a systematic review and meta analysis

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Abstract

Background Insulin resistance (IR) plays a noticeable role in the pathogenesis of non-alcoholic fatty liver disease (NAFLD). The triglyceride glucose-waist circumference (TyG-WC) index, a novel measure for assessing IR, may hold significant predictive value for NAFLD. However, the relationship between TyG-WC and the risk of NAFLD remains elusive. To investigate this association, this comprehensive meta-analysis was conducted.

Methods A systematic electronic search was conducted using the PubMed, Embase, and Web of Science databases from their inception until July 2024 to identify observational studies assessing the relationship between TyG-WC and the risk of NAFLD. Joanna Briggs Institute's critical appraisal checklist was utilized to evaluate the quality of cross-sectional studies, while the Newcastle-Ottawa Scale (NOS) score was used to assess cohort studies. The principal summary outcomes included the mean difference (MD) and the corresponding 95% confidence interval (CI).

Results In total, 10 studies comprising 38,518 participants were included in this meta-analysis, of whom 37% were diagnosed with NAFLD. The analysis revealed a significant MD between NAFLD and non-NAFLD cases (MD, 137.41; [95% CI, 121.52-153.31]).

Conclusion A significant MD was identified between NAFLD and non-NAFLD cases. The TyG-WC index was found to be positively correlated with the risk of NAFLD, suggesting that it may serve as a potential indicator for NAFLD.

Keywords TyG-WC index, Non-alcoholic fatty liver disease, Meta-analysis, Insulin resistance

Introduction

Following the proposal to redefine non-alcoholic fatty liver disease (NAFLD) as metabolic dysfunction-associated fatty liver disease (MAFLD), the condition has now been officially reclassified as metabolic dysfunction-associated steatotic liver disease (MASLD) [1]. Currently, the global prevalence of NAFLD is approximately 30.2%, with regional variations of 30.9% in Asia, 16.1% in Australia, 30.2% in Europe, 29% in North America, and 34% in South America [2]. Given its high prevalence, this condition has become a major public health concern, particularly due to its strong association with metabolic

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comorbidities, including obesity, type 2 diabetes, hyperlipidemia, hypertension, and metabolic syndrome [3]. In addition, NAFLD has the potential to progress to nonalcoholic steatohepatitis, compensated/decompensated cirrhosis, or even hepatocellular carcinoma [4, 5]. To date, no agents have been approved by the U.S. Food and Drug Administration (FDA) for the treatment of NAFLD, although several drugs are in various stages of development. The primary treatment for NAFLD remains weight loss [6]. When weight loss through diet and exercise is difficult to achieve or sustain, bariatric surgery can facilitate long-term weight reduction [7]. In clinical practice, most NAFLD diagnoses rely on abdominal ultrasound, which has limited ability to quantify fat infiltration. Although it is highly sensitive for detecting moderate-to-severe fatty liver, its accuracy may be reduced in individuals with abdominal obesity [8, 9]. Magnetic resonance imaging (MRI), including MRI-proton density fat fraction (MRI-PDFF) and magnetic resonance elastography (MRE), provides an accurate and noninvasive assessment of hepatic steatosis and fibrosis [10]. However, its implementation remains constrained by technical feasibility and the time required to complete the examination. The gold diagnostic standard for NAFLD relies on liver biopsy results. However, it has well-known limitations, including invasiveness, poor acceptability, sampling variability, and high cost [11]. Therefore, early identifying at-risk populations for NAFLD using simple and effective diagnostic tools is essential.

The homeostatic model assessment for insulin resistance (HOMA-IR), an important marker for evaluating IR [12], has been extensively applied to IR-related diseases and serves as a diagnostic criterion for NAFLD. However, in primary care, as circulating insulin concentrations are rarely measured, alternative indices, such as the Fatty Liver Index (FLI) [13], triglyceride-glucose (TyG) index, have been developed to assess IR [14, 15]. The prevalence of NAFLD has exhibited to increase progressively with higher TyG index values [16], highlighting the role of elevated levels of triglycerides in liver fat accumulation. Moreover, TyG-associated parameters, including triglyceride glucose-waist-to-height ratio (TyG-WHtR), triglyceride glucose-waist circumference (TyG-WC), and triglyceride glucose-body mass index (TyG-BMI) can effectively identify NAFLD in the Japanese population [17]. These indicators are easy to measure and can be obtained through routine medical examinations.

To date, few studies have concentrated on the correlation between TyG-WC and the risk of NAFLD, and it remains controversial whether an increase in TyG-WC is indicative of NAFLD in the general adult population. Therefore, this meta-analysis aimed to comprehensively explore the association between TyG-WC and the risk of NAFLD.

Methods

Protocol registration and search strategy

The study protocol was registered in the PROSPERO database (International Prospective Register of Systematic Reviews, http://www.york.ac.uk/inst/crd) under registration number of CRD42024580557. A comprehensive search was carried out using the Cochrane Library, Embase, Web of Science, PubMed, China Biomedical Literature Database (CBM), China National Knowledge Infrastructure (CNKI), Database for Chinese Technical Periodicals (VIP), Wanfang Database, and other relevant databases, covering publications from their inception until July 2024. The specific retrieval strategy is detailed in Supplementary Table 1.

Study selection and eligibility criteria

According to the PICOS criteria (Population, Intervention, Comparison, Outcome, and Study Design), the inclusion criteria were summarized as follows: (1) adults (age > 18 years old); (2) hepatic steatosis confirmed histologically through ultrasonography, by computed tomography (CT), or using noninvasive biomarkers and scores; (3) comparison of high TyG-WC index versus low TyG-WC index; (4) availability of mean and standard deviation (SD), or ability to calculate them; (5) observational studies published as full-length articles. The exclusion criteria were defined as follows: (1) studies involving patients with secondary causes of hepatic steatosis; (2) studies lacking relevant data or from which data could not be extracted; (3) reviews, meta-analyses, congress abstracts, nonhuman studies, or in vitro studies; (4) publications in languages other than English. Two investigators (Ziyi Xin and Lanlan Feng) independently conducted each phase of the study from screening of the included studies to data analysis, and the results of the searches were imported into EndNote 21 software (Clarivate, 2021). Following removal of duplicates, the included articles were finally selected by reviewing titles, abstracts, and full texts. Any disagreements were resolved through consultation or, if necessary, by a third investigator (Qingwen Yu). The calculation formulas used in the analysis are as follows: BMI = weight (kg)/height^2 (m^2); TyG-WC = Ln [TG (mg/dL) × FPG (mg/dL)/2] × WC (cm).

Data collection and assessment of the quality of the included studies

The relevant characteristics of the included studies were extracted into an electronic database, including: (1) study details, such as the first author's name, year of publication, country or region, and study design; (2) participants' information, including the number, age, and sex of participants in both the NAFLD and non-NAFLD groups; (3) diagnostic methods used for NAFLD; and (4) comparison of TyG-WC level in the NAFLD group with

that in the control group. The quality of the cross-sectional studies was assessed using Joanna Briggs Institute's critical appraisal checklist, with responses categorized as "yes", "no", "unclear", or "not applicable". For cohort studies, quality was evaluated using the Newcastle-Ottawa Scale (NOS) score, assigning a quality score ranging from 1 to 9 stars based on eight criteria, with a higher number of stars indicating a higher study quality (Supplementary Table 2). The certainty of evidence for each outcome was appraised using the GRADE approach, in which factors, such as risk of bias, inconsistency, indirectness, imprecision, and publication bias were considered (Supplementary Table 4). The risk of bias in the included studies was assessed using the ROBINS-E tool, which biases were evaluated across seven domains (Supplementary Table 5).

Statistical analysis

The statistical analysis was conducted using the Review Manager (RevMan) 5.4 and Stata 14.0 software. For studies that reported the median and interquartile range (IQR), the mean and SD were calculated. This meta-analysis used TyG-WC as the primary outcome, and TyG-WC was presented as mean ± SD. Heterogeneity was assessed using the I^2 statistics and the Chi-squared (X^2) test; an I^2 value greater than 50% was indicative of high heterogeneity. A random-effects model was used to synthesize the data, as it is considered as a more robust approach for accounting for potential heterogeneity among the included studies. To assess publication bias, a funnel plot, Egger's test, and Begg's test were conducted. The leave-one-out sensitivity analysis was performed by removing each study individually to assess its impact on the overall effect estimate. If a study was identified as contributing to high heterogeneity, subgroup analysis was conducted to explore the sources of the heterogeneity.

Results

Search results

The process of literature search and screening is summarized in a PRISMA flowchart (Fig. 1). A total of 114 articles were initially retrieved, involving 26 from the PubMed, 26 from the EMBASE, 25 from the Web of Science, 24 from the VIP database, 7 from the Wanfang database, 4 from the CNKI, and 2 from the CBM. After removing duplicate records and reviewing titles and abstracts, 89 studies were excluded. One study was excluded due to the unavailability of the full text. The full texts of the remaining 24 studies were reviewed, and 14 were excluded for the following reasons: (1) lack of relevant data; (2) concentration on different populations, exposures, or outcomes; and (3) publication in languages other than English.

Characteristics and quality assessment of the included studies

The characteristics of the included studies are presented in Table 1. In this meta-analysis, 10 studies comprising 14,473 NAFLD cases and 38,518 participants were included [18–27]. Overall, the sample sizes of the included studies ranged from 175 to 20,922, and the mean age ranged from 43.9 to 52.6 years old. Besides, ultrasound or CT was used in all the included studies for diagnosing NAFLD. Among these articles, 9 cross-sectional studies were assessed by the Joanna Briggs Institute's critical appraisal checklist, and the remaining were cohort studies that were evaluated by NOS scores. After evaluation of selection, comparability, and outcomes, the studies were regarded as high-quality. All the included studies were assessed using the ROBINS-E tool, and they were judged to have a low risk of bias across all domains. Therefore, the conclusions of this meta-analysis are considered reliable and not significantly affected by bias. Based on the GRADE approach, the overall quality of evidence was rated as low. Despite this, the findings remain valuable for understanding the association between TyG-WC level and the risk of NAFLD.

Association between TyG-WC and the risk of NAFLD

Ten studies compared TyG-WC level between NAFLD patients and non-NAFLD controls. The results of the summary analysis are illustrated in Fig. 2. The results revealed an overall mean difference (MD) of 137.41 (95% confidence interval (CI): 121.52-153.31). A significant heterogeneity was also found ($I^2 = 96\%$, $P < 0.00001$). The study [27], due to its large combined sample size, might significantly contribute to the high heterogeneity (I^2 = 96%) found in the meta-analysis.

Sensitivity analysis and publication bias

The combined results remained consistent with the original results when any study was omitted from the sensitivity analysis. The results were stable when the fixed-effects model was used, yielding a MD of 147.01 (95% CI, 144.88-149.15) (Fig. 3).

The funnel plot is displayed in Fig. 4. Moreover, the Begg's test (P=0.592) and Egger's test (P=0.526) were conducted, indicating no publication bias in either test (Supplementary Fig. 1).

Subgroup analysis

Taking into account the influences of regional dietary habits, lifestyle, and genetic factors, subgroup analysis was conducted based on geographical region, age, and BMI. The results indicated that the interaction between mean age, BMI, geographical region, and TyG-WC was not significant (Fig. 5). Significant heterogeneity was found in these subgroups, suggesting that these factors

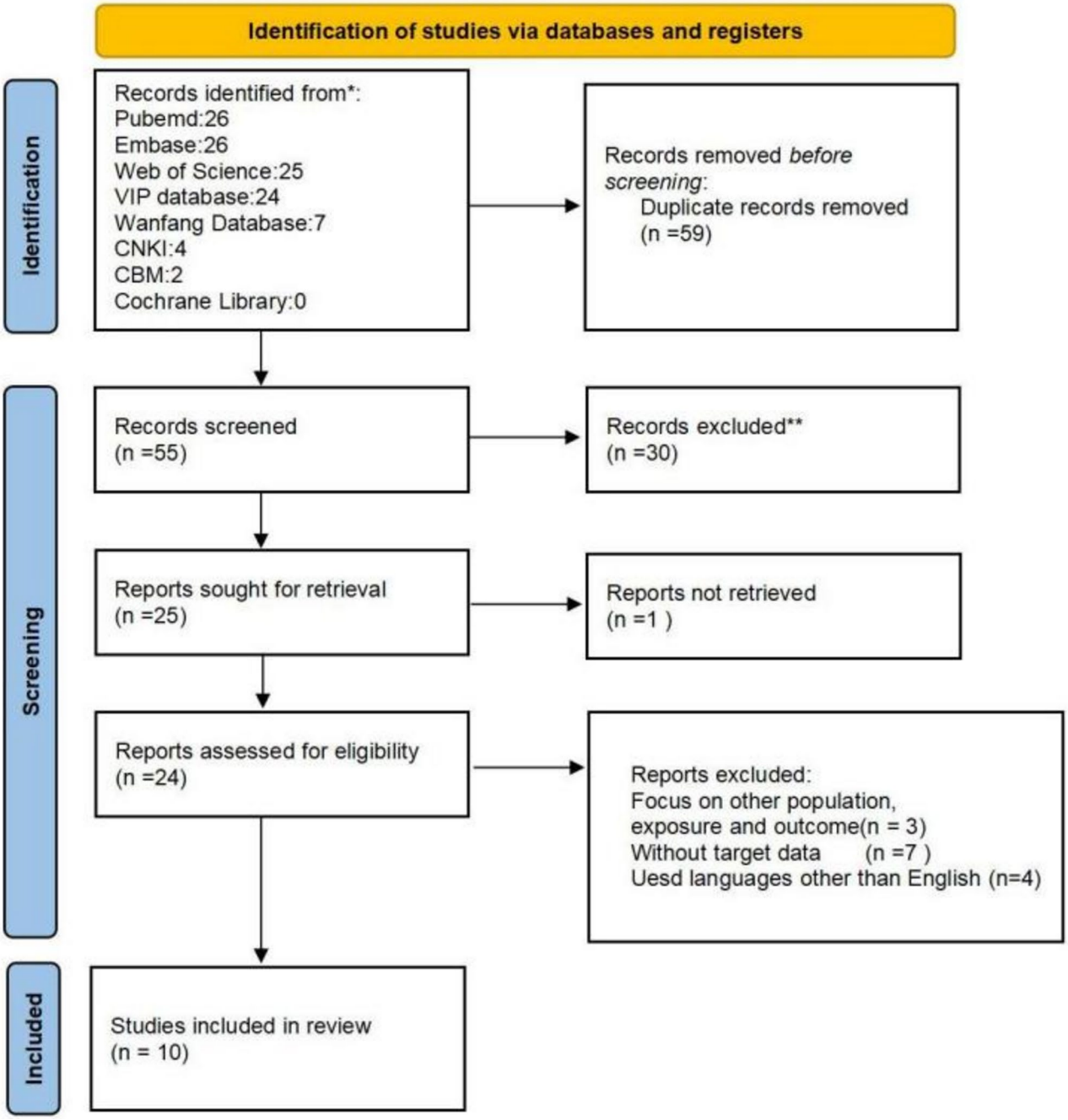

Fig. 1 Flow chart of the study selection process

were not the primary sources of heterogeneity. This finding supports the generalizability of TyG-WC as a potential predictor of NAFLD risk across various regions, age groups, and BMI categories.

Meta-regression analysis

A univariate meta-regression analysis was conducted to explore study-level factors that may account for the high heterogeneity observed across studies. NAFLD diagnosis, population type, and study type were not found to be sources of heterogeneity(Supplementary Table 3). Due to the limited number of studies included in the analysis, a multivariable meta-regression could not be performed.

Discussion

The present meta-analysis included 10 high-quality clinical studies, comprising 38,518 participants and 14,473 NAFLD cases. TyG-WC levels were significantly higher

Table 1 Characteristics of studies contained in the meta-analyses

References (First Author, Year, Country/ Region)	Source of participants	Participant Characteristics	NAFLD diagnosis	Study design	Case /*N*	Mean age (years), Male (%)	Mean BMI (kg/m^2)
Chang,2023, China	the Affiliated Hospital of Xuzhou Medical University	General population	Ultrasound	cross-sectional study	8099/ 20,922	43.9, 58.9	24.4
Han,2024, Korea	NA	General population	Abdominopelvic CT scan	cross-sectional study	150/ 852	52.60, 59.7	24.6
Xue,2022, China	NHANES	General population	Vibration controlled transient elastography	cross-sectional study	737/ 1727	51.2, 47.8	28.4
Khamseh,2024, Iran	Iran University of Medical Sciences	General population	FibroScan	cross-sectional study	320/ 644	50.2, 46.9	29.7
Chen,2024, China	NHANES	General population	Ultrasound	cohort study	3672/ 10,390	45, 51.6	26.7
Yu,2023, China	First Hospital of Nanping City, Fujian Medical University	General population	Ultrasound	cross-sectional study	726/ 2605	45.0, 56.5	22.9
Bockarie,2023, Ghana	Cape Coast Teaching Hospita	General population	Ultrasound	cross-sectional study	52/ 210	51.3, 27.8	27.5
Peng,2023, China	NHANES	General population	Ultrasound	cross-sectional study	499/ 809	45.9, 50.4	28.3
Khamseh,2021, Iran	NR	Patients with overweight/ obese	FibroScan	cross-sectional study	96/ 184	44.7, 50.5	30.4
Malek,2021, Iran	Iran University of Medical sciences	Patients with T2DM	FibroScan	cross-sectional study	122/ 175	48.9, 45.7	30.2

NAFLD, nonalcoholic fatty liver disease; BMI, body mass index; NR, not reported

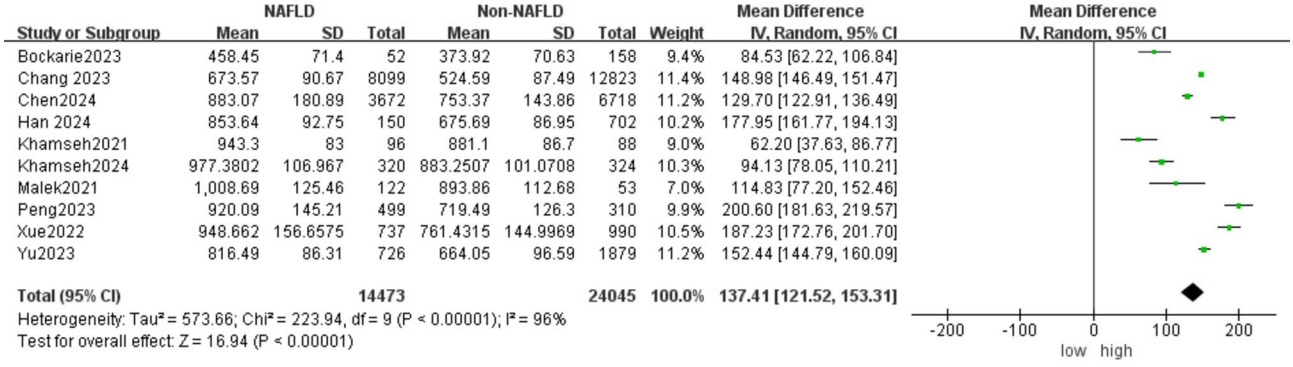

Fig. 2 Meta-analysis of studies reporting TyG-WC in NAFLD vs. non-NAFLD subjects using a random-effects model and a MD with 95% CI

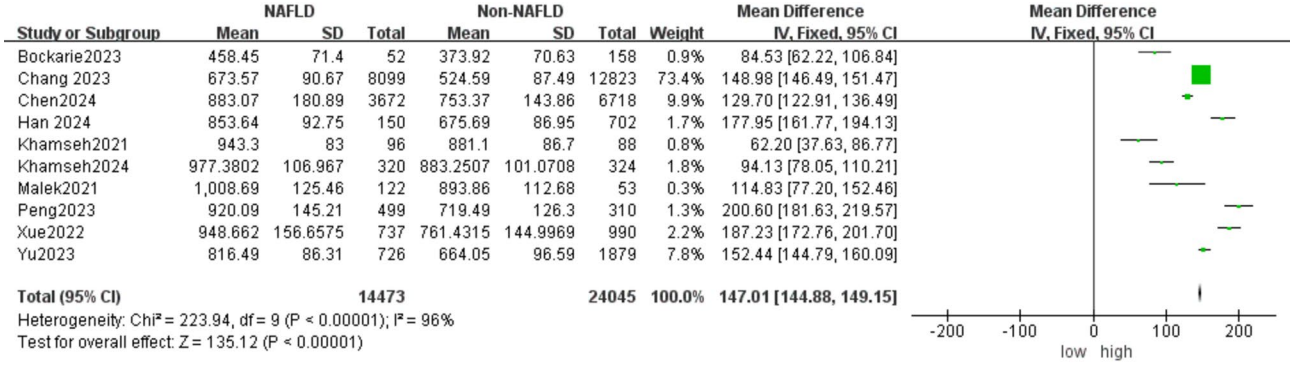

Fig. 3 Meta-analysis of studies reporting TyG-WC in NAFLD vs. non-NAFLD subjects using a fix-effects model and a MD with 95% CI

in patients with NAFLD compared with the controls (MD: 137.41, 95% CI: 121.52-153.31, $P<0.00001$). Subgroup analysis indicated that the association between the TyG-WC level and the subsequent incidence of NAFLD was not significantly affected by the factors, including participants' geographical regions, age, or BMI. Populations in non-Asian countries, primarily the United States, have higher TyG-WC levels, requiring greater attention to the risks of NAFLD and metabolic syndrome. Future research should further explore the impact of TyG-WC across different racial and socioeconomic backgrounds to develop more targeted interventions. The increased risk of NAFLD reflects the exacerbation of various health concerns, including the progression of liver disease and the occurrence of other complications. The pathogenesis of NAFLD is multifactorial, involving IR, genetic predisposition, gut dysbiosis, and dietary habits. The PNPLA3 variant has been identified as the primary genetic determinant of NAFLD, while variants in TM6SF2, MBOAT7, and GCKR also contribute significantly, albeit with moderate effect sizes [28]. Altered gut microbiota in abundance and diversity can influence NAFLD through multiple bacterial metabolites, including bile acids, butyrate, choline, amino acids, ethanol, lipopolysaccharides (LPS), and short-chain fatty acids (SCFAs) [29, 30]. Recent findings suggest that modulating these microbial interactions may help slow disease progression. Administration of prebiotics, probiotics, and synbiotics as gut microbiota therapies in NAFLD patients exerts beneficial effects on HOMA-IR and fasting insulin (FI) levels [31] and can significantly reduce BMI [32]. Meanwhile, prebiotics and probiotics demonstrate a significant overall effect on lowering TNF-α and CRP levels in NAFLD patients [33]. Notably, IR, a core factor in the pathogenesis of NAFLD [34, 35], is characterized by the reduced insulin sensitivity throughout the body, particularly in the liver and adipose tissue [36]. This reduction in insulin sensitivity impairs its ability to facilitate glucose utilization, which subsequently triggers de novo lipogenesis (DNL) and gluconeogenesis in the liver, resulting in excessive fat accumulation in the organ [24, 37]. In the development of IR, two main components of TyG-WC (TG and FPG) are associated with "glucotoxicity"and "lipotoxicity", playing pivotal roles [38, 39]. Moreover, WC is a key indicator for assessing obesity and potential atherogenic metabolic disturbances [40], is also linked to an increased risk of IR [41]. Notably, IR significantly influences the onset and progression of NAFLD by disrupting glucose and lipid metabolism, as well as promoting excessive fat accumulation in hepatocytes. This reciprocal relationship between IR and hepatocellular fat storage establishes a detrimental cycle that constantly promotes

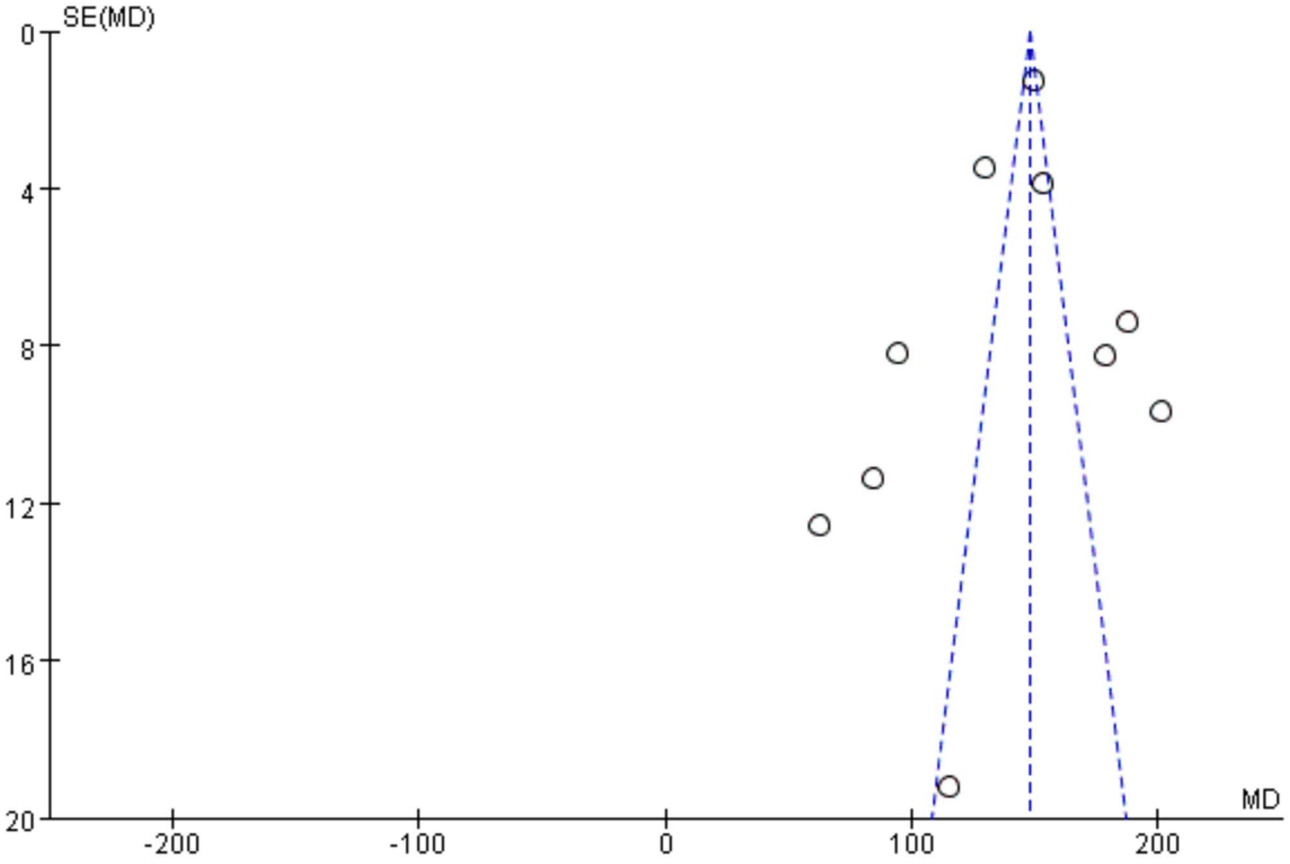

Fig. 4 Funnel plot of meta-analysis

the development and progression of NAFLD [34, 42] (Fig. 6). TyG-WC is derived by multiplying two indicators associated with the IR. Therefore, TyG-WC can be a risk factor for NAFLD. A previous meta-analysis reported a significant association between the risk of NAFLD and TyG-WC level in the Japanese population, specifically when the TyG-WC level was between 480 and 800. It was also demonstrated that TyG-WC level was not associated with the risk of NAFLD when TyG-WC level was ≤480 or ≥800 [43]. While previous studies have primarily concentrated on TyG-WC level in NAFLD, the present study distinguished between NAFLD and non-NAFLD cases, incorporating data from populations across four countries. Given the unclear relationship between TyG-WC level and the risk of NAFLD, this indicator was selected for comprehensive retrieval and discussion.

One previous Nigerian study assessed the utility of novel indices, including the TyG index, TyG-WC, TyG-BMI, and TyG-WHtR, to evaluate their efficacy as predictors of metabolic syndrome (MetS). The mentioned study found that all these indices significantly identified MetS among participants [44]. Notably, several studies have demonstrated that TyG-WC exhibits superior diagnostic performance than HOMA-IR, TyG, and TyG-BMI in diagnosing NAFLD [21, 24, 45]. The most likely explanation for this phenomenon is that BMI serves as a recognized indicator of general obesity, while WC reflects visceral fat accumulation, which is associated with IR, metabolic disorders, and hepatic steatosis [46]. Moreover, the index reflects the correlation between IR and visceral fat [45]. Visceral fat buildup plays a mediating role in obesity-induced liver fat accumulation, this mediation effect is more pronounced in overweight and obese women, accounting for 53.85% of liver fat accumulation, compared to 26.51% in men [47]. So far, there is no universally accepted TyG-WC cutoff value for clinical practice, a cutoff of 637.8369 has been reported in a Japanese population [17], while a cutoff of 790.927 has been reported in an American population [21], and further research is needed to validate these values. Additionally, studies suggested that TyG-WC indices exhibited strong relationships with all-cause mortality, cardiovascular mortality, and diabetes mortality among patients with NAFLD [19, 48–50]. Therefore, TyG-WC may serve as a predictive index capable of identifying high-risk patients, allowing for timely and appropriate interventions. This has significant clinical implications for preventing the occurrence and development of NAFLD.

The combined results remained consistent with the original findings when any study was omitted from the

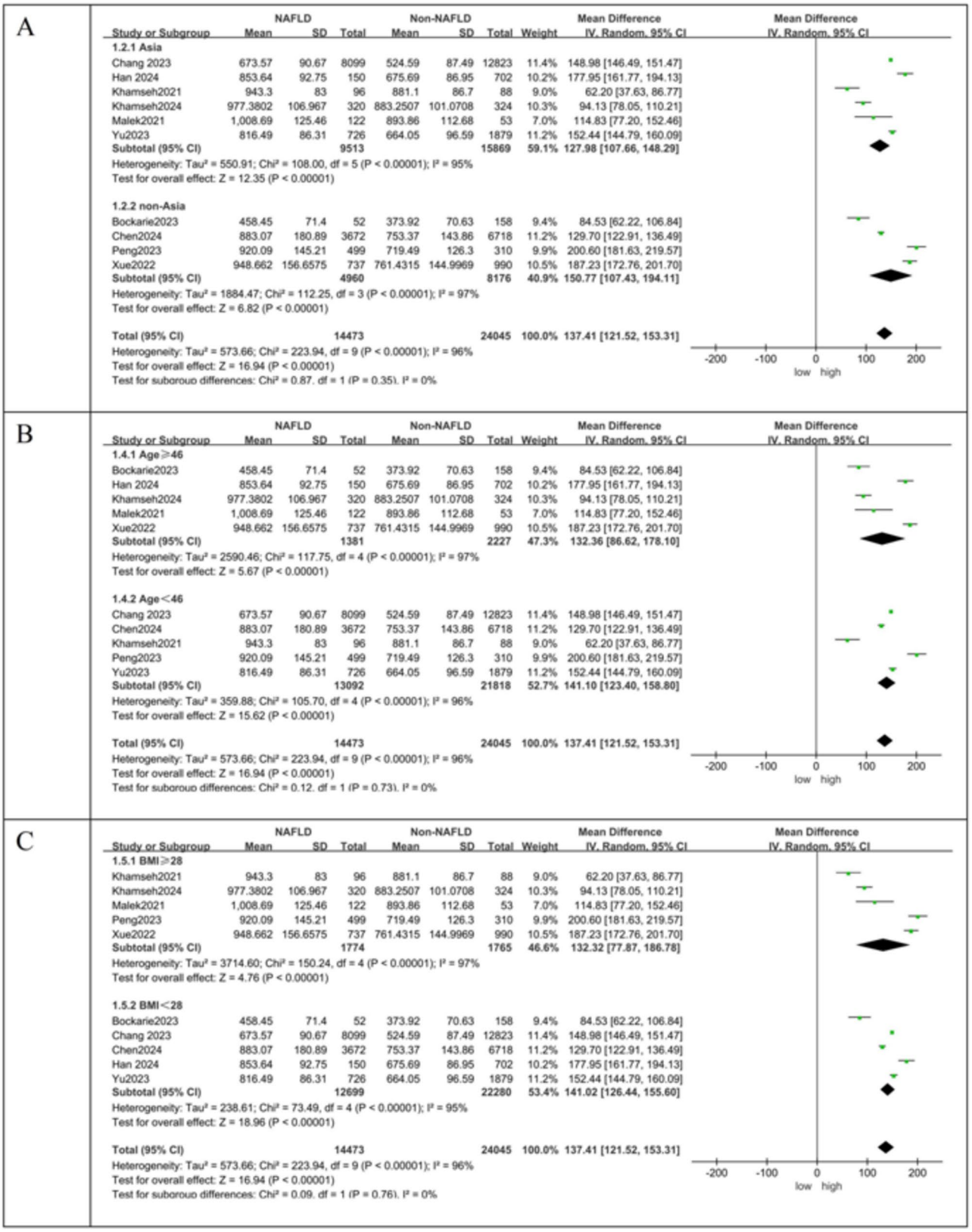

Fig. 5 Subgroup analysis of TyG-WC and risk of NAFLD. (**A**) Subgroup analysis according to Asia and non-Asia. (**B**) Subgroup analysis according to age. (**C**) Subgroup analysis according to BMI

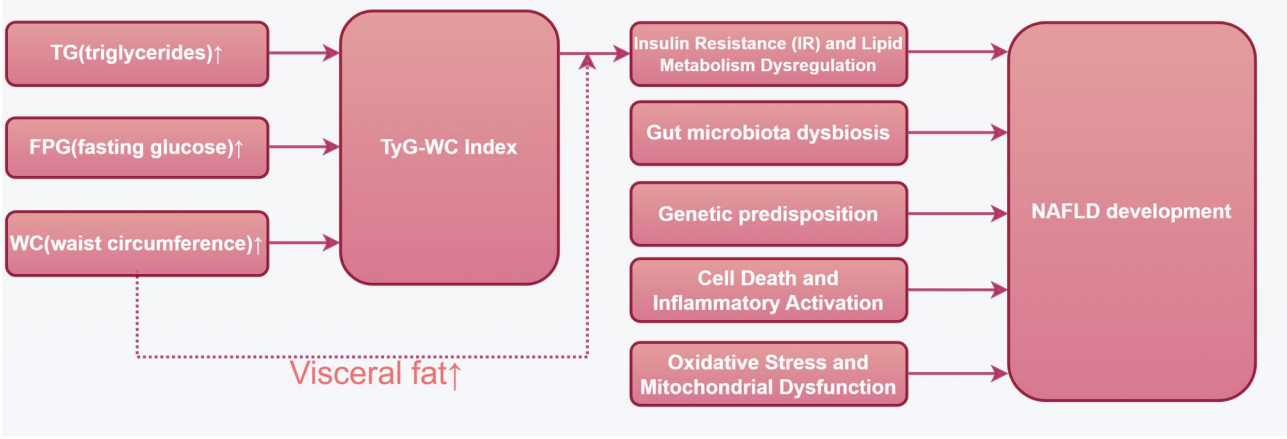

Fig. 6 TyG-WC Index in NAFLD Progression

sensitivity analysis. Similarly, the application of the fixed-effects model for analysis yielded results that were not significantly altered. Both Begg's test ($P = 0.592$) and Egger's test ($P = 0.526$) demonstrated an absence of publication bias. This study systematically synthesized research from the past five years on the association between TyG-WC and the risk of NAFLD.

Nonetheless, several limitations warrant consideration. Firstly, as the diagnosis of NAFLD was confirmed through ultrasonography rather than liver biopsy, the prevalence of NAFLD might be underestimated. Secondly, a substantial proportion of participants were predominantly recruited from three countries: Iran, China, and the United States, potentially limiting the generalizability of the findings. Although we performed univariate meta-regression analysis, residual confounding may still affect our results. In particular, the TyG-WC index in individuals with hyperglycemia or hyperlipidemia may be influenced by pharmacological interventions. Furthermore, due to the limited number of included studies, we were unable to impose restrictions on dietary habits and lifestyle factors, which may contribute to additional heterogeneity. More studies focusing on populations with different characteristics are needed in the future.

Conclusions

In conclusion, our findings demonstrate a significant difference in the TyG-WC index between individuals with NAFLD and those without. This suggests that elevated TyG-WC levels may act as a potential risk factor for NAFLD. Early identification of high-risk individuals using TyG-WC could facilitate timely recognition and intervention, emphasizing the need for close monitoring and targeted dietary modifications in those with elevated levels. Nevertheless, further research is warranted due to the limited available data on the relationship between TyG-WC, liver fibrosis, and diabetic NAFLD, as well as the absence of a definitive diagnostic cut-off for TyG-WC. These future investigations could advance our understanding of the role of TyG-WC in disease onset, progression, and management, ultimately enhancing early diagnosis, clinical decision-making, and personalized treatment strategies for NAFLD.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12876-025-03888-x.

Supplementary Material 1

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None.

Author contributions
Ziyi Xin, Lanlan Feng, Siqi Hu, and Qingwen Yu: writing—original draft/conceptualization/formal analysis/visualization, Yongmin Shi, Ting Tang and Xuhan Tong: supervision/writing—review & editingMingwei Wang and Jiake Tang: supervision/writing—review & editingYao You, Shenghui Zhang, Xingwei Zhang: writing - review & editing. All authors read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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