

REVIEW

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Diagnostic and prognostic value of triglyceride glucose index: a comprehensive evaluation of meta-analysis

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Abstract

Objective The present umbrella review aims to collate and summarize the findings from previous meta-analyses on the Triglyceride and Glucose (TyG) Index, providing insights to clinicians, researchers, and policymakers regarding the usefulness of this biomarker in various clinical settings.

Methods A comprehensive search was conducted in PubMed, Scopus, and Web of Science up to April 14, 2024, without language restrictions. The AMSTAR2 checklist assessed the methodological quality of the included meta-analyses. Statistical analyses were performed using Comprehensive Meta-Analysis (CMA) software.

Results A total of 32 studies were finally included. The results revealed significant associations between the TyG index and various health outcomes. For kidney outcomes, a high TyG index was significantly associated with an increased risk of contrast-induced nephropathy (CIN) (OR = 2.24, 95% CI: 1.82–2.77) and chronic kidney disease (CKD) (RR = 1.46, 95% CI: 1.32–1.63). High TyG index was significantly associated with an increased risk of type 2 diabetes mellitus (T2DM) (RR = 3.53, 95% CI: 2.74–4.54), gestational diabetes mellitus (GDM) (OR = 2.41, 95% CI: 1.48–3.91), and diabetic retinopathy (DR) (OR = 2.34, 95% CI: 1.31–4.19). Regarding metabolic diseases, the TyG index was significantly higher in patients with obstructive sleep apnea (OSA) (SMD = 0.86, 95% CI: 0.57–1.15), metabolic syndrome (MD = 0.83, 95% CI: 0.74–0.93), and non-alcoholic fatty liver disease (NAFLD) (OR = 2.36, 95% CI: 1.88–2.97) compared to those without these conditions. In cerebrovascular diseases, a higher TyG index was significantly associated with an increased risk of dementia (OR = 1.14, 95% CI: 1.12–1.16), cognitive impairment (OR = 2.31, 95% CI: 1.38–3.86), and ischemic stroke (OR = 1.37, 95% CI: 1.22–1.54). For cardiovascular outcomes, the TyG index showed significant associations with an increased risk of heart failure (HF) (HR = 1.21, 95% CI: 1.12–1.30), atrial fibrillation (AF) (SMD = 1.22, 95% CI: 0.57–1.87), and hypertension (HTN) (RR = 1.52, 95% CI: 1.25–1.85).

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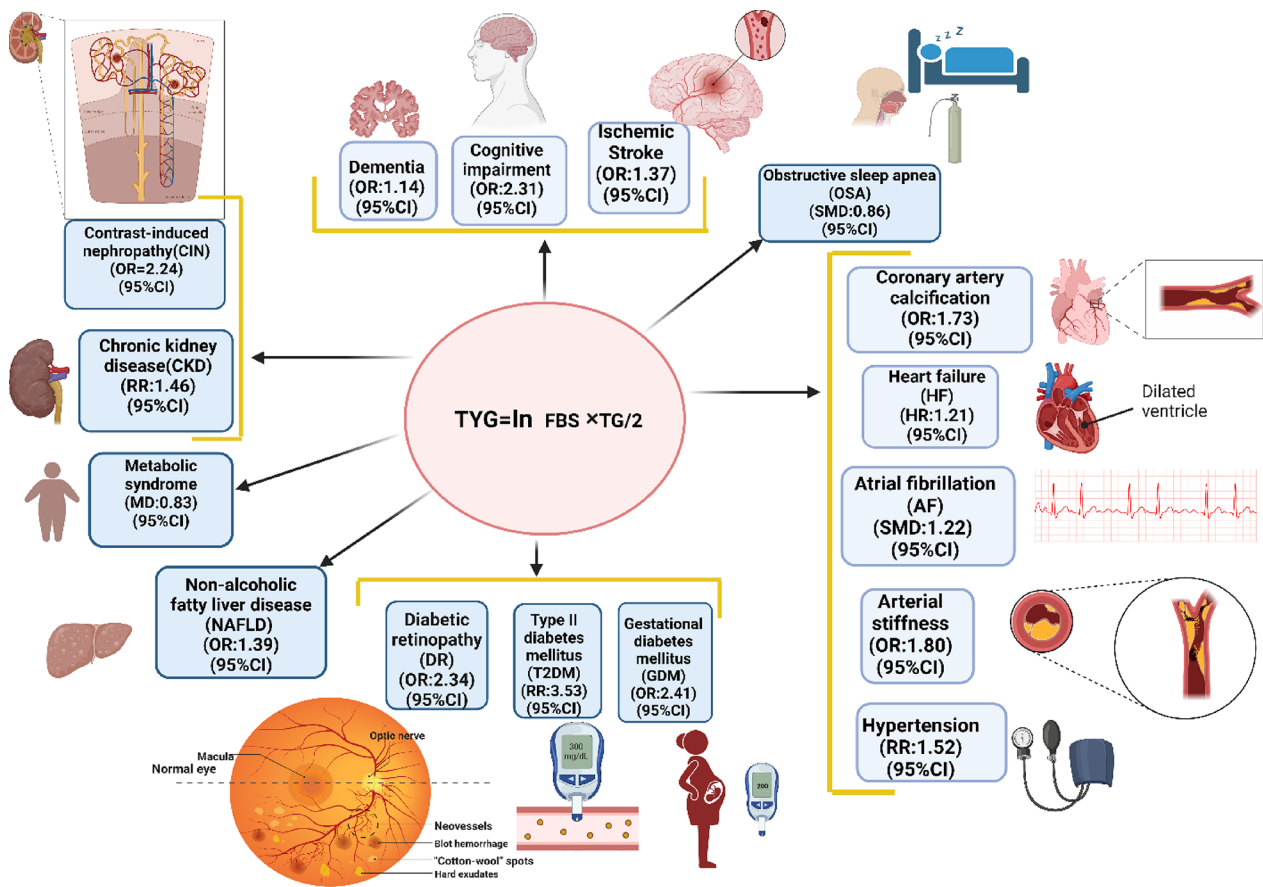
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Conclusion The TyG index is a promising biomarker for screening and predicting various medical conditions, particularly those related to insulin resistance and metabolic disorders. However, the heterogeneity and methodological quality of the included studies suggest the need for further high-quality research to confirm these findings and refine the clinical utility of the TyG index.

Graphical abstract



Keywords Triglyceride and glucose (TyG) index, TyG, Meta-analysis, Umbrella review, Cardiovascular outcomes, Insulin resistance, Clinical significance

Introduction

In the field of medical diagnostics, finding affordable yet valid biomarkers is crucial for efficient disease detection and treatment [1, 2]. One such biomarker that has gained significant attention is the Triglyceride and Glucose (TyG) Index due to its potential as a cost-effective diagnostic tool for various medical conditions [3, 4]. The TyG Index is derived from fasting triglyceride and glucose levels, and is known for its simplicity of calculation [5]. It is believed to reflect underlying insulin resistance, which is a key factor in many metabolic disorders [6].

The TyG Index holds promise as a surrogate marker for insulin resistance and metabolic dysregulation. Its calculation— natural logarithm of glucose times triglycerides

divided by 2 —renders it a practical and accessible metric in clinical settings [7, 8]. This index underscores the intricate interplay between triglyceride and glucose metabolism, offering insights into metabolic disturbances implicated in various medical conditions [9–12].

So far, numerous original studies have been undertaken to assess the diagnostic effectiveness of the TyG index across diverse medical conditions. This growing body of research has led to the publication of several meta-analyses examining the diagnostic and prognostic potential of the TyG index in conditions such as cardiovascular diseases, neurological disorders, endocrine ailments, and renal conditions [13–16].

While there has been a recent increase in the number of meta-analyses examining the diagnostic ability of the TyG index, there remains substantial heterogeneity and controversies among these studies. Moreover, the reported findings from these meta-analyses may vary in epidemiological robustness due to differences in their quality. Consequently, there is a need for a comprehensive umbrella review to consolidate the outcomes of previous meta-analyses, evaluate their quality, delineate current findings, and provide current and up-to-date evidence-based insights into this biomarker.

This umbrella review aims to collate and summarize the findings from previous meta-analyses on the TyG Index. The goal is to provide meaningful insights to clinicians, researchers, and policymakers regarding the usefulness of this biomarker in various clinical settings.

Trend of TyG index research

The results of the bibliometric analysis revealed the increasing interest and growing research focus on the TyG index. As shown in Fig. 1A, the overlay visualization indicated that among metabolic-related keywords, the TyG index is a relatively new term (shown in yellow), which is closely related to the keyword “insulin resistance”. Furthermore, the timeline analysis demonstrated that most research topics peaked after 2021, with Percutaneous coronary intervention (PCI), hypertension (HTN), and chronic kidney disease (CKD) being the most prominent trend areas (Fig. 1B).

Methods

We adhered to the Cochrane Handbook for Systematic Reviews’ guidelines in conducting our umbrella study, which is a methodical investigation encompassing several meta-analyses [17]. The PRISMA standards were utilized when reporting the findings [18]. Using the registration number CRD42024532457, the study protocol was pre-registered in PROSPERO.

Search strategy

To uncover meta-analyses exploring the diagnostic and predictive capability of the TyG index across various contexts, two researchers devised an extensive search strategy. This strategy was employed to search three sources (PubMed, Scopus, and Web of Science) until April 14, 2024. The search terms encompassed phrases such as “Triglyceride-glucose index,” “Triacylglycerol glucose index,” “Triglyceride glucose,” “Meta-Analysis,” and “Systematic Review.” Language restrictions were not imposed. Discrepancies were resolved by a third researcher when disagreements arose. EndNote X20 was utilized for the organization and management of identified studies. The specific search strategies for each database are delineated in Table S1. To ensure the accuracy of the search methodology, the assistance of two information specialists was enlisted. Furthermore, a manual review of citations from pertinent studies was conducted.

Study selection and eligibility criteria

Two researchers independently conducted the study selection process. In cases of disagreement, resolutions were reached through correspondence involving a third researcher. Meta-analyses included in the study were required to meet specific criteria: they had to assess the TyG index as an indicator for the target disease and focus on a particular underlying condition within the study population. Original research, case reports, case series, commentaries, editorials, and narrative reviews were excluded from consideration.

Quality assessment

The AMSTAR2 checklist was implemented to determine the methodological quality of the meta-analyses. Two impartial reviewers appraised each study using the 16 questions on this checklist, selecting “yes,” “no,” or “partial yes” for each item. A third researcher was consulted in order to settle any disputes. The meta-analyses were

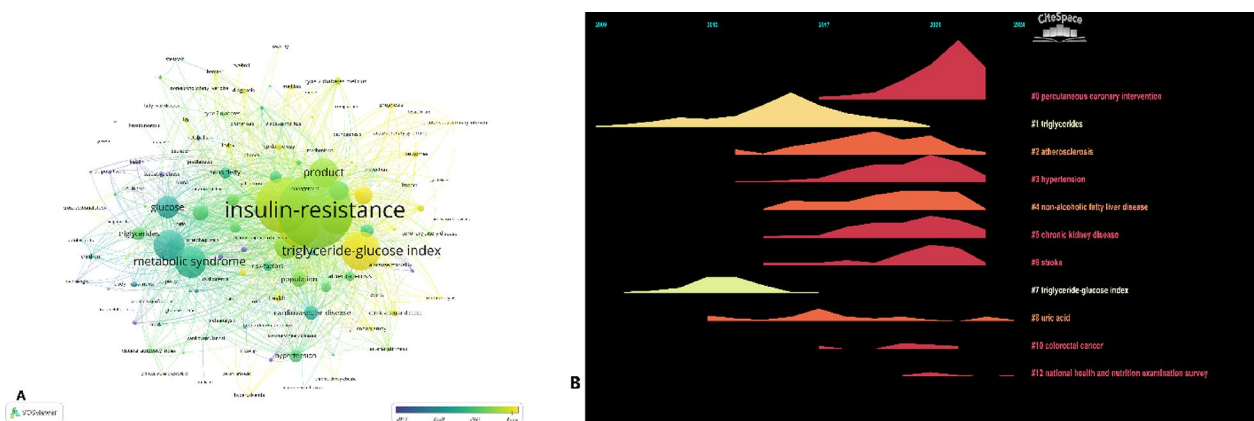


Fig. 1 Research trend of triglyceride glucose index. **A** Overlay visualization **B** Timeline visualization

subsequently separated into four groups: high-quality, moderate quality, low-quality, and critically low-quality [19].

Data extraction

The data extracted from the meta-analyses encompassed various details such as the primary author's name, publication year, journal, number of original studies included, total sample size, effect size with a 95% confidence interval of the original included studies, and the checklist utilized for assessing the original studies' quality.

To ensure the extraction comprehensiveness, the primary and the corresponding authors were contacted to address any missing information. Two researchers collaborated to gather data and consulted a third researcher to resolve any disagreements.

Statistical analyses

Comprehensive meta-analysis (CMA) software version 4 was utilized for the analysis of the current umbrella review. Furthermore, to construct summary receiver operating characteristic (SROC) charts for the TyG index across different medical conditions, STATA version 18 was employed. The results of original studies within each meta-analysis were obtained to conduct the analysis. In instances where multiple meta-analyses were available for a single outcome, original studies were identified from each meta-analysis. Following the elimination of duplicates, our meta-analysis was carried out using the results of the remaining original studies.

Between-study heterogeneity was assessed using both I^2 statistics and Cochrane's Q test. Significance in heterogeneity was determined if I^2 exceeded 50% and the P-value was found to be less than 0.1. In cases where significant heterogeneity was observed, the random effects model was applied, while in instances of non-significant heterogeneity, the fixed effects model was employed.

For every outcome, power tests were performed to check the suitability of sample sizes. Additionally, CMA software was used to establish prediction intervals (PI) for each result. The epidemiological strength of the results was evaluated using GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) assessment conducted with GRADE profiler software.

To assess publication bias, visual inspection of funnel plots was conducted, along with Egger's regression test, Begg's regression test, and trim and fill analysis [20, 21].

Results

In the first stage of the investigation, a combined total of 161 research articles were identified, sourced from PubMed (36), Scopus (73), and Web of Science (52). After removing 76 duplicate articles and reviewing the titles and abstracts of the remaining papers, 45 studies

advanced to a comprehensive evaluation of their full texts. Thirteen studies were excluded at this phase of which four were from China [12, 22–24], two were from the USA [25, 26] and one study was for each of Indonesia [27], Mexico [28], Brazil [29], Iran [30], Egypt [31], Sweden [32], and Poland [33]). Ultimately, following this thorough assessment, 32 meta-analyses met the criteria. A visual representation of the study selection process is presented in Fig. 2.

Characteristics of included studies

Table 1 provides a comprehensive summary of the 32 studies included in our meta-umbrella analysis, covering publications from 2020 to 2024 (Fig. 3A). The majority of the studies originated from China (22 articles) [13, 15, 16, 34–52] followed by Iran (4 articles) [53–56], the USA (2 articles) [57, 58], Indonesia (2 articles) [27, 59] and one each from Brazil [60] and Taiwan [61] (Fig. 3B). These studies encompassed a wide range of sample sizes, from 1,610 to a substantial 11,944,688 participants, and varied in scope, analyzing between 4 and 41 individual studies.

Included studies assessed the TyG index using the following calculation: $\text{Ln} [\text{fasting triglycerides (mg/dl)} \times \text{fasting glucose (mg/dl)} / 2]$. The outcomes of the studies included in our meta-umbrella analysis covered a diverse range of medical conditions. Four studies focused on adverse events in patients with acute coronary syndrome (ACS) [13, 35, 52, 59], while arterial stiffness was analyzed in three studies [45, 46, 57]. Hypertension (HTN) and stroke were the subjects of two [36, 44] and three studies [47–49], respectively. Non-alcoholic fatty liver disease (NAFLD) [39, 58], type 2 diabetes mellitus [27, 60], and gestational diabetes mellitus [40, 41] were each addressed in two studies. Cardiovascular diseases were examined in two other studies [34, 50]. The research scope also included single studies investigating cerebrovascular disease [37], contrast induced nephropathy (CIN) [61], diabetic retinopathy (DR) [38], heart failure (HF) [53], obstructive sleep apnea (OSA) [54], metabolic syndrome [55], atrial fibrillation (AF) [56], post percutaneous coronary intervention (PCI) major adverse cardiovascular events [42], cognitive impairment and dementia [43], and coronary artery calcification [45], ischemic stroke [15], chronic kidney disease (CKD) [16], and metabolic dysfunction-associated steatosis liver disease (MAFLD) [51].

Additionally, protocol registration details revealed that 17 studies had their protocols registered in PROSPERO [13, 34–36, 38, 39, 42, 43, 45, 46, 53–56, 59–61], one in INPLASY [15], and 14 were not registered [16, 27, 37, 40, 41, 44, 47–52, 57, 58].

In our included studies, a variety of statistical tools and review management software were employed to ensure robust data analysis. Fourteen studies utilized

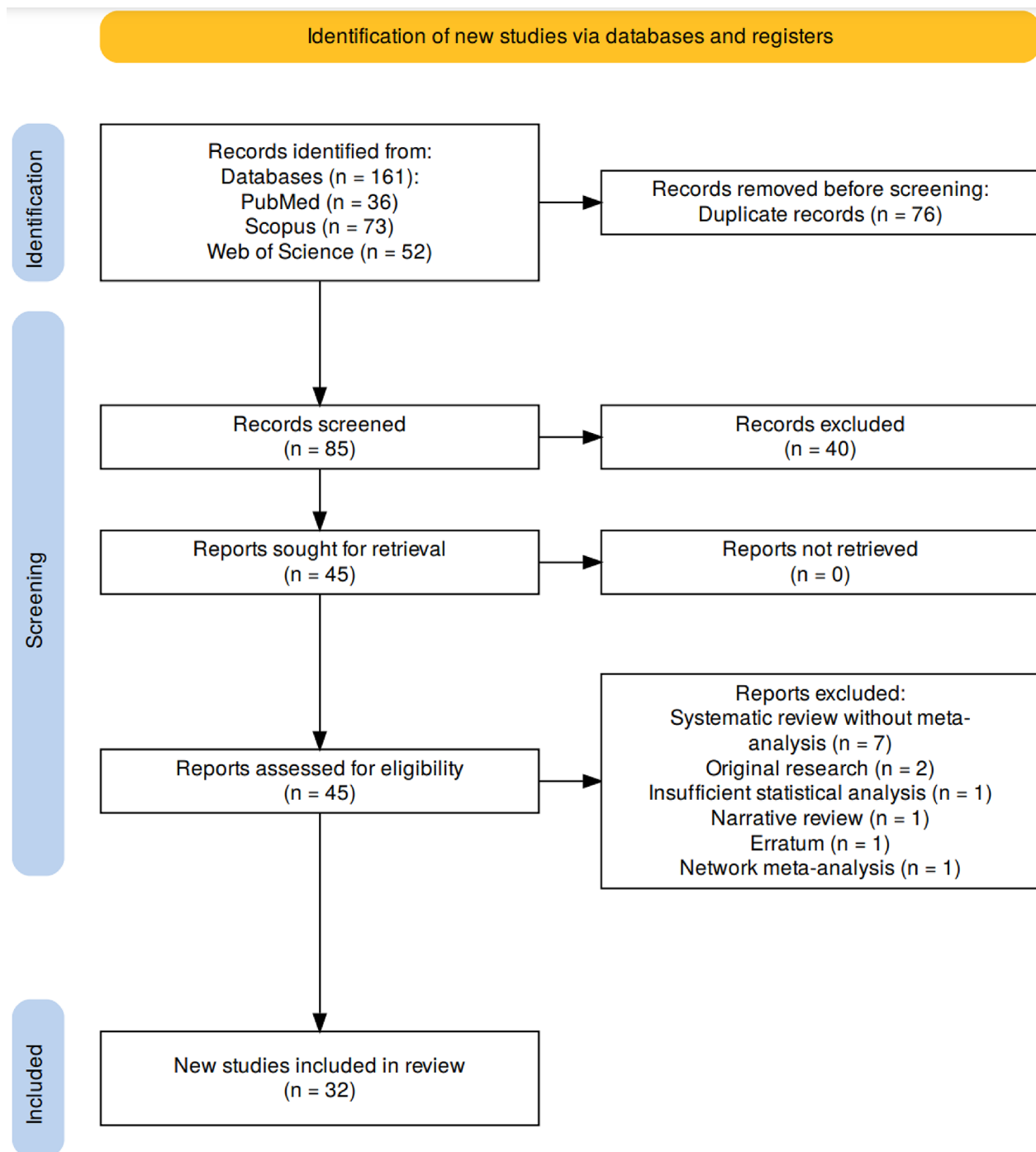


Fig. 2 Study selection process

both STATA and Revman [39–41, 43–50, 52, 55, 61], six used Revman alone [13, 34, 37, 42, 57, 60], and another five employed STATA independently [15, 16, 27, 35, 59]. Three studies chose R software [53, 54, 56] (Fig. 3C).

Quality assessments were conducted using several checklists, with the Newcastle-Ottawa Scale (NOS) being the most prevalent, used in 29 articles [13, 15, 16, 27, 34–50, 52–54, 56–60]. Other methods included the Quality

Assessment of Diagnostic Accuracy checklist (QUADS) [51, 55, 61], the Agency for Healthcare Research and Quality standards (AHQR) [15, 36, 38], and the Joanna Briggs Institute (JBI) checklist [39, 43, 45].

Search strategies varied among the studies. PubMed/Medline was the most frequently accessed database, with searches conducted in 32 studies [13, 15, 16, 27, 34–61]. EMBASE followed closely, being searched in 29 studies

Table 1 Characteristics of included studies

First author, Year of publication	Published journal	Searched databased	Date of search	Outcome	Num-ber of included studies	Total sample size	Model of analysis	Quality of assessment checklist	Registration ID	Statistical software	Publica-tion bias assessment	Country	Qual-ity as-sess-ment
Yan, 2022 [37]	Cardiovascular Diabetology	PubMed, EMBASE, Cochrane Library, Web of Science and Medline databases	From inception up to March 2022	Cerebro-vascular disease	29	11,944,688	Random-effects model	NOS	NR	Revman	Visual inspection of funnel plots, Egger's test, and trim-and-fill test	China	Criti-cally low
Chang, 2023 [61]	Frontiers in Endocrinology	Medline, Cochrane, and Embase	From inception up to August 3, 2023	Contrast induced nephropathy	5	3,518	NR	QUADAS-2	PROSPERO (CRD42023452257)	STATA and Revman	Deeks'funnel plot asymmetry test	Taiwan	Low
Sajideya, 2022 [57]	Current Problems in Cardiology	PubMed, Em-base, and Web of Science databases	From inception up to April 30, 2022	Arterial Stiffness	9	37,780	Random-effects model	NOS	NR	Revman	NA (not assessed)	USA	Criti-cally low
Zhou, 2023 [38]	Frontiers in Endocrinology	PubMed, Embase, Web of Science, and China National Knowledge Infrastructure (CNKI)	From inception up to June 2023	Diabetic Retinopathy	10	13,716	Random-effects model for hetero-genic and fixed effect model for homogenic results	NOS and AHRQ	PROSPERO (CRD42023432747)	STATA, R, and Revman	Visual inspection of funnel plots, cut-and-fill methods and Egger's regres-sion test	China	High
Khalaj, 2023 [53]	Cardiovascular Diabetology	PubMed, Em-base, Scopus, and Web of Science	From inception up to June 16, 2023	Heart failure	30	772,809	Random-effects model	NOS	PROSPERO (CRD42023437470)	R	NA	Iran	High
Beran, 2022 [58]	Journal of Clinical Medicine	PubMed, Em-base, and Web of Science	From inception up to 25 March 2022	Non-alco-holic fatty liver disease	17	121,975	Random-effects model	NOS	NR	Review Manager and Com-prehensive Meta-Anal-ysis	NA	USA	High
Ling, 2023 [39]	Frontiers in Endocrinology	Cochrane Li-brary, PubMed, and Embase	From inception up to July 18, 2022	Non-alco-holic fatty liver disease	12	105,365	Random-effects model	JBI and NOS	PROSPERO (CRD42022347813)	STATA and Revman	Visual inspection of funnel plots, Egger's test, and Begg's test	China	Mod-erate

Table 1 (continued)

First author, Year of publication	Published journal	Searched databases	Date of search	Outcome	Number of included studies	Total sample size	Model of analysis	Quality of assessment checklist	Registration ID	Statistical software	Publication bias assessment	Country	Quality assessment
Behnoush, 2024 [54]	Lipids in Health and Disease	PubMed, Scopus, the Web of Science, and Embase	From inception up to September 6, 2023	Obstructive sleep apnea	10	16,726	Random-effects model	NOS	PROSPERO (CRD42023460518)	R	Visual inspection of funnel plots, Egger's test, and Begg's test	Iran	Low
Pranata, 2021 [27]	Endocrine	PubMed, Scopus, and Embase	From inception up to February 9, 2021	Type 2 diabetes mellitus	14	270,229	Random-effects model	NOS	NR	STATA	Visual inspection of funnel plots, Egger's test and trim and fill analysis	Indonesia	High
Silva, 2020 [60]	Primary Care Diabetes	PubMed, Cochrane, Scopus, and Lilacs	From inception up to October 1, 2019.	Type 2 diabetes mellitus	13	70,380	Random-effects model	NOS	PROSPERO (CRD42018114496)	Revman	Visual inspection of funnel plots	Brazil	Moderate
Nabipourashrafi, 2022 [55]	Nutrition, Metabolism & Cardiovascular Diseases	PubMed, Scopus, and Web of Science	From inception up to February 2022	Metabolic syndrome	13	49,325	Random-effects model for heterogenic and fixed effect model for homogenic results	QUADAS-2	PROSPERO (CRD42022316209)	STATA and Revman	Visual inspection of funnel plots, Egger's test and Deeks'funnel plot asymmetry test	Iran	Low
Song, 2022 [40]	Gynecological Endocrinology	PubMed, Embase, China National Knowledge Infrastructure, and Wan Fang	From inception up to January 16, 2021	Gestational Diabetes mellitus	5	382,213	Random-effects model	NOS	NR	STATA and Revman	Visual inspection of funnel plots, and Egger's test	China	High
Liu, 2021 [41]	Endocrine Connections	PubMed, Web of Science, Cochrane Library, and Embase	From inception up to March 1, 2021	Gestational Diabetes mellitus	4	1,610	Random-effects model	NOS	NR	STATA and Revman	Visual inspection of funnel plots, and Egger's test	China	High

Table 1 (continued)

First author, Year of publication	Published journal	Searched databases	Date of search	Outcome	Number of included studies	Total sample size	Model of analysis	Quality of assessment checklist	Registration ID	Statistical software	Publication bias assessment	Country	Quality assessment
Azarboo, 2024 [56]	European Journal of Medical Research	PubMed, Embase, Scopus, and Web of Science	From inception up to September 2023	Atrial fibrillation	9	6,171	Random-effects model	NOS	PROSPERO (CRD42023456875)	R	Visual inspection of funnel plots, Egger's test and trim and fill analysis	Iran	Low
Sun, 2024 [42]	ESC Heart Failure	Embase, PubMed, Cochrane Library, and Web of Science	From inception up to March 3, 2023	Post percutaneous coronary intervention major adverse cardiovascular events	9	10,164	Random-effects model	NOS	PROSPERO (CRD42023387411)	Revman	NA	China	Low
Wang, 2023 [43]	Frontiers in Aging Neuroscience	PubMed, Cochrane Library, and Embase	From inception up to February 2023	Cognitive impairment and dementia	10	8,443,279	Random-effects model	JBI and NOS	PROSPERO (CRD42023388028)	STATA and Revman	NA	China	High
Wang, 2021 [44]	Frontiers in Cardiovascular Medicine	PubMed, Embase, Web of Science, Wan fang data, and Chinese National Knowledge Infrastructure	From inception up to March 10, 2021	Hypertension	8	200,044	Random-effects model	NOS	NR	STATA and Revman	Visual inspection of funnel plots, Egger's test, and Begg's test	China	High
Liu, 2023 [45]	Cardiovascular Diabetology	Embase, Cochrane Library, and PubMed	From inception up to September 9, 2022	Arterial stiffness and coronary artery calcification	26	87,307	Random-effects model	JBI and NOS	PROSPERO (CRD42022360981)	STATA and Revman	Visual inspection of funnel plots, Egger's test, and Begg's test	China	High
Zhong, 2023 [46]	Medicine	PubMed, Embase, and Scopus	From inception up to July 31, 2022	Arterial stiffness	13	48,332	Random-effects model	NOS	PROSPERO (CRD42022330963)	STATA and Revman	Visual inspection of funnel plots, and Egger's test	China	Low

Table 1 (continued)

First author, Year of publication	Published journal	Searched databased	Date of search	Outcome	Number of included studies	Total sample size	Model of analysis	Quality of assessment checklist	Registration ID	Statistical software	Publication bias assessment	Country	Quality assessment
Yang, 2023 [15]	Cardiovascular Diabetology	Cochrane, Embase, Medline, Web of Science, PubMed	From inception up to April 4, 2022	Ischemic stroke	18	592,635	Random-effects model	NOS and AHRQ	INPLASY (INPLASY2022110145)	STATA	Visual inspection of funnel plots, clip-and-complement method, Egger's test, and Begg's test	China	Low
Liao, 2022 [47]	Frontiers in Neurology	PubMed, Cochrane Library, and Embase	From inception up to December 16, 2021	Stroke	8	5,804,215	Random-effects model	NOS	NR	STATA and Revman	Visual inspection of funnel plots	China	High
Feng, 2022 [48]	Hormone and Metabolic Research	PubMed, Embase, Cochrane Library and Web of science.	From inception up to October 26, 2021	Stroke	11	5,721,077	Random effects model for heterogenic and fixed effect model for homogenic results	NOS	NR	STATA and Revman	Egger's test, and Begg's test	China	High
Ma, 2022 [49]	Hormone and Metabolic Research	PubMed, Embase, Web of Science, Wan fang, and China National Knowledge Infrastructure	From the inception up to February 20, 2022	Stroke	6	34,076	Random-effects model	NOS	NR	STATA and Revman	Visual inspection of funnel plots and Egger's test	China	High
Ding, 2021 [50]	Cardiovascular Diabetology	PubMed and Embase	From the inception up to January 5, 2021	Cardiovascular diseases	8	5,731,294	Random-effects model	NOS	NR	STATA and Revman	Visual inspection of funnel plots and Egger's test	China	Low

Table 1 (continued)

First author, Year of publication	Published Journal	Searched databases	Date of search	Outcome	Number of included studies	Total sample size	Model of analysis	Quality of assessment checklist	Registration ID	Statistical software	Publication bias assessment	Country	Quality assessment
Liang, 2023 [13]	Cardiovascular Diabetology	PubMed, Embase, The Cochrane Library, and Web of Science	From the inception up to May 1, 2023	Adverse events in patients with acute coronary syndrome	41	65,974	Random effects model for heterogenic and fixed effect model for homogenic results	NOS	PROSPERO (CRD42023422917)	Revman	Visual inspection of funnel plots	China	Low
Ren, 2023 [16]	Nutrition, Metabolism and Cardiovascular Diseases	PubMed and Web of Science	From inception to March 2023	Chronic kidney diseases	13	80,777	NR	NOS	NR	STATA	Egger's test, and Begg's test	China	Critically low
Wang, 2022 [51]	Nutrients	PubMed, Medline, Web of Science, Embase and the Cochrane Library	From inception to April 23, 2022	Metabolic dysfunction associated steatotic liver disease	20	165,725	Random effects model	QUADAS-2	NR	Meta-Disc and STATA	Deeks'funnel plot asymmetry test	China	High
Li, 2021 [52]	Hormone and Metabolic Research	PubMed, Embase, and Web of Science	From inception to January 18, 2021	Adverse events in patients with acute coronary syndrome	8	19,611	Random effects model	NOS	NR	STATA and Revman	Visual inspection of funnel plots and Egger's test	China	High
Akbar, 2021 [59]	Nutrition, Metabolism and Cardiovascular Diseases	PubMed, Scopus, and Embase	From inception up to February 7, 2021	Adverse events in patients with acute coronary syndrome	4	13,684	Random effects model	NOS	PROSPERO (CRD42021235765)	STATA	Funnel plots and Egger's test	Indonesia	High
Xu, 2023 [36]	Frontiers in Cardiovascular Medicine	CNKI, VIP, Wan Fang, CBM, PubMed, Embase, Web of Science, and Cochrane Library	From inception up to May 10, 2023	Hypertension	22	668,486	Random effects model for heterogenic and fixed effect model for homogenic results	AHRQ and NOS	PROSPERO (CRD42023425836)	STATA and R	Visual inspection of funnel plots, Egger's test, Begg's test and trim and fill methods	China	Low

Table 1 (continued)

First author, Year of publication	Published journal	Searched databased	Date of search	Outcome	Num-ber of included studies	Total sample size	Model of analysis	Quality of assess-ment checklist	Registration ID	Statistical software	Publica-tion bias assessment	Country	Qual-ity as-sess-ment
Luo, 2021 [35]	Frontiers in Cardiovascular Medicine	Scopus, PubMed, Em-base, and Web of Science	From in-ception up to October 5, 2021	Adverse events in patients with acute coronary syndrome	12	28,795	Random effects model	NOS	PROSPERO (CRD42021228521)	STATA	Egger's test, and Begg's test	China	Low
Liu, 2022 [34]	Cardiovascular Diabetology	PubMed, Co-chrane Library and Embase	From incep-tion to April 16, 2022	Cardio-vascular diseases	12	6,354,990	Random effects model	NOS	PROSPERO (CRD42022296235)	Revman	Visual inspection of funnel plots	China	Low

AHOR: Agency for Healthcare Research and Quality, JBI: Joanna Briggs Institute, NA: Not assessed, NOS: Newcastle-Ottawa scale Studies, NR: Not reported, QUADS: Quality Assessment of Diagnostic Accuracy

[13, 15, 27, 34–54, 56–59, 61]. The Cochrane Library was utilized in 15 studies [13, 15, 34, 36, 37, 39, 41–43, 45, 47, 48, 51, 60, 61], while Web of Science was searched in 20 studies [13, 15, 16, 35–38, 41, 42, 44, 48, 49, 51–58]. Scopus was used for literature searches in 9 studies [27, 35, 46, 53–56, 59, 60], and more region-specific databases like China National Knowledge Infrastructure (CNKI) [36, 38, 40, 44, 49] and Wan Fang [36, 40, 44, 49] were searched in 5 and 4 studies, respectively. Less commonly, Lilacs [60], VIP [36], and CBM [36] were each searched in one study.

Quality assessment

Among the included studies, 15 were assessed as high quality [27, 38, 40, 41, 43–45, 47–49, 51–53, 58, 59], two were of moderate quality [39, 60], and 12 were determined to have low quality [13, 15, 34–36, 42, 46, 50, 54–56, 61]. Furthermore, the AMSTAR2 evaluation determined that three of the meta-analyses had critically low methodological quality [16, 37, 57] (Table 1; Fig. 4).

Results of meta-analysis

TyG index and kidney outcomes

The correlation between TyG index and CIN A total of five studies, comprising a combined sample size of 3518 individuals, investigated the relationship between the TyG index and CIN following coronary interventions (Table 2). The analysis revealed that a high TyG index was significantly associated with CIN (OR=2.24, 95%CI:1.82–2.77, $P<0.01$) (Fig. 5A). The studies demonstrated low heterogeneity ($I^2 = 35.42\%$, $P=0.18$), and no significant publication bias was detected based on Egger’s and Begg’s tests ($P=0.33$ and $P=0.80$, respectively). Additionally, the trim and fill analysis, which included two imputed studies, adjusted the OR to 2.13 (95% CI: 1.70–2.67) (Fig. 5B). The results of the sensitivity analysis indicated that the total effect size remained stable and did not show any significant change after the sequential deletion of each study (Fig. 5C). Moreover, the prediction interval for the relationship between TyG and CIN ranged from 1.29 to 3.92(Fig. 5D). The results of the power analysis indicated high statistical power ($1-\beta=1$), suggesting the sample size was adequate (Fig. 5E). The epidemiological strength of the association between TyG and CIN was low based on the GRADE criteria (Table 3).

The correlation between TyG index and CKD A total of 13 studies, comprising a combined sample size of 70,279 individuals, investigated the relationship between the TyG index and CKD (Table 2). The analysis revealed that a high TyG index was significantly associated with CKD (RR=1.46, 95%CI: 1.32–1.63, $P<0.01$) (Fig. 6A). The studies demonstrated moderate heterogeneity ($I^2 = 50.44\%$,

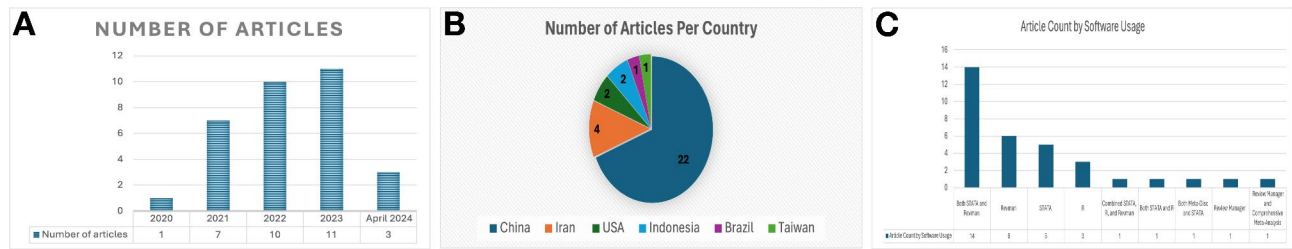


Fig. 3 Summary of study characteristics. **A** Distribution of studies by country: Annual publication trends of articles. **C** Usage of statistical software and analysis tools across the studies

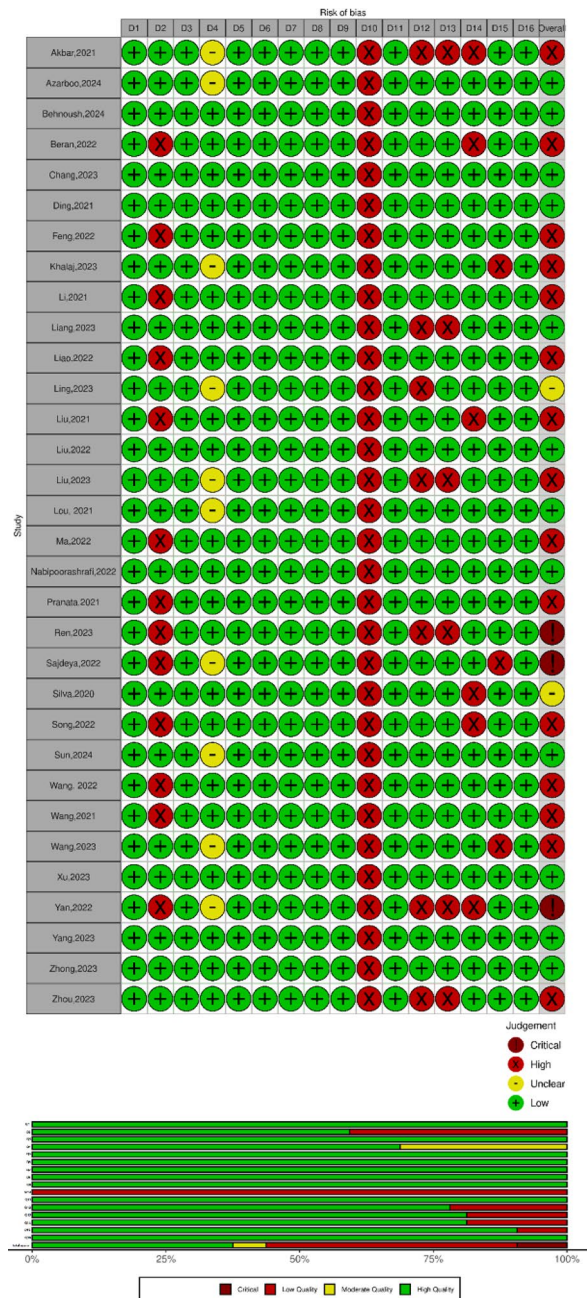


Fig. 4 Quality assessment of included studies based on AMSTAR 2 appraisal tool

$P=0.01$), and significant publication bias was detected based on Egger’s and Begg’s tests ($P<0.01$). Additionally, the trim and fill analysis, which included six imputed studies, adjusted the RR to 1.37 (95% CI: 1.24–1.53) (Fig. 6B). The results of the sensitivity analysis indicated that the total effect size remained stable and did not show any significant change after the sequential deletion of each study (Fig. 6C). Moreover, the prediction interval for the relationship between TyG and CKD ranged from 1.06 to 2.03 (Fig. 6D). The calculation of power analysis was not possible because the results were reported as relative risk. The epidemiological strength of the association between TyG index and CKD was very low based on GRADE criteria (Table 3).

TyG index and diabetes mellitus

The correlation between TyG index and T2DM Among the included studies assessing the relationship between the TyG index and T2DM, two statistical measures were reported: risk ratio (RR) and hazard ratio (HR) (Table 2). The TyG index was significantly associated with T2DM when reported as a risk ratio (RR=3.53, 95% CI: 2.74–4.54, $P<0.01$) (Fig. 7A). This association was accompanied by significant heterogeneity ($I^2 = 83.70\%$, $P<0.01$). No significant publication bias was found based on Egger’s regression test ($P=0.79$) and Begg’s regression test ($P=0.19$). The results of the trim-and-fill analysis with five imputed studies yielded an RR of 2.93 (95% CI: 2.25–3.82) (Fig. 7B). The sensitivity analysis results indicate that the total effect size remained stable, showing no significant change after sequentially deleting each study (Fig. 7C). The prediction interval was 1.36–9.16 (Fig. 7D). The calculation of power analysis was not possible because the results were reported as relative risks.

The association between the TyG index and T2DM was significant when calculated as a hazard ratio (HR=2.60, 95% CI: 2.19–3.09, $P<0.01$) (Fig. 8A). Significant heterogeneity was observed ($I^2 = 79.05\%$, $P<0.01$). Although the Eggers regression test showed significant publication bias ($P<0.01$), no significant publication bias was found based on the Begg’s regression test ($P=0.06$). The results of the Trim and Fill analysis with 8 studies yielded an HR

Table 2 Results of the meta-analyses of the correlation between TyG index and various health outcomes

Variable	Effect size	Prediction interval	Heterogeneity	Egger's regression test P value	Begg's regression test P value	Number of imputes studies in trim and fill analysis	Trim and Fill analysis	Power analysis
CIN	OR = 2.24, 95% CI: 1.82–2.77, $P < 0.01$	1.29–3.92	35.42%, $P = 0.18$	0.33	0.80	2	OR = 2.13, 95% CI: 1.70–2.67	1-b = 1
Diabetic Retinopathy	OR = 2.34, 95% CI: 1.31–4.19, $P < 0.01$	0.31–1.782	89.70%, $P < 0.01$	$P < 0.01$	$P < 0.01$	2	OR = 1.79, 95% CI: 1.06–3.03	1-b = 1
Continuous	OR = 1.48, 95% CI: 1.11–1.97, $P < 0.01$	0.59–3.72	83.46%, $P < 0.01$	0.01	0.25	2	OR = 1.33, 95% CI: 1.03–1.71	1-b = 1
Obstructive sleep apnea	SMD = 0.86, 95% CI: 0.57–1.15, $P < 0.01$	-1.89–3.61	36.74%, $P = 0.20$	0.36	0.29	0	0.86, 95% CI: 0.57–1.15	1-b = 1
Gestational diabetes mellitus	OR = 2.41, 95% CI: 1.48–3.91, $P < 0.01$	0.61–9.47	59.48%, $P = 0.03$	0.15	0.13	2	OR = 1.83, 95% CI: 1.11–3.01	1-b = 1
Metabolic syndrome	MD = 0.83, 95% CI: 0.74–0.93, $P < 0.01$	0.47–1.20	98.18%, $P < 0.01$	0.43	0.76	0	MD = 0.83, 95% CI: 0.74–0.93	1-b = 1
Nonalcoholic fatty liver disease	OR = 6.00, 95% CI: 4.12–8.74, $P < 0.01$	1.64–21.98	91.80%, $P < 0.01$	0.89	0.75	0	OR = 6.00, 95% CI: 4.12–8.73	1-b = 1
Chronic kidney disease	OR = 2.36, 95% CI: 1.88–2.97, $P < 0.01$	0.99–5.68	98.13%, $P < 0.01$	0 < 0.01	0.24	0	OR = 2.36, 95% CI: 1.88–2.97	1-b = 1
Type 2 diabetes mellitus	RR = 1.46, 95% CI: 1.32–1.63, $P < 0.01$	1.06–2.03	50.44%, $P = 0.01$	0 < 0.01	0 < 0.01	6	RR = 1.37, 95% CI: 1.24–1.53	–
Hazard ratio	RR = 3.53, 95% CI: 2.74–4.54, $P < 0.01$	1.36–9.16	83.70%, $P < 0.01$	0.79	0.19	5	RR = 2.93, 95% CI: 2.25–3.82	–
Dementia	HR = 2.60, 95% CI: 2.19–3.09, $P < 0.01$	1.33–5.12	79.05%, $P < 0.01$	0 < 0.01	0.067	8	2.09, 95% CI: 1.77–2.46	–
Cognitive impairment	OR = 1.14, 95% CI: 1.12–1.16, $P < 0.01$	LN	0.00%, $P = 0.32$	LN	LN	LN	LN	1-b = 1
Ischemic stroke	OR = 1.37, 95% CI: 1.03–1.82, $P = 0.03$	LN	0.00%, $P = 0.77$	LN	LN	LN	LN	1-b = 1
Ischemic stroke association	OR = 2.31, 95% CI: 1.38–3.86, $P < 0.01$	0.37–14.26	84.75%, $P < 0.01$	< 0.01	0.46	2	OR = 1.67, 95% CI: 1.05–2.64	1-b = 1
Ischemic stroke recurrence	OR = 3.38, 95% CI: 1.67–6.83, $P < 0.01$	0.16–72.58	81.56%, $P < 0.01$	0.84	0.73	0	OR = 3.38, 95% CI: 1.67–6.83	1-b = 1
Ischemic stroke poor functional outcomes	OR = 1.50, 95% CI: 1.19–1.89, $P < 0.01$	0.75–2.99	74.18%, $P < 0.01$	0.04	0.90	1	OR = 1.35, 95% CI: 1.20–1.52	1-b = 1
Ischemic stroke mortality	OR = 1.36, 95% CI: 1.10–1.69, $P < 0.01$	0.74–2.54	56.22%, $P = 0.05$	0.02	0.08	2	OR = 1.33, 95% CI: 1.04–1.70	1-b = 1
Ischemic stroke neurological worsening	OR = 1.40, 95% CI: 1.14–1.71, $P < 0.01$	0.76–2.57	71.40%, $P < 0.01$	< 0.01	0.02	2	OR = 1.25, 95% CI: 1.01–1.54	1-b = 1
Ischemic stroke neurological worsening	OR = 1.33, 95% CI: 1.09–1.63, $P < 0.01$	LN	70.70%, $P < 0.01$	0.19	0.70	0	OR = 1.40, 95% CI: 1.14–1.71	1-b = 1
Ischemic stroke neurological worsening	OR = 1.33, 95% CI: 1.09–1.63, $P < 0.01$	LN	76.57%, $P = 0.03$	LN	LN	LN	LN	1-b = 0.99

Table 2 (continued)

Variable	Effect size	Prediction interval	Heterogeneity	Egger's regression test P value	Begg's regression test P value	Number of imputes in trim and fill analysis	Trim and Fill analysis	Power analysis
Heart Failure	Categorical HR = 1.21, 95% CI: 1.12–1.30, $P < 0.01$	1.04–1.41	21.43%, $P = 0.26$	0.29	0.76	1	HR = 1.19, 95% CI: 1.08–1.31	–
Continues	HR = 1.16, 95% CI: 1.11–1.21, $P < 0.01$	0.86–1.57	0.64%, $P = 0.36$	0.40	1	1	HR = 1.15, 95% CI: 1.09–1.21	–
Atrial fibrillation	SMD: 1.22, 95% CI: 0.57–1.87, $P < 0.01$	-1.18–3.63	98.04%, $P < 0.01$	0.64	1	0	SMD: 1.22, 95% CI: 0.57–1.87	1-b=1
Hypertension	RR = 1.52, 95% CI: 1.25–1.85, $P < 0.01$	0.78–2.98	85.67%, $P < 0.01$	<0.01	0.28	1	RR = 1.44, 95% CI: 1.20–1.74	–
Atrial stiffness	Categorical OR = 1.80, 95% CI: 1.53–2.10, $P < 0.01$	1.07–3.03	66.26%, $P < 0.01$	0.35	0.20	0	OR = 1.80, 95% CI: 1.53–2.10	1-b=1
Continuous	OR = 1.50, 95% CI: 1.34–1.69, $P < 0.01$	1.03–2.21	81.66%, $P < 0.01$	0.10	0.16	4	OR = 1.39, 95% CI: 1.23–1.56	1-b=1
Coronary artery calcification	Continuous OR = 1.73, 95% CI: 1.36–2.20, $P < 0.01$	0.84–3.59	50.81%, $P = 0.08$	0.08	0.22	0	OR = 1.73, 95% CI: 1.36–2.20	1-b=1
Categorical	OR = 1.65, 95% CI: 1.50–1.82, $P < 0.01$	1.51–1.83	0.00%, $P = 0.72$	0.21	1	0	OR = 1.65, 95% CI: 1.50–1.82	1-b=1
Post percutaneous coronary intervention events	Categorical HR = 2.03, 95% CI: 1.64–2.51, $P < 0.01$	1.01–4.11	77.09%, $P < 0.01$	0.05	0.25	0	HR = 2.03, 95% CI: 1.64–2.51	–
Continuous	HR = 1.81, 95% CI: 1.34–2.46, $P < 0.01$	0.58–5.75	91.72%, $P < 0.01$	0.02	0.02	0	HR = 1.81, 95% CI: 1.34–2.46	–
Post-PCI all-cause mortality	Categorical HR = 1.92, 95% CI: 1.35–2.74, $P < 0.01$	0.01–16638.72	50.91%, $P = 0.13$	0.15	1	2	HR = 2.18, 95% CI: 0.97–4.87	–
Continuous	HR = 0.94, 95% CI: 0.28–3.12, $P = 0.92$	0.01–975086.18	73.95%, $P = 0.02$	0.09	1	0	HR = 0.94, 95% CI: 0.28–3.12	–
Post-PCI revascularization	Categorical HR = 2.61, 95% CI: 1.46–4.65, $P < 0.01$	0.01–2851.01	83.56%, $P < 0.01$	0.58	1	0	HR = 2.61, 95% CI: 1.46–4.65	–
Continuous	HR = 2.05, 95% CI: 1.20–3.50, $P < 0.01$	0.01–1552.36	89.78%, $P < 0.01$	0.20	1	0	HR = 2.05, 95% CI: 1.20–3.50	–
Post-PCI non-fatal MI	Categorical HR = 2.02, 95% CI: 1.31–3.10, $P < 0.01$	1.32–3.10	00.00%, $P = 0.96$	0.57	0.29	0	HR = 2.02, 95% CI: 1.31–3.10	–
Continuous	HR = 2.56, 95% CI: 1.49–4.400, $P < 0.01$	0.01–1013.95	63.41%, $P = 0.06$	0.12	1	0	HR = 2.56, 95% CI: 1.49–4.400	–

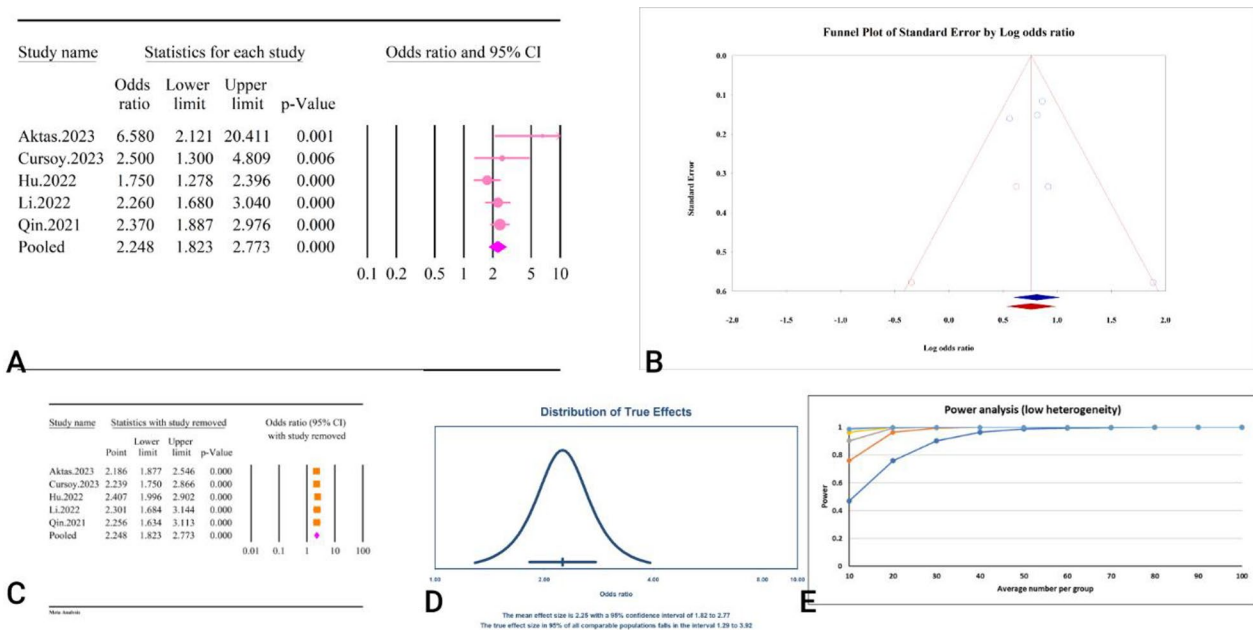


Fig. 5 The association between TyG index and CIN. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval **E** Power analysis

of 2.09, with a 95% CI of 1.77–2.46 (Fig. 8B). Sensitivity analyses showed no effect of each study on the pooled effect (Fig. 8C). The result of the prediction interval was 1.33–5.12 (Fig. 8D). The epidemiological strength of the association between TyG index and T2DM was low based on GRADE criteria (Table 3).

The correlation between TyG index and GDM A total of 6 studies, comprising a combined sample size of 18,038 individuals, investigated the relationship between the TyG index and GDM (Table 2). The analysis revealed that a high TyG index was significantly associated with GDM (OR=2.41, 95% CI: 1.48–3.91, $P<0.01$) (Fig. 9A). These studies demonstrated high heterogeneity (59.48%, $P=0.03$), with no significant publication bias detected based on Egger’s and Begg’s tests ($P=0.15$ and $P=0.13$, respectively). Additionally, the trim and fill analysis, which included two imputed studies, adjusted OR to 1.83 (95% CI: 1.11–3.01) (Fig. 9B). The sensitivity analysis indicated that the total effect size remained stable without significant change after the sequential deletion of each study (Fig. 9C). Moreover, the prediction interval for the TyG and GDM relationship ranged from 0.61 to 9.47 (Fig. 9D). The power analysis indicated high statistical power ($1-\beta=1$), suggesting adequate sample size (Fig. 9E). The epidemiological strength of the relationship between TyG index and GDM was accompanied by low evidence (Table 3).

The correlation between TyG index and DR A total of 10 studies comprising 13,716 individuals assessed the relationship between TyG and DR (Table 2). The included

meta-analyses assessed the TyG as both a continuous and categorical variable.

The analysis revealed that a high TyG index was significantly associated with DR (OR=2.34, 95% CI: 1.31–4.19, $P<0.01$) as a categorical variable (Fig. 10A). These studies demonstrated high heterogeneity ($I^2=89.7%$, $P<0.01$), with significant publication bias detected based on Egger’s and Begg’s tests ($P<0.01$). Additionally, the trim and fill analysis, which included two imputed studies, adjusted the OR to 1.79 (95% CI: 1.06–3.03) (Fig. 10B). The sensitivity analysis showed that the total effect size remained stable without significant change after sequentially deleting each study (Fig. 10C). Moreover, the prediction interval for the TyG as a categorical variable and DR relationship ranged from 0.31 to 17.82 (Fig. 10D). The power analysis indicated high statistical power ($1-\beta=1$), suggesting adequate sample size (Fig. 10E).

The study found a significant association between TyG and DR when TyG was considered as a continuous variable (OR=1.48, 95% CI: 1.11–1.97, $p<0.01$) (Fig. 11A). This relationship was accompanied by substantial heterogeneity ($I^2 = 83.4%$, $p<0.01$). While the Egger’s regression test indicated the presence of significant publication bias ($p<0.01$), the Begg’s regression test did not find evidence of publication bias ($p=0.25$). The results of the trim and fill analysis, which imputed two additional studies, yielded an adjusted odds ratio of 1.33 (95% CI: 1.03–1.71) (Fig. 11B). The sensitivity analysis demonstrated that the overall effect size remained stable without significant changes after sequentially removing each study (Fig. 11C). Furthermore, the prediction interval for the relationship between TyG as a continuous variable and

Table 3 GRADE assessment of the correlation of TyG index with various outcomes

GRADE assessment							
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
CIN							
5	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	⊕⊕OO LOW
Arterial stiffness							
13	Observational studies	Serious	Serious	No serious indirectness	No serious imprecision	None	⊕OOO VERY LOW
Diabetic retinopathy							
10	Observational studies	No serious risk of bias	Serious	No serious indirectness	No serious imprecision	Reporting bias Strong association	⊕OOO VERY LOW
Heart failure (categorical)							
7	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	⊕⊕OO LOW
Non-alcoholic fatty liver disease (categorical)							
12	Observational studies	No serious risk of bias	Very serious	No serious indirectness	No serious imprecision	Strong association	⊕OOO VERY LOW
Obstructive sleep apnea							
3	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	⊕⊕OO LOW
Type 2 diabetes mellitus							
12	Observational studies	No serious risk of bias	Serious	No serious indirectness	No serious imprecision	Strong association	⊕⊕OO LOW
Metabolic syndrome							
13	Observational studies	Serious	Serious	No serious indirectness	No serious imprecision	Very strong association	⊕⊕OO LOW
Gestational diabetes mellitus							
6	Observational studies	No serious risk of bias	Serious	No serious indirectness	No serious imprecision	Strong association	⊕⊕OO LOW
Atrial fibrillation							
6	Observational studies	No serious risk of bias	Very serious	No serious indirectness	No serious imprecision	Very strong association	⊕⊕OO LOW
Post-PCI major cardiovascular outcomes							
9	Observational studies	No serious risk of bias	Serious	No serious indirectness	No serious imprecision	Strong association	⊕⊕OO LOW
Post-PCI all-cause mortality							
4	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	⊕⊕OO LOW
Post-PCI revascularization							
3	Observational studies	No serious risk of bias	Very serious	No serious indirectness	No serious imprecision	Strong association	⊕OOO VERY LOW
Post-PCI non-fatal MI							
3	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	Strong association	⊕⊕⊕O MODERATE
Cognitive impairment							
7	Observational studies	No serious risk of bias	Very serious	No serious indirectness	No serious imprecision	Strong association	⊕OOO VERY LOW
Hypertension							
7	Observational studies	No serious risk of bias	Very serious	No serious indirectness	No serious imprecision	None	⊕OOO VERY LOW
Coronary artery calcification							
5	Observational studies	Serious	No serious inconsistency	No serious indirectness	No serious imprecision	None	⊕OOO VERY LOW
Ischemic stroke							

Table 3 (continued)

GRADE assessment							
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
8	Observational studies	No serious risk of bias	Serious	No serious indirectness	No serious imprecision	None	⊕○○○ VERY LOW
Ischemic stroke recurrence							
5	Observational studies	No serious risk of bias	Serious	No serious indirectness	No serious imprecision	None	⊕○○○ VERY LOW
Ischemic stroke mortality							
6	Observational studies	No serious risk of bias	Serious	No serious indirectness	No serious imprecision	None	⊕○○○ VERY LOW
Ischemic stroke poor functional outcomes							
6	Observational studies	No serious risk of bias	Serious	No serious indirectness	No serious imprecision	Reporting bias	⊕○○○ VERY LOW
Chronic kidney disease							
13	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	Reporting bias	⊕○○○ VERY LOW

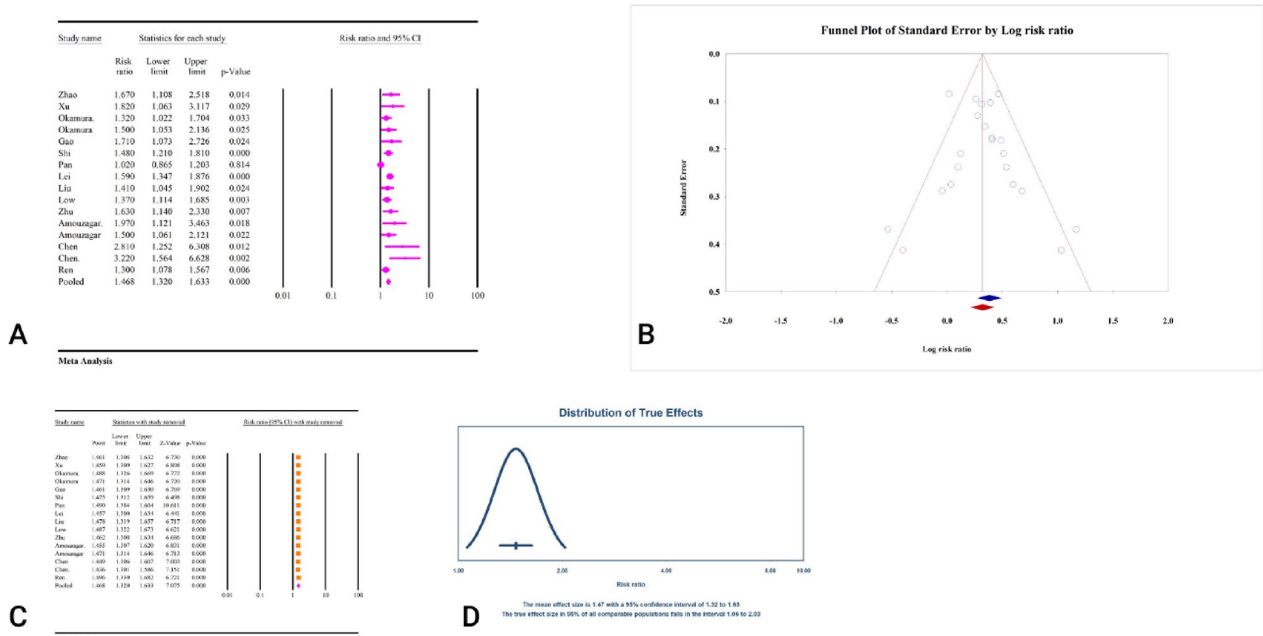


Fig. 6 The association between TyG index and CKD. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval

DR ranged from 0.59 to 3.72 (Fig. 11D). The power analysis indicated a high statistical power, suggesting that the sample size was adequate to detect the observed effect (Fig. 11E). The epidemiological strength between TyG and DR was very low regarding GRADE criteria (Table 3).

TyG index and metabolic diseases

The correlation between TyG index and OSA A collective effort from 3 studies, involving a combined sample size of 437 individuals, examined the relationship between the TyG index and OSA (Table 2). The analysis revealed a significant association between a heightened TyG index and OSA (SMD=0.86, 95% CI: 0.57–1.15,

$P<0.01$) (Fig. 12A). The results showed minimal heterogeneity (36.74%, $P=0.20$), with no noticeable publication bias evident through both Egger’s and Begg’s tests ($P=0.36$ and $P=0.29$). Additionally, the trim and fill analysis, free of any imputed studies, tuned the standardized SMD to 0.86 (95% CI: 0.57–1.15) (Fig. 12B). The sensitivity analysis indicated that the total effect size remained stable without significant change after the sequential deletion of each study (Fig. 12C). Noteworthy also is the prediction interval for the TyG and OSA relationship, spanning from -1.89 to 3.61 (Fig. 12D). Furthermore, the power analysis reflected a commendable statistical power ($1-\beta=1$), underscoring the adequacy of the sample size for reliable

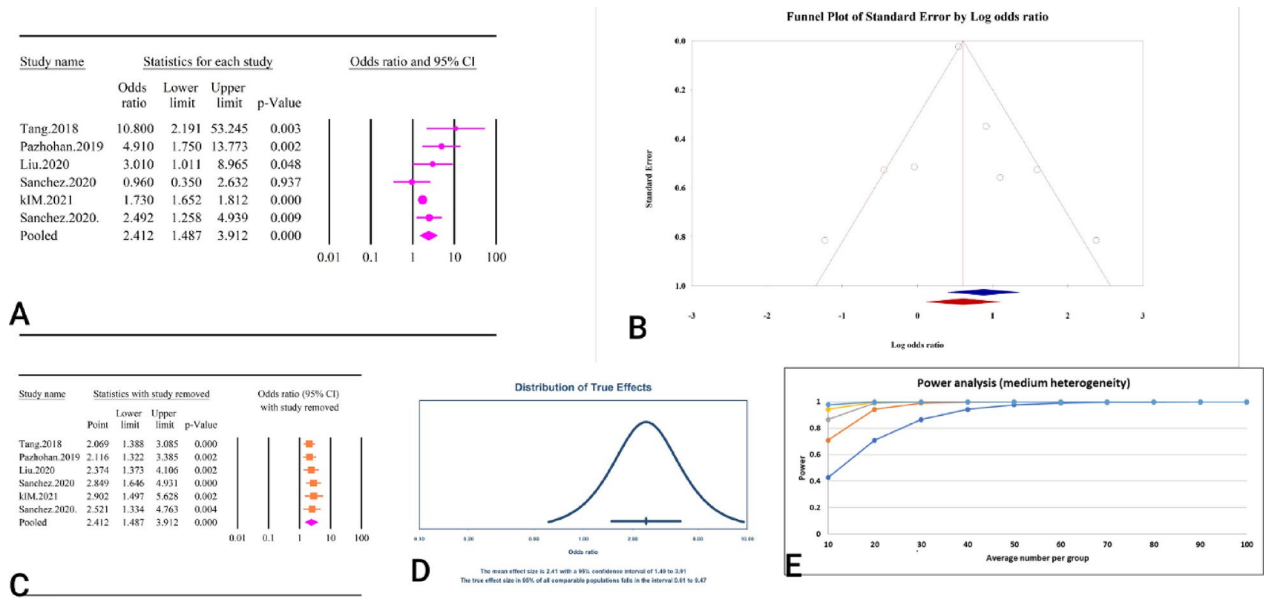


Fig. 9 The association between TyG index and GDM. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval. **E** Power analysis

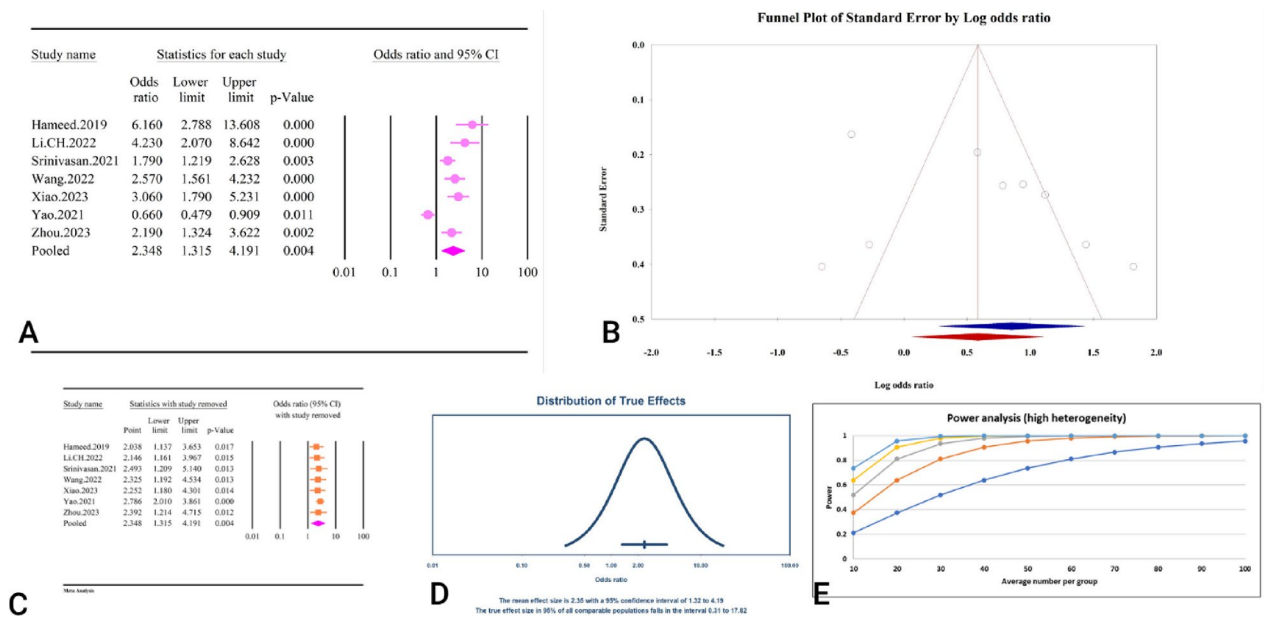


Fig. 10 The association between TyG index and DR as a categorical variable. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval. **E** Power analysis

based on Egger’s and Begg’s tests ($P=0.43$ and $P=0.76$). Additionally, the trim and fill analysis, which did not include any imputed studies, adjusted the MD to 0.83 (95% CI: 0.74–0.93) (Fig. 13B). The sensitivity analysis indicated that the total effect size remained stable without significant change after the sequential deletion of each study (Fig. 13C). Moreover, the prediction interval for the TyG and metabolic syndrome relationship ranged from 0.47 to 1.20 (Fig. 13D). The power analysis indicated high statistical power ($1-\beta=1$), suggesting adequate sample

size (Fig. 10E). The epidemiological strength of the relationship between TyG index and metabolic syndrome was accompanied by low evidence (Table 3).

The correlation between TyG index and NAFLD A total of 17 studies, comprising a combined sample size of 121,975 individuals, investigated the relationship between the TyG index and NAFLD (Table 2). The included meta-analyses assessed the TyG as both a continuous and categorical variable.

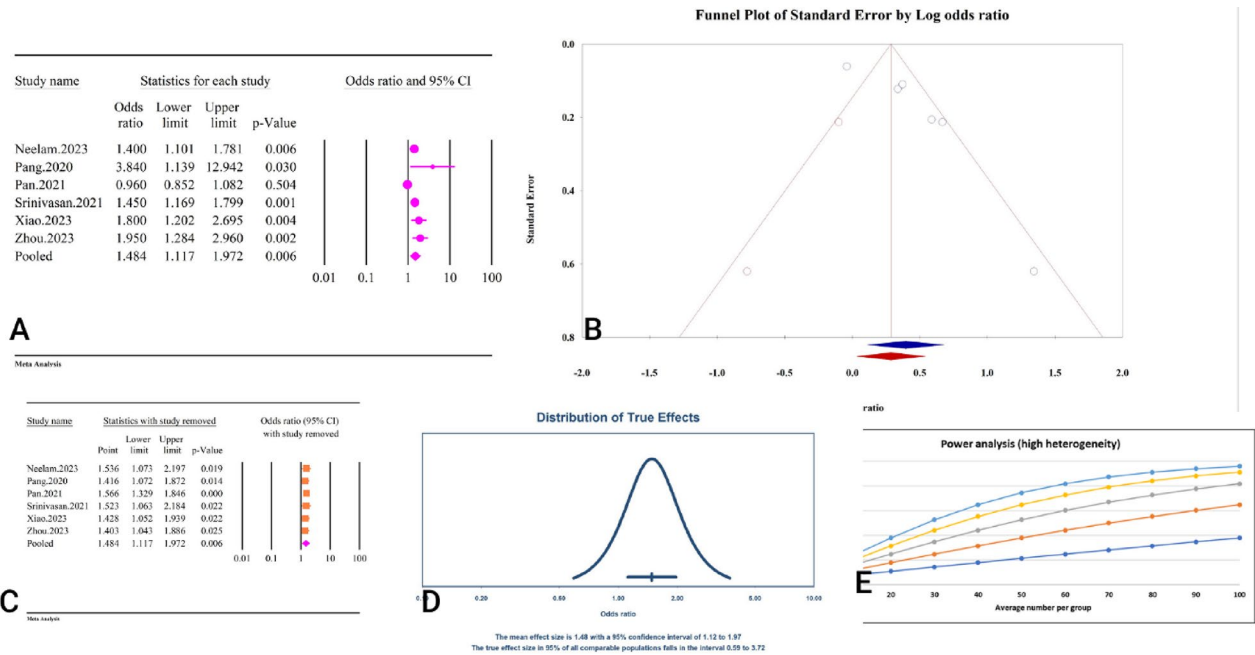


Fig. 11 The association between TyG index and DR as a continuous variable. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval. **E** Power analysis

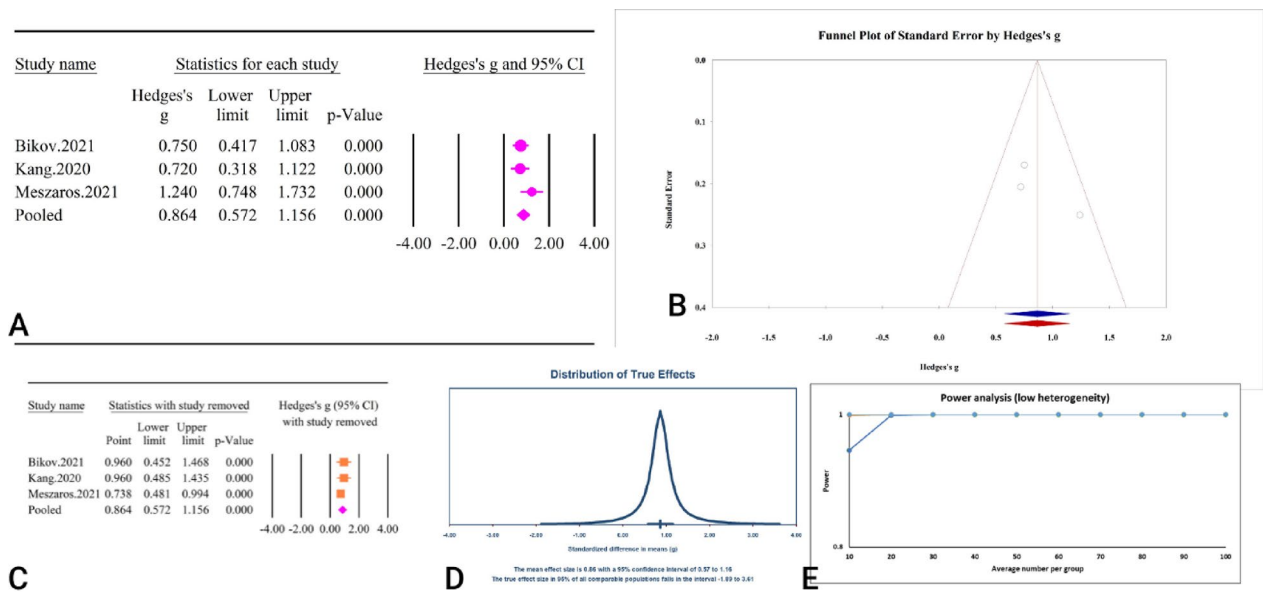


Fig. 12 The association between TyG index and OSA. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval. **E** Power analysis

The meta-analysis demonstrated that the TyG index was significantly associated with NAFLD as a continuous variable (OR=2.36, 95% CI: 1.88–2.97, $P<0.01$) (Fig. 14A). The Egger’s regression test showed a significant publication bias ($P<0.01$), while the Begg’s regression test did not indicate a significant publication bias ($P=0.24$). Additionally, the trim and fill analysis, which did not include any imputed studies, adjusted the OR to 2.36 (95% CI: 1.88–2.97) (Fig. 14B). The sensitivity

analysis indicated that the total effect size remained stable without a significant change after the sequential deletion of each study (Fig. 14C). Moreover, the prediction interval for the TyG and metabolic syndrome relationship ranged from 0.99 to 5.68 (Fig. 14D). The power analysis indicated high statistical power ($1-\beta=1$), suggesting an adequate sample size (Fig. 14E).

The meta-analysis results showed a significant association between the TyG index and NAFLD when TyG

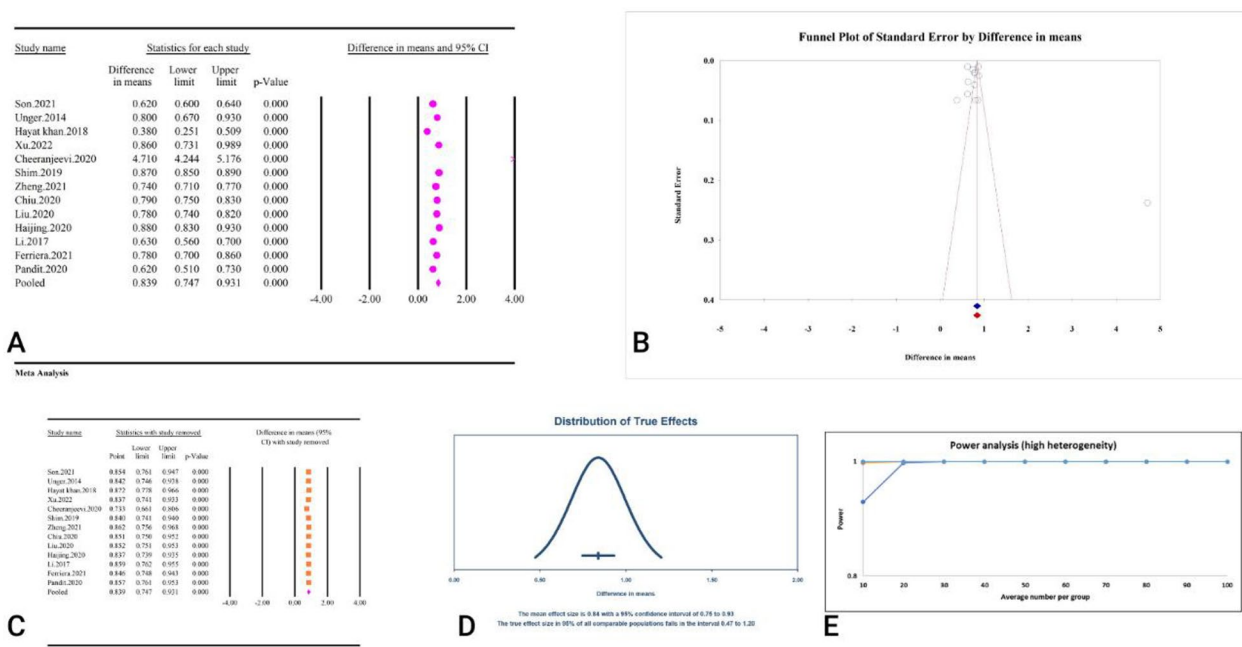


Fig. 13 The association between TyG index and metabolic syndrome. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval. **E** Power analysis

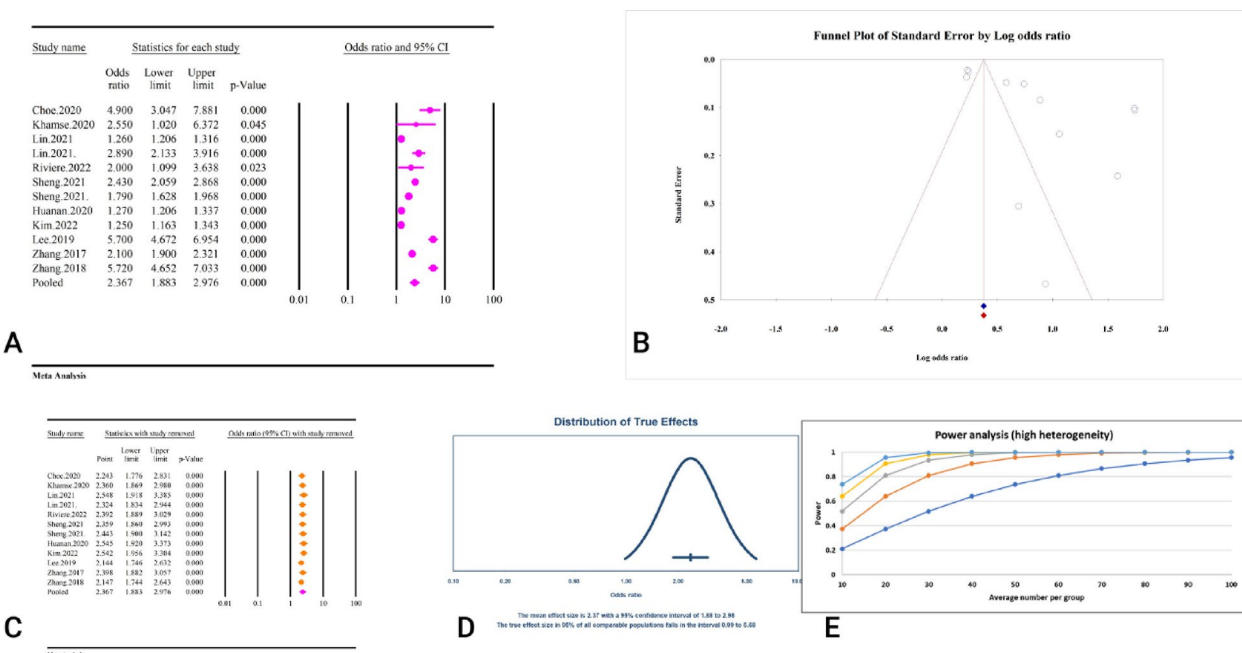


Fig. 14 The association between TyG index and NAFLD as a continuous variable. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval. **E** Power analysis

was considered as a categorical variable (OR=6.00, 95% CI: 4.12–8.73, $P < 0.01$) (Fig. 15A). However, the analysis also revealed significant heterogeneity (91.80%, $P < 0.01$) in the included studies. The Egger’s and Begg’s regression tests did not show any significant publication bias ($P = 0.89$ and $P = 0.75$, respectively). Trim and Fill analysis,

without imputing any additional studies, resulted in an odds ratio of 6.00 (95% CI: 4.12–8.73) (Fig. 15B). The sensitivity analysis demonstrated the stability of the overall effect size, as it remained consistent after the sequential removal of each individual study (Fig. 15C). The prediction interval for the relationship between TyG and

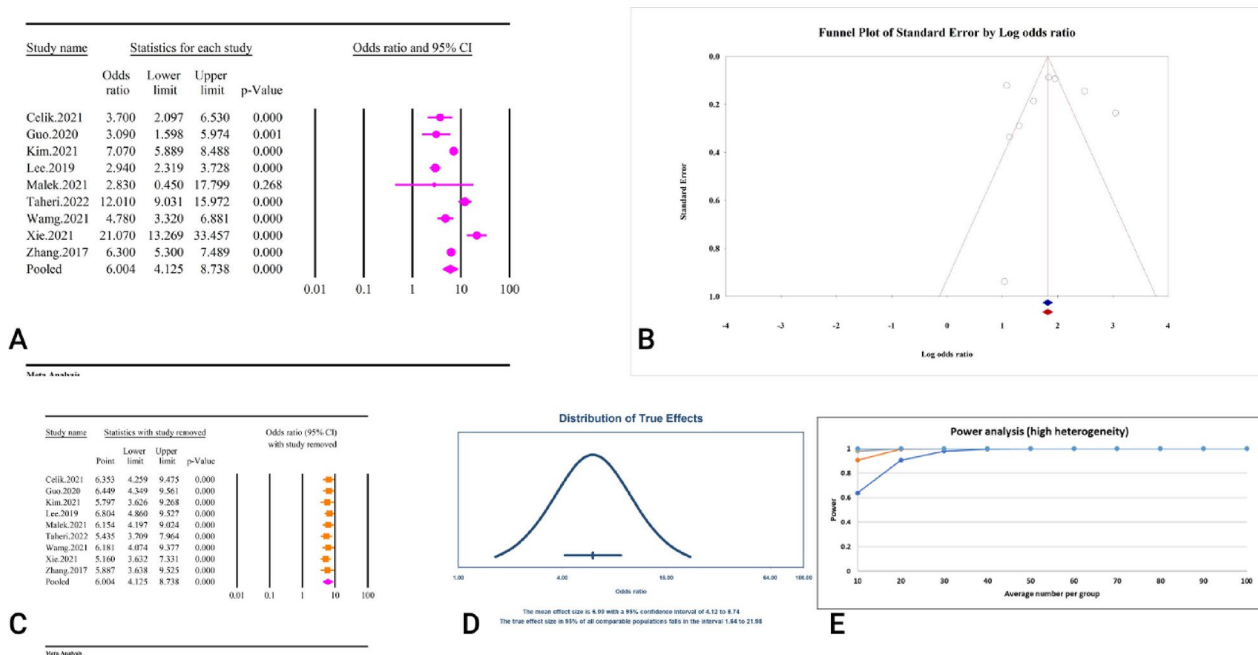


Fig. 15 The association between TyG index and NAFLD as a categorical variable. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval. **E** Power analysis

metabolic syndrome ranged from 1.64 to 21.98, indicating the potential variation in the true effect size across different settings (Fig. 15D). Finally, the power analysis revealed a high statistical power ($1-\beta=1$), suggesting that the sample size used in the meta-analysis was adequate to detect the observed effect (Fig. 15E). The GRADE criteria showed very low evidence of the association between TyG and NAFLD (Table 3).

TyG index and cerebrovascular diseases

The correlation between TyG index and dementia The relationship between TyG index and dementia was assessed considering TyG as both a continuous and categorical variable (Table 2). Two studies with a total sample size of 8,435,216 participants assessed TyG as a categorical variable. The results of the meta-analysis showed that a higher TyG index was significantly associated with an increased risk of dementia (OR=1.14, 95% CI: 1.12–1.16, $P<0.01$) (Fig. 16A). No significant heterogeneity was found across the studies ($I^2=0.00\%$, $P=0.32$). Due to the low number of studies, it was not possible to assess publication bias, prediction interval, and epidemiological robustness. The results of the power analysis showed high statistical power, indicating that the sample size was adequate (Fig. 16B).

TyG was also significantly associated with dementia as a continuous variable based on the results of two studies with a total sample size of 2,524 participants (OR=1.37, 95% CI: 1.03–1.82, $P=0.03$) (Fig. 16C). No significant

heterogeneity was observed ($I^2=0.00\%$, $P=0.77$). However, due to the low number of studies, it was not possible to assess publication bias, prediction interval, and epidemiological robustness. The results of the power analysis showed high statistical power, indicating that the sample size was sufficient (Fig. 16D).

The correlation between TyG index and cognitive impairment

Based on the meta-analysis of five studies including 7,057 participants, TyG index was significantly associated with cognitive impairment as a categorical variable (OR=2.31, 95% CI: 1.38–3.86, $P<0.01$) (Fig. 17A) (Table 2). Significant heterogeneity ($I^2=84.75\%$, $P<0.01$) accompanied the results. While there was no obvious publication bias in the Begg’s regression test ($P=0.46$), the Egger’s regression test revealed considerable publication bias ($P<0.01$). The OR was modified to 1.67 (95% CI: 1.05–2.64) by the trim and fill analysis results using two imputed trials (Fig. 17B). The removal of each study did not significantly alter the pooled effect, according to the results of the sensitivity analysis (Fig. 17C). The power analysis revealed strong statistical power, indicating that the overall sample size was sufficient, and the prediction interval was 0.37–14.26 (Fig. 17D) (Fig. 17E).

A total of four studies comprising 1,235 individuals assessed the relationship between cognitive impairment and TyG index and as a continuous variable. This association was statistically significant (OR=3.38, 95% CI: 1.67–6.83, $P<0.01$) (Fig. 18A), however, it was accompanied by significant heterogeneity ($I^2=81.56\%$). No significant

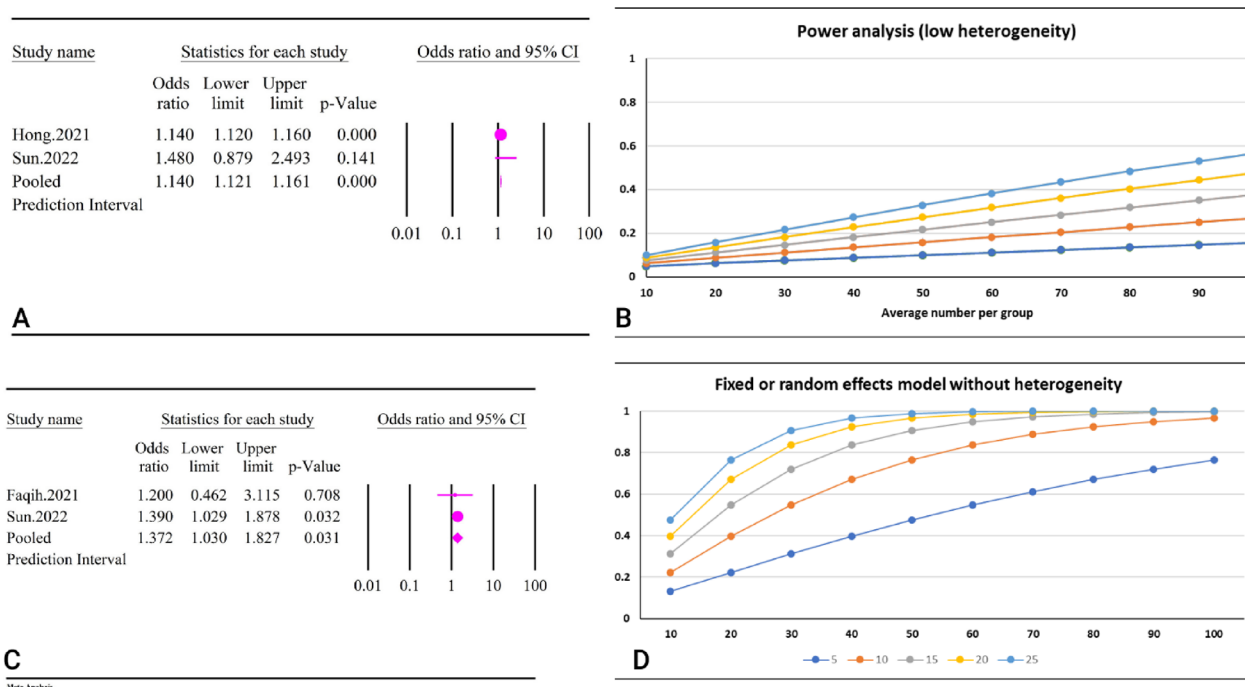


Fig. 16 The association between TyG index and dementia. **A** Forest plot of TyG as a categorical index **B** Power analysis of TyG as a categorical index. **C** Forest plot of TyG as a continuous index. **D** Power analysis of TyG as a continuous index

publication bias was found based on the Egger’s and Begg’s regression tests ($P=0.84$ and $P=0.73$, respectively). The results of the trim and fill analysis adjusted the OR to 3.38 (95% CI: 1.67–6.83) without imputing any additional studies (Fig. 18B). The results of the sensitivity analysis indicated that the removal of each individual study did not significantly affect the total estimate (Fig. 18C). Prediction interval ranged from 0.16 to 72.58 (Fig. 18D). The power analysis showed high statistical power, reflecting the adequacy of the sample size (Fig. 18E). The epidemiological strength of the association between TyG index and cognitive impairment was very low based on GRADE criteria (Table 3).

The correlation between TyG index and ischemic stroke Among the included studies, the correlation between the TyG index and the following outcomes was examined: ischemic stroke, ischemic stroke recurrence, ischemic stroke mortality, ischemic stroke poor functional outcomes, and ischemic stroke neurological worsening (Table 2).

Based on the results of 8 studies including 554,334 individuals, the TyG index was significantly associated with an increased risk of stroke (OR=1.37, 95% CI: 1.22–1.54, $P<0.01$) (Fig. 19A). The results were accompanied by significant heterogeneity ($I^2=74.18\%$, $P<0.01$). The results of the publication bias assessment showed significant bias based on the Egger’s regression test ($P=0.04$), however, the Begg’s regression test was not significant

($P=0.90$). The results of the trim and fill analysis with one imputed study adjusted the OR to 1.35 (95% CI: 1.20–1.52) (Fig. 19B). The results of the sensitivity analysis showed no significant change in the pooled estimate after the removal of each individual study (Fig. 19C). The prediction interval was calculated as 0.99–1.91, and the power analysis indicated high statistical power (Fig. 19D and E).

The results of five studies including 84,774 individuals showed that the TyG index was significantly associated with an increased risk of ischemic stroke recurrence (OR=1.50, 95% CI: 1.19–1.89, $P<0.01$) (Fig. 20A). The analysis exhibited moderate heterogeneity among the included studies ($I^2=56.22\%$, $P=0.05$). The assessment of publication bias suggested the presence of bias based on Egger’s regression test ($P=0.02$), but Begg’s regression test was not significant ($P=0.08$). The trim and fill analysis, which adjusts for publication bias, estimated the adjusted OR as 1.33 (95% CI: 1.04–1.70) (Fig. 20B). The sensitivity analysis indicated that the pooled estimate was stable (Fig. 20C). The prediction interval calculated was 0.75–2.99, indicating the range of true effect sizes (Fig. 20E). The power analysis showed high statistical power (Fig. 20D).

The results of the analysis including six studies with total sample size of 31,465 showed that the higher TyG index was significantly associated with an increased risk of poor functional outcomes following an ischemic stroke (OR=1.36, 95% CI: 1.10–1.69, $P<0.01$) (Fig. 21A). The

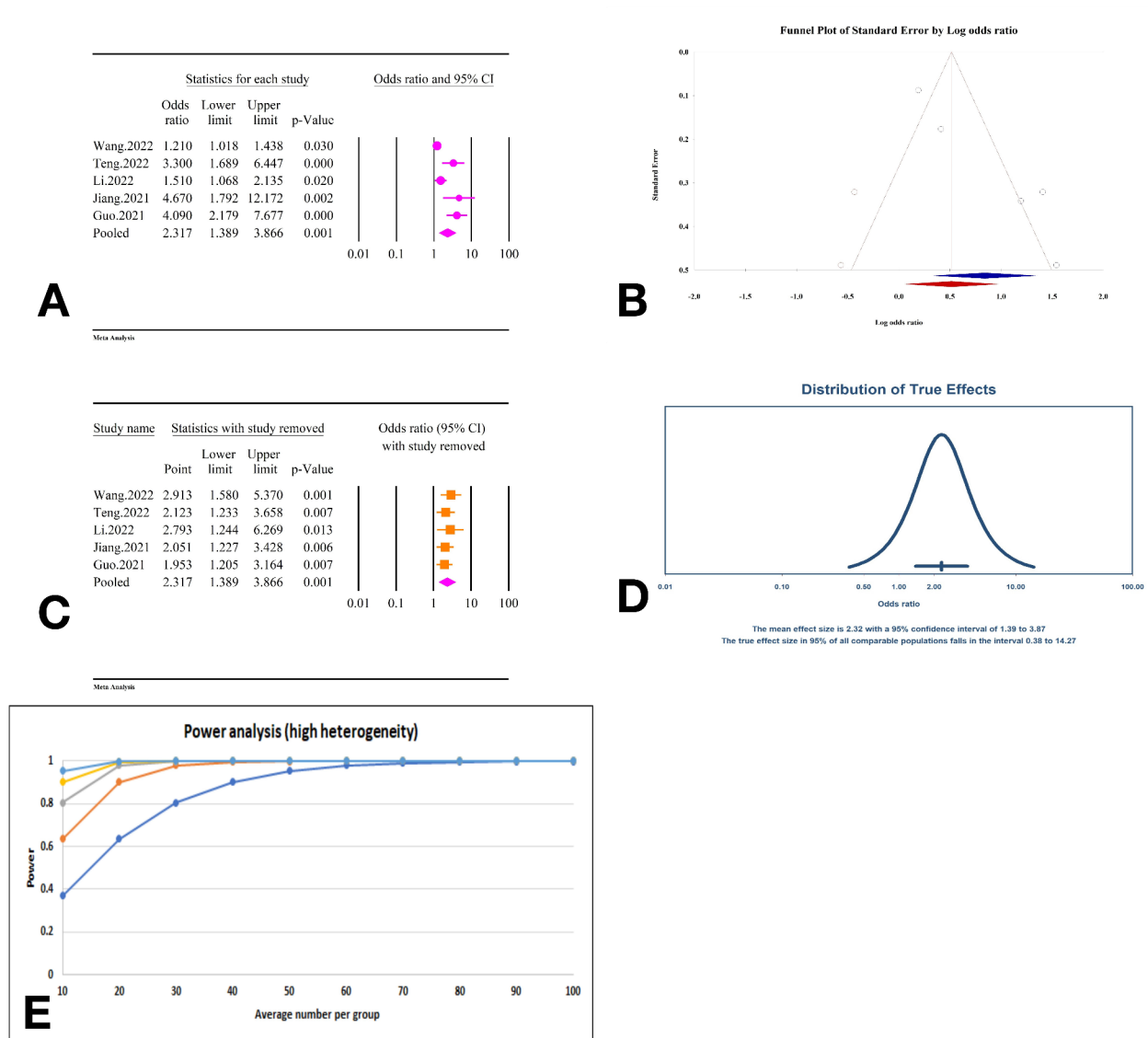


Fig. 17 The association between TyG index as a categorical variable and cognitive impairment. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval. **E** Power analysis

analysis exhibited high heterogeneity among the included studies ($I^2 = 71.40\%$, $P < 0.01$). The assessment of publication bias suggested the presence of bias based on both Egger’s regression test ($P < 0.01$) and Begg’s regression test ($P = 0.02$). The trim and fill analysis, which adjusts for publication bias, estimated the adjusted OR as 1.25 (95% CI: 1.01–1.54) with two studies imputed (Fig. 21B). The sensitivity analysis indicated that the pooled estimate was stable (Fig. 21C). The prediction interval for the true effect sizes was calculated to be between 0.74 and 2.54, indicating variability in the potential outcomes (Fig. 21D). The power analysis demonstrated high statistical power (Fig. 21E).

The results of the analysis showed that the TyG index was significantly associated with an increased risk of

ischemic stroke mortality (OR=1.40, 95% CI: 1.14–1.71, $P < 0.01$) (Fig. 22A). The analysis exhibited high heterogeneity among the included studies ($I^2 = 70.70\%$, $P < 0.01$). The assessment of publication bias using Egger’s regression test ($P = 0.19$) and Begg’s regression test ($P = 0.70$) was not significant. The trim and fill analysis did not impute any studies, and thus the adjusted OR remained the same (OR=1.40, 95% CI: 1.14–1.71) (Fig. 22B). The sensitivity analysis indicated that the pooled estimate was stable (Fig. 22C). The prediction interval for the true effect sizes was calculated to be between 0.76 and 2.57, indicating variability in the potential outcomes (Fig. 22D). The power analysis demonstrated high statistical power (Fig. 22E). The epidemiological strength of the association between TyG index and ischemic

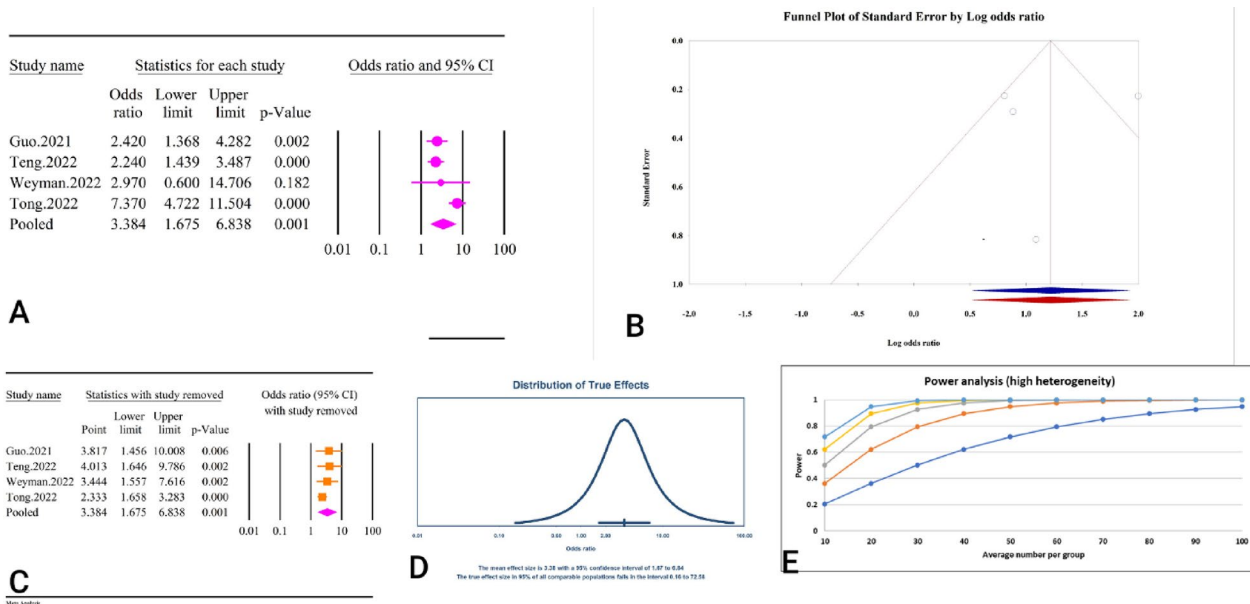


Fig. 18 The association between TyG index as a continuous variable and cognitive impairment. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval. **E** Power analysis

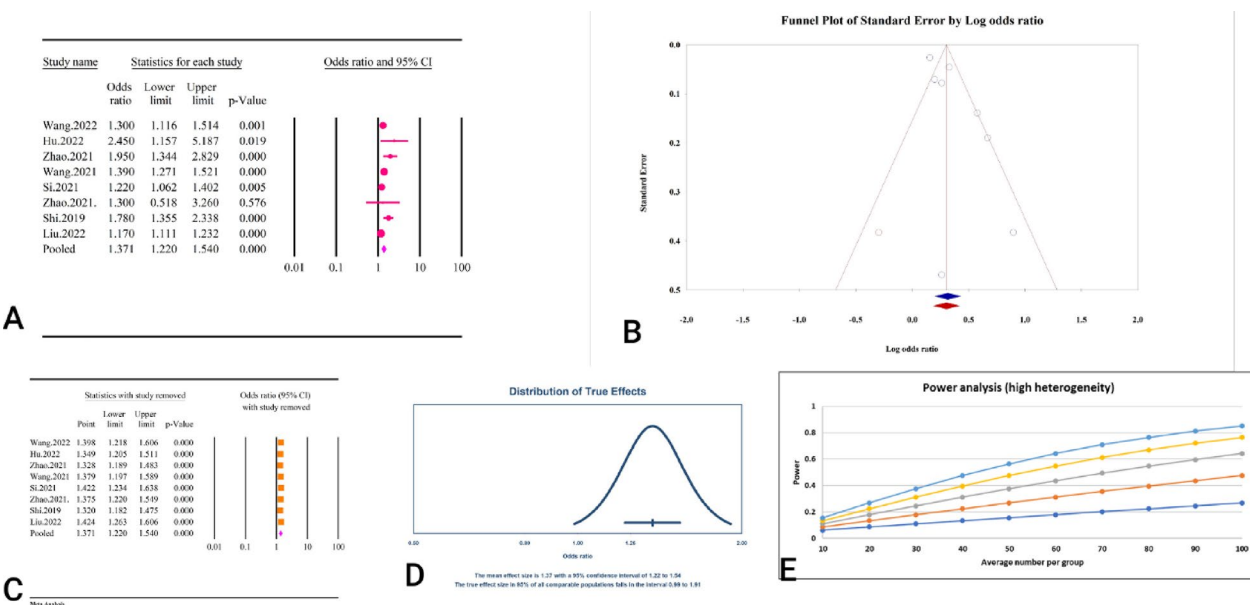


Fig. 19 The association between TyG index and ischemic stroke. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval. **E** Power analysis

stroke mortality was very low based on GRADE criteria (Table 3).

TyG index and cardiovascular outcomes

The correlation between TyG index and HF Among the included studies, the relationship between TyG index and

HF was evaluated as both a continuous and categorical variable (Table 2).

The results of the analysis showed that the TyG index as a categorical variable was significantly associated with an increased risk of heart failure (HR=1.21, 95% CI: 1.12–1.30, $P < 0.01$) (Fig. 23A). The analysis exhibited low heterogeneity among the included studies ($I^2 = 21.43\%$, $P = 0.26$). The assessment of publication bias using Egger’s regression test ($P = 0.29$) and Begg’s regression test

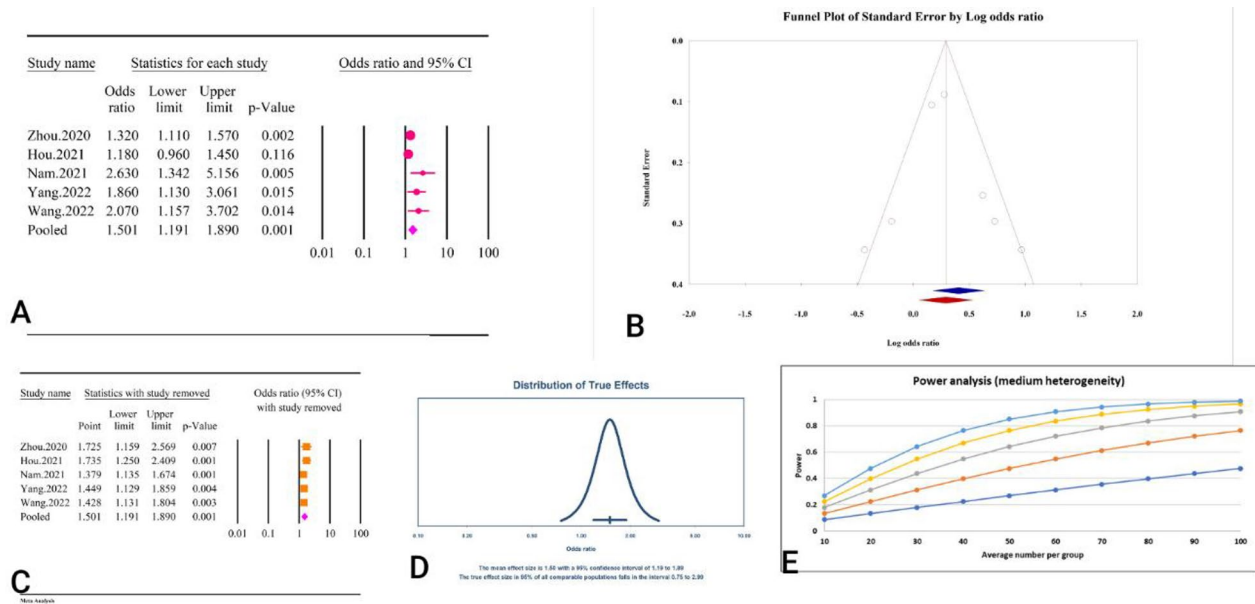


Fig. 20 The association between TyG index and ischemic stroke recurrence. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval. **E** Power analysis

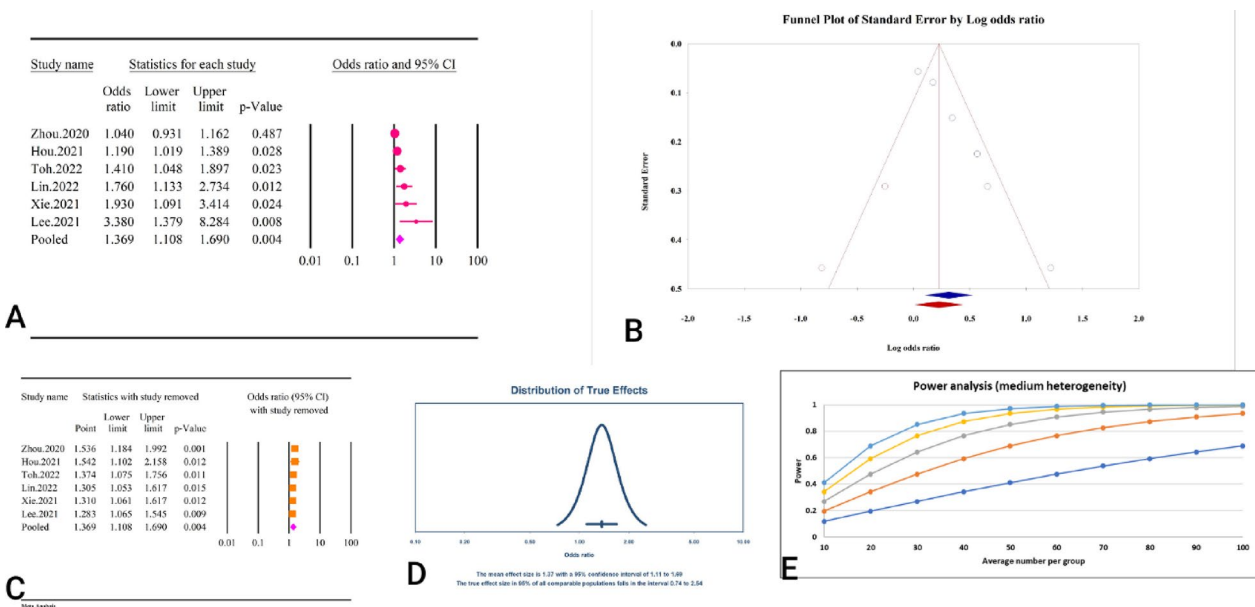


Fig. 21 The association between TyG index and ischemic stroke poor functional outcomes. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval. **E** Power analysis

($P=0.76$) was not significant. The trim and fill analysis estimated the adjusted HR as 1.19 (95% CI: 1.08–1.31) with one study imputed (Fig. 23B). The sensitivity analysis indicated that the pooled estimate was stable (Fig. 23C). The prediction interval for the true effect sizes was calculated to be between 1.04 and 1.41, indicating variability in the potential outcomes (Fig. 23D). Because the reported results were presented as HR, the assessment of power analysis was not possible.

The results of the analysis showed that the TyG index was significantly associated with an increased risk of HF as a continuous variable (HR=1.16, 95% CI: 1.11–1.21, $P<0.01$) (Fig. 24A). The analysis exhibited very low heterogeneity among the included studies ($I^2 = 0.64\%$, $P=0.36$). The assessment of publication bias using Egger’s regression test ($P=0.40$) and Begg’s regression test ($P=1$) was not significant. The trim and fill analysis, which adjusts for publication bias, estimated the adjusted HR as 1.15 (95% CI: 1.09–1.21) with one study

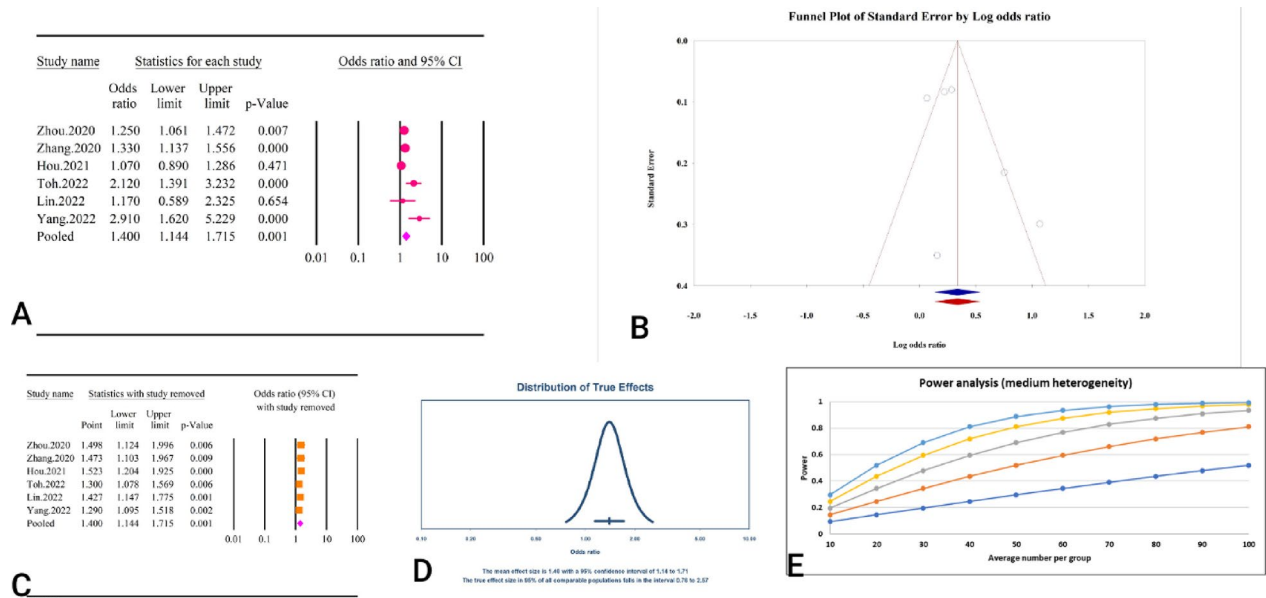


Fig. 22 The association between TyG index and ischemic stroke mortality. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval. **E** Power analysis

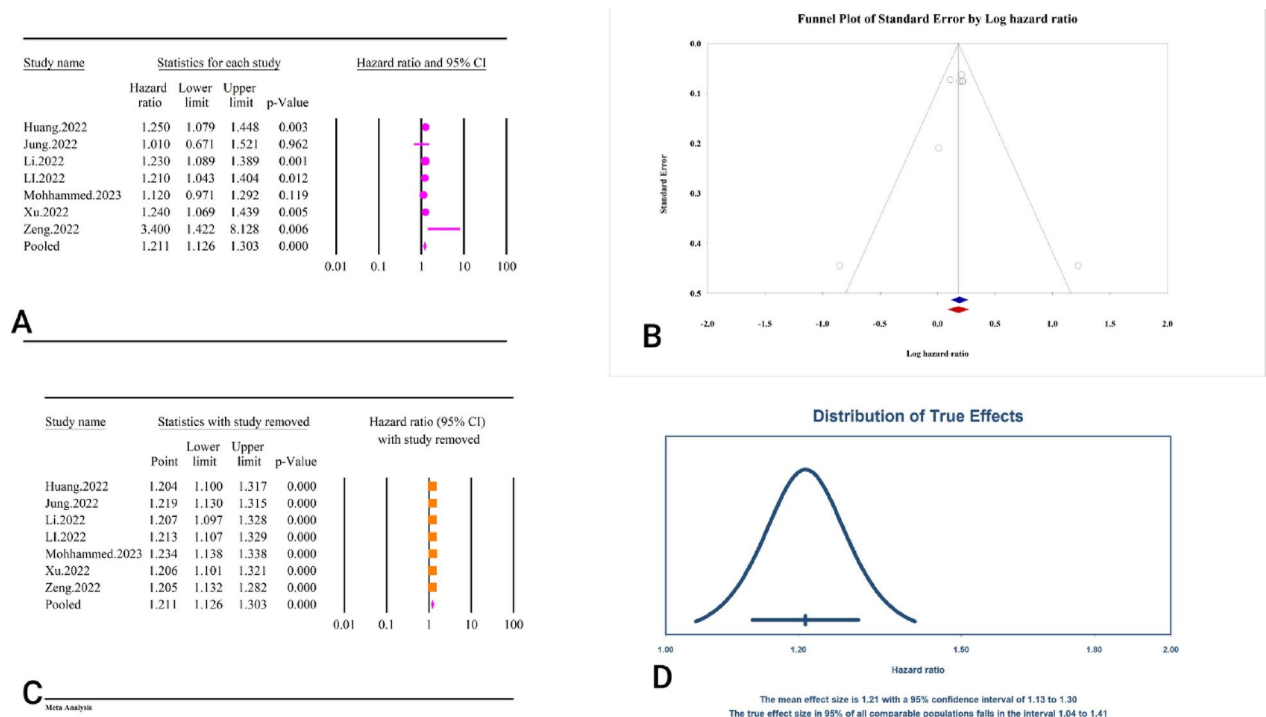
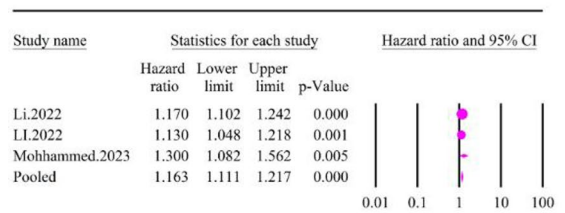


Fig. 23 The association between TyG index and heart failure as a categorical variable. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval

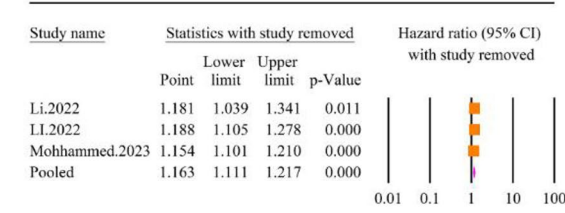
imputed (Fig. 24B). The sensitivity analysis indicated that the pooled estimate was stable (Fig. 24C). The prediction interval for the true effect sizes was calculated to be between 0.86 and 1.57, indicating variability in the potential outcomes (Fig. 24D). The epidemiological strength

of the association between TyG index and HF was low based on GRADE criteria (Table 3).

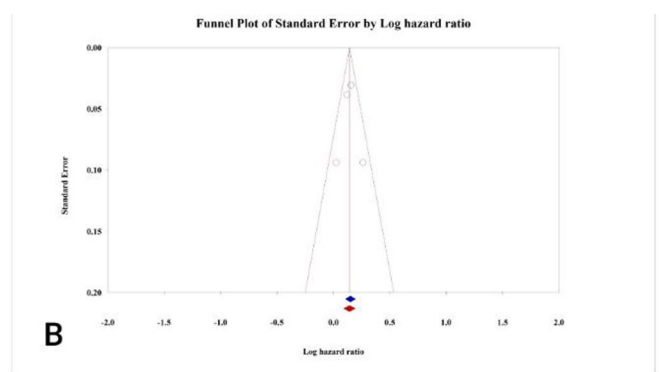
The correlation between TyG index and AF The analysis of six studies comprising 5813 participants revealed a significant association between the TyG index and



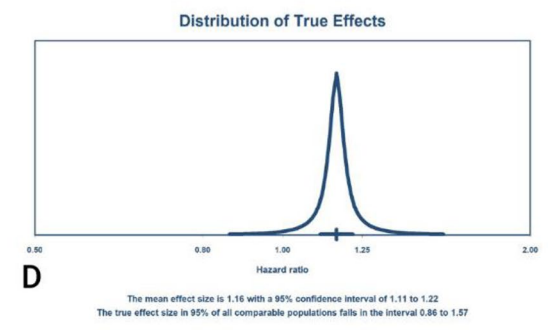
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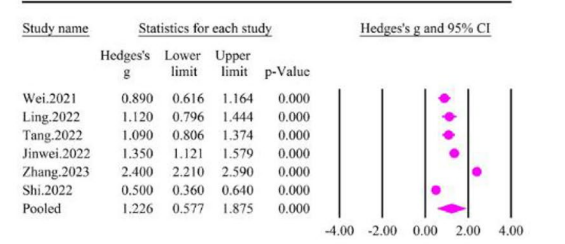


B

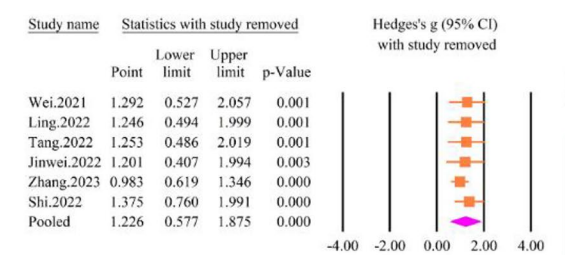


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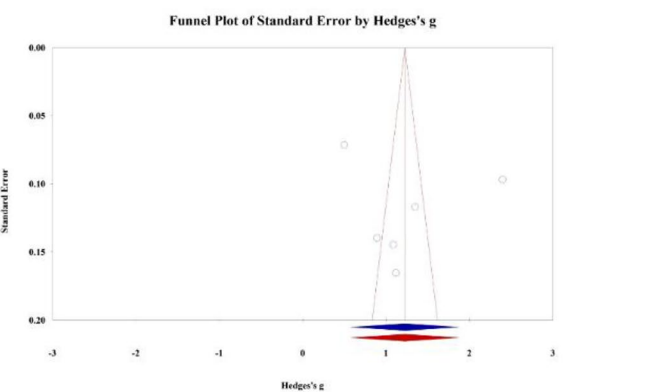
Fig. 24 The association between TyG index and heart failure as a continues variable. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval



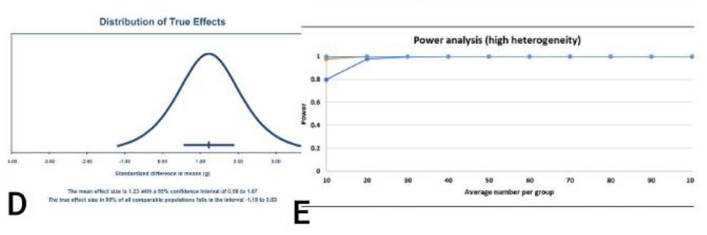
A



C



B



D

E

Fig. 25 The association between TyG index and atrial fibrillation. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval. **E** Power analysis

an increased risk of AF, with an SMD of 1.22 (95% CI: 0.57–1.87, $P < 0.01$) (Fig. 25A) (Table 2). The heterogeneity among the included studies was extremely high ($I^2 = 98.04\%$, $P < 0.01$). Evaluations for publication bias indi-

cated no significant bias, as evidenced by Egger's regression test ($P = 0.64$) and Begg's regression test ($P = 1$). The trim and fill method did not identify any missing studies, thus the adjusted SMD remained unchanged (SMD = 1.22,

95% CI: 0.57–1.87) (Fig. 25B). Sensitivity analysis confirmed the robustness of the pooled estimate (Fig. 25C). The prediction interval, ranging from –1.18 to 3.63, highlighted substantial variability in the possible effect sizes. The power analysis confirmed a high level of statistical power (Fig. 25D). The epidemiological strength of the association between TyG index and AF was low based on GRADE criteria (Table 3).

The correlation between TyG index and HTN The analysis of 6 studies and 200,044 individuals demonstrated that the TyG index was significantly associated with an increased risk of HTN (RR=1.52, 95% CI: 1.25–1.85, $P<0.01$) (Fig. 26A) (Table 2). The included studies exhibited considerable heterogeneity ($I^2 = 85.67%$, $P<0.01$). The evaluation of publication bias showed mixed results: Egger’s regression test indicated the presence of bias ($P<0.01$), whereas Begg’s regression test did not show significant bias ($P=0.28$). The trim and fill analysis, which corrects for potential publication bias, adjusted the risk ratio to 1.44 (95% CI: 1.20–1.74) with one study imputed (Fig. 26B). The sensitivity analysis confirmed the stability of the pooled estimate (Fig. 26C). The prediction interval for the true effect sizes ranged from 0.78 to 2.98, indicating variability in the potential outcomes (Fig. 26D). The epidemiological strength of the association between TyG index and HTN was very low based on GRADE criteria (Table 3). Because the reported results were presented as RR, the assessment of power analysis was not possible.

The correlation between TyG index and arterial stiffness Among the 16 included studies with 59,851 individuals, the relationship between TyG index and arterial stiffness was evaluated as both a continuous and categorical variable (Table 2).

The analysis demonstrated a significant association between the TyG index as a categorical variable and an increased risk of arterial stiffness, with an OR of 1.80 (95% CI: 1.53–2.10, $P<0.01$) (Fig. 27A). The studies included exhibited moderate heterogeneity ($I^2 = 66.26%$, $P<0.01$). Assessments for publication bias showed no significant bias according to Egger’s regression test ($P=0.35$) and Begg’s regression test ($P=0.20$). The trim and fill method did not identify any missing studies, thus the adjusted OR remained the same (OR=1.80, 95% CI: 1.53–2.10) (Fig. 27B). Sensitivity analysis confirmed the robustness of the pooled estimate (Fig. 27C). The prediction interval for the true effect sizes ranged from 1.07 to 3.03, indicating some variability in the potential outcomes (Fig. 27D). The power analysis demonstrated a high level of statistical power (Fig. 27E).

The findings revealed a significant association between the TyG index as a continuous variable and increased risk of arterial stiffness, with an OR of 1.50 (95% CI: 1.34–1.69, $P<0.01$) (Fig. 28A). The studies included in the analysis exhibited substantial heterogeneity ($I^2 = 81.66%$, $P<0.01$). Tests for publication bias were not significant, as shown by Egger’s regression test ($P=0.10$) and Begg’s regression test ($P=0.16$). The trim and fill method

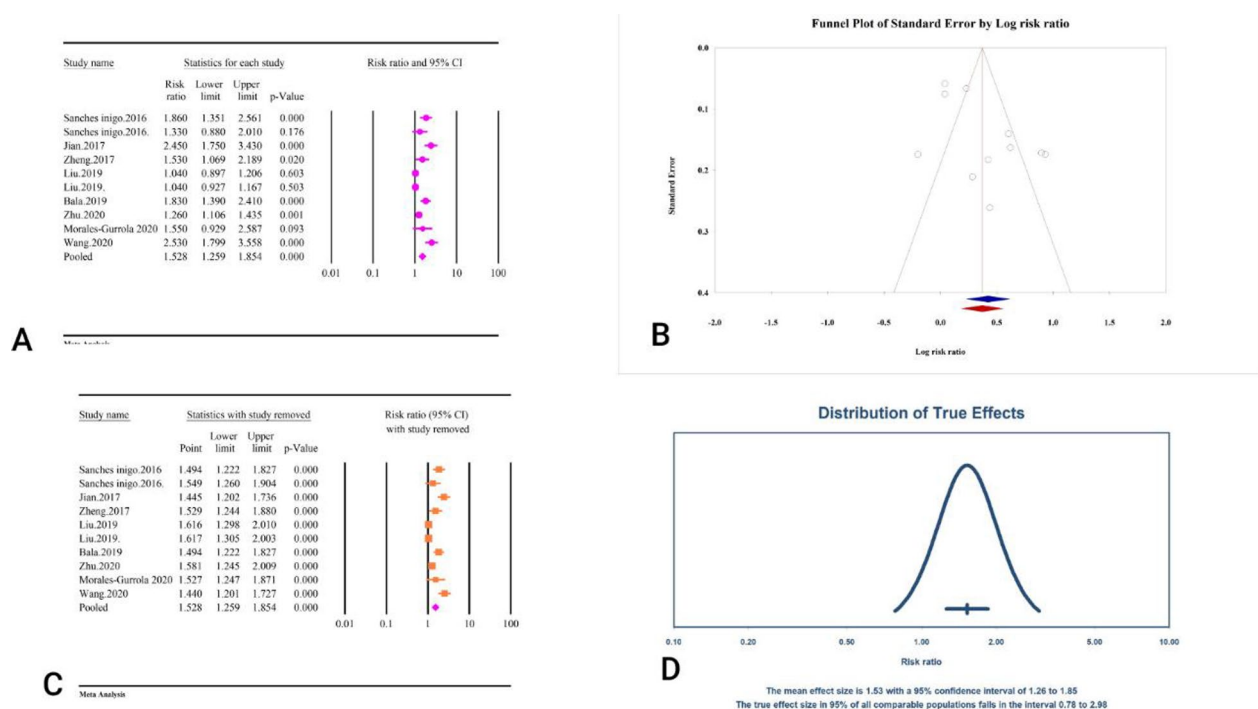


Fig. 26 The association between TyG index and hypertension. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval

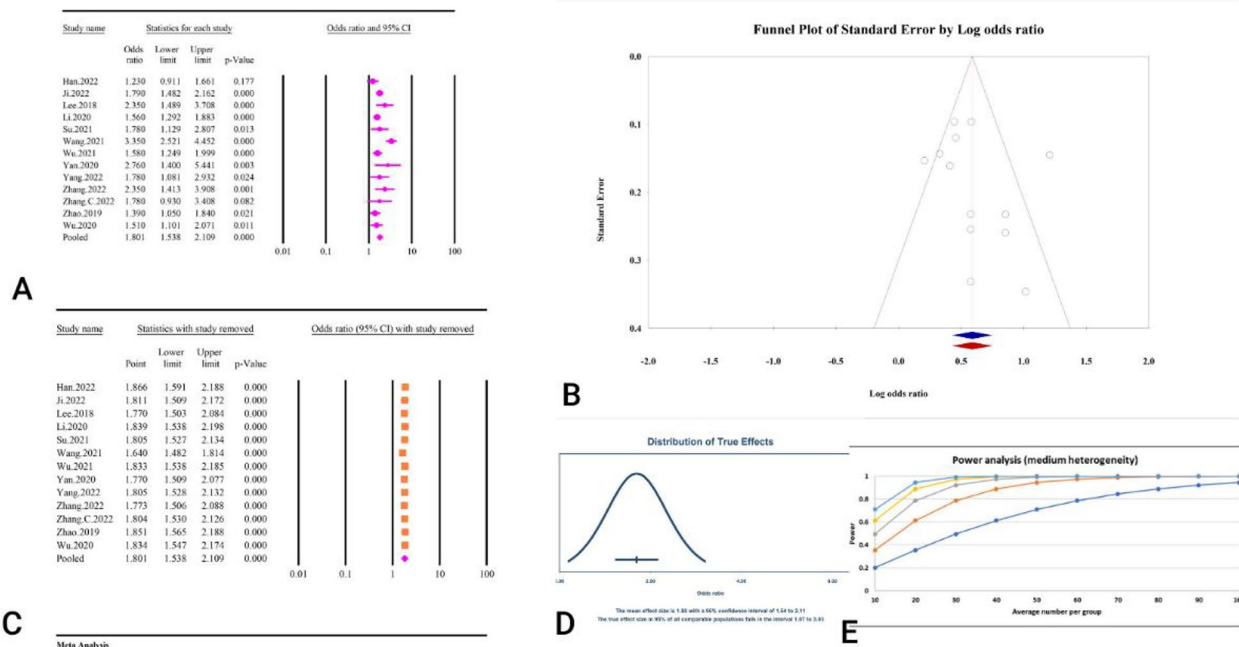


Fig. 27 The association between TyG index as a categorical variable and atrial stiffness. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval **E** Power analysis

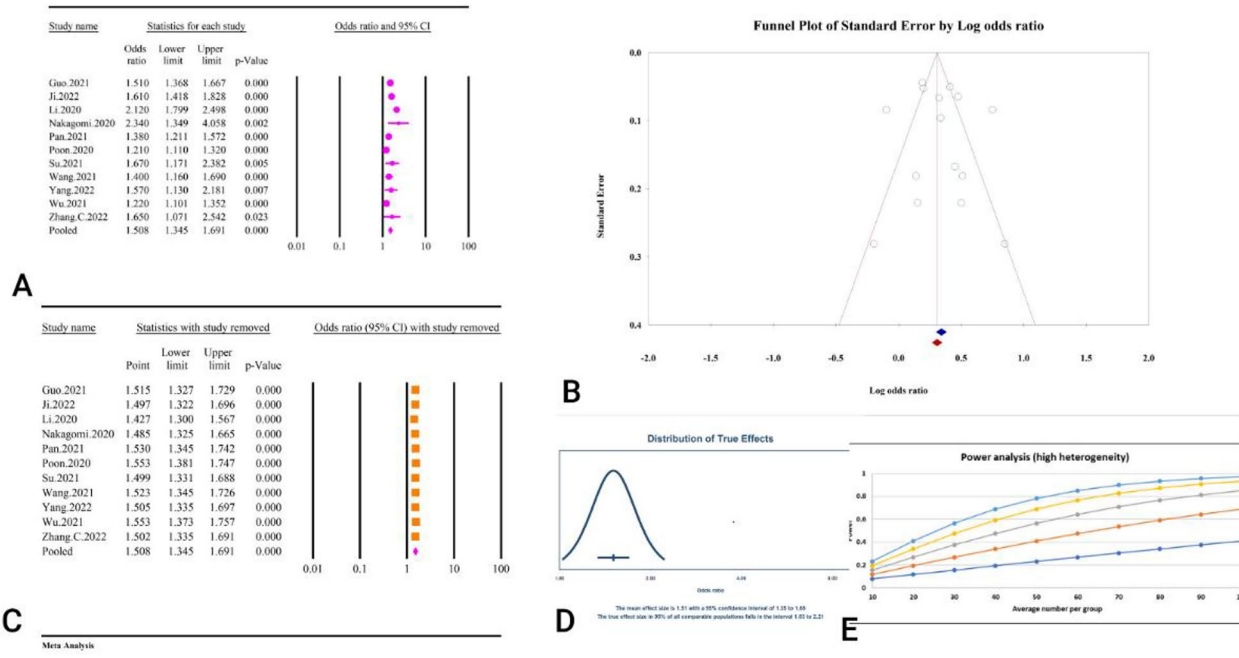


Fig. 28 The association between TyG index as a continuous variable and atrial stiffness. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval **E** Power analysis

suggested the addition of four missing studies, leaving the adjusted OR unchanged (OR=1.39, 95% CI: 1.23–1.56) (Fig. 28B). Sensitivity analysis indicated the robustness of the combined estimate (Fig. 28C). The prediction interval for the true effect sizes was between 1.03 and 2.21(Fig. 27D). The results demonstrated high statistical

power (Fig. 28E). According to the GRADE criteria, the epidemiological strength of the association between the TyG index and arterial stiffness was found to be very low (Table 3).

The correlation between TyG index and coronary artery calcification In the 10 included studies, encompassing 27,456 individuals, the relationship between the TyG index and coronary artery calcification was assessed both as a continuous and a categorical variable (Table 2).

Employing the TyG index as a continuous variable, the analysis showed a significant correlation (OR of 1.73 (95% CI: 1.36–2.20, $P < 0.01$) with an increased risk of coronary artery calcification (Fig. 29A). The included studies demonstrated moderate heterogeneity ($I^2 = 50.81\%$, $P = 0.08$). Tests for publication bias were not significant, as indicated by Egger’s regression test ($P = 0.08$) and Begg’s regression test ($P = 0.22$). The trim and fill analysis did not identify any missing studies, thus the adjusted OR remained unchanged (OR = 1.73, 95% CI: 1.36–2.20) (Fig. 29B). Sensitivity analysis confirmed the robustness of the pooled estimate. The prediction interval for the true effect sizes ranged from 0.84 to 3.59, indicating some variability in outcomes (Fig. 29C). The power analysis demonstrated high statistical power (Fig. 29D).

With an OR of 1.65 (95% CI: 1.50–1.82, $P < 0.01$), our findings demonstrated a strong correlation between the TyG index as a categorical variable and an elevated risk of coronary artery calcification (Fig. 30A). There was no heterogeneity detected among the studies ($I^2 = 0.00\%$, $P = 0.72$). Evaluation for publication bias showed no significant issues according to Egger’s regression test ($P = 0.21$) and Begg’s regression test ($P = 1$). The trim and fill method did not indicate any missing studies, so the adjusted OR remained unchanged (OR = 1.65, 95% CI:

1.50–1.82) (Fig. 30B). Sensitivity analysis confirmed the robustness of the pooled estimate (Fig. 30C). The prediction interval, matching the confidence interval from 1.51 to 1.83, suggested consistency in the effect sizes (Fig. 30D). The power analysis indicated high statistical power (Fig. 30E). According to the GRADE criteria, the epidemiological strength of the association between the TyG index and coronary artery calcification was found to be very low (Table 3).

The correlation between TyG index and post PCI events A total of nine studies including 10, 164 participants assessed the correlation between TyG index and post PCI events (Table 2).

The analysis revealed a significant association between the TyG index as a categorical variable and an increased risk of major cardiovascular outcomes following PCI (HR = 2.03, 95% CI: 1.64–2.51, $P < 0.01$) (Fig. 31A). The included studies showed considerable heterogeneity ($I^2 = 77.09\%$, $P < 0.01$). Publication bias assessments indicated no significant issues according to Egger’s regression test ($P = 0.051$) and Begg’s regression test ($P = 0.25$). The trim and fill method did not suggest any missing studies, leaving the adjusted HR unchanged (HR = 2.03, 95% CI: 1.64–2.51) (Fig. 31B). Sensitivity analysis confirmed the stability of the pooled estimate (Fig. 31C). The prediction interval for the true effect sizes ranged from 1.01 to 4.11, indicating variability in the potential outcomes (Fig. 31D). The results were reported as HR and calculating power analysis was not possible.

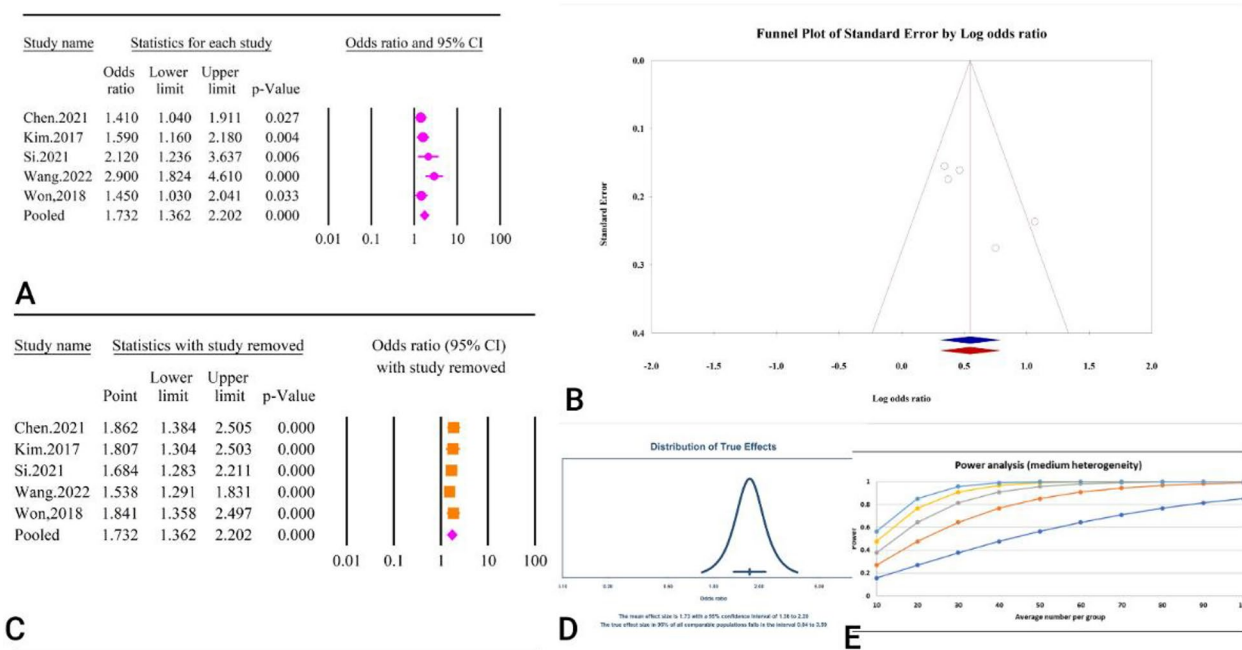


Fig. 29 The association between TyG index as a continuous variable and coronary artery calcification. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval. **E** Power analysis

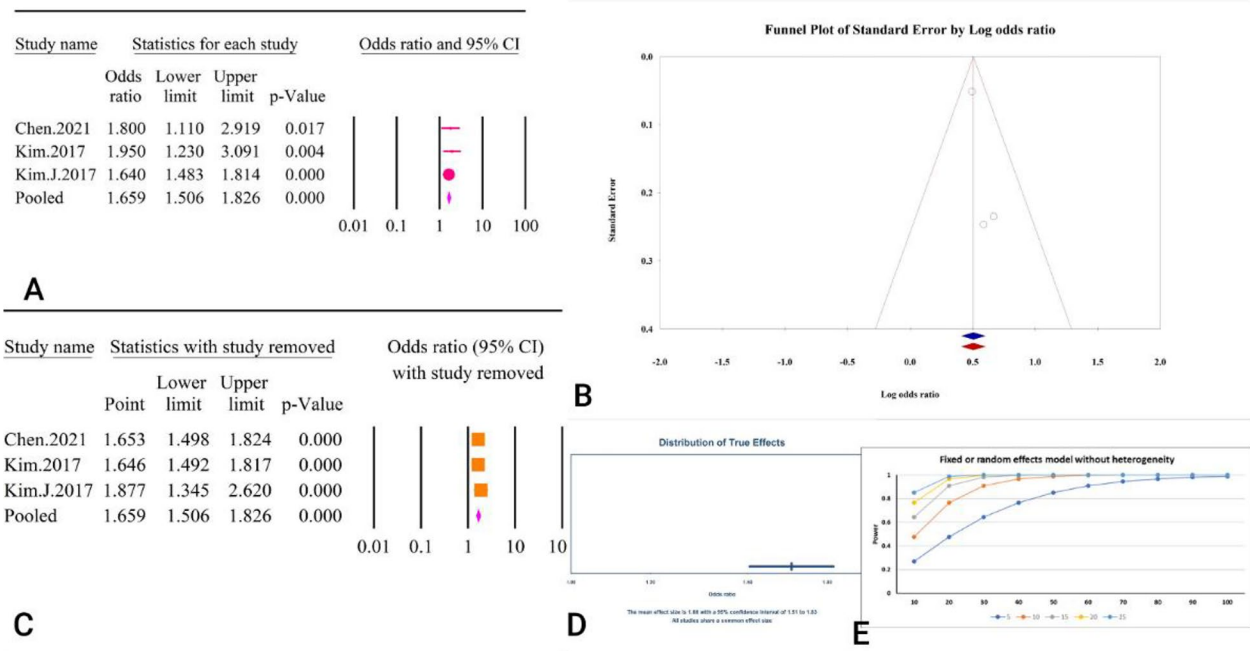


Fig. 30 The association between TyG index as a categorical variable and coronary artery calcification. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval. **E** Power analysis

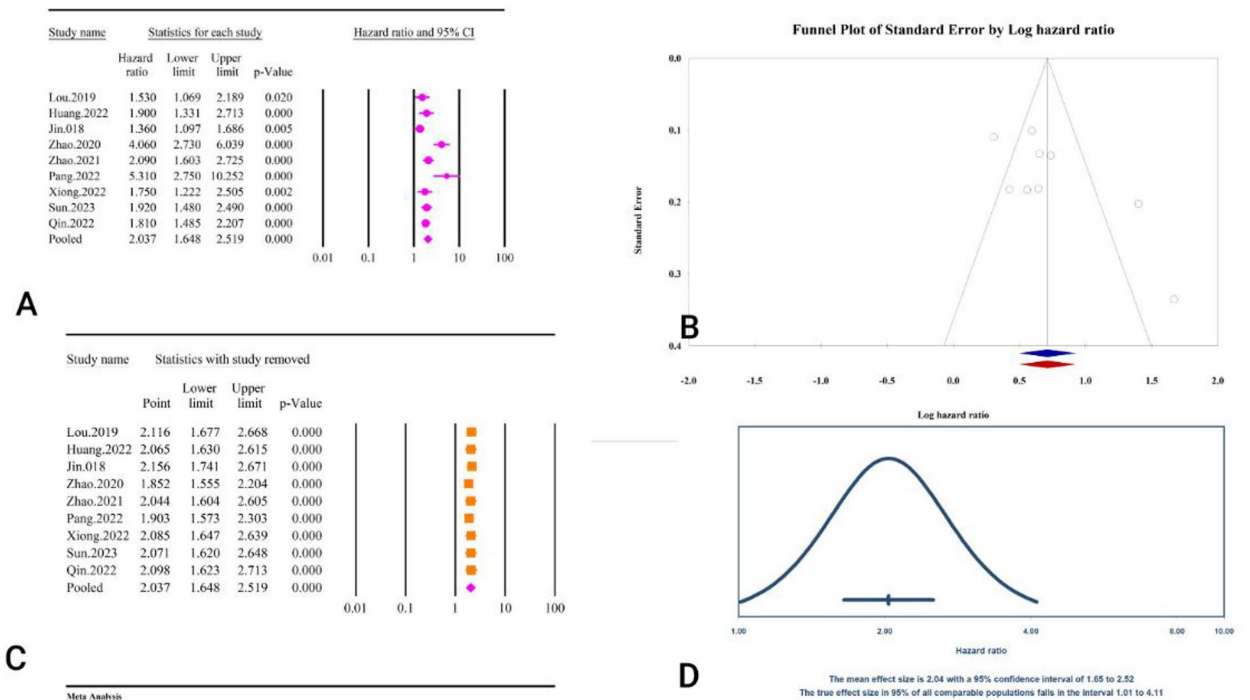


Fig. 31 The association between TyG index as a categorical variable and major cardiovascular outcomes following PCI. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval

The analysis demonstrated a significant association between the TyG index as a continuous variable and an increased risk of major cardiovascular outcomes following PCI, with HR of 1.81 (95% CI: 1.34–2.46, $P < 0.01$)

(Fig. 32A). The included studies exhibited very high heterogeneity ($I^2 = 91.72\%$, $P < 0.01$). Tests for publication bias indicated significant bias according to both Egger’s regression test ($P = 0.02$) and Begg’s regression test

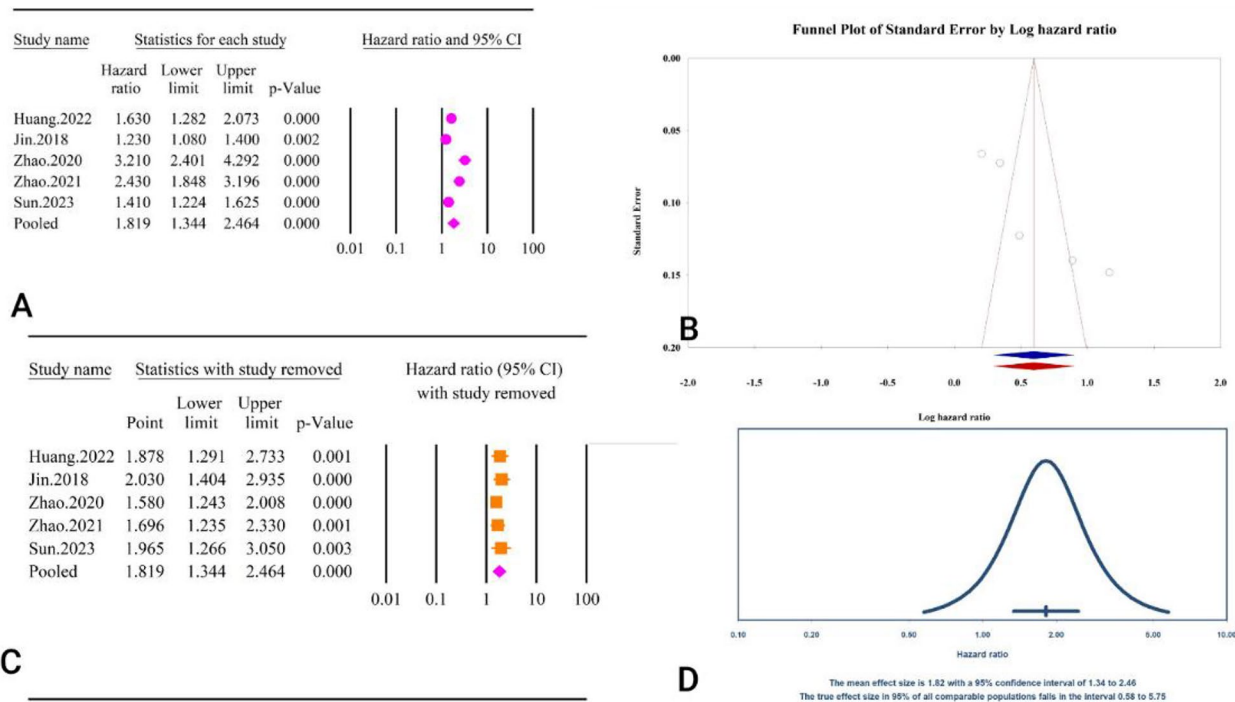


Fig. 32 The association between TyG index as a continuous variable and major cardiovascular outcomes following PCI. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval

($P=0.02$). The trim and fill method did not impute any missing studies, so the adjusted HR remained unchanged (HR=1.81, 95% CI: 1.34–2.46) (Fig. 32B). Sensitivity analysis confirmed the robustness of the pooled estimate (Fig. 32C). The prediction interval for the true effect sizes ranged from 0.58 to 5.75, reflecting a wide variability in potential outcomes (Fig. 32D). The results were reported as HR and calculating power analysis was not possible.

The epidemiological strength of the association between TyG and post-PCI major cardiovascular outcomes was low based on the GRADE criteria (Table 3).

The analysis revealed a significant association between the TyG index as a categorical variable and post-PCI all-cause mortality (HR=1.92, 95% CI: 1.35–2.74, $P<0.01$) (Fig. 33A). The included studies showed moderate heterogeneity ($I^2 = 50.91\%$, $P=0.13$). Publication bias assessments indicated minimal effects, with Egger’s regression test ($P=0.15$) and Begg’s regression test ($P=1.00$) showing no significant bias. The trim and fill method did not suggest any missing studies, leaving the adjusted HR unchanged (HR=2.18, 95% CI: 0.97–4.87) (Fig. 33B). Sensitivity analysis showed significant change in pooled result after removal of Sun, 2023 [62] (HR=0.68, 95% CI: 0.23–2.02, $P=0.49$) (Fig. 33C). The prediction interval for the true effect sizes ranged from 0.01 to 16638.72, indicating considerable variability in potential outcomes (Fig. 33D). The results were reported as HR and calculating power analysis was not possible.

For the TyG index as a continuous variable, the analysis did not show a significant association with post-PCI all-cause mortality (HR=0.94, 95% CI: 0.28–3.12, $P=0.92$) (Fig. 34A). The included studies exhibited high heterogeneity ($I^2 = 73.95\%$, $P=0.02$). Tests for publication bias indicated no significant bias according to both Egger’s regression test ($P=0.09$) and Begg’s regression test ($P=1.00$). The trim and fill method did not impute any missing studies, so the adjusted HR remained unchanged (HR=0.94, 95% CI: 0.28–3.12) (Fig. 34B). The sensitivity analysis showed a significant change in the pooled results after the removal of Zhao.2020 [63] (HR=1.34, 95% CI: 0.37–4.18, $P=0.65$), Zhao,2021 [64] (HR=1.11, 95% CI: 0.23–5.32, $P=0.89$), and Sun, 2023 [62] (HR=0.48, 95% CI: 0.17–1.31, $P=0.15$) (Fig. 34C). The prediction interval for the true effect sizes ranged from 0.01 to 975086.18, indicating wide variability in potential outcomes (Fig. 34D). The results were reported as HR and calculating power analysis was not possible.

The epidemiological strength of the association between TyG and post-PCI all cause mortality was low based on the GRADE criteria (Table 3).

The analysis revealed a significant association between the TyG index as a categorical variable and post-PCI revascularization (HR=2.61, 95% CI: 1.46–4.65, $P<0.01$) (Fig. 35A). The included studies exhibited high heterogeneity ($I^2 = 83.56\%$, $P<0.01$). Tests for publication bias indicated minimal effects, with Egger’s regression test

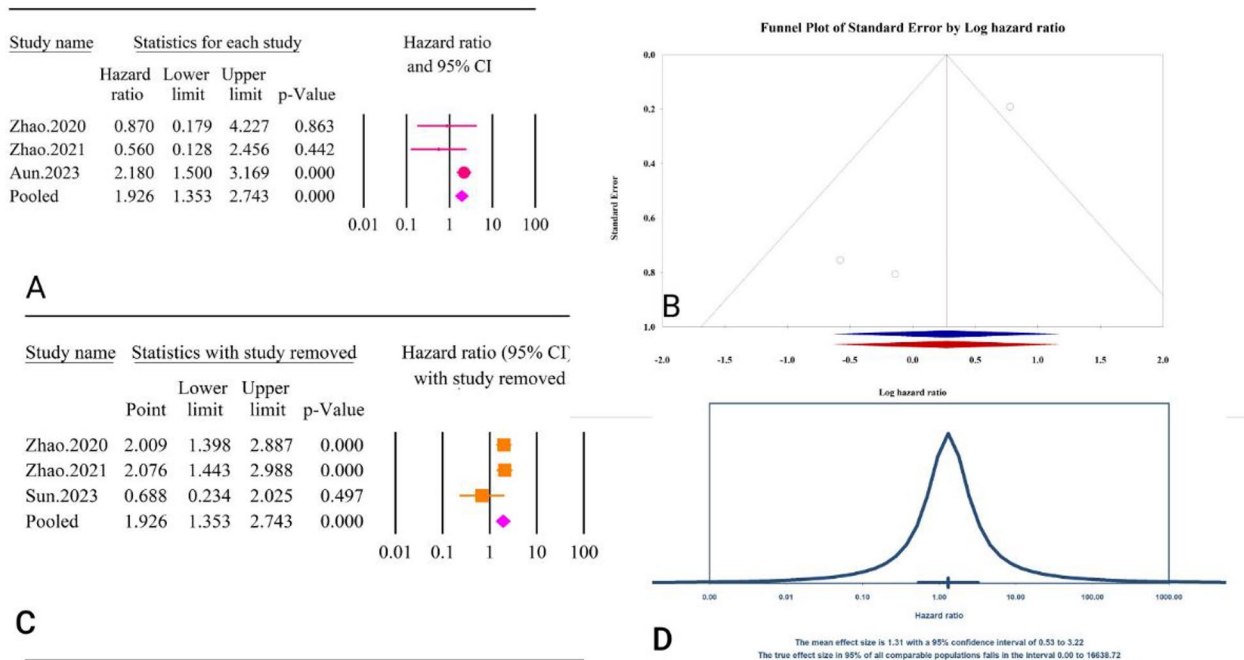


Fig. 33 The association between TyG index as a categorical variable and all-cause mortality following PCI. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval

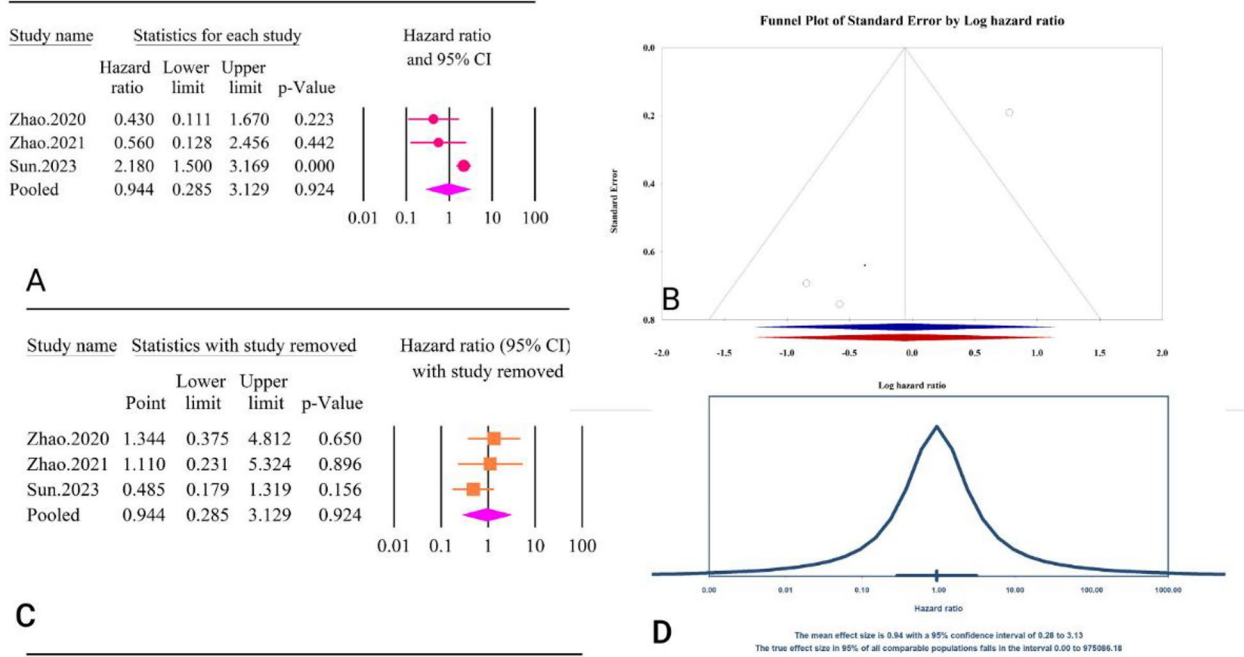


Fig. 34 The association between TyG index as a continuous variable and all-cause mortality outcomes following PCI. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval

($P=0.58$) and Begg’s regression test ($P=1.00$) showing no significant bias. The trim and fill method did not suggest any missing studies, leaving the adjusted HR unchanged (HR=2.61, 95% CI: 1.46–4.65) (Fig. 35B). Sensitivity analysis showed that after the elimination of the Zhao.2021

study, the association became insignificant (HR=2.83, 95% CI: 0.05–8.41, $P=0.06$) [64] (Fig. 35C). The prediction interval for the true effect sizes ranged from 0.01 to 2851.01, indicating considerable variability in potential

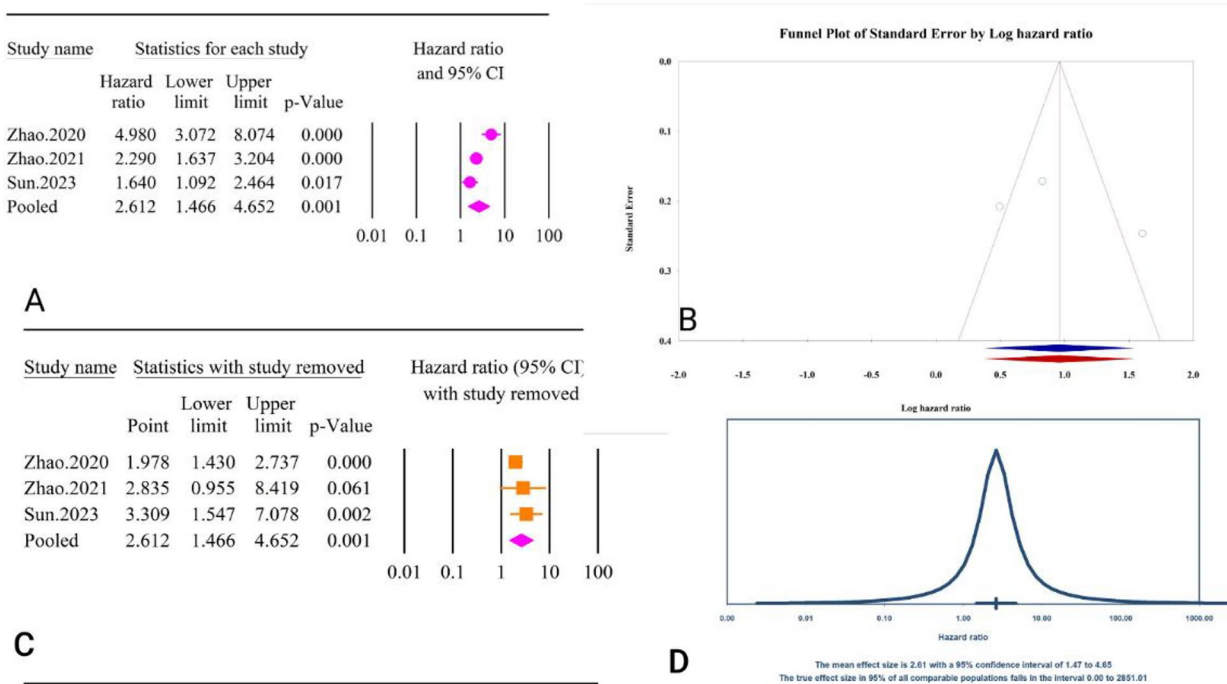


Fig. 35 The association between TyG index as a categorical variable and post-PCI revascularization. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval

outcomes (Fig. 35D). Calculating power analysis was not possible due to reported results in HR.

For post-PCI revascularization and TyG index as a continuous variable, the analysis revealed a significant association (HR=2.05, 95% CI: 1.20–3.50, $P<0.01$) (Fig. 36A). The included studies exhibited high heterogeneity ($I^2 = 89.78\%$, $P<0.01$). Tests for publication bias indicated minimal effects, with Egger’s regression test ($P=0.20$) and Begg’s regression test ($P=1.00$) showing no significant bias. The trim and fill method did not suggest any missing studies, leaving the adjusted HR unchanged (HR=2.05, 95% CI: 1.20–3.50) (Fig. 36B). Sensitivity analysis showed changes in the overall summary after elimination Zhao, 2021 (HR=1.96, 95% CI: 0.86–4.48, $P=0.10$) [64] and Zhao, 2020 (HR=1.69, 95% CI: 0.97–2.95, $P=0.06$) (Fig. 36C) [63]. The prediction interval for the true effect sizes ranged from 0.01 to 1552.36, indicating considerable variability in potential outcomes (Fig. 36D).

The epidemiological strength of the association between TyG and post-PCI revascularization was very low based on the GRADE criteria (Table 3).

The analysis revealed a significant association between the TyG index as a categorical variable and post-PCI non-fatal MI (HR=2.02, 95% CI: 1.31–3.10, $P<0.01$) (Fig. 37A). The included studies exhibited no heterogeneity ($I^2 = 0.00\%$, $P=0.96$). Tests for publication bias indicated minimal effects, with Egger’s regression test ($P=0.57$) and Begg’s regression test ($P=0.29$) showing no significant bias. The trim and fill method did not suggest

any missing studies, leaving the adjusted HR unchanged (HR=2.02, 95% CI: 1.31–3.10) (Fig. 37B). Sensitivity analysis showed no significant effect of any single study on the overall sample size (Fig. 37C). The prediction interval for the true effect sizes ranged from 1.32 to 3.10, indicating limited variability in potential outcomes (Fig. 37D).

When examining post-PCI non-fatal MI as a continuous variable, the analysis identified a significant association (HR=2.56, 95% CI: 1.49–4.40, $P<0.01$) (Fig. 38A). The included studies displayed moderate heterogeneity ($I^2 = 63.41\%$, $P=0.06$). Assessment for publication bias revealed minimal influence, with Egger’s regression test ($P=0.12$) and Begg’s regression test ($P=1.00$) both showing no significant bias. The trim and fill method did not indicate any missing studies, and the adjusted HR remained unchanged (HR=2.56, 95% CI: 1.49–4.40) (Fig. 38B). Sensitivity analysis demonstrated that the exclusion of any single study did not significantly impact the overall sample size (Fig. 38C). The prediction interval for true effect sizes spanned from 0.01 to 1013.95, reflecting substantial variability in possible outcomes (Fig. 38D).

The epidemiological strength of the association between TyG and post-PCI MI was moderate based on the GRADE criteria (Table 3).

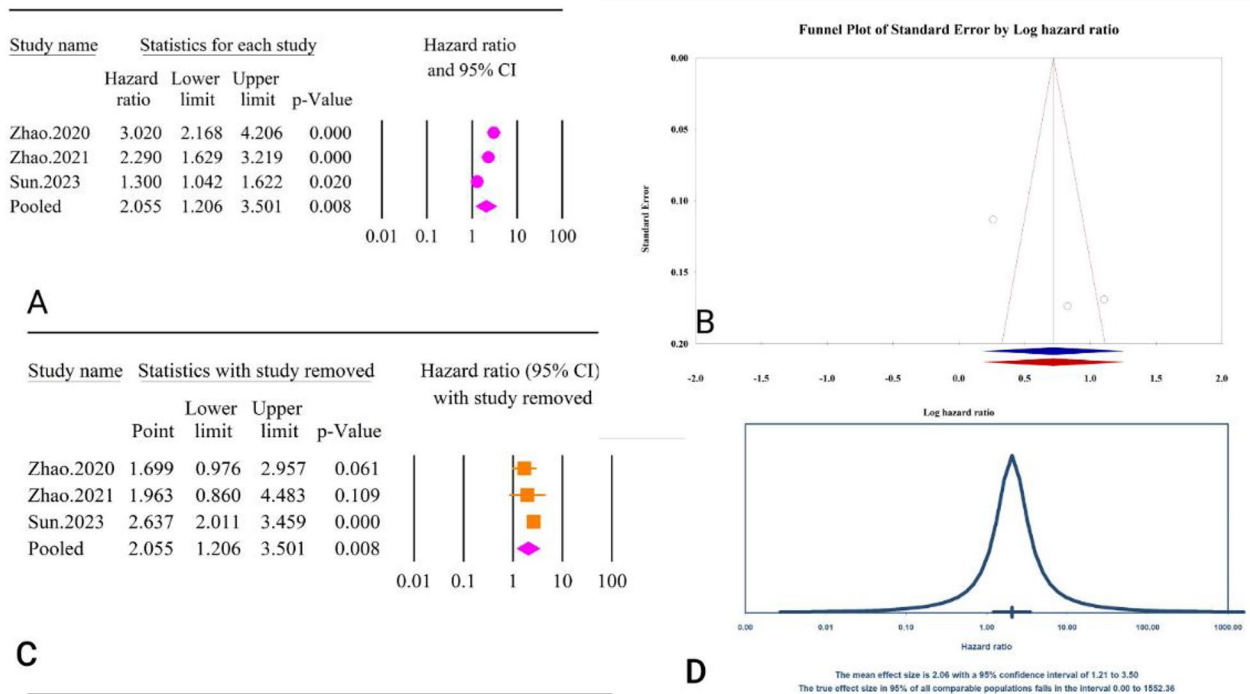


Fig. 36 The association between TyG index as a continuous variable and post-PCI revascularization. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval

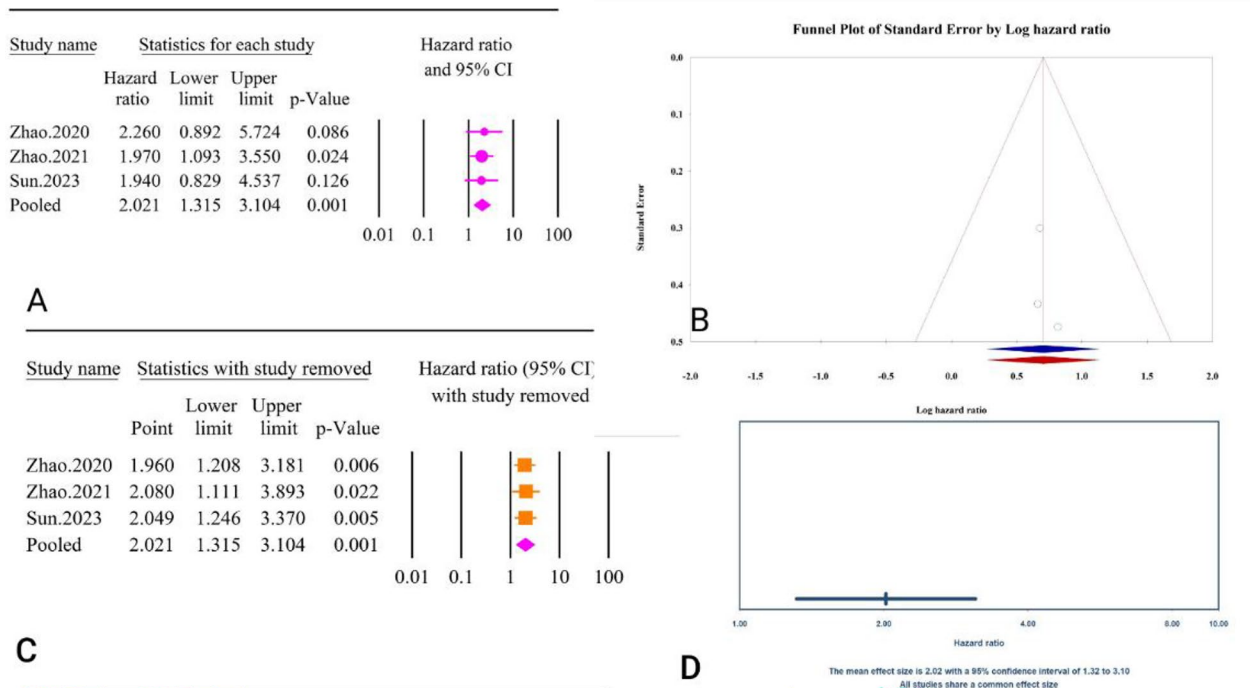


Fig. 37 The association between TyG index as a categorical variable and post-PCI myocardial infarction. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval

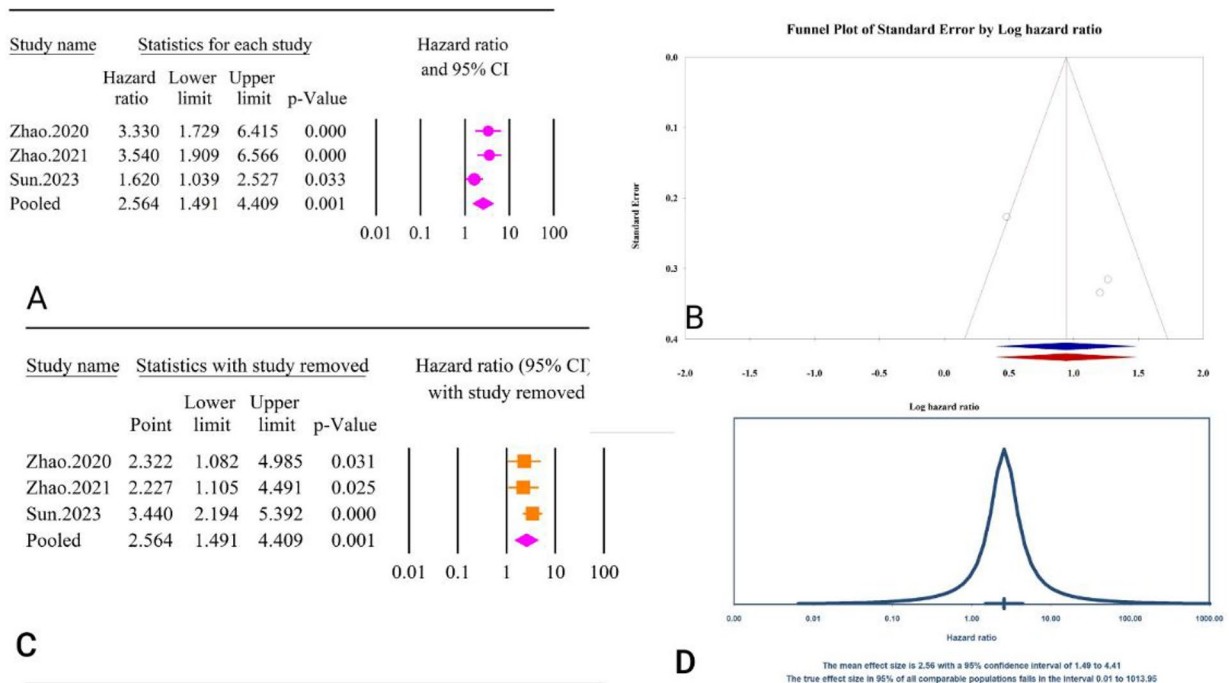


Fig. 38 The association between TyG index as a continuous variable and post-PCI myocardial infarction. **A** Forest plot. **B** Publication bias. **C** Sensitivity analysis. **D** Prediction interval

Discussion

It has been proposed that the triglyceride-glucose (TyG) index can be used as an accessible, practical, and affordable substitute marker for the hyperglycemic-hyperinsulinemic clamp test in order to measure insulin resistance (IR) [65]. The TyG index has been manifested to better predict and identify the presence of insulin resistance than the homeostasis model assessment of insulin resistance (HOMA-IR) method, as shown in several studies [66–69]. As the TyG index is highly relevant in predicting IR, it can be used to identify the risk level of various metabolic conditions, such as metabolic syndrome, type 2 diabetes mellitus, non-alcoholic fatty liver disease, cardiovascular disease, and atherosclerosis [70, 71]. A large volume of original and meta-analysis studies has been conducted to evaluate the prognostic and diagnostic value of TyG across various medical conditions.

Our analysis showed a significant relationship between the TyG index and T2DM. Elevated fasting plasma glucose and triglyceride levels are two components of the metabolic syndrome linked to IR and the development of chronic diseases [72]. It is important to note that IR usually appears about 1–2 decades before T2DM is diagnosed [73]. Consequently, early detection of IR is crucial for devising effective health interventions to prevent the onset of T2DM [74]. Multiple studies conducted with populations from America, Europe, and Asia have found that a higher TyG index is significantly associated with

IR, despite some baseline variables being influenced by ethnicity [75–81].

Research has found that over 60% of individuals diagnosed with T2DM will go on to develop DR within the first 10 years of their disease onset [82]. Recent studies have shown a strong association between IR and DR [83]. In the early stages of DR, there are typically no obvious symptoms [84]. As a result, many patients only seek medical attention when they start experiencing blurred vision and vision loss, which indicates a serious stage. This late presentation is not favorable for subsequent recovery and prognosis. Accordingly, early detection of DR is crucial. Therefore, a noninvasive and convenient index should be identified for screening and detecting early-stage patients [38]. Our final analysis found a link between a higher TyG index and an increased risk of developing DR. Therefore, the TyG index, as an easily accessible and routinely available indicator, may represent a potentially valuable clinical option for the early diagnosis of DR.

Our research discovered that a high TyG index could indicate or predict GDM. The available evidence suggests that the main cause or pathogenesis of GDM is associated with IR and decreased insulin secretion during pregnancy [85]. Previous studies have found a relationship between a high TyG index and the development of GDM [86–88]. However, other studies failed to find such a correlation [87]. Previous research has shown that triglyceride (TG) levels fluctuate during pregnancy to meet fetal needs [89]. TG levels decrease in the first 2 months, then

gradually increase over the next 7 months. Therefore, comparing the TyG index before or around 2 months of pregnancy may be more sensitive. In addition, individual differences among the study participants may contribute to the inconsistency and heterogeneity observed in TyG index levels. For example, it's important to consider potential racial differences in physiology that could impact the TyG index [41].

Our study showed that individuals with a higher TyG index are more susceptible to developing coronary artery disease. The TyG index is a highly accurate and precise indicator for detecting IR, which increases the risk of developing cardiovascular disease [90]. Normally, insulin promotes vasodilation by stimulating nitric oxide production. However, when insulin signaling is dysregulated, it can reduce the availability of nitric oxide, leading to increased vascular stiffness [91]. The nonenzymatic glycosylation of lipids is a factor that contributes to atherosclerosis, along with hypertriglyceridemia and hyperglycemia. Hypertriglyceridemia can result in the production of low-density lipoproteins, promoting atherosclerosis and weakening the protective impact of high-density lipoproteins [92]. Additionally, hyperglycemia can accelerate atherosclerosis directly or indirectly [93]. Our study demonstrated that a higher TyG index is associated with the development and progression of heart failure. Indeed, IR is widely recognized for its harmful effects, such as oxidative stress, endothelial dysfunction, and myocardial remodeling. These contribute to defective cardiac function and the development of heart failure [23, 94].

Various biomarkers have been identified and evaluated for the risk assessment of AF, such as high-sensitivity troponin I [95], C-reactive protein (CRP) [96], fibroblast growth factor-23 (FGF-23) [97], the N-terminal pro-B-type natriuretic peptide (NT-proBNP) [96, 98], Galectin-3 [99], and several micro-RNAs [100]. Other biomarkers related to baseline risk factors, such as diabetes [101] and IR [87], have also been examined for their dual diagnostic and prognostic purposes. Our final analysis found an essential relationship between a higher TyG index and the development of AF. Therefore, the TyG index, as an established, cost-effective, and easily measurable indicator of IR, may assist clinicians in identifying patients with a higher risk of atrial fibrillation (AF). This could help in the early detection of atrial fibrillation, allowing for timely intervention and management [56].

Our final analysis also found a positive relationship between the TyG index and the development of HTN. Previous research has indicated that IR is associated with low-level systemic inflammation, which may contribute to endothelial dysfunction [102–104]. Additionally, IR may also affect the metabolism of sodium in the kidneys, stimulate the sympathetic nervous system's activity [105],

and modulate the secretion of vasoactive substances [106]. All of these factors have been linked to the development of hypertension.

In the context of OSA, research has shown a positive correlation between the TYG index and the presence of the condition. Chronic intermittent hypoxia and sleep deprivation have been extensively linked to the development of IR through multiple pathways. [107] The activation of Hypoxia-Inducible Factor 1 (HIF-1) triggers a cascade of inflammatory signaling and impairs insulin signaling, contributing to the onset of IR [108, 109]. Additionally, hypoxia disrupts sympathetic nervous system function, leading to increased oxidative stress and altered adipokine secretion, which can further exacerbate IR [110]. Although confounding factors like obesity and other metabolic conditions play a role in this regard, Bikov's research has shown that even after adjusting for factors like body mass index (BMI), there remains a positive correlation between the presence of OSA and the TYG index [111].

Clinical studies have established a clear association between the presence of IR and CKD, and these IR levels have been shown to rise progressively alongside the worsening stages of CKD [112, 113]. TYG, as a promising marker of IR, has been closely linked to an increased risk and prevalence of CKD in this study and previous ones [114, 115]. Multiple mechanisms underlie the association between IR and CKD. IR disrupts the delicate balance between vasodilation and vasoconstriction within the kidney, ultimately leading to glomerular hyperfiltration [116]. It can interfere with mitochondrial function and energy metabolism in proximal tubular cells and disrupt the cytoskeletal architecture of podocytes, ultimately leading to dysfunction in the filtration barrier and proteinuria [117–120]. By addressing the important role of IR in the pathogenesis of CKD, TYG as a reliable surrogate marker of IR can play a crucial role first in the identification of the risk of developing CKD, second in predicting its progression to end-stage levels (ESRD), and third in identifying the risk of all-cause mortality in patients with CKD [121, 16].

CIN, a form of acute kidney injury following contrast exposure, is typically seen in patients undergoing invasive treatments for non-ST-segment elevation myocardial infarction (NSTEMI) [122, 123]. It can occur even in patients with normal baseline kidney function and is associated with higher mortality rates and hospital stays [124]. Therefore, a proper risk assessment and finding high-risk patients for timely prophylactic management are crucial. As reported in previous studies, diabetes is a well-established risk factor for the development of CIN [125, 126]. Thus, TyG index was evaluated in nondiabetic NSTEMI patients after percutaneous coronary intervention, and several original investigations

discovered a high association between the TyG index and the risk of CIN. These findings were consistent with our results [127, 128].

NAFLD and MAFLD are two terms used to describe metabolic diseases related to steatosis in the liver, which are closely associated with the underlying condition of IR [129]. In this meta-umbrella study, after considering all original articles within various meta-analyses, there was a close relationship between metabolic syndrome and NAFLD with the TyG index. IR can manifest in both the liver and peripheral tissues. Hepatic IR impairs the liver's ability to suppress glucose production, leading to hyperglycemia [130]. Peripheral IR, on the other hand, reduces the inhibitory effect of insulin on lipolysis, resulting in an increased flow of free fatty acids to the liver [131]. This excessive influx of fatty acids, combined with impaired fat metabolism in the liver, ultimately contributes to the development of hepatic steatosis, the hallmark of NAFLD and MAFLD [132]. Given the central role of IR in the pathogenesis of these metabolic liver diseases, it is crucial to identify a reliable marker that can accurately assess IR. Recent evidence suggests that the TyG index may be a more sensitive and reliable indicator of IR compared to the traditional HOMA-IR, particularly in the context of NAFLD and metabolic syndrome [67, 133].

There aren't so many studies assessing the relationship between TyG and the risk of cognitive impairment and dementia. In the last meta-analysis assessing this correlation, there were only 10 studies included [43]. However, in our study, it was demonstrated that there is a significant association between TyG and both cognitive impairment and dementia. Drugs such as statins and hypoglycemic agents like metformin are important to consider as they are known to decrease the risk of cognitive impairment as well as affect the TyG index measurement [134, 135]. In addition, other factors like ethnicity, APOE genotype, and underlying diseases such as diabetes and hypertension are important factors that should be taken into consideration in future studies to make further rational analyses [136].

Stroke, as an acute neurological condition, greatly reduces the quality of life of patients and causes significant social and economic burdens in societies [137]. In our study, after assuming all the data, the results revealed that the risk of ischemic stroke and its recurrence was significantly related to the value of the TyG index. In a study on 10,132 participants of American adults without a history of stroke at baseline with a median follow-up of 26.6 years and after considering potential confounders, they reported that for each unit increase in the TyG index, there is an increase of 32.1% in the risk of stroke incidence [138]. Also, in our results, it was demonstrated that many complications of stroke, such as poor functional outcome, worsening of neurological state, and risk

of mortality, have a significant correlation with the TyG index. However, data on stroke adverse events is controversial in different studies [139]. Yang et al. revealed that although the relationship between mortality and TyG is significant, they didn't find a significant association in terms of poor functional outcomes and neurological worsening [15]. This could be explained by some sources of heterogeneity in these studies, such as the severity of the stroke itself, the quality of rehabilitation, secondary prevention methods, the existence of CYP2C19 polymorphisms, family support, and so many other factors that should be taken into consideration to better understand these relationships [15, 140, 141]. Ultimately, TyG could be considered to optimize risk stratification for stroke in the general population and could be a valuable marker for screening and management of high-risk patients.

Strengths, limitations, and future suggestions

This umbrella review has several strengths. It integrates findings from 32 meta-analyses, offering a comprehensive and detailed synthesis of the evidence on the diagnostic utility of the TyG Index across various medical conditions. The review follows rigorous methodology by adhering to established guidelines from the Cochrane Handbook and PRISMA standards, ensuring a systematic and transparent approach to study selection, data extraction, and analysis. Furthermore, the use of the AMSTAR2 checklist for quality assessment and GRADE criteria for evaluating the epidemiological strength of the associations adds robustness to the review process.

However, there are several limitations to consider. The included meta-analyses exhibited substantial heterogeneity, which could affect the reliability of the pooled estimates. The heterogeneity might stem from differences in study populations, diagnostic criteria, and analytical methods across the original studies. Moreover, the definitions of the TyG index and the cut-off values varied among the included studies in the meta-analyses, which is another source of heterogeneity. Additionally, while publication bias was generally low, it cannot be entirely ruled out, particularly in areas with fewer studies. Another limitation was that 22 of the 32 included studies were from a single nationality (China), which may impact the robustness and comprehensiveness of the results. In addition, the overall quality of the included meta-analyses varied, with some being assessed as low or critically low quality, which may influence the robustness of the conclusions drawn.

Future research should focus on addressing the sources of heterogeneity identified in this review. High-quality, large-scale prospective studies are needed to validate the associations between the TyG Index and various medical conditions. Standardizing the diagnostic criteria and analytical methods used in studies involving the TyG Index

could help reduce variability and improve comparability. Moreover, there are metabolic diseases such as polycystic ovarian syndrome, obesity, and dyslipidemia for which meta-analyses should be conducted to evaluate the prognostic value of the TyG index. Additionally, further research should explore the potential mechanisms underlying the associations between the TyG Index and different diseases, which could provide deeper insights into its clinical utility. Investigating the TyG Index in diverse populations and settings would also enhance the generalizability of the findings, supporting its broader application in clinical practice.

Conclusion

The TyG Index shows significant promise as a screening marker for a wide range of medical conditions, including chronic kidney disease, type 2 diabetes mellitus, ischemic stroke, non-alcoholic fatty liver disease, cognitive impairment, coronary artery calcification, obstructive sleep apnea, gestational diabetes mellitus, metabolic syndrome, dementia, heart failure, atrial fibrillation, hypertension, and post-percutaneous coronary intervention events. Despite the encouraging associations, the substantial heterogeneity and varying quality of the included studies indicate the necessity for further rigorous research to confirm these findings. This comprehensive umbrella review provides valuable insights into the current evidence, supporting the potential clinical utility of the TyG Index and guiding future research efforts.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12933-024-02392-y>.

Supplementary Material 1

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Author contributions

The concept development for this research was carried out by E.A.S, S.S.N, and L.D.P. The design and planning of the methodology to generate the results were handled by E.A.S and S.S.N. Supervision, including oversight, organization, implementation, and manuscript writing, was provided by E.A.S, S.N, P.B, and M.T.U. Data collection and processing, which involved conducting experiments, organizing data, and reporting findings, were managed by E.A.S, M.H.K, N.L, and A.H. The analysis and interpretation of the data, including statistical analysis, evaluation, and presentation of the results, were the responsibility of A.A and M.H.K. The literature search was performed by E.A.S and D.A. All authors contributed substantively to writing the manuscript.

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Data availability

No datasets were generated or analysed during the current study. The datasets used and/or analyzed during the current study can be provided from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

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Consent for publication

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Competing interests

The authors declare no competing interests.

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