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Association between triglyceride-glucose index and risk of chronic kidney disease: a systematic review and meta-analysis

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ABSTRACT

Introduction: The triglyceride-glucose index (TyG) is a reliable alternative marker for insulin resistance. Since insulin resistance is a risk factor for chronic kidney disease (CKD).
Objectives: This study aimed to investigate the relationship between the TyG index and CKD using the systematic review method and meta-analysis.
Material and Methods: The required sources were searched using the databases Cochrane, Web of Science, PubMed, ProQuest, and Google Scholar Search Engine without a time limit. STATA 14 software was conducted for data analysis, and tests with p-values lower than 0.05 ($P < 0.05$) were considered statistically significant.
Results: Findings from 20 research with a total of 277986 samples demonstrated that high TyG index increased the risk of CKD in the total population, female patients, and male patients by 37% (OR: 1.37, 95% CI: 1.25, 1.5), 38% (OR: 1.38, 95% CI: 1.19, 1.61), and 31% (OR: 1.31, 95% CI: 1.13, 1.50), respectively. Furthermore, high TyG levels in individuals younger than 55 and those aged 55 or higher increased the risk of CKD by 54% (OR: 1.54, 95% CI: 1.36, 1.74) and 23% (OR: 1.23, 95% CI: 1.14, 1.32), respectively. Nevertheless, Australia (OR: 1.68, 95% CI: 1.56, 1.81) indicated the strongest and Singapore (OR: 1.21, 95% CI: 1.06, 1.38) showed the weakest relationship between the TyG index and the risk of CKD. However, higher TyG indices increased the risk of CKD in cohort and cross-sectional studies by 35% (OR: 1.35, 95% CI: 1.20, 1.51) and 41% (OR: 1.41, 95% CI: 1.29, 1.55), respectively.
Conclusion: A high TyG index increases the risk of CKD, and women and individuals younger than 55 are the high-risk groups
Registration: This study has been compiled based on the PRISMA checklist, and its protocol was registered on the PROSPERO (ID: CRD42024544037) and Research Registry (UIN: reviewregistry1829) website.

Implication for health policy/practice/research/medical education:
Our systematic review and meta-analysis showed that, high triglyceride-glucose index increases the risk of chronic kidney disease.

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Meta-analysis

Introduction

Based on the Global Burden of Disease (GDB), chronic kidney disease (CKD) is ranked twelfth cause of death among the 133 diseases (1). A study conducted between 1990 and 2017 on the burden of kidney diseases identified 697.5 million cases of CKD worldwide (2). Population aging, hypertension, and increased rate of diabetes mellitus incidence were among the causes of increasing CKD frequency (3,4). Moreover, the mortality rate due to CKD in 2017 was 1.2 million deaths in the world, with estimates of an increase to 2.2 million deaths by 2040 in the best-case scenario and 4 million deaths in the worst-

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case scenario (2), as CKD has turned into one of the primary causes of death in the 21st century, affecting more than 10 percent of the general population (5).

Insulin resistance and metabolic syndrome are among the factors significantly associated with albuminuria (6,7), since insulin resistance is one of the top risk factors for the development of CKD (8). The triglyceride-glucose index (TyG) is a simple and reliable marker for insulin resistance, calculated using the fasting triglyceride (TG) and fasting blood glucose (FBG) values (9,10). The TyG index in patients with type 2 diabetes mellitus is significantly higher than in the general population, which can be conducted to identify high-risk individuals (5).

Objectives

The TyG index was found to be significantly correlated with the incidence of cardiovascular illnesses, including hypertension, myocardial infarction, and coronary heart disease (11-13). The relationship between the TyG index and CKD is debatable, however, other studies showed different results (14,15). Accordingly, this study aimed to investigate the association between the TyG and CKD using the systematic review method and meta-analysis.

Material and Methods

This study was conducted according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) (16), and its protocol was registered on the PROSPERO (International Prospective Register of Systematic Reviews) and Research registry websites.

Search strategy

Two authors conducted searches in databases Web of Science, Cochrane, ProQuest, PubMed, and Google Scholar Search Engine for articles published before May 1, 2024. The searches applied the Medical Subject Heading (MeSH) keywords and their equivalents. Combinations of keywords "Triglyceride-Glucose index; TyG index; chronic kidney disease; CKD; Renal insufficiency; Chronic" were conducted for advanced search. The keywords were combined using the "AND" and "OR" operators. The manual search included an investigation of the list of primary references. The search strategy for the database Web of Science was as follows; Triglyceride-glucose index OR TyG index (All Fields) AND Chronic kidney disease OR CKD OR Renal Insufficiency, Chronic (All Fields).

PICO components

- Population: The observational studies investigating the relationship between the TyG and the risk of CKD.
- Intervention/Exposure: The TyG index.
- Comparison: Individuals without CKD or patients at the early stages.
- Outcomes: The association between the TyG index and the risk of CKD.

Inclusion criteria

The observational studies evaluating the relationship between the TyG index and the risk of CKD entered this study.

Exclusion criteria

Duplicate studies, review articles, meta-analyses, low-quality studies, abstracts, experimental studies, those with inaccessible full text, posters, and studies with incomplete data.

Quality assessment

Two authors evaluated the quality of the studies using the Newcastle-Ottawa Scale questionnaire. This tool comprised nine questions, and the authors could assign a maximum of one star to each question, except for the comparison question, which they could assign two. Accordingly, the lowest and highest scores for this tool were zero (lowest quality) and ten (highest quality). Studies that received seven or more stars from this tool entered the present tool (17).

Data extraction

The crucial data needed for this investigation was extracted by two authors. The data included the first author's name, study type, mean age, sample size, mean TyG index, country of origin, study duration, publication year, and the relationship between the TyG index and the risk of CKD.

Statistical analysis

The logarithm of the odds ratio (OR) and hazard ratio (HR) were applied for each study and the combination of all studies. The I^2 index was used to assess the heterogeneity and heterogeneities lower than 25%, between 25 and 75, and those higher than 75% were considered low, moderate, and extreme. The random effects model was employed due to the great heterogeneity of the current investigation. The subgroup analysis was conducted to evaluate the effect of variables such as age, country of origin, and study type. Further analyses were conducted using meta-regression and publication bias. The statistical analysis was conducted using the STATA 14 software, and tests with P values lower than 0.05 ($P < 0.05$) were considered statistically significant.

Results

The current study excluded 306 articles from the studies that were retrieved from the aforementioned databases since 134 of them were duplicates. The abstracts of the remaining 172 articles were evaluated, and 23 studies without accessible full texts were dismissed. Out of the other 149 articles, 28 lacked the required data, 101 others were reviews or had low qualities, which were removed, and 20 studies remained for the systematic review process and meta-analysis (Figure 1).

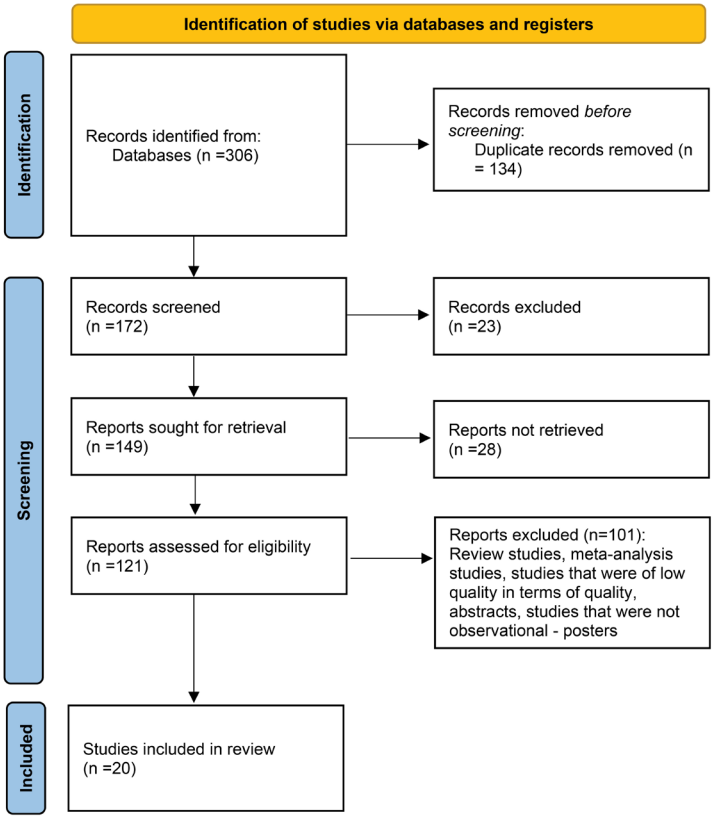

Figure 1. The PRISMA flow chart of study selection

A total of 20 observational studies with 277 986 samples were examined, 14 of which were cohort studies and 6 were cross-sectional studies. Fourteen studies were conducted in China, whereas the remaining six were conducted in the United States, England, Singapore, Australia, Japan, and South Korea (Table 1).

The highest TyG level significantly increased the risk of CKD (OR: 1.37, 95% CI: 1.25, 1.50) compared with the lowest TyG level (Figure 2).

The highest level of the TyG index, compared with the lowest level, increased the risk of CKD in patients younger than 55 and those aged 55 or higher by 54% (OR: 1.54, 95% CI: 1.36, 1.74) and 23% (OR: 1.23, 95% CI: 1.14, 1.32), respectively (Figure 3).

Figure 4 demonstrates that the highest level of the TyG index increased the risk of CKD compared with the lowest TyG level in all of the investigated countries. Nevertheless, studies reported the most substantial relationship between the TyG index and CKD in Australia (OR: 1.68, 95% CI: 1.56, 1.81) and the weakest association in Singapore (OR: 1.21, 95% CI: 1.06, 1.38).

Figure 5 shows that the highest TyG index level increased the risk of CKD compared with the lowest level in the cohort (OR: 1.35, 95% CI: 1.20, 1.51) and cross-sectional (OR: 1.41, 95% CI: 1.29, 1.55) studies.

The highest level of TyG index increased the risk of CKD in female (OR: 1.38, 95% CI: 1.19, 1.61) and male (OR: 1.31, 95% CI: 1.13, 1.50) patients compared with the lowest level. The higher observed levels of TyG index in female patients than in males increase the risk of CKD (Figures 6 and 7).

Meta-regression plots indicated that the relationship between the "TyG index and risk of CKD" and the article's publication year ($P=0.509$) and sample size ($P=0.089$) was statistically insignificant (Figures 8 and 9).

The publication bias plot shows that there was no publication bias in the present study ($P=0.221$), and regardless of the significance of the final results, all the studies entered this meta-analysis (Figure 10).

Discussion

The present study demonstrated that high TyG index levels increased the risk of CKD in the study population, women, men, individuals younger than 55, and those aged 55 or higher by 37%, 38%, 31%, 54%, and 23%, respectively. The most substantial relationship between the TyG index and CKD was reported in Australia (68%). In contrast, the weakest relationship between the TyG index and the risk of CKD was reported in Singapore (21%).

Based on the result of a meta-analysis by Ren et al investigating the relationship between TyG index and CKD, the relative risk of the highest level compared with the lowest TyG level was (RR: 1.47, 95% CI: 1.32, 1.63), indicating a statistically significant relationship (25). The mentioned study was consistent with the present study. On one hand, the previous meta-analysis reviewed the articles

Table 1. Summarized information of the studies

Index	Author, Year	Country	Design	Total number	Mean age (year)	Duration of study	Follow-Up (year)	Mean TyG index
HR	Kunutsor SK, 2024 (15)	UK	Cohort	2362	53	NR	17.5	8.5
HR	Chen N, 2024 (18)	China	Cohort	5484	52.49	2015-2017	3.82	8.72
HR	Yu C, 2024 (19)	China	Cohort	8418	63.09	NR	4	Per 1 unit TyG change
OR	Fu X, 2023 (20)	China	Cross-sectional	288	NR	between January 2018 and January 2022	NR	9.11
OR	Kim B, 2023 (21)	South Korea	Cross-sectional	7326	66.1	2014-2018	NR	8.6
HR	Duan S, 2023 (22)	China	Cohort	179	52.28	January 2011 to December 2020	NR	9.07
OR	Wang Z, 2023 (23)	USA	Cross-sectional	9872	46.81	2011-2018	NR	8.53
OR	Liu N, 2023 (24)	China	Cross-sectional	4361	NR	2015-2018	NR	8.6
HR	Ren X, 2023 (25)	China	Cohort	10498	59	2013-2018	NR	≥9.07
HR	Low S, 2022 (26)	Singapore	Cohort	1571	57.3	March 2011 to March 2014	8.6	9.1
OR	Shi Y, 2022 (27)	China	Cross-sectional	13055	63.81	from March 2018 to August 2018	NR	8.87
HR	Zhu Q, 2022 (28)	China	Cohort	2033	55.5	between January 2012 and May 2019	2.5	8.94
HR	Lei L, 2022 (29)	China	Cohort	7822	70.84	between January 2017 and July 2021	2.04	8.65
HR	Fritz J, 2021 (30)	Austria	Cohort	176420	42.5	1988-2020	22.7	8.5
OR	Gao W, 2021 (31)	China	Cohort	2446	59.17	June to August 2009	3.9	8.74
OR	Pan Y, 2021 (14)	China	Cohort	4721	59.56	between January 2015 and November 2020	NR	9.2
OR	Xu X, 2021 (32)	China	Cohort	3868	NR	From May to September, 2011	3.1	9.01
OR	Chen T, 2020 (33)	China	Cross-sectional	2720	54.87	From January to April 2018	NR	8.6
OR	Zhao S, 2019 (34)	China	Cohort	2830	71.5	From June 2014 to August 2018	NR	8.75
HR	Okamura T, 2019 (35)	Japan	Cohort	11712	41	from 1994 to 2016	4	8

NR: Not reported; TyG: Triglyceride-glucose; OR: Odds ratio; HR: Hazard ratio.

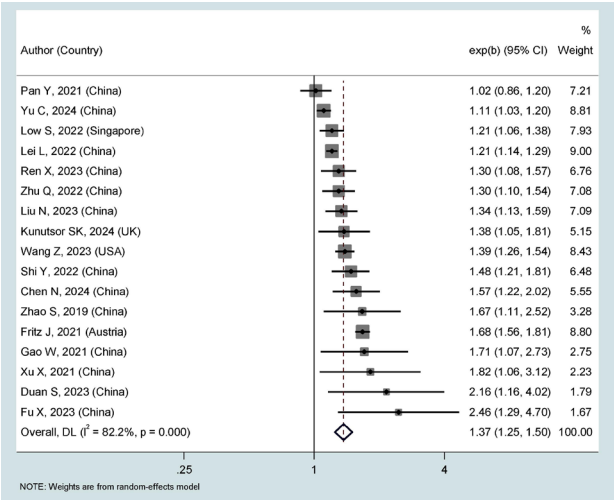

Figure 2. Association between triglyceride-glucose index and risk of CKD.

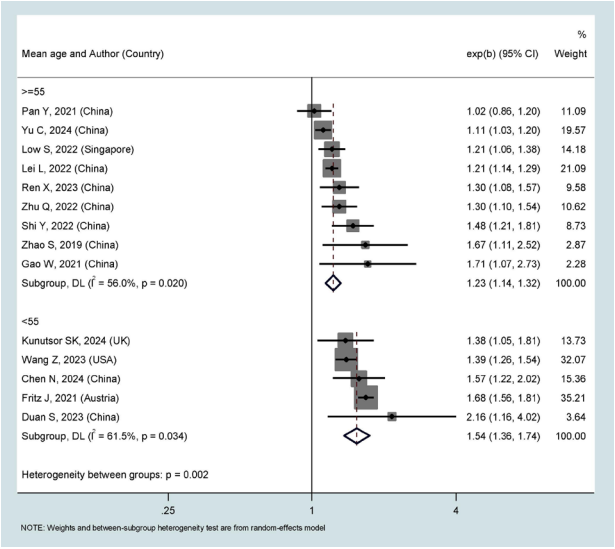

Figure 3. Association between triglyceride-glucose index and risk of CKD by mean age.

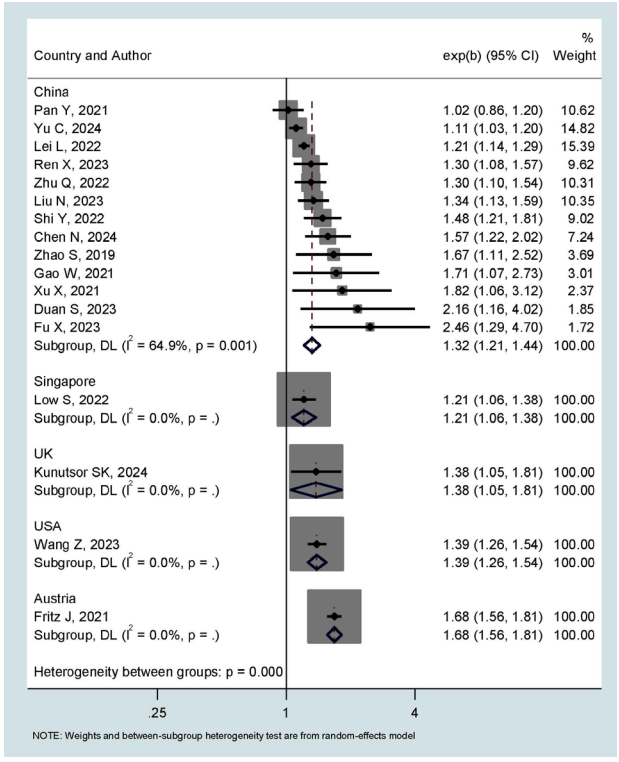

Figure 4. Association between triglyceride-glucose index and risk of CKD by country.

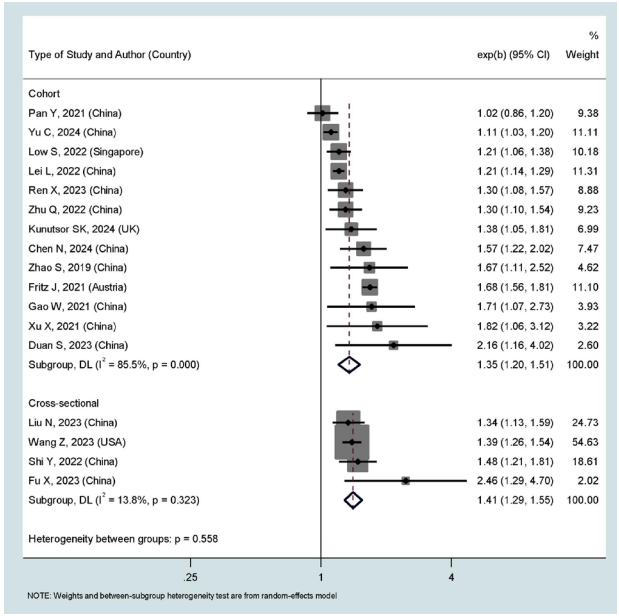

Figure 5. Association between triglyceride-glucose index and risk of CKD by design.

in PubMed and Web of Science published by March 2023. On the other hand, the present study reviewed articles in databases Cochrane, Web of Science, PubMed, and ProQuest published by May 2024, since the total number of studies in the previous meta-analysis (n = 12) increased to 20 in our study. Furthermore, unlike the previous meta-analysis, the current study conducted subgroup analysis and meta-regression.

According to the study by Qin et al evaluating the association between TyG index and kidney stones in United States adults using the cross-sectional method, each unit of increase in TyG index increased the risk of kidney stones by 12% (OR: 1.12, 95% CI: 1.02, 1.22) and its recurrence by 26% (OR: 1.26, 95% CI: 1.08, 1.4) (36). The mentioned study demonstrated that higher TyG index levels are a risk factor for kidney stones, besides increasing the risk of CKD.

Wang et al conducted a meta-analysis to examine the association between the TyG index and hypertension. They combined eight studies and demonstrated that the highest level of TyG index increased the risk of hypertension compared with the lowest level (RR: 1.53, 95% CI: 1.26, 1.85) (37). Similarly, the results of a meta-

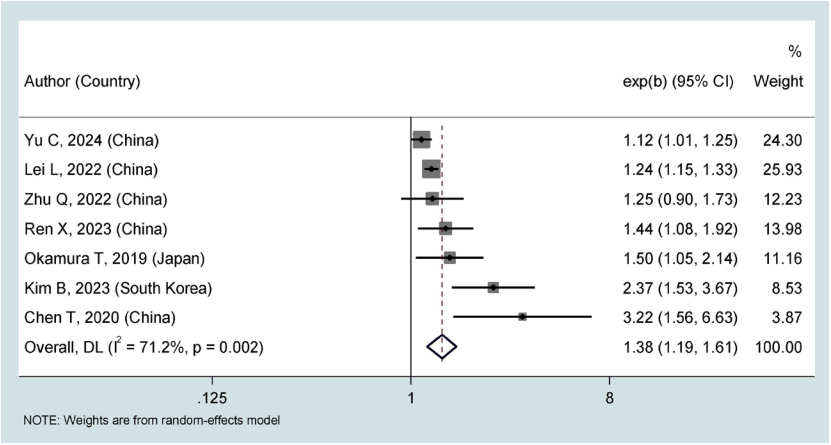

Figure 6. Association between triglyceride-glucose index and risk of CKD in women.

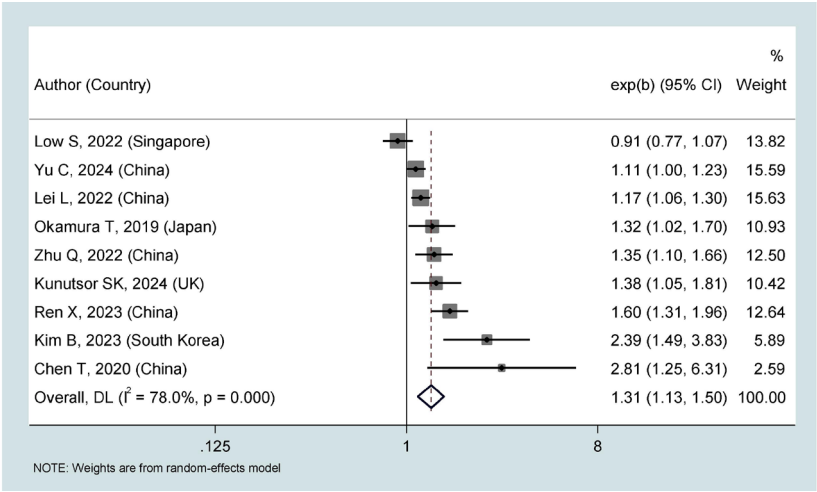

Figure 7. Association between triglyceride-glucose index and risk of CKD in men.

analysis study conducted by Xu et al in China showed higher TyG index levels increased the risk of developing hypertension (OR/HR: 1.36, 95% CI: 1.28, 1.45) (38). The mentioned studies confirmed the result of the present study and displayed that high TyG index levels increased the risk for individuals to develop hypertension.

Based on the findings of a meta-analysis by Luo et al, the highest TyG index level increased the risk of major cardiovascular adverse events in coronary patients by approximately 100% compared with the lowest TyG index level (HR: 2.14, 95% CI: 1.69, 2.71) (39). In another meta-analysis, Ding et al believed that the risk of atherosclerotic cardiovascular diseases in individuals with higher TyG index levels was significantly higher than in those with low TyG index levels (HR: 1.61, 95% CI: 1.29, 2.01) (40). Moreover, Liu et al confirmed in their meta-analysis that the highest TyG index level significantly increased the risk of coronary artery disease (HR: 2.01, 95% CI: 1.68, 2.40), myocardial infarction (HR: 1.36, 95% CI: 1.18, 1.56), and complex cardiovascular diseases (HR: 1.46, 95% CI: 1.23, 1.74) compared with the lowest TyG index level (41). According to a meta-analysis by Liang et al, the highest TyG index level is a risk factor that can increase the risk of coronary artery disease (OR: 1.94, 95% CI: 1.20, 3.14) compared with the lowest TyG index level (42). Since the mentioned studies reported that high TyG index levels were a notable risk factor for cardiovascular diseases, they were consistent with our study.

Besides hypertension and related kidney and heart diseases, high TyG index level is a potential risk factor for several diseases, including cancer, cerebrovascular disease, and non-alcoholic fatty liver disease, which we will discuss some of the related studies in the following section. In the meta-analysis by Yan, high TyG index levels increased the risk of cerebrovascular disease (RR/HR: 1.22, 95% CI: 1.14, 1.30) compared with low TyG index levels (43). A meta-analysis by Ling et al reported that the TyG index could be a new risk factor for non-alcoholic fatty liver disease (OR: 2.84, 95% CI: 2.01, 4.01) (44). Regarding cancer, a previous meta-analysis by Wang et al concluded that higher TyG index levels increased the risk of cancer (total effect size: 1.14, 95% CI: 1.08, 1.20) (45).

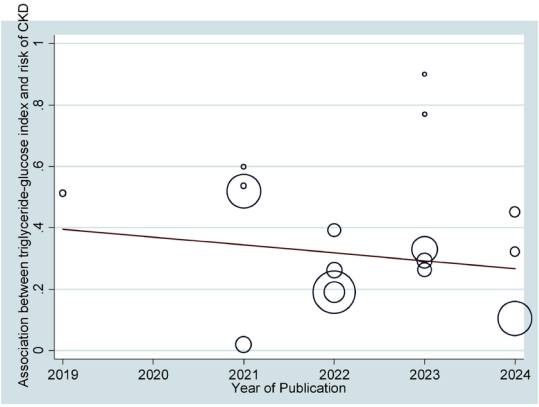

Figure 8. The meta-regression diagram showing the association between triglyceride-glucose index and risk of CKD by year of publication.

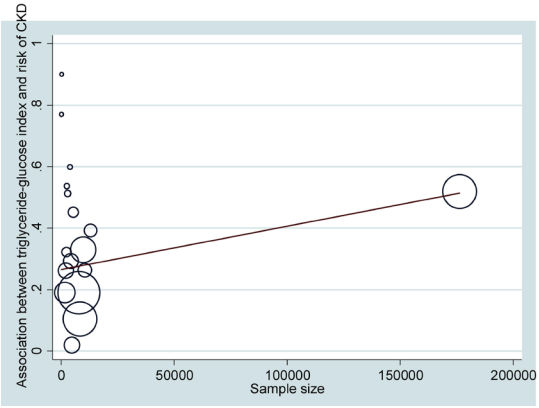

Figure 9. The meta-regression diagram showing the association between triglyceride-glucose index and risk of CKD by sample size.

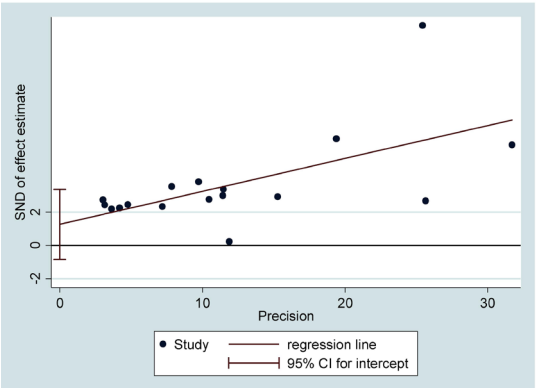

Figure 10. Publication bias chart.

The mentioned studies showed a significant relationship between high TyG index levels and the occurrence of several diseases. Accordingly, we recommend using the TyG index as a marker to identify the at-risk groups and prevent the development of diseases, including CKD, to some extent.

Conclusion

Generally, high TyG levels increase the risk of CKD. Furthermore, women with high TyG index levels were exposed to higher risks of CKD than men. Among individuals with high TyG index levels, those aged under 55 faced approximately twice the risk of CKD compared with individuals aged 55 or higher. Accordingly, women and individuals under 55 are categorized as high-risk groups. Furthermore, a greater number of published studies in different nations is required to determine whether high TyG index values in the Australian population are more harmful than in other countries.

Limitations of the study

1) Numerous investigations looked into a diverse population. For instance, some of the researchers conducted their studies on diabetic patients, whereas others selected the general population or patients with hypertension as their target. 2) Most studies were conducted in China. 3) Since most studies did not report the individual's BMI, this variable was not analyzed. The aforementioned limitations were unavoidable given that this study was a systematic review and meta-analysis. This study recommended that researchers address these limitations in future original studies.

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Authors' contribution

Conceptualization: Muhanad Muhussin Ali.
Data curation: Muhanad Muhussin Ali, Raed Muslim Mhaibes.
Formal analysis: All authors.
Investigation: Muhanad Muhussin Ali, Raed Muslim Mhaibes, Mohammed Jasim Qasim.
Methodology: All authors.
Resources: Mohammed Abdul-Mounther Othman, Qais R. Lahhob.
Supervision: Muhanad Muhussin Ali.
Validation: Muhanad Muhussin Ali, Raed Muslim Mhaibes.
Visualization: Mohammed Abdul-Mounther Othman, Qais R. Lahhob.
Writing–original draft: All authors.
Writing–review & editing: All authors.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

This study has been compiled based on the PRISMA checklist, and its protocol was registered on the PROSPERO website (ID: CRD42024544037) and Research Registry website (Unique Identifying Number (UIN) reviewregistry1829). Besides, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the author.

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