

REVIEW

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Association between the triglyceride-glucose index (TyG Index) and risk of colorectal cancer: a systematic review and meta-analysis

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Abstract

Background Colorectal cancer (CRC) is one of the most common malignancies worldwide, with increasing evidence linking metabolic dysregulation, such as insulin resistance and chronic inflammation, to its development and progression. A potential useful predictor of CRC risk is the triglyceride-glucose (TyG) index, a marker for insulin resistance that is determined using fasting triglyceride and glucose levels. The purpose of this systematic review was to assess the relationship between the TyG index and CRC and ascertain whether the TyG index is associated with the development and outcomes of CRC.

Methods A systematic review and meta-analysis was reported in accordance with the PRISMA guidelines. Comprehensive searches of PubMed, Web of Science, Scopus, and World Health Organization Virtual Health Library were conducted in 24th March 2025 to find studies assessing the relationship between the TyG index and CRC. Results of association between TyG index and CRC were summarized and a meta-analysis was done to calculate pooled hazard ratio (HR) with 95% confidence interval (CI).

Results A total of eight studies were included in the systematic review, of which five met the criteria for inclusion in the quantitative synthesis. The pooled analysis showed that the hazard of developing CRC was significantly greater for those with a higher TyG index (HR = 1.18; 95% CI: 1.12–1.25; $P < .001$). In addition, meta-analysis indicated that hazard of developing CRC significantly increased for each one-unit increase in the TyG index (HR = 1.28, 95% CI: 1.18 to 1.39, $P < .001$).

Conclusion Higher TyG index level is substantially linked to an elevated hazard of developing CRC. Therefore, the TyG index can be a useful tool for CRC risk identification. Standardizing cut-off values and researching clinical applicability in various populations should be the main goals of future research. Due to the limitations posed by the small number of studies, further prospective studies are needed to generate more robust and generalizable evidence.

Keywords Triglyceride-glucose index, Colorectal cancer, Systematic review

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Background

Colorectal cancer (CRC) is one of the most common types of cancers and is the third leading cause of cancer-related deaths globally, with recent increasing trends in CRC incidence worldwide [1–3]. The number of incident cases and deaths from CRC have more than doubled worldwide in the past three decades in several parts of the world [1]. Currently, it is the most common malignant cancer in the gastrointestinal tract, representing 13% of all malignant tumors [3]. The incidence of CRC is increasing, and the number of CRC cases could rise to 3.2 million by 2040 [4]. CRC is influenced by several risk factors such as age and inflammatory bowel disease, as well as smoking, which could elevate the CRC risk by 40% [4].

Studies have showed that CRC is influenced by insulin resistance and lipid profile changes, which are key components of metabolic dysfunction that have been extensively studied in relation to CRC [5–7]. Insulin resistance is marked by diminished cellular response to insulin, resulting in metabolic dysregulation and it is one of the metabolic abnormalities leading to the onset of multiple chronic diseases ([7, 8]). By stimulating pro-mitogenic and anti-apoptotic effects, insulin resistance promotes cell proliferation and inhibits apoptosis, potentially contributing to tumor growth and progression [5–9]. In addition, dyslipidemia has been linked to CRC risk [8, 9].

Determining prognostic factors is important for effective CRC management. The clinical importance of developing optimal biomarkers for CRC lies in their ability to predict risk or poor prognosis, which enables the identification of relevant patient populations. Given the link between metabolic dysfunction and CRC, markers reflecting such changes are of interest. The triglyceride-glucose (TyG) index has been described as a reliable, highly available, and inexpensive biochemical marker of insulin resistance [10]. It represents an interplay between triglyceride and glucose metabolism, offering insights into metabolic disturbances associated with several medical conditions ([11]–[12]).

The TyG index has been utilized in clinical settings and has been found to be positively associated with various chronic diseases, mainly cardiovascular diseases [10–12]. The present literature shows general support for a positive association between the TyG index and CRC, though some variability exists in reported effect sizes and statistical significance. Although prior reviews have examined the TyG index in relation to overall cancer risk [10, 12], CRC is biologically distinct, with unique pathophysiological mechanisms. A focused systematic review and meta-analysis on CRC is needed to clarify this specific relationship, which is underexplored and not consistently reported across studies. However, the literature lacks a systematic review of studies that investigated the

relationship between a high TyG index and CRC. There is a need to define and solidify how the TyG index can be effectively used in patient care in context of CRC. The aim of this systematic review and meta-analysis is to evaluate the association between the TyG index and the hazard of developing CRC. The findings will provide insights and guidance for healthcare practitioners and researchers.

Methods

Search approach and studies inclusion criteria

This systematic review was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Additional file 1) [13]. The protocol for this systematic review was registered on the Open Science Framework platform (<https://osf.io/7bgds>). In order to identify all relevant published research, we undertook an inclusive electronic literature search across PubMed, Web of Science, Scopus, and World Health Organization Virtual Health Library Regional Portal (WHO-VHL). The search strategy did not impose any limitations based on geographical location or publication date, aiming to capture the widest possible range of relevant studies.

The search involved the published studies from the earliest records to March 2025, using the following search keywords: (“triglyceride glucose index” OR “triglyceride–glucose index” OR “TyG” OR “TyG index” OR “triacylglycerol glucose index” OR “triacylglycerol-glucose index”) AND (“colorectal cancer” OR “colorectal tumor” OR “colorectal carcinoma” OR “colorectal neoplasm” OR “colon cancer” OR “rectal cancer” OR “CRC”) (Additional file 2). The keywords were selected based on a review of relevant literature, terms used in previous systematic reviews on related topics, and terms commonly associated with the TyG index and colorectal cancer.

The references in the included articles were screened to make sure that no relevant studies have been missed. In addition, we conducted a search in Google Scholar along with our searches in major databases to identify potentially relevant grey literature. All publications were uploaded to EndNote software for initial screening of titles and abstracts as well as to remove duplicates.

Inclusion and exclusion criteria

Following the literature search, the selection procedure involved a two-step approach. Initially, four independent reviewers screened titles and abstracts of all identified articles to identify potentially relevant studies. Those judged to be relevant studies then underwent full-text evaluation to determine their final eligibility based on the pre-defined inclusion criteria.

Studies were included if they met the following criteria, structured according to the PECOS framework:

(Population): Adult individuals, (Exposure): TyG index, (Comparator): individuals with a lower TyG index, (Outcome): developing CRC, (Study design): observational studies for descriptive review of all aspect of association between TyG index and CRC. To be further included in the meta-analysis, studies needed to provide extractable hazard ratios (HRs) with 95% confidence intervals (CIs) comparing the highest versus lowest TyG index groups to assess hazard of developing CRC, and/or survival outcomes, or HR per one-unit TyG index increase. Studies were excluded if they lacked sufficient data for extracting the HR and its 95% CIs or did not evaluate hazard of developing CRC or survival outcomes. In addition, we excluded case reports, editorials, review articles, conference abstracts, and studies published in languages other than English.

Quality assessment and data extraction

The quality of included studies was assessed for potential bias using Joanna Briggs Institute critical appraisal checklists (<https://jbi.global/critical-appraisal-tools>). The tool aided in assessing the risk of bias related to study design, implementation, and data analysis. For each included study, the following data were extracted: author(s), publication year, geographic region, number of patients, age range of participants, mean age, outcome measures, and summary of the clinical outcome results related to the TyG index analyses. Any discrepancies encountered throughout the quality assessment and data extraction were effectively resolved through discussion.

Statistical analysis

Statistical analyses were conducted using the meta package in R version 4.4.3. Before pooling HRs in the meta-analysis, a log transformation of HRs and their associated CIs was applied to normalize the data and improve accuracy of the analysis. The meta-analysis was then conducted using the log-transformed HRs and their corresponding standard errors (SE), with subsequent exponentiation of results to present them in a more interpretable HR scale. A random-effects model, using Restricted Maximum Likelihood (REML) estimator, was used for calculation of the pooled effect sizes due to the methodological heterogeneity between studies included in the meta-analysis, which was evaluated using the I^2 statistic. To test for the presence of publication bias, we performed statistical analyses using both Begg's and Egger's regression tests [14]–[15]. The significance level for both tests was set at 0.1. The Duval and Tweedie trim-and-fill method was applied to account for potentially missing studies when there is evidence of a publication bias [16]. Meta-regression analyses were done to investigate heterogeneity and assess how specific study characteristics are associated with the effect size. In addition,

leave-one-out sensitivity analyses were conducted, to evaluate the robustness of the meta-analyses by assessing the influence of individual studies on the outcomes.

Results

Studies characteristics

The schematic flow of the process employed for study identification and selection is presented in Fig. 1. The initial database search yielded 69 records. After removing duplicates, 39 studies remained for title/abstract screening. During this stage, 30 studies were excluded due to irrelevance. Full texts of the remaining nine records were screened, resulting in exclusion of one study due to overlapping populations. Ultimately, a total of eight studies were selected for the systematic review (Table 1) [17–24].

The included studies, published between 2020 and 2025, were conducted in the United States, China, Japan, South Korea, Turkey, and across multiple European countries (Norway, Austria, and Sweden). The study sample sizes ranged from a relatively small cohort of 67 participants in Gündoğdu et al. to very large population-based studies, with over 300,000 participants in Son et al. study and over 500,000 participants in Fritz et al. study. The studies identified CRC cases by imaging, colonoscopy, and histopathological confirmation of biopsies. Some of the studies were based on national cancer registries and indicated that CRC cases were classified as C18–21 using the International Classification of Diseases, Tenth Revision (ICD-10). The TyG index was calculated by all of the included studies using the following formula: $\ln[\text{triglyceride} \times \text{fasting blood glucose} / 2]$, where: \ln represents the natural logarithm. Fasting triglycerides and fasting blood glucose were measured in milligrams per deciliter (mg/dL). The studies examining TyG index and CRC included comprehensive demographic data and adjusted their analyses for them as potential confounding factors in the TyG-CRC relationship (Additional file 3). The main features of the selected studies and summary of the main results of association between TyG index and CRC, as well as risk of bias assessment, were presented in Table 1. Detailed risk of bias assessment was presented in (Additional file 4).

Association between the TyG index and CRC

A meta-analysis comparing the highest versus lowest categories of TyG index was conducted to assess association with hazard of developing CRC. One of the included studies (Fritz et al.) presented results for each cancer separately (4032 patients with colon cancer and 2430 patients with rectal cancer). Therefore, it was included as two studies in the analysis. The meta-analysis indicated a significant association, with HR of 1.18 (95% CI: 1.12 to 1.25, $P < .001$) (Fig. 2). The heterogeneity was moderate according to the I^2 test (40.6%), with non-significant

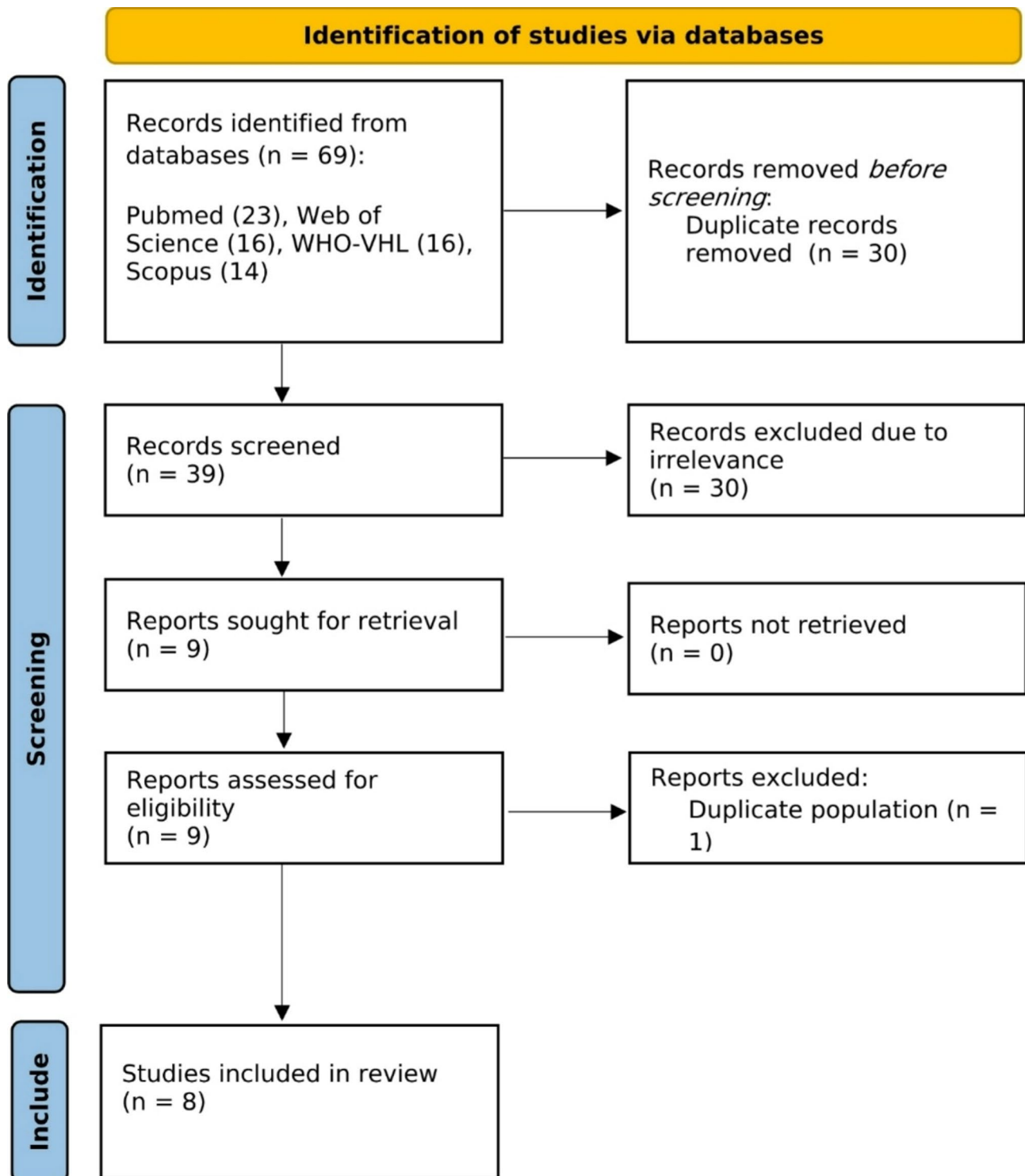


Fig. 1 Flow chart for studies selection process

Cochran's Q-test results ($Q=5.05$, $P=.168$) and small between-study variance ($\text{Tau}^2 = 0.0069$, 95% CI: 0.0009 to 0.260). The publication bias tests were not significant for Begg's test ($P=.174$), but not for Egger's test results ($P=.089$). After applying trim and fill method,

the estimate was slightly lower but significant ($\text{HR}=1.17$ (95% CI: 1.06 to 1.29, $P=.011$).

To further evaluate hazard of developing CRC associated with each unit increment in TyG index, we conducted a meta-analysis on three studies that reported HR

Table 1 Baseline characteristics of the studies included in the review

Study	Study design	Country	Total sample size	No. of cases	Male %	BMI mean	Age mean	Main findings	Quality assessment
Aksoy et al. (2024)	Case-control	Turkey	256	124	53.5	27.6	62.1 ± 10.2	Mean level of TyG index was higher in CRC patients than healthy participants. The ROC curve analysis for TyG index, based on a cut-off of 4.49, was highly accurate for the presence of CRC (AUC = 0.782), with a sensitivity of 77% and a specificity of 78.4%.	9/10
Fritz et al. (2020)	Cohort study	Norway, Sweden, and Austria	510471	6462	50.5	25.2	43.1 ± 10.6	TyG index was associated with an increased risk of several cancers, including those of colon cancer and rectal cancer. Substantial proportions of the effect of BMI were mediated by TyG index for both cancers.	10/11
Gündoğdu et al. (2021)	Case-control	Turkey	67	30	NR	NR	NR	Median level of TyG index was higher in CRC patients than healthy participants.	7/10
Hu et al. (2025)	Case-control	China	1311	277	63.5	23.78	66.54 ± 10.91	The ROC curve analysis for TyG index, based on a cut-off of 8.63, was moderately accurate for the presence of CRC (AUC = 0.668). Combining TyG index, carcinoembryonic antigen, and carbohydrate antigen 19–9 yielded a higher positive prediction rate.	10/10
kityo et al. (2024)	Cohort study	South Korea	98800	699	33.45	NR	53.2 ± 8.3	Significant association between higher TyG index and presence of CRC. Association was dose-dependent. The risk was highest among participants with a high BMI, low fruit and vegetable intake, and high intake of red meat.	9/11
Liu et al. (2022)	Cohort study	China	93659	593	79.73	25.05	51.44 ± 12.45	TyG index was significantly associated with a higher risk of developing CRC. The ROC curve analysis for TyG index, based on a cut-off of 9.06, was weakly accurate for the presence of CRC (AUC = 0.611),	11/11
Okamura et al. (2020)	Cohort study	Japan	27921	116	58.9	22.6	45.7 ± 10.1	TyG index was significantly associated with an increased risk of developing CRC. The ROC curve analysis for TyG index, based on a cut-off of 8.27, was moderately accurate for the presence of CRC (AUC = 0.682), with a sensitivity of 62% and a specificity of 66.8%.	9/11
Son et al. (2024)	Cohort study	South Korea	314141	6112	53.9	24	58.82 ± 8.72	Significant association between insulin resistance markers, including TyG index, and the incidence of CRC. The study also found disease-free probabilities decrease with higher quartiles of the TyG index.	11/11

TyG: triglycerides-glucose index, CRC: colorectal cancer, AUC: area under the curve, ROC: receiver operating characteristics, BMI: body mass index

per one-unit increase in the TyG index. The meta-analysis indicated that hazard of developing CRC significantly increased for each one-unit increase in the TyG index (HR = 1.28, 95% CI: 1.18 to 1.39, $P < .001$) (Additional file 5).

Meta-regression analyses

Meta-regression analyses were conducted to analyze the effect of various variables on the association between TyG index and CRC. The results showed that none of the other variables had a moderating effect on the outcome; number of participants (coefficient < -0.001 , $P = .161$), mean age (coefficient < 0.001 , $P = .984$), mean BMI (coefficient = 0.047, $P = .649$), male ratio (coefficient = 0.008,

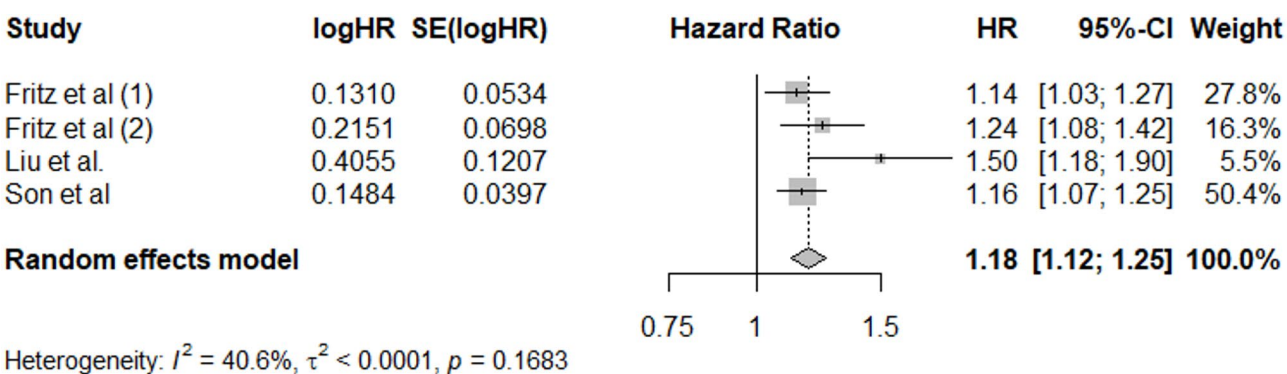


Fig. 2 Forest plot for the association of TyG index with hazard of developing CRC

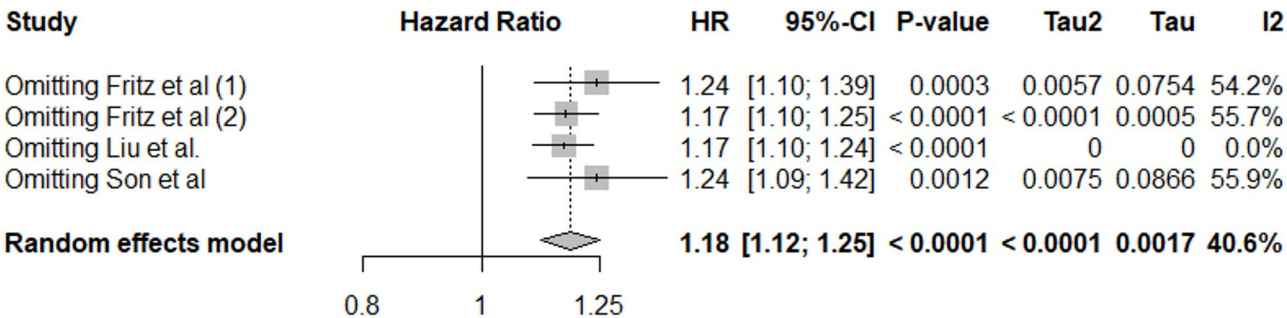


Fig. 3 Sensitivity analysis for the results of association of TyG index with hazard of developing CRC

$P=.058$), publication year (coefficient <-0.001 , $P=.979$), and TyG index cut-off values (coefficient $= -0.478$, $P=.098$) (Additional file 6).

Sensitivity analysis

A leave-one-out sensitivity analysis was conducted to assess the influence of individual studies on the pooled effect estimates. The results showed that all re-analyses, where each study was removed one at a time, yielded a statistically significant pooled effect estimates, indicating that the effect size from each individual study did not cause excessive change to the pooled estimate (Fig. 3).

Discussion

The main finding of this systematic review is the presence of a consistent and reliable evidence of a clear link between high levels of the TyG index and an increased hazard of developing CRC across diverse populations. The pooled results of categorical analysis revealed that individuals with elevated TyG index had a 18% greater hazard of developing CRC compared to those with lower levels.

The findings of this systematic review are consistent with a previous review examining the relationship between TyG index and overall cancer risk, which included data from near one-million participants, found that higher TyG index was associated with a 14% increased overall cancer risk [25]. Our findings build

upon this cancer-related review by providing CRC-specific pooled estimates. This suggests that the association extends beyond CRC to other malignancies. In addition, a recent large cohort found that TyG index was positively associated with both the incidence of colorectal adenoma and multiple adenomas in asymptomatic subjects with high TyG index compared to subjects with the lowest TyG index [26].

From a mechanistic perspective, the TyG index may reflect underlying biological processes involved in colorectal carcinogenesis. Several studies identified other mediators which are linked to insulin resistance and were recognized as contributors to tumorigenesis through several metabolic pathways, stimulating cellular proliferation and inhibit apoptosis in colonic epithelial cells, potentially facilitating cancer development and progression [19, 25]. The predictive performance of the TyG index varied across studies. However, the accuracy improved when TyG index was combined with other factors. Despite these variations, the overall discriminative ability of the TyG index across studies was sufficient to support its potential as a predictive tool for CRC risk.

key advantage of the TyG index is its low cost and practicality for primary care settings, as it integrates readily available fasting triglyceride and glucose measurements. Unlike more complex and expensive measures of insulin resistance, the TyG index offers a convenient and cost-effective alternative for clinical assessment [25]. However,

its clinical application requires establishing population-specific cut-off values to enhance screening protocols for high-risk individuals.

Given the consistent association between TyG index and CRC, monitoring TyG index may be valuable in the comprehensive management of CRC patients. It could serve as accessible biomarkers for monitoring disease severity, predicting clinical outcomes, and suggesting potential pathways for risk stratification. Future studies should establish population specific TyG thresholds, given the variability of cut-off values across studies. While TyG alone demonstrated moderate predictive accuracy, integrating it with complementary biomarkers such as done by Gündoğdu et al. and Li et al. with atherogenic indices and inflammatory markers may enhance utility. Although the meta-regression showed a non-significant trend ($P=.058$), the result suggests a possible sex-related difference in the association between TyG index and colorectal cancer risk. However, further studies are needed to clarify this potential moderating effect and to identify the sex-specific TyG index cut-off values to improve the CRC risk detection in more diverse populations.

Strengths and limitations

One of the main strengths of this systematic review is the large pooled sample size from diverse populations and regions included in global cohorts. Another strength is that most of the included studies used well-established methods for diagnosing CRC and used standardized TyG index calculations. However, several limitations should be acknowledged, mainly the limited number of studies and limitations in the available data. This small number reduces the power of the pooled estimates and the ability to explore heterogeneity or publication bias meaningfully. The limited stratification by CRC subtypes restricts insights into potential differences associations, meaning that more stratification of tumor types and locations may help understanding if TyG index predicts all CRC types equally. In addition, most of the studies focused of Asian and European cohorts, thus, more research in African and Latin American populations is needed. Another important limitation is the inherent risk of residual confounding within the included observational studies. Despite most studies adjusting for several known confounders such as age and BMI, unmeasured or inadequately controlled variables may still bias the observed associations. Future research should also focus on prospective studies to further validate the TyG index in CRC screening.

Conclusion

This systematic review and meta-analysis evaluated the association between the TyG index and hazard of developing CRC. The results showed that the TyG index can be considered as a prognostic indicator for the development of CRC. To increase therapeutic usefulness, future studies should concentrate on standardizing TyG thresholds, assessing dynamic variations in TyG levels over time, and confirming results across a diverse range of ethnic groups. Due to the limitations posed by the small number of included studies and the resulting low statistical power, further large-scale and prospective studies are recommended to generate more robust and generalizable evidence.

Abbreviations

CRC	Colorectal cancer
TyG	Triglyceride-glucose
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
WHO-VHL	World Health Organization Virtual Health Library
HR	Hazard ratio
CI	Confidence interval
AUC	Area under the curve
ROC	Receiver operating characteristics

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12957-025-03930-y>.

Supplementary Material 1

Supplementary Material 2

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Author contributions

Authors' contributions SM conceptualized the research idea, HO and SM managed and planned the research process. HO, EY, MAA, NH, and YE undertook database searches and articles screening. MI, MA, and NA undertook risk of bias assessment. AM, YN, MI and AA extracted and summarized data. SM analyzed data. HO, MA, MI, and AA drafted the manuscript. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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