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Investigating the relationship between triglyceride glucose index and the risk of colorectal neoplasm; a systematic review and meta-analysis

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Abstract

Introduction: One of the most common cancers in the world is colorectal cancer (CRC). Various studies yielded contradictory findings about the relationship between triglyceride-glucose (TyG) index and colorectal neoplasm. Therefore, this study aims to investigate the correlation between TyG index and colorectal neoplasm through systematic review and meta-analysis.

Materials and Methods: The following databases were searched until January 1, 2025: Cochrane, ProQuest, Embase, Web of Science, PubMed, and Google Scholar. Statistical analysis was performed with STATA 14, and $P < 0.05$ indicated significance of the tests.

Results: Increased TyG index increased the risk of colorectal (OR: 1.25, 95% CI: 1.16, 1.33), colon (OR: 1.11, 95% CI: 1.04, 1.19), and rectal (OR: 1.21, 95% CI: 1.11, 1.32) cancers. Compared to the Q1, the Q2 of TyG index (OR: 1.10, 95% CI: 1.03, 1.18), the Q3 (OR: 1.27, 95% CI: 1.07, 1.50) and the Q4 (OR: 1.41, 95% CI: 1.12, 1.77) increased the risk of CRC (CRC). Similarly, the following increased the risk of CRC: increased TyG index in men (OR: 1.30, 95% CI: 1.16, 1.45), women (OR: 1.23, 95% CI: 1.12, 1.36), individuals aged 50 to 59 (OR: 1.19, 95% CI: 1.11, 1.28), people aged 60 to 69 (OR: 1.64, 95% CI: 1.12, 2.38), in Korea (OR: 1.11, 95% CI: 1.06, 1.16), China (OR: 1.36, 95% CI: 1.23, 1.49), Japan (OR: 1.38, 95% CI: 1, 1.91), in cohort studies (OR: 1.21, 95% CI: 1.11, 1.33) and in a case-control study (OR: 1.30, 95% CI: 1.14, 1.48).

Conclusion: Increased TyG index raised the risk of rectal, colorectal, and colon neoplasms, since men were at higher risk of CRC than women. Our study showed, the higher the TyG index level and the older the participants, resulted in the higher the risk of CRC.

Registration: This study has been compiled based on the PRISMA checklist, and its protocol was registered on the PROSPERO (ID: CRD42025634667) and Research Registry (UIN: reviewregistry1942) websites.

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Introduction

Colorectal cancer (CRC) and colorectal adenoma are colorectal neoplasms that place a remarkable economic burden on governments (1). Colorectal adenoma is usually regarded as a precursor lesion for most CRCs (2,3). Likewise, CRC is the third most common cancer worldwide (4). It is also responsible for more than 10% of all neoplasm cases all over the world (5). According to the World Health Organization (WHO) GLOBOCAN database, more than 1.9 million new cases of CRC were diagnosed, 930,000 deaths from CRC were estimated to have occurred in 2020 (6), and the incidence of CRC and its mortality rate is predicted to increase significantly by 2040 (6). This cancer has many risk factors, including metabolic syndrome, alcohol consumption, obesity, hypertension (7), red meat consumption (8), and physical inactivity (9). There are some etiological factors common between metabolic syndrome and insulin resistance. This connection has resulted in the hypothesis that there might be a relationship between the triglyceride-glucose (TyG) index and CRC (10). The TyG index is calculated by testing fasting blood sugar and fasting triglycerides and is a biomarker of insulin resistance (11).

On the one hand, different studies have produced various findings concerning the relationship between the TyG index and CRC risk. Certain studies have shown that the second quartile (Q2) of the TyG index does not increase the risk of CRC compared to the quartile 1 (Q1) (12-14). On the other hand, some other studies have indicated that a high TyG index increases the risk of CRC (15-17).

Key point

The rising triglyceride-glucose (TyG) index intensified the risk of colorectal cancer (CRC) by 25%, colon cancer by 11%, and rectal cancer by 21%. Additionally, compared to the first quartile, other quartiles raised the risk of CRC; the second quartile of TyG index (10%), the third quartile (27%), and the fourth quartile (41%). On the other hand, the surging TyG index boosted the risk of CRC by 19% in the age group 50 to 59 years, 64% in the age group 60 to 69 years, 11% in Korea, 36% in China, 38% in Japan, 30% in men, and 23% in women.

Considering the contradictory results of previous studies, the present research sought to provide thorough and up-to-date results – was the first to examine the relationship between TyG index and CRC risk through a systematic review and meta-analysis.

Materials and Methods

The protocol for this research was registered on the PROSPERO (International Prospective Register of Systematic Reviews) and research registry websites. The PRISMA checklist was used to prepare the above protocols (18).

Search strategy

The authors searched the Cochrane, Web of Science, PubMed, ProQuest, Embase, and Google Scholar databases with no language or time filters until January 1, 2025. Medical Subject Headings (MeSH) words and operators (AND, OR) were utilized for the search, and the reference lists of primary studies were manually screened. This was the search strategy in the Web of Science database: Colorectal Neoplasms OR Colorectal Tumor OR Colorectal Cancer (All Fields) AND Triglyceride-glucose index OR TyG index (All Fields).

PECO components

- Population: Studies that evaluated the correlation between the TyG index and CRC.
- Exposure: TyG index.
- Comparison: Healthy individuals.
- Outcomes: correlation between the TyG index and the risk of colorectal, colon, and rectal cancers.

Inclusion criteria

- Observational studies that examined the correlation between the TyG index and the risk of CRC.

Exclusion criteria

- Studies of low quality,
- Letters to the editor,
- Studies that did not provide the necessary data for data analysis,
- Preprints or repetitive studies,
- Studies that were published as abstracts in conferences,
- Studies whose full text was not accessible.

Quality assessment

The authors assessed the quality of researches, making use of the Newcastle Ottawa Scale, which conducted a scoring method that ranged from 0 to 10, with a score of 0 indicating the lowest quality and a score of 10 showing the highest quality. The cut-off point of this instrument was a score of 6 (19).

Data extraction

The researchers extracted the data which included; the name of research authors, measurement indexes (odds ratio [OR] and hazard ratio [HR]), the type of studies, time, place, and duration of studies, sample sizes, the age of their participants, the level of TyG indexes, relationship between TyG index and risk of colon, colorectal, and rectal cancers with its upper and lower limits, etc.

Statistical analysis

For each study, the logarithm of OR and HR were calculated, and then the results of all studies were combined for analysis. To assess heterogeneity, the I^2 index was employed. For low-heterogeneity, the fixed effects model was applied, and for high heterogeneity, the random effects model was capitalized on. Moreover, subgroup analysis was run to examine the correlation between TyG index and CRC risk with the variables of TyG index level, study type, age, and location. Finally, data analysis was performed with STATA 14 software, with a significance level of $P < 0.05$.

Results

In total, 198 articles were searched, of which 101 were duplicates. The abstracts of the remaining 97 articles were evaluated, and 9 articles having full text were excluded. This left 88 studies, of which 38 articles were excluded because they lacked the data required for analysis. Of the remaining 50 articles, 42 more were excluded based on other exclusion standards, leaving 6 articles (Figure 1).

In this meta-analysis, six observational studies (five cohort studies and one case-control research) were reviewed, and in total data of 459 855 individuals were included in it (Table 1).

As displayed in Figure 2, increasing TyG index heightened the risk of CRC (OR: 1.25, 95% CI: 1.16, 1.33). Subgroup analysis depicted that the Q2 of TyG index (OR: 1.10, 95% CI: 1.03, 1.18), the Q3 (OR: 1.27, 95% CI: 1.07, 1.50) and the Q4 (OR: 1.41, 95% CI: 1.12, 1.77) raised the risk of CRC compared to the Q1 (Figure 3).

The rising TyG index in the age group 50 to 59 years (OR: 1.19, 95% CI: 1.11, 1.28) and 60 to 69 years (OR: 1.64, 95% CI: 1.12, 2.38) raised the risk of CRC (Figure 4).

The increasing TyG index in Korea (OR: 1.11, 95% CI: 1.06, 1.16), China (OR: 1.36, 95% CI: 1.23, 1.49) and Japan (OR: 1.38, 95% CI: 1, 1.91) heightened the risk of CRC (Figure 5).

The surging TyG index in cohort studies (OR: 1.21, 95%

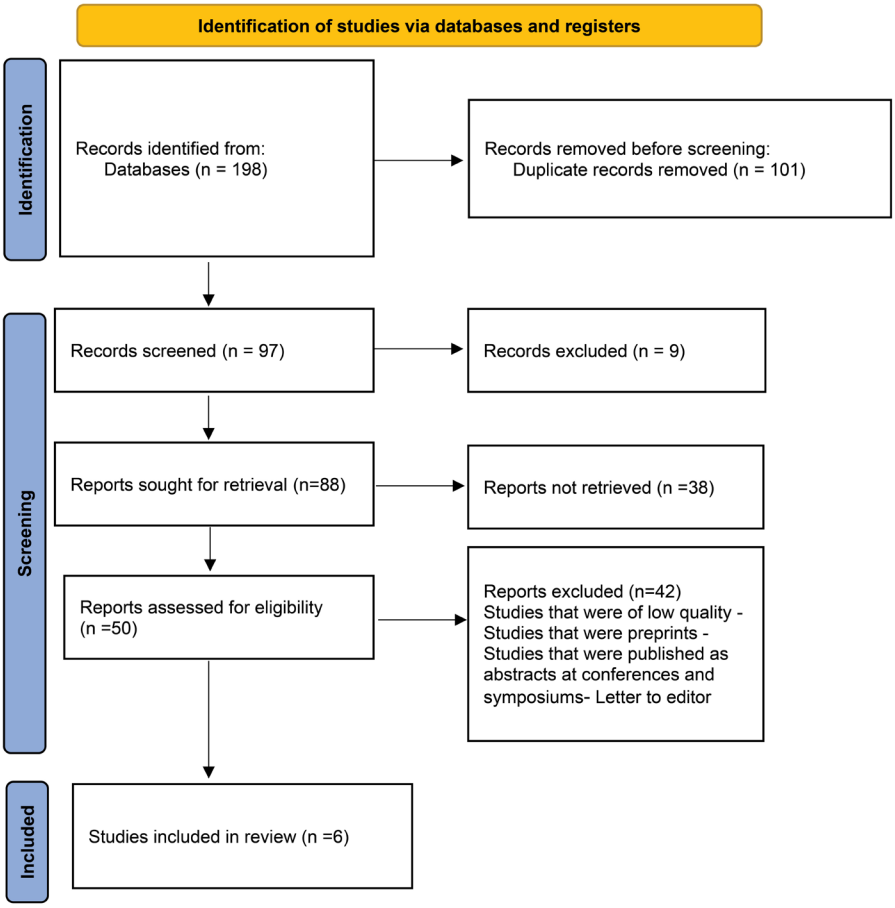

Figure 1. The PRISMA flowchart of study selection.

Table 1. Summary of data extracted from the reviewed articles

Author, year	Index	Country	Type of study	Duration of study	Sample size	Mean age (year)	TyG level	Association between TyG index and colorectal neoplasm risk		
								OR/HR	Low limit	Up limit
Son M, 2024 (16)	HR	Korea	Cohort	From 2009 to 2010	77345	59	Q2	1.08	1	1.16
					78955	59.4	Q3	1.1	1.02	1.19
					79228	59.1	Q4	1.16	1.07	1.25
Zhu Z, 2024 (13)	OR	China	Cohort	2008-2023	1538	60.5	Total	1.26	1.04	1.54
							Q2	1.36	0.96	1.91
							Q3	1.52	1.02	2.25
							Q4	3.36	1.44	7.73
Kityo A, 2024 (17)	HR	Korea	Cohort	Between 2004 and 2013	98800	53.2	Total	1.28	1.12	1.46
Han M, 2022 (12)	OR	China	Case-control	Jan 1, 2016 to Dec 31, 2019	2409	57.18	Total	1.23	1.08	1.41
							Q2	1.21	0.96	1.52
							Q3	1.31	1.04	1.65
							Q4	1.38	1.09	1.73
Liu T, 2022 (14)	HR	China	Cohort	between Jul 2006 and Oct 2007	93659	51.44	Total	1.21	1.08	1.36
							Q2	1.13	0.88	1.46
							Q3	1.43	1.12	1.83
							Q4	1.53	1.2	1.93
Okamura T, 2020 (15)	HR	Japan	Cohort	From Jan 1st in 2004 to Dec 31st in 2016	27921	45.7	Total	1.38	1	1.91

NR: Not reported; HR: Hazard ratio; OR: odds ratio; TyG index: Triglyceride-glucose index; Q2: Quartile 2; Q3: Quartile 3; Q4: Quartile 4.

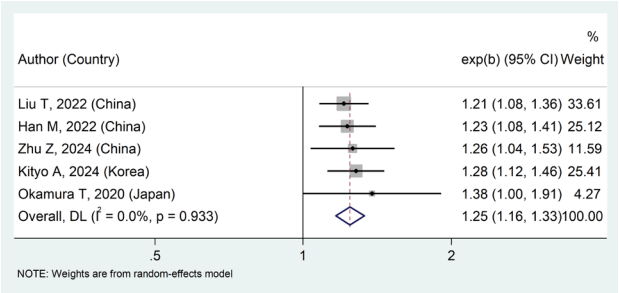

Figure 2. Forest plot showing the relationship between TyG index and risk of CRC.

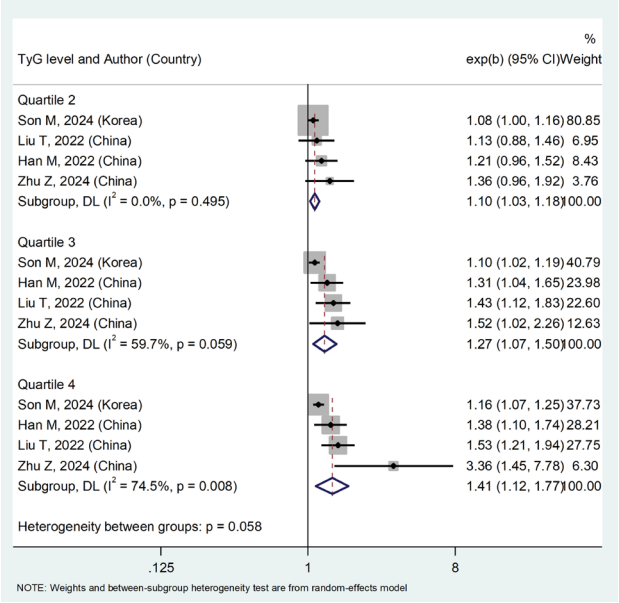

Figure 3. Forest plot showing the relationship between TyG index and risk of CRC by level of TyG.

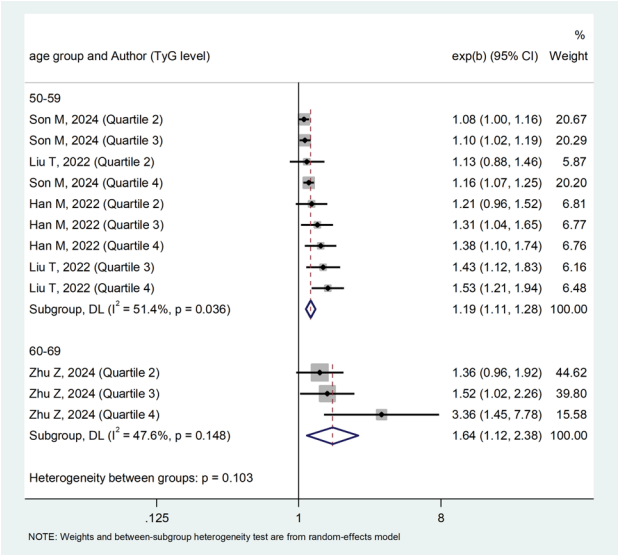

Figure 4. Forest plot showing the relationship between TyG index and risk of CRC by age group.

CI: 1.11, 1.33) and in case-control studies (OR: 1.30, 95% CI: 1.14, 1.48), raised the risk of CRC (Figure 6).

Among individuals with a high TyG index, men (OR: 1.30, 95% CI: 1.16, 1.45) were at a higher risk of CRC than women (OR: 1.23, 95% CI: 1.12, 1.36) (Figures 7 and 8).

The surging TyG index intensified the risk of colon cancer (OR: 1.11, 95% CI: 1.04, 1.19) and rectal cancer risk (OR: 1.21, 95% CI: 1.11, 1.32) (Figures 9 and 10).

Meta-regression analysis indicated that the "correlation between TyG index and CRC risk" was not significantly related to the sample sizes ($P=0.954$) and the year of research publication ($P=0.846$; Figures 11 and 12).

The publication bias plot depicted that there was no

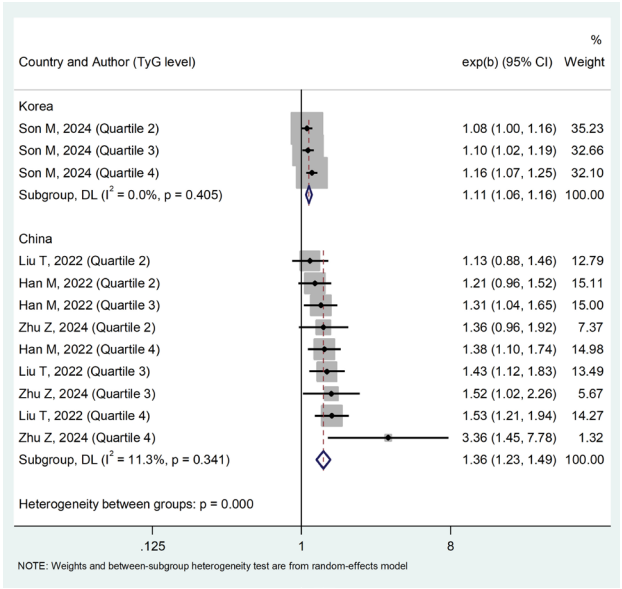

Figure 5. Forest plot showing the relationship between TyG index and risk of CRC by countries.

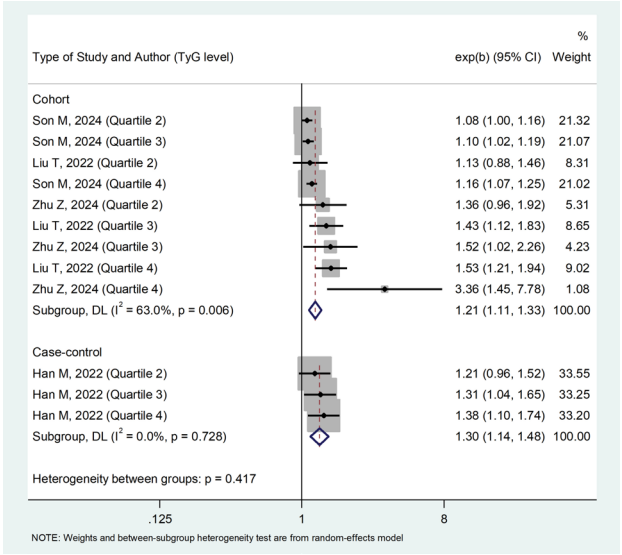

Figure 6. Forest plot showing the relationship between TyG index and risk of CRC by type of studies

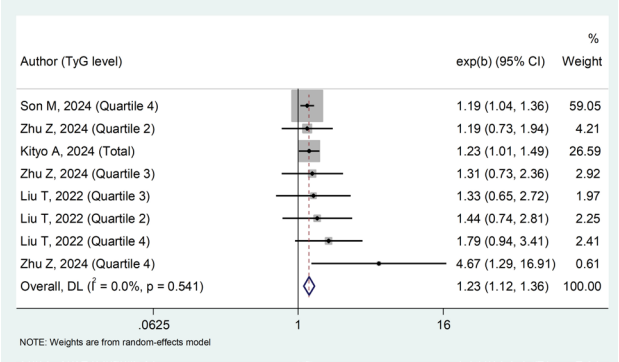

Figure 7. Forest plot showing the relationship between TyG index and risk of CRC in females

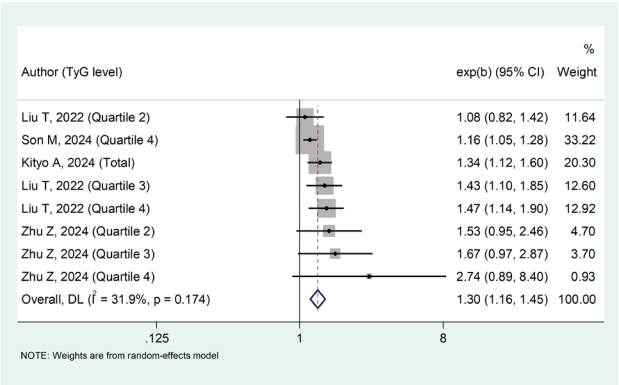

Figure 8. Forest plot showing the relationship between TyG index and risk of CRC in males.

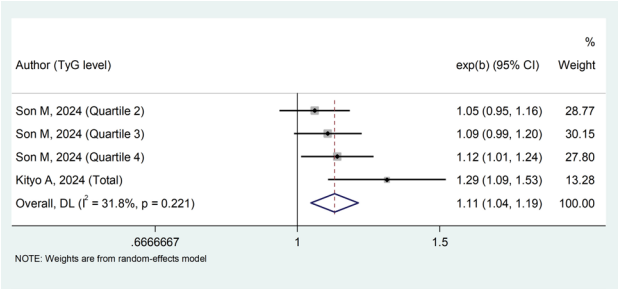

Figure 9. Forest plot showing the relationship between TyG index and risk of colon cancer.

such publication bias in this study ($P = 0.124$). Therefore, it can be concluded that the search of the reference lists was carried out thoroughly and unbiasedly (Figure 13).

Discussion

The rising TyG index intensified the risk of CRC by 25%, colon cancer by 11%, and rectal cancer by 21%. Additionally, compared to the Q1, other quartiles raised the risk of CRC; the second quartile of TyG index (10%), the Q3 (27%), and the Q4 (41%). On the other hand, the surging TyG index boosted the risk of CRC by 19% in the age group 50 to 59 years, 64% in the age group 60 to 69 years, 11% in Korea, 36% in China, 38% in Japan, 30% in men, and 23% in women.

A retrospective study was conducted by Han et al. Their aimed was to examine the relation between TyG index and plasma atherogenic index to predict CRC in patients with no cardiovascular diseases. The findings revealed that boosted levels of TyG index was associated with enlarged risk of colorectal neoplasms (OR: 1.23, 95% CI: 1.08, 1.41) (12). In the recent study by Okamura et al, elevated levels

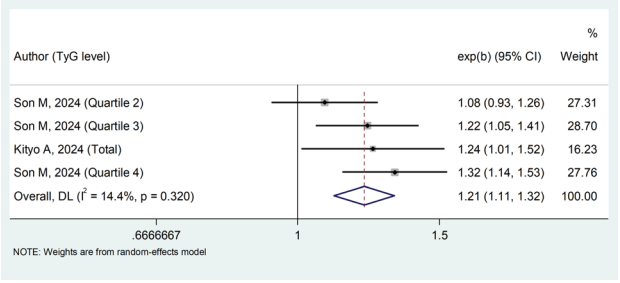

Figure 10. Forest plot showing the relationship between TyG index and risk of rectal cancer.

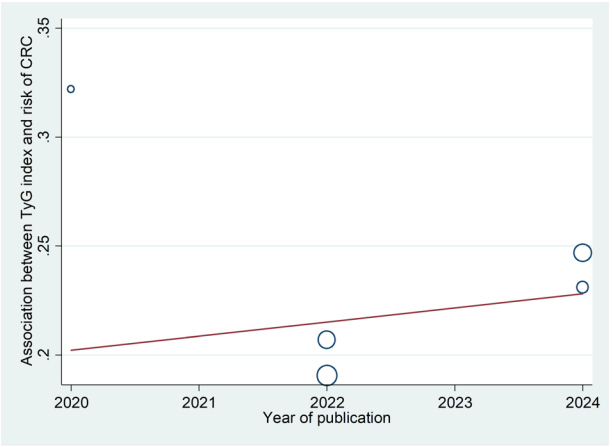

Figure 11. Meta-regression showing the relationship between TyG index and risk of CRC with year

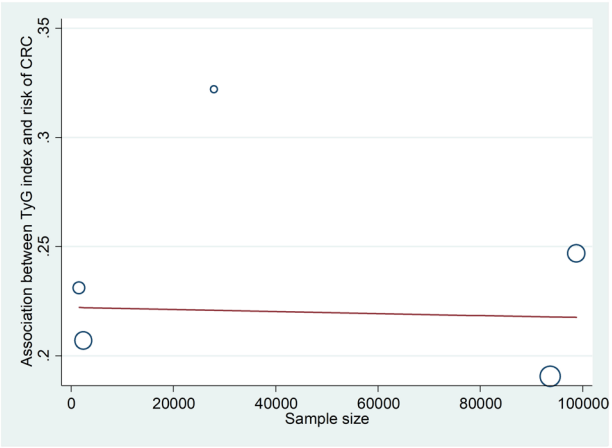

Figure 12. Meta-regression showing the relationship between TyG index and risk of CRC with the sample size.

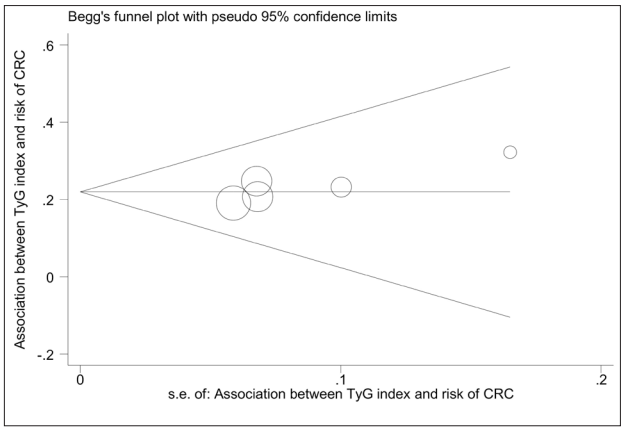

Figure 13. Publication bias diagram.

of TyG could predict CRC incidence (HR: 1.38, 95% CI: 1.00, 1.91) (15). According to the cohort study by Liu et al, the risk of CRC was higher in third (HR: 1.36, 95% CI: 1.06, 1.76), and fourth (HR: 1.50, 95% CI: 1.19, 1.9) quartiles of TyG index, compared to Q1 (14). Likewise, in Kityo and Lee's cohort study in South Korea, an increased TyG index was associated by boosted CRC risk (HR: 1.28, 95% CI: 1.12–1.46), colon (HR:1.29, 95% CI:1.10, 1.54) and rectal cancer (HR:1.24, 95% CI: 1.01, 1.52) (17). By combining the findings of these observational studies, this study has concluded that high levels of TyG index is a risk factor for emergence of rectal, colorectal, and colon tumors. Thus, the findings of this study were consistent with those of the above-mentioned ones.

In the more recent US cohort study by Zha et al, the results demonstrated that a raised TyG index (Q4 vs. Q1: OR: 2.08, 95% CI: 1.01, 4.26) was related to an increased risk of gastrointestinal cancers (20). Another cohort study by Kim et al illustrated that the increasing TyG index was correlated with the risk of increased gastric cancer (Q2 (OR = 1.61), Q3 (OR = 2.18), and Q4 (OR = 2.36)) (21). Likewise, in a prospective study by Yang et al, a high TyG index was a risk factor for hepatic cancers in patients with liver cirrhosis (OR: 2.60, 95% CI: 1.43, 4.70) (22). Our findings were in line with those obtained in the above studies, demonstrating that a high TyG index is a risk factor for gastrointestinal cancers.

In the previous retrospective study by Yan et al in China, a high TyG index (OR: 3.65, 95% CI: 2.46, 5.41) was significantly associated with an increased risk of non-small cell lung cancer (23). Similarly, in another retrospective study by Zhou et al, the risk of prostate cancer was higher in the highest quartile of TyG index (Q4) than in the lowest quartile (Q1) (OR: 3.38, 95% CI: 1.51, 7.59) (24). Furthermore, in a meta-analysis by Wang et al, high TyG index increased the risk of cancers in comparison to low-TyG (total effect size = 1.14, 95% CI: 1.08, 1.20) (25). In addition to gastrointestinal cancers, high TyG index is an independent predictor for other cancers. Hence, TyG index, as an indicator for insulin resistance, can foretell the occurrence of various cancers.

Conclusion

Increased TyG index was an important risk factor for colorectal, colon, and rectal cancers. Male gender and Japanese ethnicity were factors that aggravated the incidence of CRC. However, it should be noted that only one study was carried out in Japan. Additionally, the higher the level of TyG index and the age of the individuals, the higher the risk of CRC. Therefore, measurement of TyG index is a good predictor of the incidence of this cancer, since CRCs can be prevented by this reducing level. Given the small number of reviewed studies, it is recommended that future studies be conducted on this topic to increase the generalizability of the results. Moreover, all of the studies reviewed were carried out in Asia, hence further studies in other continents are also recommended.

Limitations of the study

- The number of studies included was limited, with all studies conducted in Asia.
- Only one case-control study was carried out.
- Only one study focused on participants aged 40 to 49 years.
- Most studies did not report the exact level of the TyG index in participants, making it impossible to perform a subgroup analysis based on TyG levels.

Authors' contribution

Conceptualization: Rohollah Masumi.
Data curation: Rohollah Masumi, Diana Sarokhani.
Formal analysis: Diana Sarokhani.
Investigation: Kiavash Fekri.
Methodology: Rohollah Masumi, Kiavash Fekri.
Project administration: Kiavash Fekri.
Resources: Rohollah Masumi.
Software: Diana Sarokhani.
Supervision: Rohollah Masumi.
Validation: Diana Sarokhani.
Visualization: Kiavash Fekri.
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 with (ID: CRD42025634667) and Research Registry website (Unique Identifying Number (UIN): reviewregistry1942). Besides, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the author.

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