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Triglyceride-Glucose Index is A Novel Predictor of Colorectal Cancer

Trigliserit-Glikoz İndeksi, Kolorektal Kanserin Yeni Bir Belirleyicisidir

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Abstract

Aim Colorectal cancer (CRC) is the leading cause of cancer-related mortality. Metabolic syndrome is associated with obesity, pre-diabetes, and dyslipidemia. Triglyceride-Glucose Index (TyG) is a simple, reliable, easily accessible, cost-effective screening method that has been recently used in screening. The purpose of the study was to investigate the effects of TyG as a novel biomarker on CRC risk.

Material and Method The study was conducted with 256 people in total, including the CRC (n=124) and Control Groups (n=132). TyG Index was calculated by using fasting triglycerides and glucose with the formula Ln [fasting TGs (mg/dL) x fasting glucose (mg/dL)/2]. The performance of the TyG Index to predict the presence of CRC was also evaluated.

Results Metabolic parameters associated with insulin resistance were found to be at statistically significant levels in the CRC Group. Fasting plasma glucose, triglyceride, insulin, hemoglobin A1c, and GGT were also statistically significant. It was also determined that the cut-off value of the TyG Index for the presence of CRC was 4.49 (AUC = 0.782, sensitivity 77%, specificity = 78.4%, and p=0.002).

Conclusion In the present study, it was found that the TyG Index is associated with the risk of CRC and can be used as a novel biomarker in high-risk CRC cases.

Keywords Colorectal cancer, insulin resistance, TyG index

Özet

Amaç *Kolorektal kanser (KRK), kansere bağlı ölümlerin önde gelen nedelerinden biridir. Metabolik sendrom, obezite, pre-diyabet ve dislipidemi ile ilişkilidir. Trigliserit-Glikoz İndeksi (TyG), taramada son zamanlarda kullanılmaya başlanan basit, güvenilir, kolay erişilebilir, uygun maliyetli bir tarama yöntemidir. Çalışmanın amacı, yeni bir biyobelirteç olarak TyG'nin KRK riski üzerindeki etkilerini araştırmaktır.*

Gereç ve Yöntem *Çalışma, KRK (n=124) ve Kontrol Grubu (n=132) olmak üzere toplam 256 kişi ile gerçekleştirildi. TyG İndeksi, Ln [açlık TG'ler (mg/dL) x açlık glikozu (mg/dL)/2] formülü ile açlık trigliseritleri ve glikoz kullanılarak hesaplandı. TyG İndeksinin KRK varlığını tahmin etme performansı da değerlendirildi.*

Bulgular *İnsülin direnci ile ilişkili metabolik parametrelerin KRK grubunda istatistiksel olarak anlamlı düzeyde olduğu bulundu. Açlık plazma glikozu, trigliserit, insülin, hemoglobin A1c ve GGT de istatistiksel olarak anlamlıydı. TyG Index'in KRK varlığı için cut-off değerinin de 4,49 olduğu saptandı (EAA=0,782, sensitivite %77, spesifite=%78,4 ve p=0,002).*

Sonuç *Bu çalışmada, TyG İndeksinin KRK riski ile ilişkili olduğu ve yüksek riskli KRK olgularında yeni bir biyobelirteç olarak kullanılabileceği bulundu.*

Anahtar Kelimeler *Kolorektal kanser, insülin direnci, TyG indeksi*

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INTRODUCTION

Colorectal Cancer (CRC) is the third leading cause of cancer-related mortality.[1] It was reported that CRC is associated with metabolic syndrome, obesity, pre-diabetes, and dyslipidemia.[2] Especially insulin resistance, hyperinsulinemia, increased Insulin-like Growth factors (IGF) levels, and changes in Peroxisome Proliferator-Activated Receptor Gamma (PPARy) signal play key roles in the pathogenesis of CRC.[3-4]

Triglyceride-Glucose (TyG) Index correlates with insulin resistance and is calculated with fasting plasma glucose and triglycerides.[5] Increasing TyG Index is an important risk factor for metabolic syndrome.[6] There are common etiological factors (e.g. obesity, sedentary lifestyle, and western diet) between metabolic syndrome and insulin resistance. This association gave rise to the hypothesis that there might be an association between the TyG Index and CRC.[7]

It is considered that the mitogenic and growth-stimulating effects of Insulin-like Growth Factors may play roles in CRC. Any direct relationship between circulating insulin levels and the risk of CRC remains unclear. In the present study, the purpose was to investigate the direct relationship between the TyG Index and the incidence of CRC. Very few studies investigated this relationship previously.

MATERIALS and METHODS

A total of 124 CRC patients who were diagnosed in our general surgery clinic between February 2014 and June 2022 were included in the study. Patients diagnosed with CRC "CRC Group"; Patients without CRC were included in the "Control Group". The demographics, biochemical data, Computed Tomography results, Magnetic Resonance Imaging results, colonoscopy results (Figure 1), biopsy and histopathology reports were collected from patient files and electronic records. The ethichs committee of this study was obtained from Sakarya University Faculty of Medicine ethics committee (Number no: E-71522473-050.04-330368-31)

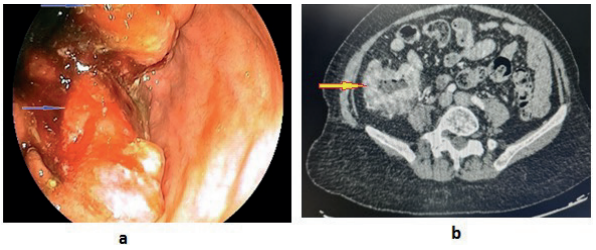

Figure 1. Colonoscopy image of CRC (a) and its computed tomography image (b).

Patients who had inflammatory bowel disease, other cancer, gastrointestinal surgery and bariatric surgery, pregnant women, those under the age of 18, those who used immunosuppressive drugs, steroid and lipid-lowering drugs, metformin and antidiabetic drugs were not included in the study.

Serum fasting plasma glucose, triglyceride, insulin, hemoglobin A1c (HbA1c), Alanine Transaminase (ALT), and Gamma-Glutamyl Transferase (GGT) serum levels of the patients were measured in the biochemistry laboratory of our hospital by using the standard laboratory techniques. Plasma glucose (cut-off level 70-100 mg/dL) was determined with the Glucose Oxidase Method. Triglyceride (cut-off level 0-150 mg/dL) was determined with the Enzymatic Method. Among other parameters, insulin (cut-off level 0-25 uIU/mL), ALT (cut-off level 0-41 U/L), GGT (cut-off level 0-65 U / L) values were obtained with Roche Hitachi 912 Chemistry Analyzer with fasting plasma glucose and insulin homeostasis model assessment for insulin resistance (HOMA-IR: fasting insulin (uIU/mL) x fasting glucose (mg/dL)/405).[5,8]

TyG Index is a simple, reliable, easily accessible, cost-effective screening method that has been recently used in screening. When the literature is examined; It has been observed that the relationship between the TyG index level and the disease has been investigated in diseases such as thyroid diseases, Diabetes mellitus (DM), Gonatosis,

ST-segment elevation myocardial infarction.[9-13] The effect of TyG Index on CRC risk was investigated in the present study. TyG Index was calculated by using fasting triglycerides and glucose with the formula Ln [fasting TGs (mg/dL) x fasting glucose (mg/dL)/2]. The performance of the TyG Index to predict the presence of CRC was also evaluated.

Statistical Analysis

Kolmogorov-Smirnov test was performed to check the normality, and the nonparametric tests were performed given the groups' non-normality before the statistical analyses. Mean and standard deviations (SD) were measured to check each continuous variable. Data analysis was done with SPSS 22.0 statistics software (SPSS, Inc., Chicago, IL, USA) and studied at a 95% confidence level. Statistical data were considered significant at $p<0.05$. The Chi-Square Statistics were used for categorical data, and the categorical variables (n) were compared using percentages, and the analysis of the variables according to the group was examined with the parametric t-test. The cut-off value was calculated by ROC analysis.

RESULTS

The study was conducted with a total of 256 people, 124 in the CRC Group and 132 in the Control Group. The mean age was found to be 60.7±10.7 years. Women constituted 47.5% of the CRC Group and 45.4% of the Control Group. CRC was detected 1.10-fold more frequently in men. In the CRC group, 25.8% (n=32) were currently smoking, physical activity was in 12.9% (n=16) of the participants, physical activity was detected in 16.9% (n=21) patients, 16.9% (n=21) patients were overweight (BMI: 27.6±6.2 kg/m2), 15.3% (n=19) patients had DM, and 17.7% (n=22) had hypertension. The demographic characteristics of the Control Group were similar to those of the CRC Group. However, smoking and alcohol consumption were significantly higher in the CRC Group and physical activity was significantly higher in the Control Group. The demographic characteristics of the CRC and Control Groups are shown in Table 1.

Table 1. Demographic characteristics of the CRC and Control Group

Parameters	CRC (n=124)	Control Groups (n=132)	p
Age	62.1±10.2	59.6±11.3	0.697
Female, sex [%]	59 (47.5%)	60 (45.4%)	0.594
Current smoking, n (%)	32 (25.8%)	18 (13.6%)	0.005
Consumption of alcohol, n (%)	16 (12.9%)	4 (5.3%)	0.001
Physical activity, n (%)	21 (16.9%)	38 (28. 7%)	0.012
BMI, kg/m2	27.6±6.2	26.7±8.5	0.751
Diabetes mellitus, n (%)	19 (15.3%)	15 (11.3%)	0.089
Hypertension, n (%)	22 (17.7%)	25 (18.9%)	0.523

Data are expressed as mean ± SD, median or number (%). BMI; Body Mass Index

It was found that metabolic parameters were higher in the CRC group at statistically significant levels. Fasting plasma glucose, triglyceride, insulin, hemoglobin A1c, and GGT were found to be statistically significant ($p<0.05$). HOMA-IR, one of the indicators of insulin resistance, was calculated high in the CRC Group. Fatty liver, alcohol consumption, high triglycerides and GGT, which is one of the indicators of insulin resistance, were significantly higher in the CRC Group. ALT was similar in both groups. TyG Index was calculated high in the CRC group at a statistically significant level ($p=0.002$). The clinical and biochemical characteristics of the participants are given in Table 2.

Table 2. Clinical and biochemical characteristics of the participants

Parameters	CRC (n=124)	Control Groups (n=132)	p
Fasting plasma glucose (mg/dL)	106.7 ± 12.8	92.5±10.3	0.032
Triglycerides (mg/dL)	98.3±8.6	80.4±6.9	0.014
Insulin (uIU/mL)	18.5±4.6	10.5±2.1	0.011
TyG Index	4.69 ±0.14	4.45±0.10	0.002
HOMA-IR	4.7±1.1	2.4±0.8	0.001
HbA1c, %	5.9±0.6	5.4±0.3	0.046
ALT, IU/L	24.4±12.5	25.1±10.5	0.683
GGT, IU/L	79.8±25.6	68.4±20.9	0.036

Data are expressed as mean ± SD, median, TyG Index; triglyceride glucose index, HOMA-IR; homeostasis model assessment of insulin resistance, HbA1c; hemoglobin A1c, ALT; alanine transaminase, GGT; gamma-glutamyl transferase.

The ability of the TyG Index to predict the presence of CRC was evaluated with the ROC Analysis. The cut-off value of the TyG Index for the presence of CRC was found to be 4.49 (AUC = 0.782, sensitivity 77%, specificity = 78.4%, and p=0.002) as the AUC under the ROC analysis curve. ROC analysis of TyG Index is given in Figure 2.

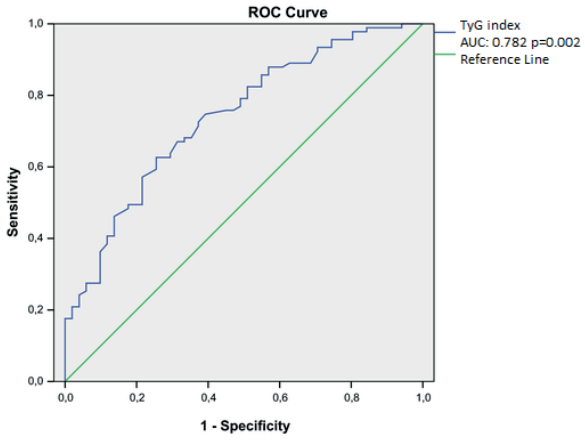

Figure 2: ROC Analysis of TyG Index effect on colorectal cancer development

DISCUSSION

In the present study, it was showed that the TyG Index can predict the presence of CRC on 124 newly diagnosed CRC cases and that beyond predicting insulin resistance, the TyG Index is a predictor of CRC risk. A positive relationship was shown between metabolic parameters and CRC. Previous studies also showed that TyG Index is associated with DM, cardiovascular disease, obesity hypoventilation syndrome, ischemic stroke, pancreatitis, and fatty liver.[13-16]

Very few studies reported that metabolic parameters associated with insulin resistance and insulin resistance increase the risk of colorectal cancer.[13] Studies conducted on this subject are very insufficient. Hyperinsulinemia, IGF levels, changes in PPARγ signaling were blamed for the pathogenesis of CRC.[14-16] In the present study, it was found that the metabolic parameters associated with insulin resistance and the insulin resistance indicator HOMA-IR increase the risk of CRC. Metabolic parameters and HOMA-IR CRC were significantly higher in the CRC group than in the control group. However, in some studies, the published results on insulin resistance are not consistent. The results of hyperinsulinemia, which is one of the components of insulin resistance, were associated with CRC and colorectal adenomatous polyps positively.[17-18]

In the present study, smoking and alcohol consumption were found to be significantly higher in the CRC Group and physical activity was significantly higher in the Control Group. BMI, DM, and hypertension were similar in the groups. This finding can be explained by the fact that some metabolic syndrome parameters are associated with CRC, which may be why studies report inconsistent results.[18-23] In the present study, fasting plasma glucose, insulin, HOMA-IR, and GGT levels were significantly higher in the CRC Group. Based on the results of the previous studies, it is clear that insulin resistance and central obesity support the development of CRC. The use of low-dose metformin was shown to reduce the average number of abnormal crypt fossi significantly, which may prevent the

development of a CRC in the future.[24] The present study and its findings show that some metabolic parameters and insulin resistance increase the risk of CRC.

Serum plasma glucose and triglyceride levels were associated with the risk of CRC in humans in a recent study.[25] In the present study, it was found that fasting plasma glucose and triglyceride levels were higher in the CRC Group. In a study conducted on the TyG Index, it was shown to be a more useful risk marker for CRC. The ability of the TyG Index to predict the presence of CRC was evaluated in the present study. It was found that the cut-off value of the TyG Index was 4.49 for the presence of CRC. A sensitivity of 77% and specificity of 78.4% detects the presence of CRC.

CONCLUSION

It was found in the present study that metabolic parameters regarding insulin resistance and TyG Index were associated with the risk of CRC. TyG Index should be used as a novel biomarker in high-risk cases. The next study should be on the effects of breaking insulin resistance on CRC risk in patients who have high risks in this regard.

Ethical Approval

The ethichs committee of this study was obtained from Sakarya University Faculty of Medicine ethics committee (Number no: E-71522473-050.04-330368-31).

Peer-review

Externally and internally peer-reviewed.

Author Contributions

Concept: E.A., Z.E., H.E., K.G., F.G., Design: E.A., Z.E., H.E., K.G., F.G., Data Collection or Processing: E.A., K.G., F.G., Analysis or Interpretation E.A., Z.E., H.E., K.G., F.G., Literature Search: E.A., Z.E., H.E., K.G., F.G., Writing: E.A., Z.E., H.E., K.G., F.G.

Conflict of Interest

All the authors declare that there is no conflict of interest with regard to the authorship and/or publication of this article.

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