RESEARCH ARTICLE / *Araştırma Makalesi*

Association Between Triglyceride Glucose Index and Neutrophil Lymphocyte Ratio in Patients with Gonarthrosis

Gonartrozlu Hastalarda Trigliserit Glikoz İndeksi ile Nötrofil Lenfosit Oranı Arasındaki İlişki

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Abstract

Introduction	This study investigated the relationship between Triglyceride Glucose (TyG) index, Neutrophil Lymphocyte Ratio (NLR) and gonarthrosis disease and investigated the role of these indicators in the development of gonarthrosis.
Materials and Methods	This study was carried out at Ayancık State Hospital between August 15 and September 15, 2022. The information of the patients who met the inclusion criteria of the retrospectively planned study was obtained from the hospital information system. Patients diagnosed with gonatrosis were divided into the study group and healthy patients were divided into the control group. NLR and TyG index were calculated for each patient, and the demographic characteristics and biochemical data of the patients were examined comparatively.
Results	The mean age of the patients included in the study was 54.10±12.5 (18-75) years. In the gonatrosis group, plasma glucose was 129.6 ± 65.6 mg/dL and triglyceride was 150.1 ± 111.9 mg/dL, and blood plasma glucose level was significantly higher than the control group (p=0.000). The TyG index level was 4.30±0.22 in the gonatrosis group and 4.21±0.08 in the control group, and there was a significant difference between the two groups in the TyG index level (p=0.008). The mean NLR level in the gonarthrosis group was 3.02±5.55, while it was 1.37±0.53 in the control group, and there was a significant difference between the two groups in terms of NLR levels (p=0.025).
Conclusion	In our study, TyG index and NLR levels were found to be significantly higher in patients with gonatrosis compared to patients in the control group. Metabolic syndrome indices such as TyG and NLR should be carefully monitored in the clinical follow-up of patients with gonatrosis.
Keywords	Triglyceride Glucose Index; Neutrophil Lymphocyte Ratio; Gonarthrosis

Öz

Amaç	*Bu çalışma, Trigliserit Glikoz (TyG) indeksi, Nötrofil Lenfosit Oranı (NLR) ve gonartroz hastalığı arasındaki ilişkiyi inceleyerek bu göstergelerin gonartroz gelişimindeki rolünü araştırmıştır.*
Yöntem ve Gereçler	*Bu çalışma 15 Ağustos-15 Eylül 2022 tarihleri arasında Ayancık devlet Hastanesi'nde yapıldı. Retrospektif olarak planlanan çalışmanın dahil edilme kriterlerine uyan hastaların bilgileri hastane bilgi sisteminden elde edildi. Gonatroz tanısı alan hastalar çalışma grubu ve sağlıklı hastalar ise kontrol grubu olarak ayrıldı. NLR ve TyG indeksi her hasta için hesaplandı ve hastaların demografik özellikleri ve biyokimyasal verileri karşılaştırmalı olarak incelendi.*
Bulgular	*Çalışmaya alınan hastaların yaş ortalaması 54,10±12,5 (18-75) yıldı. Gonatroz grubunda plazma glukozu 129,6 ± 65,6 mg/dL ve trigliserit 150,1 ± 111,9 mg/dL idi ve kan plazma glukoz düzeyi kontrol grubuna göre anlamlı düzeyde yüksekti (p=0.000). TyG indeksi düzeyi Gonatroz grubunda 4.30±0.22, kontrol grubunda ise 4.21±0.08 idi ve iki grup arasında TyG indeksi düzeyi arasında anlamlı fark vardı (p=0.008). Gonartoz grubunda NLR düzeyi ortalama 3.02±5.55 iken kontrol grubunda ortalama 1.37±0.53 idi ve iki grup arasında NLR düzeyi açısından anlamlı fark vardı (p=0.025).*
Sonuç	*Çalışmamızda, Gonatroz hastalarında kontrol grubu hastalara göre TyG indeksi ve NLR düzeyleri anlamlı düzeyde yüksek olduğu saptanmıştır. Gonatroz hastalarının klinik takibinde TyG ve NLR gibi metabolik sendrom indeksleri düzeyleri dikkatle izlenmelidir.*
Anahtar Kelimeler	*Trigliserit Glikoz İndeksi; Nötrofil Lenfosit Oranı; Gonartroz*

INTRODUCTION

The American Society of Rheumatology defined osteoarthritis as a group of heterogeneous conditions leading to joint symptoms and complications with articular cartilage defects and causing the underlying bone changes at the border of the joint.[1] Gonarthrosis is the leading cause of disability and pain in the elderly and the most common form of arthritis.[2] Recent studies on the pathophysiology of the disease have recognized the disease as a condition related to genetics, age, trauma, and metabolic conditions.[3] Metabolic conditions play a significant role in the development and progression of this disease, such as adipokines, high blood sugar, hormonal changes, and free radicals, which lead to the development of this complication in middle age (45-65 years old) and brings pain and disability.[4]

While the prevalence rate of metabolic syndrome for people without osteoarthritis is about 23%, studies show that this prevalence rate for osteoarthritis patients is 59%.[5] The findings of studies also show a relationship between having metabolic syndrome and developing arthritis at a younger age, and these patients usually have more pain and general symptoms than patients without metabolic syndrome.[2,4,5] Today, gonarthrosis is a systemic and inhomogeneous disease, and its structural and clinical aspects have been greatly improved over the past years, improving our understanding of its pathology. Age-related, metabolic, genetic, and pain-related phenotypes are hypothesized for this disease.[6,7] Aging is still recognized as the leading risk factor for gonarthrosis, but the metabolic phenotype of the disease is becoming the second sub-unit of the disease in clinical studies.[7]

On the other hand, oxidative stress can be defined as an imbalance between the production and destruction of free radicals.[8] The results of studies indicate that increased oxidative stress plays a significant role in developing diseases related to metabolic syndromes such as atherosclerosis, high blood pressure, and type 2 diabetes.[6,8] Oxidative stress has also been associated with obesity and insulin resistance in men[9] and metabolic syndrome in American adults.[10] Several studies indicate that metabolic syndrome can be considered a pre-oxidative condition.[8-10] Over time and with the increase of our knowledge about the relationship between the four main aspects of metabolic syndrome and the disease, today, efforts are underway to study the relationship between metabolic syndrome as a whole and osteoarthritis disease.[6-10] In this study, we investigate the relationship between the indicators of metabolic syndrome (Triglyceride Glucose-TyG), inflammation (Neutrophil Lymphocyte Ratio-NLR), and gonarthrosis disease to investigate the relationship between these factors and study the role of these indicators in the development of gonarthrosis.

MATERIALS and METHODS

The study was carried out in the Orthopedics and traumatology clinic of Ayancık State Hospital between August 15 and September 15, 2022. Ethics committee approval was obtained before starting the study (dated 08.08.2022 and numbered E-715222473-050.01.04-155161-230). Retrospectively planned study data were obtained from the hospital information system. The study population consisted of patients hospitalized in the orthopedics clinic between 01.20.2021 and 01.06.2022. Patients diagnosed with pregnancy status, acute inflammation, alcohol use, malignancy history, kidney or infectious disease, viral hepatitis (HBs Ag or anti-hepatitis C positive) and liver cirrhosis were excluded from this study. Persons with a history of diabetes mellitus or newly diagnosed diabetes and taking triglyceride-lowering drugs (statins, fibrates, omega-3, thiazolidinediones or insulin) were also excluded. Participants were divided into two groups as control and study groups. Participants diagnosed with gonarthrosis were included in the study group and healthy controls were included in the control group.

Laboratory examination results of the patients were obtained from the hospital information system. Fasting

blood glucose and triglyceride levels were obtained from the hospital information system from the examinations of the patients studied in the biochemistry laboratory. Plasma glucose (cut-off level 70-100 mg/dL) was determined by the glucose oxidase method. Triglyceride (cut-off level 0-150 mg/dL) was determined by enzymatic method. TyG index was calculated using fasting triglyceride and glucose with the following formula: [fasting TGs (mg/dL) x fasting glucose (mg)/dL)/2]. Demographic characteristics and biochemical data of the patients were obtained from patient file records and electronic records.

Analysis Method

The 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 21.0 and studied at a 95% confidence level. The analysis of the variables according to the group was examined with the parametric t-test. The Chi-square test analyzed the relationship between the group and gender and the TyG Index group. The cut-off value was calculated by ROC analysis.

RESULTS

Of the 141 patients included in the study, 83 were female and 58 were male. Gender distribution according to the Gonarthrosis and control groups is shown in Table 1. There was a significant difference between the gender distribution of the patients in the gonatrosis group and the patients in the control group (p=0.000).

Table 1: Distribution of Gonarthrosis and control group patients by gender

		Gonarthrosis (n=67)		Control (n=74)		p
		N	%	N	%	
GENDER	Male	15	25.9	43	74.1	0.000
	Woman	52	62.7	31	37.3	

*p<0.05 Chi-square test

While the mean age of the patients in the gonatrosis group was 68.43±8.13 years, the mean age of the patients in the control group was 32.3±10.3 years, and there is a significant difference between the mean age of both groups (p=0.000).

Granulocyte, Glucose, CRP, TyG index and NLR levels of biochemical parameters were significantly higher in patients in the gonatrosis group compared to the control group (respectively; p= 0.004, p=0.000, p=0.016, p=0.025, Table 2). Albumin and Protein levels were significantly lower in the gonatros group than in the control group (Respectively, p=0.000, p=0.001, Table 2). The distribution of laboratory parameters of patients with gonarthrosis and control group is shown in Table 2.

Table 2: Comparison of laboratory parameters of gonarthrosis and control group

Laboratory parameters	Gonarthrosis (n=67)	Control (n=74)	P value
Age, year	68.43±8.13	32.3±10.3	0.000*
Lym	1.96±0.99	2.23±0.58	0.060
Granulocyte	9.06±14.3	3.71±1.23	0.004*
Glucose	129.6±65.63	95±10.58	0.000*
Albumin	28.26±19.14	45.66±5.82	0.000*
Protein	58.19±26.43	72.15±3.75	0.001*
HDL	46.99±12.62	49.54±10.00	0.202
LDL	103.02±36.17	109.63±56.38	0.456
Triglyceride	150.14±111.9	125.41±90.04	0.165
CRP	19.28±50.15	3.21±3.06	0.016*
TyG index	4.30±0.22	4.21±0.08	0.008*
NLR	3.02±5.55	1.37±0.53	0.025*

*p<0.05 t-test; Lym: Lymphocytes; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; CRP: C- reactive protein; NLR: Neutrophil-to-lymphocyte ratio

The cut-off value calculation of TyG Index and NLR levels according to gonarthrosis and control groups is shown in Table 3.

Table 3: TyG Index and NLR Cut-off Value Calculation by Groups

Laboratory parameters	Sensitivity	Specificity	area	Std. error	P value	Asymptotic 95% Confidence Interval	
						lower limit	upper limit
TyG index	0.750	0.531	0.658	0.057	0.003	0.546	0.769
NLR	0.688	0.563	0.581	0.059	0.127	0.465	0.697

***p<0.05 ROC Analysis**

The area under the curve for the TyG Index was 0.658, relative to the gonatros and control groups. This area is significantly higher (p<0.05). When the results are examined, the best discrimination value for the TyG Index is 4.33. The value of the area under the curve for the NLR is 0.581. This area is not significantly high (p>0.05). The relationship between the TyG Index group in the gonatrosis and control group is shown in Table 4. There is a significant relationship between groups regarding TyG Index (p<0.05). 69.5% of those with a TyG Index value of less than 4.33 were in the control group, and all those above 4.33 were in the gonarthrosis group (Table 4).

Table 4: Examining the Relationship Between the Groups and the TyG Index

		Gonarthrosis		Control		p
		n	%	n	%	
TyG Index	under 4.33	32	30.5	73	69.5	0.000
	over 4.33	22	100.0	0	0.0	

*p<0.05 Chi-square test

The specificity of the variables and the sensitivity of the ROC curves are presented in Figure 1.

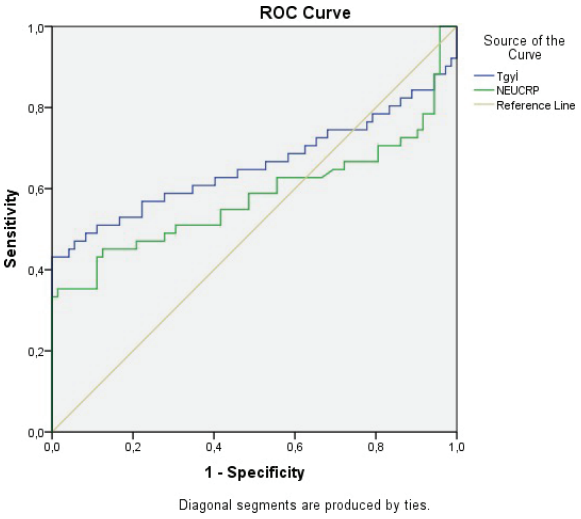

Figure 1. The variables' specificity and sensitivity of the ROC curves

DISCUSSION

Arthritis is the leading cause of pain and disability in the elderly, and gonarthrosis is the most common form of arthritis.[5] Therefore, more knowledge about the risk factors and their predisposing factors can help to prevent it and minimize the amount of disability caused by it in the elderly. New studies suggest that metabolic syndrome, due to its range of complications and different dimensions involving many organs, is probably the cause and facilitator of osteoarthritis.[5,6,8,9]

The present study investigated the relationship between

Triglyceride Glucose Index and Neutrophil Lymphocyte Ratio in patients with gonarthrosis. The results showed that these two variables are significantly higher in the gonarthrosis group. Therefore, these two variables can be considered significant indicators of metabolic syndrome and systemic inflammation in gonarthrosis populations. The findings of this study are consistent with the previous studies.[7-11] In the third round of the National Health and Nutrition Examination Survey (NHANES) study (1994-1988), metabolic syndrome was more prevalent in people with gonarthrosis.[11] In the Michigan Bone Metabolism and Health Study, obese women with two or more cardiovascular disease risk factors reported more knee pain in the past three years.[12] In the Japanese ROAD study, the risk of osteoarthritis increased with the presence of each component of the metabolic syndrome.[13] In addition, in a study in Russia with the presence of 1,350 people with osteoarthritis, 56.62% had metabolic syndrome.[14] Also, other studies have discussed the relationship between the components of metabolic syndrome and osteoarthritis.[12,13,15] Arthritis and obesity have been known to be related to each other in many studies.[14-16] Although the exact association mechanism between obesity and arthritis is unknown, studies report metabolic and mechanical factors in this relationship.[13-17]

Regarding mechanical factors, joints, especially cartilage and subchondral bone, are exposed to mechanical pressures.[9] Studies have shown that increased pressure hinders the cartilage matrix synthesis and increases the expression of pro-inflammatory factors and degrading enzymes by activating ERK, NF-KB, and Ca2+ pathways.[11,17] Also, studies showed that the reduction of body fat could have a better impact than reducing body weight in the treatment of gonarthrosis patients.[14] It has been determined that adipose tissue secretes adipokines such as leptin, adiponectin, visfatin, and resistin.[15] Dumond et al.[18] provided the first findings related to the crucial role of leptin in osteoarthritis and opened the way for further investigation of adipokines as a metabolic link between osteoarthritis and obesity.

In the present study, no significant difference was observed between the cholesterol indices of the two groups. Findings related to the relationship between cholesterol and osteoarthritis are mixed. Epidemiological studies in this field showed the relationship between increased serum cholesterol and osteoarthritis.[19] A positive correlation between serum cholesterol levels and knee and hand osteoarthritis, independent of obesity, has been shown in 1003 women aged 45-64.[20] In addition, in a study where femoral head samples were examined in 23 osteoarthritis patients, it was shown that the number of fatty acids and arachidonic acids in these samples had increased significantly concerning the severity of the disease. Apolipoprotein A1, which is part of HDL and is traditionally considered a protector against heart diseases, was shown to significantly increase in patients with osteoarthritis compared to healthy people.[21] Therefore, it seems likely that the disorder in fat metabolism plays an essential role in the development of osteoarthritis.

Another index that this study examined was the Neutrophil Lymphocyte Ratio, which was significantly higher in the patients of the study group. The relationship between the Neutrophil Lymphocyte Ratio as an index of systemic inflammation and various diseases has been of great interest in recent years. Over the past years, osteoarthritis and metabolic syndrome have been increasingly considered mild inflammatory condition that leads to increased inflammatory factors in the systemic blood flow.[22] However, it is still unclear whether the increase in inflammation leads to metabolic syndrome/osteoarthritis or whether these inflammatory mediators begin to increase following the development of the disease. One of the significant justifications is that the imbalance in the pro-inflammatory cytokines secreted from the fat tissue leads to mild insulin resistance, and in the continuation of metabolic disorders, metabolic syndrome appears.[23] As discussed in the section on the relationship between obesity and osteoarthritis, the

pro-inflammatory hormone leptin, secreted by adipose tissue macrophages and the primary mediator of obesity-related metabolic disorders, is an essential link between obesity and osteoarthritis.[22,23]

Moreover, the results of the studies indicate that the increase in oxidative stress plays a significant role in causing diseases related to metabolic syndromes, such as atherosclerosis, high blood pressure, and type 2 diabetes.[24] Oxidative stress has also been associated with obesity and insulin resistance in men[12] and metabolic syndrome in American adults.[14] Several studies indicate that

metabolic syndrome can be considered a pre-oxidative condition.[17,18,24] Studies have shown that the amount of free radicals is related to the damage of osteoarthritis due to local joint reactions to them. Increasing the level of free radicals in the systemic circulation due to their production in other places causes cell aging in the joints, cartilage apoptosis, and eventually decreases the cartilage's thickness in the joint.[16, 22-24]

Considering the relationship between gonarthrosis and metabolic syndrome, it seems that future treatment goals should consider these two conditions together. Studies on the effects of this therapeutic combination are being carried out, which have not yet led to a change in treatment recommendations. New drugs that focus on intermediate metabolites in the pathology of gonarthrosis are under study. It is hoped that the convergence of studies between clinical researchers and basic science will inspire new efforts toward better treatment and more effective prevention of this disease. The limitations of this study included the small number of samples and the collection of all samples from one treatment center. In future studies, more samples and several different treatment centers can be used to improve the results.

CONCLUSION

This study observed a significant association between metabolic syndrome indexes, such as Triglyceride Glucose Index and Neutrophil Lymphocyte Ratio, and gonarthrosis. Of course, more studies are still needed to prove the possible cause-and-effect relationship. However, the existing results sufficiently implicate at least metabolic syndrome or its components, such as obesity, blood lipid disorders, or oxidative stress, in developing gonarthrosis.

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