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Original Article

Association Between Endometrial Pathologies and Triglyceride Glucose Index & Body Shape Index: Retrospective Cohort Study

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ABSTRACT

Objective: We aimed to investigate the association between the triglyceride glucose index and body shape index in predicting premalignant-malignant endometrial pathologies.

Methods: The results of patients who presented to the Department of Gynecology and Obstetrics at our hospital due to abnormal uterine bleeding and underwent endometrial biopsy were reviewed. We formed two groups: benign pathologies and premalignant-malignant pathologies. Multiple logistic regression analysis was performed to evaluate the relationship between the triglyceride glucose index, body shape index, and premalignant-malignant endometrial pathology. The study is a retrospective cohort study.

Results: There were 579 patients whose fasting blood glucose and fasting triglycerides were measured before endometrial biopsy. After applying exclusion criteria, 330 patients (age: 43-56 years) were included in the study. Significant differences were observed between the groups in terms of age, weight, waist circumference, BMI, and body shape index Z scores ($p<0.05$). Triglyceride glucose index, anthropometric measurements, and waist circumference had the highest AUC. Regression analysis showed that a one-unit increase in the triglyceride glucose index value increased the probability of the patient having premalignant-malignant pathology by 164 times.

Conclusion: Consequently, obesity increases the likelihood of endometrial pathology. Therefore, it is recommended to assess the triglyceride glucose index and body shape index Z scores in patients with abnormal uterine bleeding. Both of these methods are simple and cost-effective to calculate. It is important to inform patients about the risks identified in these calculations and to provide preventive advice.

INTRODUCTION

Endometrial carcinoma (EC) is a common gynecologic malignancy, and its incidence is increasing.[1] Endometrial intraepithelial neoplasia often precedes it. Frequently identified risk factors include increased age, obesity (especially abdominal obesity), increased body mass index (BMI), insulin resistance, diabetes, dyslipidemia, and hormonal imbalance.[2,3]

The development of cancer is a complex process that can be traced back to serious disturbances in the regulation of cell growth and proliferation. Recent evidence has shown that insulin resistance, which is regulated in part by fasting and lifestyle, is closely associated with the morbidity and mortality of several cancers, including breast, colorectal, and cervical cancers.[4,5] This may be because insulin resistance increases cell proliferation, inhibits apoptosis, activates IGF-1 receptors, and triggers inflammation and oxidative stress, which promote cancer growth.[6,7]

Obesity is a risk factor for EC.[8] The underlying process is thought to be related to insulin resistance and the release of adipokines. Insulin resistance causes higher insulin levels that stimulate endometrial cell mitogenesis, and adipokines such as adiponectin and leptin also contribute to the development of EC.[9] In addition, hyperinsulinemia leads to excessive proliferation of granulosa cells and the production of large amounts of androgens, which are converted to estrogens by the enzyme aromatase. Insulin

resistance thus becomes a risk factor for endometrial hyperplasia and early-stage endometrial cancer.[10-12]

It is well known that insulin resistance can be measured by the Homeostatic Model Assessment and the hyperinsulinemic-euglycemic clamp test.[13] In addition, several studies have shown that the triglyceride glucose (TyG) index may be a more appropriate and reliable predictor of insulin resistance compared with these two measurement tools. Therefore, because of its availability and cost-effectiveness, the TyG index may be a promising indicator of insulin resistance in large-scale epidemiological studies.[14]

Our aim was to investigate the relationship between insulin resistance and endometrial pathologies using the TyG index, taking into account existing risk factors for EC. In addition, we investigated the relationship between endometrial pathologies and anthropometric measurements such as BMI and a body shape index (ABSI).

MATERIALS AND METHODS

Study Design

This study is a retrospective cohort study. The results of patients who presented to the Department of Gynecology and Obstetrics at our hospital with abnormal uterine bleeding and underwent endometrial biopsy between October 2022 and June 2023 were reviewed. Over the past year, 579 patients were found whose fasting blood sugar and fasting triglyceride levels were measured before biopsy. According to the study's purpose, two groups of patients were formed: benign (endometrial polyp, endometrial hyperplasia without atypia, atrophic endometrium) and premalignant (endometrial intraepithelial neoplasia)-malignant (endometrial cancer). Patients were contacted, informed about the study, and invited to the outpatient clinic. All patients were informed that their medical data and records could be used in the studies without revealing the patient's identity. Informed consent was obtained from the patients. We prepared a form including risk factors for EC. The form was completed in a face-to-face interview with the patients, and height, weight, and waist circumference were measured. All patients had a confirmed histopathological diagnosis. Patients with fasting glucose and fasting triglyceride values checked within the past year were included in the study. Patients currently taking medications due to diabetes, hyperlipidemia, and a history of cancer were excluded from the study.

The triglyceride-glucose index of the patients was calculated according to the equation TyG=ln [fasting triglyceride (mg/dl) x fasting glucose (mg/dl)] /2.[15] To determine the risk of early death due to the patients' body shape, ABSI scores were calculated by adding waist circumference, height, and BMI to sex and age, and ABSI Z-scores were calculated to compare the results with similar age groups. ABSI values were calculated using the formula ABSI=Waist circumference/(height1^11/2_22×BMI2^22/3_33), ABSI Z-score: ABSI-ABSIMean/ABSISD.[16]

RESULTS

In the past year, 579 patients whose fasting blood sugar and fasting triglyceride levels were measured before biopsy were identified. After applying the exclusion criteria, 134 patients (22%) were excluded from the study because they were taking antidiabetic drugs, 70 patients (12%) were taking antilipidemic drugs, 20 patients (3%) had a history of cancer, and 25 patients (4%) declined to participate in the study, leaving 330 patients eligible for the study. The groups formed based on the number of patients and the pathology results are shown in Figure 1.

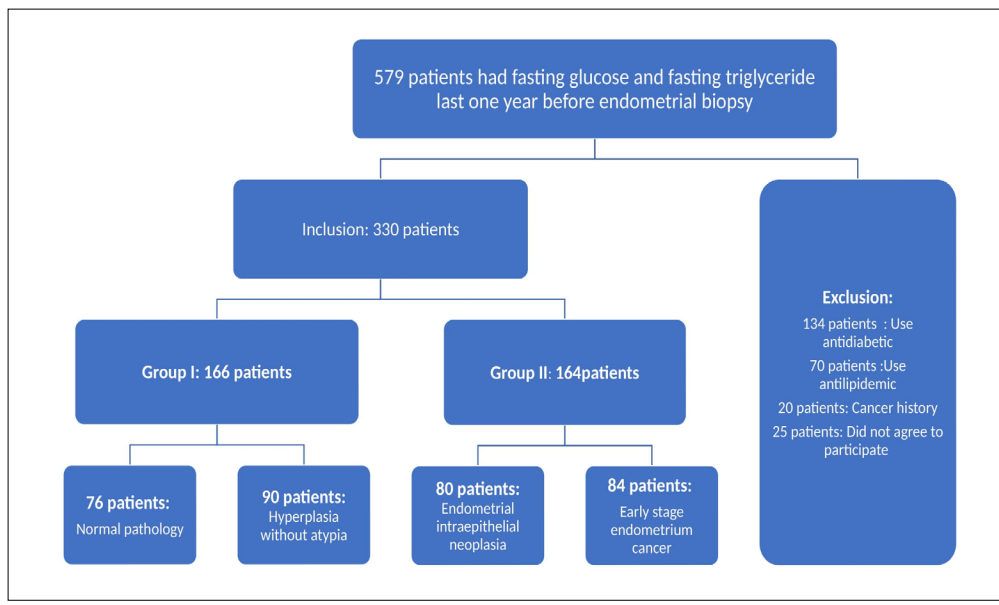

Figure 1. Flowchart.

Primary Outcome

There was a significant difference in age, weight, BMI, waist circumference, and ABSI Z-score between the two groups. Group II had a higher number of menopausal patients (p<0.05). Smoking and plasma albumin levels were statistically higher in Group I than in Group II. In Group II, plasma fasting triglyceride level, fasting blood glucose, TyG index, leukocyte count, and neutrophil count were higher than in Group I (p<0.05) (Table 1).

In evaluating the laboratory and anthropometric measurements with statistically significant differences between groups with ROC analysis, weight, waist circumference, BMI, ABSI Z-score, plasma triglyceride, fasting blood glucose, and the TyG index were found to be statistically significant (p<0.05). The TyG had the highest AUC (AUC:0.813, CI%:0.744-0.869, p<0.001, sensitivity:67.1, specificity:88, cut-off value: >4.79). Among the anthropometric measurements, waist circumference had the highest AUC value (AUC:0.779, CI%:0.708-0.840, p<0.001, sensitivity: 68.3, specificity: 45.8, cut-off value: >73 cm). The values of AUC, CI%, p-value, cut-off value, sensitivity, specificity, negative likelihood ratio, and positive likelihood ratio of each parameter are shown in Table 2. In the ROC

Table 1. Demographic and clinical characteristics of the study population

Variables	Benign (n=166)	Malign- premalignant (n=164)	Total (n=330)	p
Age	41.75 (45.5-50)	53 (47-63.5)	48 (43-56)	<0.001
Gravida	2.5 (2-3.75)	3 (2-4)	3 (2-4)	0.219
Parity	2 (2-3)	3 (2-4)	2 (2-3)	0.233
Abort	0 (0-0)	0 (0-0.75)	0 (0-0)	0.481
Menarcheal				
Age (years)	13 (12-14)	13 (12-14)	13 (12-14)	0.151
Weight (kg)	75 (66-85)	83.5 (74-97.25)	78 (71.5-90)	<0.001
BMI (kg/m^2)	29.3 (25.8-32.8)	32.1 (29.2-38.6)	35.2 (30.5-27.5)	<0.001
Waist circumference (cm)	95 (86-103)	110 (98-125.25)	102 (91-116)	<0.001
ABSI	0.0791	0.0846	0.0820	
	(0.0749-0.0840)	(0.0798-0.0886)	(0.0861-0.0770)	<0.001
ABSI Z score	0.0494	0.8403	0.4990	
	(-0.7508-1.0514)	(0.0488-1.4491)	(-0.4525-1.3128)	0.003
Fasting triglyceride level (mg/dL)	113 (78-145)	174 (117-256)	133 (97-184.5)	<0.001
Fasting glucose level (mg/dL)	88 (80-95)	100.5 (88-121)	91 (84.5-105)	<0.001
TyG index	4.58±0.242	4.90±0.267	4.74±0.300	<0.001
Hemoglobin (g/dL)	12.5 (11-13.1)	12.4 (11.5-13.4)	12.4 (11.1-13.3)	0.444
Smoking status				
No	120 (72.3)	144 (87.8)	264 (80)	0.022
Yes	46 (27.7)	20 (12.2)	66 (20)	
Previous endometrial hyperplasia diagnosis				
No	156 (94)	160 (97.6)	316 (95.8)	0.443
Yes	20 (6)	8 (2.4)	28 (4.2)	
Family history of colorectal cancer or endometrial cancer				
No	146 (88)	158 (96.3)	304 (92.1)	0.087
Yes	20 (12)	6 (3.7)	26 (7.9)	
Menopause status				
No	142 (85.5)	78 (47.6)	220 (66.7)	<0.001
Yes	24(14.5)	86 (52.4)	110 (33.3)	
Previous infertility diagnosis				
No	154 (92.8)	160 (97.6)	314 (95.2)	0.277
Yes	12 (7.2)	4 (2.4)	16 (4.8)	

kg: kilogram; BMI: body mass index; kg/m2: kilogram per square meter; cm, centimeter; ABS: A Body Shape Index; mg/dL: milligrams per decilitre; TyG: Triglyceride glucose index; g/L: gram per liter; µL: microlitre; g/dL: grams per decilitre; WBC: white blood cell. Data are expressed as the mean±SD, median (Q1-Q3), or number (percentage) where appropriate. A p value of <0.05 indicates a significant difference. Statistically significant p values are in bold.

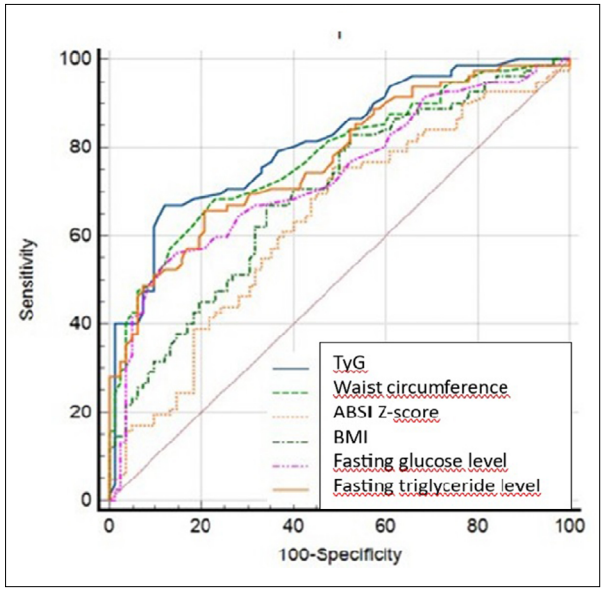

Figure 2. Comparison of the ROC graphs of various parameters.

analysis performed to determine the superiority of AUC values of all statistically significant parameters over each other, waist circumference was found to be superior to all other anthropometric measurements (waist circumference vs. BMI p:0.004; vs. ABSI p:0.023; vs. ABSI Z-score p<0.001) (Figure 2). The TyG index has better sensitivity and specificity values than other laboratory parameters and has a statistically significantly higher AUC value (TyG vs. Plasma triglyceride level p:0.015; vs. fasting glucose level p:0.045). The p-values expressing the superiority and difference of all parameters in terms of AUC values are shown in Table 3.

Secondary Outcomes

In the regression analysis performed to determine the risk factors for premalignant-malignant pathologies and the rates of risk increase among the categorical variables, not smoking (OR:2.871, p: 0.047) is considered a risk factor, while premenopause appears to be a protective factor with a 6.41-fold reduction in risk (OR:0.156, p<0.001). However, each year, the patient's age increases, resulting in a 1.089-fold increase in the risk of premalignant-malignant pathology (p<0.001). Of the anthropometric measurements, only waist circumference (OR:1.056, p: 0.001) showed a statistically significant risk increase, while of the laboratory measurements, plasma triglyceride level (OR:1.02, p<0.001), fasting blood glucose (OR:1.025, p: 0.024), and TyG index (OR:164.67, p<0.001) showed significantly increased risk. A one-unit increase in the patient's TyG index value increases the likelihood of the patient having premalignant-malignant pathology 164-fold. Weight, ABSI Z-score, white blood cell count, neutrophil count, and albumin levels alone were not sufficient to determine the risk increase (p>0.05) (Table 4).

DISCUSSION

Endometrial cancer is increasing daily due to rising obesity worldwide. Obesity, metabolic disorders, and insulin resistance pose serious risks, especially for estrogen-related EC.[17] In our study, we wanted to draw attention to the relationship between endometrial pathologies and obesity by calculating waist circumference, weight, BMI, ABSI, and

Table 2. The results of ROC curve analysis for various parameters that can be used to predict the outcome of a premalignant-malignant biopsy

Variables	AUC	CI 95%	p	Cut-off value	Sensitivity (%)	Specificity (%)	LR+	LR-
Weight	0.670	0.592-0.741	<0.001	>73	80.5	45.8	1.48	0.43
Waist circumference	0.779 0.840	0.708-<0.001	103	68.3	77.1	2.98	0.41	
BMI	0.693	0.617-0.763	<0.001	>30.45	67.1	65.1	1.92	0.51
ABSI Z-score	0.636	0.557-0.709	0.001	>0.0667	75.6	51.2	1.55	0.48
Fasting triglyceride level	0.755	0.703-0.836	<0.001	>150	65.9	79.5	3.22	0.43
Fasting glucose level	0.728	0.653-0.794	<0.001	>97	56.1	84.3	3.58	0.52
TyG	0.813	0.744-0.869	<0.001	>4.79	67.1	88	5.57	0.37

ROC: receiver operating characteristic; AUC: the area under the curve; C: confidence interval; LR+: positive likelihood ratio; LR: negative likelihood ratio; BMI: body mass index; ABSI: A Body Shape Index; TyG: Triglyceride glucose index; p-value of <0.05 indicates a significant difference. Statistically significant p-values are in bold.

Table 3. The p-values obtained when the parameters for which ROC calculations were performed are compared using the AUC values

Variables	Height	Weight	Waist circumference	BMI	ABSI	ABSI z score	TyG	Fasting glucose level
Height		0.215	<0.001$^{\Phi}$	0.040$^{\Phi}$	0.091	0.489	<0.001$^{\Phi}$	0.024$^{\Phi}$
Weight	0.215		0.002$^{\Phi}$	0.209	0.755	0.572	0.002$^{\Phi}$	0.285
Waist circumference	<0.001$^{\Phi}$	0.002$^{\Phi}$		0.004$^{\Phi}$	0.023$^{\Phi}$	<0.001$^{\Phi}$	0.456	0.378
BMI	0.040$^{\Phi}$	0.209	0.004$^{\Phi}$		0.938	0.330	0.010$^{\Phi}$	0.489
ABSI	0.091	0.755	0.023$^{\Phi}$	0.938		<0.001$^{\Phi}$	0.027$^{\Phi}$	0.458
ABSI z score	0.489	0.572	<0.001$^{\Phi}$	0.330	<0.001$^{\Phi}$		0.001$^{\Phi}$	0.097
TyG	<0.001$^{\Phi}$	0.002$^{\Phi}$	0.456	0.010$^{\Phi}$	0.027$^{\Phi}$	0.001$^{\Phi}$		0.045$^{\Phi}$
Plasma Triglyceride level	0.001$^{\Phi}$	0.034	0.910	0.108	0.161	0.020$^{\Phi}$	0.015$^{\Phi}$	0.372

ROC: receiver operating characteristic; BMI: body-mass index; ABSI: A Body Shape Index; TyG: Triglyceride glucose index; p value of <0.05 indicates a significant difference. Statistically significant p-values are in bold. $^{\Phi}$For comparisons where the p value is significant, the parameter with the higher AUC value in Table 2 is superior in predicting the outcome of a premalignant-malignant biopsy.

Table 4. Results of regression analysis showing the risk of a premalignant-malignant pathological outcome for statistically significant variables

Variables	OR	95% CI	p
Age$^{¥}$	1.089	1.044-1.135	<0.001
Premenopause$^{¥}$	0.156	0.062-0.389	<0.001
Smoking status (no)$^{¥}$	2.871	1.012-8.147	0.047
Weight$^{£}$	1.019	0.991-1.047	0.192
BMI$^{£}$	1.044	0.975-1.118	0.219
Waist circumference$^{£}$	1.056	1.024-1.088	0.001
ABSI Z-score$^{£}$	1.285	0.995-1.661	0.055
Fasting triglyceride level$^{\Omega}$	1.020	1.011-1.029	<0.001
Fasting glucose level$^{\Omega}$	1.025	1.003-1.048	0.024
TyG$^{\Omega}$	164.67	21.635-1253.415	<0.001
WBC$^{\Omega}$	1.000	0.999-1.000	0.143
Albumin$^{\Omega}$	0.895	0.791-1.013	0.078

OR: odds ratio; CI: confidence interval; BMI: body mass index; ABSI: A Body Shape Index; TyG: triglyceride glucose index; WBC: white blood count. A p-value of <0.05 indicates a significant difference. Statistically significant p-values are in bold. $^{¥}$In modeling involving only demographic data, all demographic data were adjusted with statistically significant parameters. $^{£}$Each anthropometric measurement was adjusted for statistically significant demographic data and the laboratory parameter (TyG) with the highest AUC in the ROC analysis. $^{\Omega}$Each laboratory measurement and index were adjusted with statistically significant demographic data and anthropometric measurement (waist circumference) with the highest AUC in the ROC analysis.

ABSI Z-score of the patients participating in the study.

Metabolic syndrome is a combination of various metabolic abnormalities such as obesity, insulin resistance, hypertension, and dyslipidemia.[18] Studies suggest that metabolic abnormalities and obesity may be important risk factors for the development of EC.[19]

Obesity is associated with gynecological cancers in women. Alsansan et al.[20] showed that EC is common in women with obesity. Nicholson et al.[21] found that there is a linear relationship between increasing BMI scores and early-stage endometrial intraepithelial neoplasia in premenopausal patients. Laslov et al.[22] concluded that patients with a higher BMI increase during follow-up had higher recurrence rates of EC.

In our study, we observed a significant association between increased BMI and endometrial pathologies, consistent with previous findings. It is important to note that BMI has limitations. It cannot distinguish between fat and lean mass or central and peripheral obesity. To overcome these limitations, a new anthropometric index called the body shape index (ABSI) has been proposed as an alternative. ABSI values are associated with all-cause mortality, metabolic syndrome, diabetes, and hypertension, making it useful in estimating the risk of diseases that BMI cannot detect easily.[23,24]

Our study focused on waist circumference as one of the diagnostic criteria for metabolic syndrome. We calculated ABSI scores to predict the risk of early mortality. Our results showed that increased waist circumference, especially due to abdominal adipose tissue, was more closely

associated with premalignant endometrial pathologies. In addition, the ABSI Z-scores of patients in the premalignant-malignant group were higher. Although there have been studies on the association between metabolic disorders and endometrial pathology, none have considered ABSI and endometrial pathology outcomes. Our study suggests that ABSI should be considered an important parameter for determining the risk of premalignant and malignant endometrial pathology.

It is well known that smoking increases the risk of many chronic diseases and cancers. However, it has been shown to have an estrogen-inhibiting effect due to the changes it causes in the estrogen mechanism. Smoking can reduce estrogen-induced cell proliferation in the endometrial glands. This effect may contribute to protection against the development of endometrial cancer. In our study, we found that smoking was more frequent in the benign group, which is consistent with the results reported in the literature.[25]

Dyslipidemia is an independent risk factor for EC.[26] Sethre et al.[27] found a positive correlation between serum lipid/lipoprotein levels (e.g., triglycerides) and EC risk in a cohort of 31,473 women.[27] Abnormal lipid metabolism increases the risk of endometrial cancer through several mechanisms. High triglyceride levels resulting from abnormal lipid metabolism increase free estrogen levels by decreasing the binding of the sex hormone to proteins (e.g., globulin).[9,28] The TyG index results evaluated in our study show that dyslipidemia and insulin resistance increase the risk of EC, which is consistent with the literature. It is noteworthy that the TyG index is particularly high in the endometrial intraepithelial neoplasia group. This may suggest that the association between endometrial cancer and diabetes in the population may be due to previously untreated insulin resistance. Most of the literature has examined the relationship between the TyG index and cardiovascular disease. In the article that examined the association between the TyG index and obesity-related cancers, no association was found between ovarian and endometrial cancer and the TyG index.[20] There was only one study that examined the association between endometrial cancer and the triglyceride glucose index, and it found that the index was high in premalignant-malignant endometrial pathologies, which was consistent with our study.[29]

The strength of our study is that, using indices calculated with a simple method, we can predict people's risk of endometrial pathologies and provide opportunities for preventive medicine. It is important to point out that this study has certain limitations. First, the patients were selected from only one institution, and the sample size is relatively small. Therefore, our results may not be fully representative of the wider population. However, if multicenter studies with larger patient cohorts are conducted in the future, we may obtain more precise and accurate results that reflect the general population.

Conclusion

The triglyceride glucose index provides information about insulin resistance. It is determined using a simple method and helps to assess a patient's risk of endometrial cancer. In this way, we can explain the current risk to the patient and make recommendations to reduce the risk through lifestyle changes and an appropriate dietary program. These parameters, which we have examined in diagnosed patients, can be used as a screening program in primary care to calculate individual risk by examining all women over the age of 35.

Ethics Committee Approval

The study was approved by the Ankara Etlik City Hospital Ethics Committee (Date: 19.07.2023, Decision No: AESH-EK1-2023/332).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: S.T.S., T.K.G.; Design: S.T.S., S.Ö.Ş.; Supervision: S.T.S., C.H., Ç.S.; Fundings: S.T.S.; Materials: T.K.G., E.G.T.; Data: T.K.G., C.H.; Analysis: S.Ö.Ç., E.G.T., Ç.S.; Literature search: S.T.S., C.H., E.G.T.; Writing: S.T.S., S.Ö.Ş.; Critical revision: S.T.S., Ç.S.

Conflict of Interest

None declared.

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Endometriyal Patolojiler ile Trigliserit Glikoz İndeksi ve Vücut Şekli İndeksi Arasındaki İlişki: Retrospektif Kohort Çalışması

Amaç: Bu çalışmada, premalign-malign endometrial patolojileri öngörmede trigliserid glukoz indeksi ve vücut şekil indeksi arasındaki ilişkiyi araştırmayı amaçladık.

Gereç ve Yöntem: Hastanemiz Kadın Hastalıkları ve Doğum Kliniğine anormal uterin kanama nedeniyle başvuran ve endometrial biyopsi yapılan hastaların sonuçları tarandı. Benign patolojiler ve premalign-malign patolojiler olmak üzere iki grup oluşturuldu. Trigliserid glukoz indeksi, vücut şekil indeksi ve premalign-malign endometriyal patoloji arasındaki ilişkiyi değerlendirmek için çoklu lojistik regresyon analizi yapıldı. Çalışma retrospektif bir kohort çalışmasıdır.

Bulgular: Endometriyal biyopsi öncesinde açlık kan şekeri ve açlık trigliseritleri ölçülen 579 hasta vardı. Dışlama kriterleri uygulandıktan sonra 330 hasta (yaş: 43-56) çalışmaya dahil edildi. Gruplar arasında yaş, kilo, bel çevresi, VKİ ve vücut şekil indeksi Z skorları açısından anlamlı farklılıklar gözlendi ($p<0.05$). Trigliserid glukoz indeksi, antropometrik ölçümler ve bel çevresi en yüksek AUC'ye sahipti. Regresyon analizi, trigliserit glukoz indeksi değerindeki bir birimlik artışın hastanın premalign-malign patolojiye sahip olma olasılığını 164 kat artırdığını göstermiştir.

Sonuç: Obezite endometriyal patoloji olasılığını artırmaktadır. Bu nedenle, anormal uterin kanaması olan hastalarda trigliserit glukoz indeksi ile vücut şekil indeksi Z skorları arasındaki ilişkiye bakılması önerilmektedir. Bu yöntemlerin her ikisinin de hesaplanması basit ve uygun maliyetlidir. Hastaları bu hesaplamalarda belirlenen riskler hakkında bilgilendirmek ve önleyici tavsiyelerde bulunmak önemlidir.

Anahtar Sözcükler: Endometrioid; insülin direnci; karsinom; obezite.