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ORIGINAL ARTICLE/ORİJİNAL MAKALE

The relationship between serum adropin levels, body mass index and blood pressure values in endometrial carcinoma

Endometrial karsinomda serum adropin düzeyleri, vücut kitle indeksi ve kan basıncı değerleri arasındaki ilişki

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ABSTRACT

Aim: Adropin is a protein that has been found in the brain, liver, and peripheral tissues in terms of energy homeostasis. Serum adropin levels were lower in hypertension, diabetes mellitus, and metabolic syndrome. This study aimed to investigate the relationship between adropin levels, body mass index (BMI), and blood pressure values in endometrial carcinoma (EC).

Material and Methods: Fourty healthy and 50 EC patients' demographic information, including characteristics of obstetric history, diabetes mellitus (DM), hypertension (HT), and family history were recorded. Fasting insulin, homeostasis model assessment for insulin resistance (HOMA-IR), high-density lipoprotein (HDL), low-density lipoprotein (LDL), total cholesterol (TC), triglyceride (TG), and adropin levels were obtained from venous blood samples.

Results: We found no statistically significant difference between the control and EC groups at the serum adropin level. However, adropin was found to be significantly lower in type 2 EC (OR=0.350; 95%CI 0.156-0.783; p=0.011). Optimal cut-off value was calculated in ROC curve analysis as 0.4 ng/mL for adropin (63.6% sensitivity, 64.7% specificity). Positive Likelihood ratio (LR+) was 1.8 and the negative Likelihood ratio (LR-) was 0.56.

Conclusion: Adropin may be a promising marker for the differential diagnosis of type 1 and type 2 endometrial carcinoma before surgery and needs to be confirmed by further studies.

Keywords: Adropin, Body Mass Index, Blood Pressure, Endometrial Carcinoma

ÖZET

Amaç: Adropin, enerji homeostazı açısından beyin, karaciğer ve periferik dokularda bulunan bir proteindir. Serum adropin düzeyleri hipertansiyon, diabetes mellitus ve metabolik sendromda daha düşük bulunmuştur. Bu çalışmanın amacı endometriyal karsinomlu (EC) hastalarda adropin düzeyleri, vücut kitle indeksi (VKİ) ve kan basıncı değerleri arasındaki ilişkiyi araştırmaktır.

Gereç ve Yöntemler: Toplam 40 sağlıklı ve 50 EC hastanın obstetrik öykü, diabetes mellitus (DM), hipertansiyon (HT) ve aile öyküsü özelliklerini içeren demografik bilgileri kaydedildi. Venöz kan örneklerinden açlık insülini, insülin direnci için homeostaz modeli değerlendirmesi (HOMA-IR), yüksek yoğunluklu lipoprotein (HDL), düşük yoğunluklu lipoprotein (LDL), total kolesterol (TK), trigliserit (TG) ve adropin düzeyleri elde edildi.

Bulgular: Kontrol ve EC grupları arasında serum adropin düzeyi açısından istatistiksel olarak anlamlı bir fark bulunmamıştır. Ancak tip 2 EC'de adropin anlamlı derecede düşük bulunmuştur (OR=0,350; %95CI 0,156-0,783; p=0,011). ROC eğrisi analizinde adropin için optimum cut-off değeri 0,4 ng/mL olarak hesaplanmıştır (%63,6 duyarlılık, %64,7 özgüllük). Pozitif Olabilirlik oranı (LR+) 1,8 ve negatif Olabilirlik oranı (LR-) 0,56 olarak hesaplanmıştır.

Sonuç: Adropin, cerrahi öncesi tip 1 ve tip 2 endometriyal karsinomun ayırıcı tanısı için umut verici bir belirteç olabilir ve daha ileri çalışmalarla doğrulanması gerekmektedir.

Anahtar Kelimeler: Adropin, Vücut Kitle İndeksi, Kan Basıncı, Endometriyal Karsinom

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INTRODUCTION

Endometrial cancer (EC) is the most common female genital tract malignancy (1). Endometrial cancer is associated with high estrogen levels and the number of women being diagnosed with EC is on the rise, mainly due to the increase in obesity (2). EC has been classified into two groups; type 1 and type 2 tumors. Type 1 carcinomas comprise 80% of EC and are associated with low-grade and endometrioid histology. They commonly originate from premalignant hyperplastic lesions, whereas Type 2 cancers cover serous, clear cell histology or grade 3 endometrioid carcinoma. They usually occur in old age and are not associated with high estrogen (3).

Adropin is a 42 amino-acid peptide hormone regarding that protects glucose homeostasis. Gao et al. indicated that adropin promotes carbohydrate oxidation rather than fat oxidation in skeletal muscles (4). In addition, the expression of inducible nitric oxide synthase was also affected by adropin (5). Adropin may therefore be able to predict endothelial dysfunction in diabetes mellitus (6).

Although there are different studies associating the relationship between adropin and coronary artery diseases (7), obesity and obesity-related cancers (8), liver cirrhosis (9), ovarian torsion (10), and sleep apnea (11), there is no consensus among the authors on the clinical availability of adropin levels in EC. The purpose of this study was to examine the relationship between EC, body mass index (BMI), high blood pressure, and serum adropin levels.

MATERIALS AND METHODS

Study procedures involving human participants followed the ethical principles of the institutional research committee and the Helsinki Declaration. Ethics approval was granted by the Department of Health Sciences Türkiye, Sisli Hamidiye Etfal Education and Research Hospital (Date: 03/10/2017 No: 1704/866). The sample size was established via a power calculation test. The sample size was found to have a 95% confidence level and an 80% power (α = 0.05). Therefore, each group needed a minimum sample size of 19 patients (effect size 0.84496) (12).

The control group consists of 40 healthy women. The study population included 50 women referred to Sisli Hamidiye Etfal Education and Research Hospital, Obstetrics and Gynecology Clinic between 2017-2018 years and ages 35-79 with a diagnosis of histologically confirmed EC. We excluded patients with endometrial hyperplasia, prior cancer diagnosis, and a history of adjuvant radiotherapy or chemotherapy. All participants gave their consent in writing after being fully informed. BMI was calculated as weight in kilograms divided square of height in meters (kg/m^2). BMI a categorized according to World Health Organization (WHO).

Normal adult blood pressure is defined as a systolic blood pressure of 120 mmHg and a diastolic blood pressure of 80 mmHg. According to the WHO, hypertension is defined as a systolic blood pressure of 140 mmHg or higher and/or a diastolic blood pressure of 90 mmHg or higher.

Every participant fasted the previous night. Participants' venous blood samples were taken two hours before surgery. Following the collection of blood samples in tubes (5 ml), the samples were centrifuged for 15 minutes at 1000 g at 4 C, and then stored at -80 C until the assay.

Fasting glucose level (FGL), fasting insulin, lipid profile and metabolic parameters were

collected. Homeostasis model assessment for insulin resistance (HOMA-IR) was computed as [fasting insulin (IU/mL) x fasting glucose (mg/dL) /405] (13). The tumor markers were measured by enzyme immunoassay. For the determination of serum adropin levels, samples were thawed at room temperature and vortexed for 30 sec. ELISA tests (Human Adropin ELISA kit; Catalog no: E-EL-H5307)) were used to measure adropin levels. (www.elabsicience.com).

An experienced pathologist reported histological type and grade of the tumor according to 2009 staging system of the International Federation of Gynaecology and Obstetrics (FIGO) (14).

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) version 15.0 (Chicago, Illinois, USA) was utilized for data entry and analysis. Median, mean, standard deviation, frequency, and ratio values were used for descriptive statistics. For categorical data, the x^2 test was used, and the variables were expressed as percentages. Spearman correlation was conducted on qualitative data. Quantitative data that are normally distributed was analyzed using Pearson correlation. Logistic regression analyses were performed for determining the statistically different values in correlation analyses. Receiver operator characteristic curve analysis and calculation of the area under the curve were performed to obtain significantly different serum adropin levels. A p-value less than 0.05 was taken statistically significant.

RESULTS

A total of 90 patients (40 healthy individuals in control group and 50 women with EC in the study group) were evaluated. Demographic, clinical, and biochemical data according to BMI are shown in Table 1.

Table 1. Demographic, clinical, biochemical and hormonal characteristics of patients with EC according to BMI

	Control Group			EC Group					
	BMI≥30 (n=20)	BMI<30 (n=20)	Total (n=40)	BMI≥30 (n=31)	BMI<30 (n=19)	Total (n=50)	p*	p**	p***
Age (years)	58.4±8.13	55.1±9.62	56.75±8.95	62.00±8.90	59.89±13.16	61.20±10.64	0.086	0.097	0.068
Gravidity (n)	5.35±2.50	4.35±2.68	4.85±2.61	4.58±2.90	3.21±1.90	4.06±2.63	0.212	0.194	0.108
Gravidity>4(n,%)	12 (60.0)	8 (40.0)	20 (50.0)	17 (54.8)	7 (36.8)	24 (48.0)	0.716	0.839	0.850
Parity (n)	4.05±2.16	3.05±2.24	3.55±2.23	3.55±2.71	2.21±1.08	3.04±2.31	0.201	0.296	0.155
Parity >2 (n,%)	15 (75.0)	8 (40.0)	23 (57.5)	18 (58.1)	5 (26.3)	23 (46.0)	0.217	0.365	0.278
DM (n,%)	15 (75.0)	4 (20.0)	19 (47.5)	17 (54.8)	9 (47.4)	26 (52.0)	0.146	0.070	0.671
DM Family (n,%)	10 (50.0)	4 (20.0)	14 (35.0)	16 (51.6)	7 (36.8)	23 (46.0)	0.910	0.243	0.292
HT (n,%)	12 (60.0)	8 (40.0)	20 (50.0)	25 (80.6)	4 (21.1)	29 (58.0)	0.107	0.200	0.449
HT Family (n,%)	12 (60.0)	8 (40.0)	20 (50.0)	22 (71.0)	5 (26.3)	27 (54.0)	0.417	0.365	0.706
HbA1c(mmol/L%)	5.85±0.77	5.35±0.47	5.60±0.68	6.38±1.64	5.99±0.71	6.23±1.37	0.080	**0.002**	**0.001**
BGL (mg/dL)	111.9±21.46	92.00±10.64	101.98±19.53	115.39±43.98	103.05±25.70	110.70±38.26	0.589	0.247	0.342
Insulin (µIU/mL)	10.16±4.43	6.98±3.18	8.57±4.13	9.01±6.63	6.71±4.15	8.14±5.87	0.143	0.428	0.264
HOMA-IR	2.80±1.36	1.63±0.86	2.21±1.27	2.51±2.03	1.77±1.32	2.23±1.82	0.123	0.835	0.467
HDL (mg/dL)	53.57±10.32	58.35±16.29	55.96±13.68	43.95±9.38	48.97±12.33	45.86±10.76	**0.001**	0.051	**0.001**
LDL (mg/dL)	144.7±30.63	141.40±24.14	143.07±27.28	125.06±32.51	124.51±42.59	124.85±36.24	**0.036**	0.134	**0.010**

TC (mg/dL)	221.9±37.18	220.97±32.24	221.44±34.35	192.89±41.65	200.97±52.26	195.96±45.62	**0.015**	0.157	**0.004**
TG (mg/dL)	117.9±48.3	106.34±44.50	112.12±46.21	131.34±67.03	149.94±115.8	138.41±88.10	0.524	0.247	0.158
VLDL (mg/dL)	23.54±9.66	21.24±8.91	22.39±9.24	26.24±13.48	30.02±23.27	27.68±17.71	0.531	0.224	0.153
CA125 (U/mL)	13.49±11.66	16.73±15.27	15.11±13.51	19.36±25.28	20.98±17.95	19.97±22.58	0.375	0.336	0.273
CA19-9 (U/mL)	8.70±10.15	10.89±15.05	9.79±12.72	14.63±16.43	14.41±17.16	14.54±16.54	0.065	0.496	0.056
CA15-3 (U/mL)	10.49±4.8	12.69±4.75	11.59±4.84	10.49±4.14	17.11±20.41	13.01±13.19	0.997	0.901	0.913
CEA (ng/mL)	1.38±0.93	1.75±1.06	1.57±1.01	1.63±1.32	1.81±1.99	1.70±1.59	0.463	0.322	0.811
Adropin (ng/ml)	0.79±0.8	1.32±0.81	1.05±0.83	0.70±0.72	0.85±0.96	0.76±0.8	0.692	0.095	0.057

EC, endometrial cancer; BMI, body mass index (kg/m^2); DM, diabetes mellitus; HT, hypertension; HbA1c, glycated hemoglobin%; BGL, blood glucose levels; HOMA-IR, homeostasis model assessment-insulin resistance; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglycerides; VLDL, very low-density lipoprotein; CEA, carcinoembryonic antigen.

p^{*} Difference between women with endometrial cancer and controls BMI≥30.

p^{**} Difference between women with endometrial cancer and controls BMI<30.

p^{***} Difference between women with endometrial cancer and controls totally, p value less than 0.05 was considered statistically significant.

HbA1c was higher in patients with EC (p=0.001). In EC group high-density lipoprotein (HDL), low density lipoprotein (LDL), total cholesterol (TC) concentrations were lower compared to the control group. Although serum adropin (ng/mL) levels were lower in the study group than in the control group, the difference was not significant (p=0.057). Differences in serum adropin levels were statistically significantly different if the parity was above 2 (p=0.002), the patient had DM (p<0.001), the patient had DM in terms of family history (p=0.002), the patient had hypertension (HT) (p=0.017) and HOMA-IR was above 2.5 (p=0.035) (Table 2).

Table 2. Comparison of adropin levels according to BMI, Gravidity, Parity, DM, DM family history, HT, HT family history and HOMA-IR

	BMI<30		**BMI≥30**		
	Mean.±SD	**Median**	**Mean.±SD**	**Median**	***p***
EC group	0.81±0.98	0.35	0.70±0.73	0.54	0.857
Control group	1.32±0.81	1.72	0.79±0.80	0.57	**0.044**
Totally	1.07±0.92	0.80	0.74±0.75	0.54	0.070
	Gravidity≤4		**Gravidity>4**		
EC group	0.70±0.79	0.46	0.79±0.87	0.28	0.823
Control group	1.31±0.88	1.48	0.79±0.73	0.60	0.064
Totally	0.96±0.88	0.66	0.79±0.80	0.48	0.408
	Parity≤2		**Parity>2**		
EC group	0.99±0.91	0.69	0.46±0.60	0.22	**0.043**
Control group	1.54±0.81	1.76	0.69±0.67	0.54	**0.004**
Totally	1.20±0.91	1.23	0.58±0.64	0.32	**0.002**
	DM (-)		**DM (+)**		
EC group	1.12±0.92	0.69	0.47±0.63	0.11	**0.001**
Control group	1.42±0.76	1.74	0.64±0.73	0.37	**0.002**
Totally	1.27±0.85	1.26	0.54±0.67	0.25	**<0.001**
	DM-Family (-)		**DM-Family (+)**		
EC group	0.95±0.88	0.59	0.50±0.69	0.10	**0.023**
Control group	1.27±0.89	1.37	0.66±0.55	0.57	**0.040**
Totally	1.10±0.89	0.88	0.56±0.64	0.27	**0.002**
	HT- Family (-)		**HT- Family (+)**		

EC group	0.83±0.89	0.52	0.67±0.77	0.30	0.619
Control group	1.26±0.88	1.37	0.85±0.76	0.60	0.172
Totally	1.03±0.90	0.69	0.75±0.76	0.41	0.162
	HT (-)		**HT (+)**		
EC group	1.00±0.93	0.63	0.55±0.69	0.25	0.091
Control group	1.26±0.88	1.37	0.85±0.76	0.60	0.172
Totally	1.13±0.90	0.97	0.67±0.73	0.37	**0.017**
	HOMA-IR ≤2.5		**HOMA-IR >2.5**		
EC group	0.81±0.85	0.54	0.60±0.76	0.25	0.244
Control group	1.25±0.85	1.33	0.69±0.71	0.44	**0.030**
Totally	0.99±0.87	0.68	0.64±0.73	0.33	**0.035**

EC, endometrial cancer; BMI, body mass index (kg/m²); DM, diabetes mellitus; HT, hypertension; HOMA-IR, homeostasis model assessment-insulin resistance.

In EC group, no significant difference was found in serum adropin levels between type of tumor (p=0.087), myometrial invasion (p=0.562), lymph node involvement (p=0.067), tumor size ≤2 cm (p=0.182), lymphovascular invasion (p=0.194), stage ≤ 1A (p=0.422). There was a significant difference in serum adropin levels between Grade ≤2 vs. Grade>2 (p=0.038) and Type 1 EC vs. Type 2 EC (p=0.02) (Table 3)

Table 3. Distribution of adropin (ng/mL) according to histopathologic characteristics

	Non-endometrioid type		**Endometrioid type**		
	Mean.±SD	**Median**	**Mean.±SD**	**Median**	***p***
EC group (n=11/39)	0.50±0.73	0.24	0.81±0.84	0.54	0.087
	Myometrial invasion ≤%25		**Myometrial invasion >%25**		
EC group (n=21/29)	0.61±0.73	0.30	0.84±0.89	0.54	0.562
	Lymph Node (-)		**Lymph Node (+)**		
EC group (n=43/7)	0.81±0.85	0.54	0.32±0.49	0.08	0.067
	Tumor size ≤2cm		**Tumor size >2cm**		
EC group (n=15/35)	0.92±0.93	0.39	0.67±0.77	0.25	0.182
	LVSI (-)		**LVSI (+)**		
EC group (n=40/10)	0.77±0.81	0.46	0.64±0.91	0.07	0.194
	Grade ≤2		**Grade >2**		
EC group (n=31/19)	0.93±0.87	0.63	0.44±0.65	0.11	**0.038**
	Stage ≤1A		**Stage >1A**		
EC group (n=30/20)	0.76±0.78	0.47	0.72±0.91	0.21	0.422
	Type 1		**Type 2**		
EC group (n=28/22)	0.99±0.89	0.75	0.43±0.61	0.15	**0.020**

EC, endometrial cancer; LVSI, lymphovasculer space invasion.

There was a statistically significant correlation between adropin, HDL and DM in the EC group (p=0.007, p=0.009, respectively). Type 2 EC was significantly correlated with adropin (p=0.045). In the control group, parity, insulin and HOMA-IR were statistically significantly correlated (p=0.004, p=0.017 and p=0.023, respectively). Adropin was inversely correlated with age, BMI, parity, HBA1c, insulin, HOMA-IR, HDL, HT and DM (p=0.042, p=0.006, p=0.007, p=0.010, p=0.028, p=0.012, p=0.009, p=0.042, and p = 0.001, respectively) (Table 4).

Table 4. The correlation between adropin (ng/mL) with the EC group, control group and all patients

	EC group		Control group		Total	
	Adropin		Adropin		Adropin	
	r	*p*	*r*	*p*	*r*	*p*
Age (years)	-0.145	0.313	-0.105	0.518	-0.215	**0.042**
BMI (kg/m^2)	-0.224	0.118	-0.278	0.082	-0.289	**0.006**
Gravidity (n)	-0.016	0.911	-0.262	0.103	-0.073	0.491
Parity (n)	-0.246	0.085	-0.450	**0.004**	-0.284	**0.007**
HbA1c (mmol/L%)	-0.254	0.075	-0.145	0.371	-0.271	**0.010**
BGL (mg/dL)	-0.262	0.066	-0.048	0.771	-0.199	0.060
Insulin (µIU/mL)	-0.185	0.197	-0.376	**0,017**	-0.231	**0.028**
HOMA-IR	-0.238	0.095	-0.359	**0.023**	-0.263	**0.012**
HDL (mg/dL)	0.378	**0.007**	-0.012	0.941	0.275	**0.009**
LDL (mg/dL)	0.149	0.301	-0.069	0.671	0.153	0.151
TC (mg/dL)	0.141	0.328	-0.109	0.502	0.146	0.171
TG (mg/dL)	-0.180	0.211	-0.222	0.168	-0.204	0.054
VLDL (mg/dL)	-0.177	0.219	-0.224	0.165	-0.205	0.053
CA125 (U/mL)	-0.066	0.649	0.085	0.603	-0.023	0.832
CA19-9 (U/mL)	-0.112	0.440	-0.163	0.313	-0.139	0.190
CA15-3 (U/mL)	0.001	0.996	0.039	0.812	0.006	0.954
CEA (ng/mL)	0.096	0.505	0.187	0.247	0.143	0.178
DM	-0,368	**0.009**	-0.488	**0.001**	-0.430	**0.001**
HT	-0.050	0.730	-0.219	0.175	-0.215	**0.042**
Endometrioid type	0.244	0.087				
Myometrial invasion (%)	0.092	0.525				
Lymph node involvoment	-0.246	0.085				
LVSI	-0.083	0.566				
Grade	-0.189	0.188				
Type 2 EC	-0.285	**0.045**				

EC, endometrial cancer; BMI, body mass index; HbA1c, glycated hemoglobin%; BGL, blood glucose levels; HOMA-IR, homeostasis model assessment-insulin resistance; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglycerides; VLDL, very low-density lipoprotein; CEA, carcinoembryonic antigen; DM, diabetes mellitus; HT, hipertansion; LVSI, lymphovasculer space invasion; correlation coefficient, statistical significance p<0.05.

Table 5. Binary logistic regression analysis of adropin for prediction of Type 2 EC

	OR	95 % CI		S.E.	*p*
		Min	Max		
Model 1 †	0.389	0.164	0.920	0.439	**0.032**
Model 2 ‡	0.350	0.156	0.783	0.411	**0.011**

† Type 1 vs. type 2 in EC group
‡ Type 2 vs. all participants

Minimum (0.01), maximum (2.63, 2.35, 2.68), 25-75% percentile, median (0.75, 0.27, 0.85) and mean (0.99, 0.47, 1.05) serum adropin levels in Type 1 EC, Type 2 EC and control groups are demonstrated in ***Figure 1***.

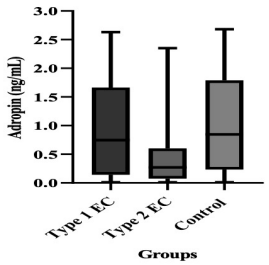

Figure 1. Minimum (0.01), maximum (2.63, 2.35, 2.68), 25-75% percentile, median (0.75, 0.27, 0.85) and mean (0.99, 0.47, 1.05) serum adropin levels in Type 1 EC, Type 2 EC and control groups. EC, endometrial cancer

Binary logistic regression analysis of adropin for prediction type 2 EC has shown in ***Table*** 5. Serum adropin levels in all participants (OR, 0.350; B, -1.05; SE, 0.411; CI, 0.156-0.783; p=0.011) and in Type 1 and Type 2 patients (OR, 0.389; B, -0.94; SE, 0.439, CI, 0.164-0.920; p=0.032) was significant predictor of EC type 2. ROC curve analysis was conducted to calculate the optimal cut-off value of adropin (***Figure 2***). Optimal cut off value was calculated as 0.4 ng / mL adropin (63.6% sensitivity and 64.7% specifity). Area under the curve (AUC) for adropin was 0.697 (95% CI 0.578-0.815). Positive Likelihood ratio (LR+) was 1.8 and the negative Likelihood ratio (LR-) was 0.56.

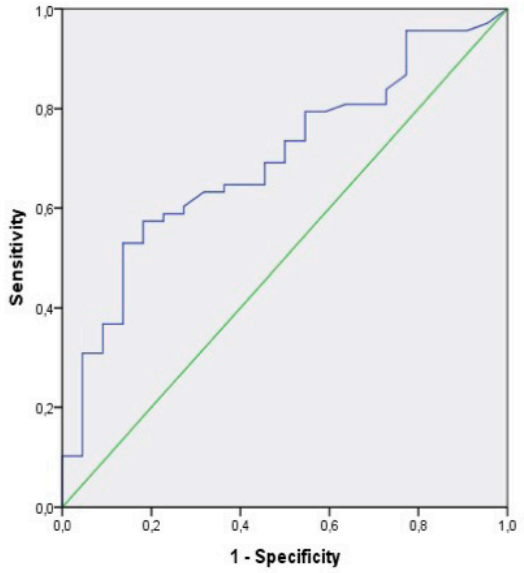

Figure 2. Receiver operating characteristic curves of the prediction Type 2 EC performance of adropin in all participants. Area under the curve (AUC) for adropin is 0,697 (95% CI 0,578-0,815) p=0.006 Sensitivity=63.6%, specifity =64.7%, Positive Likehood ratio=1.8 EC, endometrial cancer

DISCUSSION

The aim of this study was to investigate the prognostic value of adropin by determining the serum adropin level in EC patients. The prevalence of obesity and the associated cancer hazard has been ascending in the past several decades globally. In a study conducted in 2016, it was thought that approximately 2 billion adults and 340 million children worldwide have obesity problems (15). Given this increasing prevalence worldwide, the global obesity-related cancer burden is likely to increase in the future (16). Regarding gynecological cancers, an increase in BMI is associated with endometrial cancer rather than with ovarian cancer (17).

The presence of Diabetes Mellitus (DM) is associated with a worse prognosis in EC due to common risk factors such as obesity and age (18). Surveillance, Epidemiology and End Results

data show variable increases in endometrial cancer incidence over time (14). The need for early diagnosis techniques with safe, fast and easy methods for clinical applicability is increasing.

Serum adropin levels are connected with coronary artery diseases, obesity, and obesity-related cancers (7,8). Meta-analysis results showed that serum adropin levels were significantly lower in patients with coronary artery disease, and then the possible relationship between serum adropin levels and the pathogenesis of coronary artery diseases was started to be investigated (7). The strongest information available today regarding the pathophysiology of coronary artery diseases is the coexistence of vascular inflammation, endothelial dysfunction and lipid metabolism disorder. Low adropin levels weaken endothelial protection and may cause atherosclerosis (19). Atherosclerosis is accelerated in both type 1 and type 2 DM. In addition, DM leads to decrease HDL, increase triglyceride (TG), and oxidative stress-induced endothelial dysfunction. The level of adropin increased with DM, which was accompanied by a reduction in fat accumulation, plasma TG, and inflammation (8).

Adropin has been defined as a possible regulatory hormone involved in the preservation of insulin sensitivity (20). In this study, Zang et al. proposed an optimal adropin cut-off value with a high sensitivity value (81.9%) to distinguish patients with type 2 diabetes from those without. Especially in obese patients, the adropin value was quite low. According to the results, adropin level was correlated negatively with age, parity, BMI, TG, DM, HT, insulin, HOMA-IR, and HbA1c, while positively with HDL (20). In another study, adropin value was significantly lower in the patients with cardiac syndrome (1.7 ± 0.8 ng/mL vs 3.4 ± 1.8 ng/mL; P <0.001), probably due to the difference in BMI values (28.1 ± 2.4 kg/m^2 vs 26.0 ± 3.7 kg/m^2 ; P < 0.001) (21).

Although our results showed lower adropin levels in EC group than control group, the difference was not significant. Contrary to our study, decreased plasma adropin concentrations were statistically significant in women diagnosed with EC (12). The difference in results may be related to the number of the subject.

A major limitation of this study is the relatively small sample size. Moreover, serum adropin levels were not assessed both at fasting and feeding conditions or after the surgery. In our study, no statistically significant difference in serum adropin level was found between EC and the control group. However, the difference was statistically significant between Type 1 and Type 2 EC. Adropin was statistically significant in type 2 EC in Roc analysis and logistic regression analysis. The reason for this result may be either type 2 EC cases are seen in older populations or randomly increased very-low-density lipoprotein (VLDL) and TG levels in our subjects. In our opinion, the statistical difference (p=0.01) is promising and this difference should be supported by higher sample size studies.

CONCLUSİON

In recent years, innovations such as molecular classification recommended for use in the management of endometrial cancer have emerged (22). Various difficulties such as the high cost to fully transition to clinical use have not been overcome yet, so it does not seem possible to apply it preoperatively to every patient yet. We think that there is still a need for various hormonal methods that are more cost-effective. Further studies may highlight

the possible role of adropin in EC by extending the sample size with different stages of the disease and adding analyses such as molecular or genetic on endometrial tissue.

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Conflicts of interest

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Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Ethics Committee of University of Health Sciences Türkiye, Sisli Hamidiye Etfal Education and Research Hospital (Date: 03/10/2017 No: 1704/866).

Authorship Contributions

Conception and design: CMA, AEY; Acquisition of data: UKO, CMA, EK; Analysis and interpretation of data: CMA, AEY; Drafting of the manuscript: UKO, CMA, EK; Critical revision of the manuscript: CMA, AEY, UKO, EK; Statistical analysis: CMA, AEY; Administrative technical or material support: UKO, EK, CMA; Supervision: CMA, AEY.

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