

Preoperative serum leptin levels in patients with endometrial cancer and its correlation with prognostic variables

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Summary

Purpose of investigation: Since leptin is believed to be a key player in carcinogenesis, a study has been designed to investigate the relationship between leptin levels and endometrial cancer. **Methods:** A study including 30 patients with endometrial cancer and 30 healthy controls was carried out between November 2008 and July 2009 in Hacettepe University Hospital. All patients with endometrial cancer underwent a complete surgical staging procedure including lymphadenectomy. Preoperative leptin levels of endometrial cancer patients and healthy controls were compared. The relationships between leptin levels and stage, grade, histological type and lymph node status of endometrial cancer cases were evaluated. **Results:** The mean serum leptin levels were 16.9 ng/ml among endometrial cancer cases and 19.0 ng/ml among controls ($p = 0.32$). Of endometrial cancer cases, the mean leptin level was found to be 15.8 ng/ml for Stage I and 18.5 ng/ml for Stage II-IV disease ($p = 0.34$). The figure was 17.7 ng/ml for endometrioid and 13.2 ng/ml for non-endometrioid type of tumor ($p = 0.24$). The mean leptin levels of 16.3 ng/ml for grade 1 and 19.9 ng/ml for grade 2-3 tumors were observed ($p = 0.07$). The cases with positive and negative lymph nodes had leptin levels of 20.2 ng/ml and 16.1 ng/ml, respectively ($p = 0.30$). **Conclusions:** Serum leptin levels in endometrial cancer patients were similar to healthy controls. Leptin did not show any significant correlation with stage, grade, histological type and node metastases in endometrial cancer.

Key words: Leptin; Endometrial cancer; Obesity.

Introduction

Obesity has long been known to be associated with an increased risk of endometrial cancer [1]. Various bioactive substances produced by adipose tissue such as estrogens, insulin and insulin-like growth factors are believed to be involved in the association of obesity and endometrial tumorigenesis [2]. Leptin, which is a prominent type of adipokine produced by adipose tissue, is positively correlated with obesity, food intake and energy balance. Leptin is also responsible for hyperinsulinemia by reducing tissue sensitivity to insulin [3]. There is increasing evidence that leptin has an impact on development of several obesity-related cancers [4, 5].

Furthermore, leptin appears to be involved in angiogenesis and regulation of cancer progression by stimulating tumor cell migration [6, 7]. Leptin could also promote endometrial thickness and promote proliferation of endometrial cells [8, 9].

Although leptin is believed to be a key player in carcinogenesis, its role in endometrial cancer is mostly unclear. Thus, a study has been designed to investigate the relationship between leptin levels and endometrial cancer.

Materials and Methods

A study including 30 patients with endometrial cancer and 30 healthy controls was carried out between November 2008 and July 2009 in Hacettepe University Hospital, Ankara, Turkey.

The research protocol was approved by the institutional ethics committee and written informed consent for the utilization of serum samples and personal information was obtained from all subjects.

Consecutive patients with newly diagnosed and histologically confirmed endometrial cancer were enrolled in this study. All patients with endometrial cancer underwent a complete surgical staging procedure including abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy and pelvic and paraaortic lymphadenectomy. Control subjects were simultaneously recruited from the menopause clinic of the same hospital during the study period.

Preoperative leptin levels of endometrial cancer patients and healthy controls were compared. The relationships between leptin levels and stage, grade, histological type and lymph node status of endometrial cancer cases were also evaluated.

Leptin concentrations in serum were measured with enzyme-linked immunosorbent assay. Statistical analysis was carried out using SPSS 14. The categorical variables were analyzed using Pearson's chi-square test. Student's t-test was used to assess the significance of differences in continuous variables between the two groups. P values of less than 0.05 were considered to be statistically significant.

Results

The demographic characteristics of the endometrial cancer cases and controls are summarized in Table 1. There were no statistically significant differences between the mean values of the endometrial cancer cases and controls in terms of the gravida, para, height, weight and body mass index (BMI). However, the endometrial cancer group had a statistically higher mean age than the control group ($p = 0.01$).

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Table 1. — Demographic characteristics of cases.

Characteristic	Cases	Controls	<i>p</i>
Age (year)	56.8 ± 10.3	50.2 ± 8.2	0.012
Gravida	3.6 ± 1.8	3.9 ± 1.3	0.636
Para	2.9 ± 1.5	3.1 ± 1.1	0.325
Height (cm)	155 ± 0.08	1.54 ± 0.04	0.542
Weight (kg)	80.2 ± 20.1	80.5 ± 20.4	0.933
BMI (kg/m ²)	33.7 ± 6.03	32.9 ± 5.8	0.625

Table 2. — Serum leptin levels.

	Cases	Controls
Mean	16.9 ± 7.5 ng/ml	19.0 ± 8.24 ng/ml
Median	15.5 ng/ml	18.4 ng/ml
Range	4.6-32.0 ng/ml	6.5-35.5 ng/ml

Table 3. — Pathological characteristics of endometrial cancer cases.

Stage	n	%
I	18	60.0
II	6	20.0
III-IV	6	20.0
Grade		
1	17	56.7
2	9	30.0
3	4	13.3
Histology		
Endometrioid	25	83.3
Nonendometrioid	5	16.7
Lymph node status		
Negative	20	66.7
Positive	10	33.3

Table 4. — Correlation of leptin levels with prognostic parameters in endometrial cancer cases.

Endometrial cancer	Mean leptin level (ng/ml)	<i>p</i>
Stage		
I	15.8 ± 7.4	
II-IV	18.5 ± 7.6	0.349
Cell type		
Endometrioid	17.7 ± 7.1	
Non-endometrioid	13.2 ± 9.0	0.245
Grade		
1	16.3 ± 7.6	
2-3	19.9 ± 5.1	0.075
Lymph node status		
Negative	16.1 ± 7.2	
Positive	20.2 ± 8.3	0.303

The mean serum leptin levels were 16.9 ng/ml among endometrial cancer cases and 19.0 ng/ml among controls (Table 2). There was no statistically significant difference between mean values of endometrial cancer cases and controls.

Of the 30 patients with endometrial cancer, 18 (60%) had Stage I disease (Table 3). Pathological examination revealed grade 1 tumor in 17 cases. While 25 cases had endometrioid type of tumor, nonendometrioid histologic subtype cases included serous papillary in three, clear

cell in one and undifferentiated tumor in one case. The mean number of nodes removed during lymphadenectomy was found to be 33.4 ± 8.7. Of the ten cases with lymph node metastases, five had only pelvic lymph node metastases, three had only paraaortic lymph node metastases and in two patients both pelvic and paraaortic lymph node metastases were observed.

Of the endometrial cancer cases, the mean leptin level was found to be 15.8 ng/ml for Stage I and 18.5 ng/ml for Stage II-IV disease (Table 4). The figure was 17.7 ng/ml for endometrioid and 13.2 ng/ml for nonendometrioid type of tumor. Mean leptin levels of 16.3 ng/ml for grade 1 and 19.9 ng/ml for grade 2-3 tumors were observed. The cases with positive and negative lymph nodes had leptin levels of 20.2 ng/ml and 16.1 ng/ml, respectively. None of the parameters studied had a statistically significant correlation with serum leptin level.

Discussion

Endometrial cancer is a hormone-dependent neoplasm and obesity is a well known risk factor for it. Peripheral aromatization of androstenedione to estrone takes place largely in the adipose tissue and has been alleged to be responsible for development of endometrial cancer. However, the epidemiological association between obesity and endometrial cancer risk cannot be fully explained by obesity-related changes in serum levels of sex hormones. Leptin was found to be involved in neoplastic processes of hormone-dependent tumors such as breast cancer [4, 5]. Possible mechanisms resulting in the development of neoplasms are positive correlation with obesity, stimulation of angiogenesis, inducing production of cytokines, hyperinsulinemia and activation of aromatase [4, 6, 8].

Several studies investigated the correlation of leptin with endometrial cancer. Petridou *et al.* noted significantly higher leptin levels among 84 endometrial cancer patients when compared to controls [10]. Yuan *et al.* studied the expression leptin receptors in endometrial cancer cells and found higher serum concentrations of leptin in patients with endometrial cancer but the difference was not significant after normalization of body mass index [11]. Cymbaluk *et al.* found that serum concentrations of leptin in endometrial cancer and hyperplasia were higher than controls [12]. The difference was significant in all BMI groups. Ashizawa *et al.* suggested that the leptin-adiponectin ratio was independently associated with an increased risk for endometrial cancer development [13].

We have found similar serum leptin concentrations in endometrial cancer patients and controls. Thus, the present study results do not support the previous studies in terms of the role of increased leptin in endometrial carcinogenesis. It possibly results from the similar BMI values of cancer cases and controls in the current study. Higher leptin levels show a stronger correlation with obesity than endometrial cancer. Furthermore, leptin did not show any significant correlation with stage, grade, histological type and node metastases in endometrial cancer.

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