# MALİGN TÜMÖRLÜ HASTALARDA KİLO KAYBI İLE LEPTİN DÜZEYLERİ ARASINDAKİ İLİŞKİ

# THE RELATIONSHIP BETWEEN LEPTIN LEVELS AND WEIGHT LOSS IN PATIENTS WITH MALIGN TUMORS

**Fuat ERDEM, İlyas ÇAPOĞLU, Hüseyin ÇARMIK, Necdet ÜNÜVAR, Leyla YILDIZ**

Atatürk University Medical Faculty, Department of General Internal Medicine **(FE)**, Atatürk University Medical Faculty, Department of Endocrinology and Metabolism **(İÇ, HÇ, NU)**, Atatürk University Medical Faculty, Department of Biochemistry **(LY)**

**Özet**

Leptin, vücut ağırlığı ve enerji harcama ile alakalı yağ dokusundan üretilen bir obez (ob) gen ürünüdür. Bu çalışma, solid malign tümörlü hastalarda leptin seviyesi ile vücut kitle indeksi arasındaki ilişkiyi ve bu hastalarda kilo kaybından sonra leptin seviyesinde herhangi bir farklılığın olup olmadığını ortaya koymak için yapıldı. Çalışmaya histopatolojik olarak solid tümör tanısı konulan 30 hasta alınmasına rağmen 18 tanesi çalışmayı tamamladı. Hem başlangıçta hem de kilo kaybından sonra BMI ile leptin düzeyleri arasında anlamlı korelasyon tespit edildi ($r= 0.796$, $p<0.01$ and $r=0.808$, $p<0.01$, respectively). Zayıflama ile birlikte leptin seviyesindeki azalmanın solid malign tümörlü hastalardaki yağ dokusunun azalmasına bağlı olabileceği sonucuna varıldı.

**Anahtar kelimeler:** *Leptin, Malign tümör, Kilo kaybı*

**Summary**

Leptin, a product of the obese (ob) gene, produced in adipose tissue, is related to the control of body weight and energy expenditure. This study was carried out to demonstrate the relationship between body mass index and leptin levels in patients with solid malign tumor and to find out whether there was any difference in leptin levels after the weight loss in those patients**.** The study included 30 patients with confirmed solid malign tumor by biopsy. But, 18 patients completed the study. We found out a significant correlation between BMI values and leptin levels at the beginning ($r= 0.796$, $p<0.01$). Similarly, there was a significant correlation between the values of BMI and leptin levels after the weight loss ($r=0.808$, $p<0.01$). We concluded that decrease in the leptin levels occured after lost of weight is more likely to develop due to a decrease in fat mass in patients with solid malign tumor.

**Key words**: *Leptin, Malign tumor, Weight loss*

**Table 1.** *Clinical and Laboratory data for Patients Admitted to the Study*

| case no | sex/age (year) | diagnosis | height(m) | weight (kg) | | BMI (kg/m$^2$) | | leptin (ng/ml) | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | initial | 6 th month | initial | 6 th month | initial | 6 th month |
| 1. | F/44 | Breast Ca | 1.55 | 33 | 30 | 13.73 | 12.48 | 0.72 | 0.27 |
| 2. | M/47 | Stomach Ca | 1.70 | 87 | 84 | 30.10 | 29.06 | 6.58 | 3.20 |
| 3. | M/40 | Stomach Ca | 1.63 | 42 | 35 | 15.81 | 13.17 | 0.55 | 0.15 |
| 4. | F/58 | Breast Ca | 1.50 | 96 | 88 | 42.66 | 39.11 | 8.90 | 6.00 |
| 5. | M/69 | Stomach Ca | 1.69 | 85 | 74 | 29.76 | 25.91 | 9.58 | 2.71 |
| 6. | M/65 | Stomach Ca | 1.68 | 65.5 | 56 | 23.21 | 19.84 | 4.54 | 0.65 |
| 7. | M/87 | Bladder Ca | 1.66 | 65 | 59 | 23.59 | 21.41 | 7.26 | 2.90 |
| 8. | M/50 | Esophagus Ca | 1.75 | 76 | 70 | 24.82 | 22.86 | 1.97 | 0.63 |
| 9. | M/66 | Stomach Ca | 1.72 | 93 | 84 | 31.43 | 28.40 | 2.75 | 2.50 |
| 10. | M/59 | NHL* | 1.70 | 62 | 61 | 21.45 | 21.10 | 4.32 | 1.03 |
| 11. | M/68 | Stomach Ca | 1.69 | 58 | 56 | 20.31 | 19.61 | 0.56 | 0.23 |
| 12. | M/67 | Prostate Ca | 1.66 | 61 | 58 | 22.14 | 21.05 | 6.48 | 2.27 |
| 13. | M/52 | Colon Ca | 1.69 | 83 | 77 | 29.23 | 27.96 | 8.36 | 5.25 |
| 14. | F/49 | Rectum Ca | 1.60 | 71.5 | 69.5 | 27.93 | 27.15 | 14.34 | 8.00 |
| 15. | M/60 | Bladder Ca | 1.66 | 63 | 58 | 22.86 | 21.05 | 2.61 | 2.00 |
| 16. | F/53 | Colon Ca | 1.60 | 97.5 | 94 | 38.08 | 36.72 | 11.82 | 6.45 |
| 17. | M/62 | Stomach Ca | 1.65 | 65 | 61.5 | 23.87 | 22.59 | 1.10 | 0.48 |
| 18. | M/58 | Stomach Ca | 1.70 | 68 | 63.5 | 23.53 | 21.97 | 0.46 | 0.32 |

**Non-Hodgkin's lymphoma*

## Introductıon

Leptin, a product of ob gene specific to adipose tissue, is a hormone related to the regulation of metabolism and body content and has been identified recently (1-6). Besides metabolic effect of leptin (1,2,4) which is reported to be a stimulus informing the brain on the adipose tissue mass via blood, is also supposed to have a significant role on neuroendocrine system (1), reproductive system (2) and hematopoetic system (7). Leptin, found in brown adipose tissue in small quantity, is produced mainly by white adipose tissue (7).

It has been found out that the levels of serum leptin are closely related to body adipose tissue mass (8-15) and body mass index (BMI) (8,16,17) in adults, children and the newborn. Levels of serum leptin in obese individuals are significantly higher compared to the normal and thin ones (8,11,12). In addition to this, females having the same amount of adipose tissue mass have high serum leptin levels than males (12,17). Although the real mechanism is not known, it is likely that sex hormones play a role (4,18). It should be noted here that serum leptin level decreases with the loss of weight (13,19) and increases with the gain of weight (3,4).

Changes in energy intake as staying hungry and overeating also affect serum leptin levels, which are also related to leptin adipose tissue mass (11,12). However no significant change occurs in body fat during long-stay hunger, a dramatic decrease is observed in serum leptin levels (4). On the contrary, it has been found out that one day overeating increases serum leptin levels without gaining weight (3,4). The fact that leptin levels do not cause a change in food consumption indicates that leptin is not a sign of satisfaction due to eating (4).

Leptin indicates most of its metabolic effects by specific receptors that have various forms and is placed on both peripheral tissue and central nervous system (CNS) (7). Defects both within leptin itself and/or its receptor in hypothalamus result in obesity in most rodent models (11). However, no such defects have been detected in humans to date (4,8,16).

This study was carried out to indicate the relationship between BMI and leptin in patients with solid malign tumor and to find out if there was any difference in leptin levels after the loss of weight in those patients.

## Materıals and Methods

The study included 30 patients with confirmed solid malign tumor by biopsy, who received treatment between the years 1997-1999. The cases were selected randomly. After the follow-up period of six months, 12 of the patients were excluded from the study since 5 of them did not turn up for their controls,

**Table 2.** *The Values of Body Weight, Body Mass Index and Serum Leptin of the Cases (mean± SD and ranges)*

| | initial stage | six months after weight loss | statistics |
|---|---|---|---|
| body weigth (kg) | 70.7 ± 17.6 | 65.5 ± 16.8 | (t = 7.69; p < 0.001) |
| (range) | (33.0-97.5) | (30-94) | |
| BMI (kg/m$^2$) | 25.8 ± 7.1 | 23.9 ± 6.8 | (t = 7.75; p < 0.001) |
| (range) | (13.7-42.6) | (12.4-39.1) | |
| leptin (ng/ml) | 5.8 ± 5.5 | 2.6 ± 2.6 | (t = 4.20; p < 0.005) |
| (range) | (0.46-20.32) | (0.15-8.00) | |

5 did not lose weight and the remaining 2 patients died. The study was completed with 18 patients. Of the cases, 4 were females and 14 were males. Diagnoses of the cases were 8 stomach carcinoma, 3 colon carcinoma, 2 breast carcinoma, 2 bladder carcinoma, 1 non-Hodgkin's lymphoma (NHL), 1 prostate and 1 esophagus carcinoma. None of the patients had complaint of dysphagia, and took hormone replacement treatment. Also, the cases had no diabetes mellitus or any endocrine disorder.

The cases were followed-up prospectively for six months. Their body weights were measured once a month and serum samples were taken for leptin level assay. Venous blood samples (approximately 8-10 ml) were taken between 08-10 a.m after a hunger of 10-12 hours. Blood samples were centrifugated at 4000 rpm during 5 minutes. Serum samples were separated into two tubes for leptin determination and were kept at -80$^0$C in deepfreezer until their analysis.

BMI of the cases both at the beginning of the study and after the follow-up period of six month was calculated with weight (kg) / height (m$^2$) formula and leptin levels in serum samples taken in these two periods were assessed with radioimmunoassay method and by using commercial leptin kit (Sensitive Human Leptin RIA: Linco Research Inc).

Statistical analyses were performed using SPSS 7.5 computer program. Paired Student's t test and linear regression analysis were used where appropriate. P <0.05 was accepted significant.

## Results

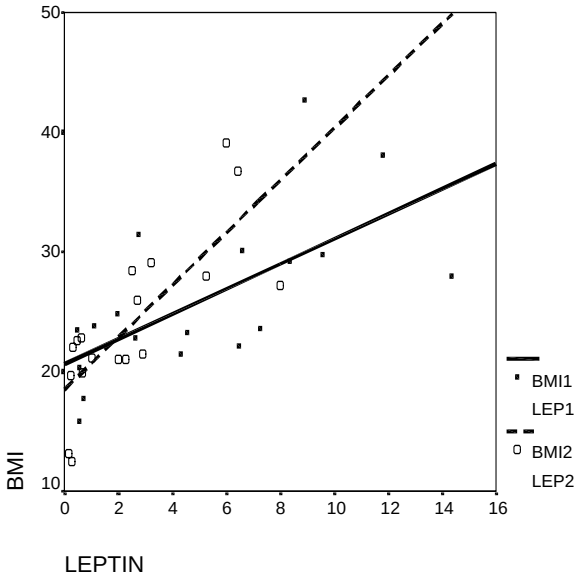
Age of the cases varied from 40 to 87 years (mean: 58.2±11.4). The heights of the cases were between 150-175 cm (mean 165.7±6.2). Their body weights were between 33.0-97.5 kg the beginning of the study (average: 70.66±17.57). Body weights were measured as 30-94 kg after the loss of weight (average: 65.47±16.82). Loss in the body weight was between 1-11 kg (average 5.19±2.86). This difference in the body weight was accepted statistically meaningful (t:7.691;p<0.001). The clinical and demographic features of the cases are shown in Table 1.

Body mass index of the cases was found as 25.87 kg/m$^2$ at the beginning and 23.96 kg/m$^2$ after weight loss. Decrease in BMI was between 0.30-3.80 kg/m$^2$ (average: 1.90±1.03). That decrease was found statistically meaningful (t:7.752; p<0.001).

Serum leptin levels of the cases were between 0.46-20.32 ng/ml at the beginning and 0.15-8.00 ng/ml after weight loss. Decrease in serum leptin levels varied between 0.14-12.54 ng/ml (average 3.19 ±3.22) (t:4.204; p<0.005). As shown in Table 2 loss of weight, decrease in BMI and decrease in serum leptin level of the cases were statistically significant.

We also found out a significant correlation between BMI values and leptin levels at the beginning (r=0.796, p<0.01). Similarly, there was a significant correlation between the values of BMI and leptin levels after the weight loss (r=0.808, p<0.01) (Fig 1).

**Figure 1.** *Correlation Between BMI and Leptin Levels at the Initial Stage and After Weight Loss*



## Discussion

Serum levels of leptin, a product of ob gene, secreted by adipose tissue, and regulating energy balance, food intake and body weight, have been found high in obese individuals (8,12,19). It was also found that serum leptin levels were low in cases with severe malnutrition (13), and recombinant leptin administration decreased food intake and weight in obese and nonobese mice (4). Studies on animals have given clues that leptin could have an important role in the regulation of energy balance. Although it is of great interest that leptin be related to unwanted and progressive loss of weight in subjects with cancer, studies on this subject are limited (5).

Leptin concentrations in circulation have been found closely related to both body fat content and BMI, so it has been emphasized that leptin is a sign of adipose tissue (10). We also evaluated BMI as a sign of adiposity.

We found out in this study that serum leptin levels were significantly correlated with BMI in patients with solid malign tumor. Besides the decrease in serum leptin levels after weight loss in those patients, a significant correlation between BMI and leptin still continued. Weight loss in patients with cancer is still a major clinical problem, which decreases the life standards of the cases. There is a limited information regarding the role of leptin in cachexia caused by cancer in humans (5).

Simons et al (22) reported that leptin concentrations in circulation were too low or could not be measured in patients with lung cancer and having weight loss. Grunfeld et al (11) found out that there was not an abnormal increase in serum leptin levels in a study carried out on AIDS patients with anorexia, weight loss and secondary infection. Lagiou et al (2) detected that leptin levels in very old patients with prostate cancer were not different from those of healthy ones. Wallace et al (5) reported that leptin concentrations did not increase in patients with gastrointestinal cancer with loss more than 5 per cent of their weight in the last 6 months and so concluded that cachexia in cancer did not result from disregulation in leptin production.

In our study we detected that serum leptin levels showed a significant decrease after loss of weight in patients with solid malignant tumor. Wallace et al (5) also found out that serum leptin levels in patients with gastrointestinal cancer that had lost more than 5 per cent of their weight were lower than those of healthy people. We did not compare leptin levels to healthy control group in our study, but observed the patients with cancer progressively and found out that such patients showed a decrease in serum leptin levels together with weight loss.

It is known that a decrease in leptin concentration stimulates neuropeptid Y from hypothalamus and causes an increase of appetite and decrease in energy use. Such changes in normal people will result in an increase of fat deposits later and this will ultimately start an increase in leptin production. But studies carried out in patients with cancer indicated no such increase in appetite and decrease in energy consumption. This brings to mind that there could be a block in hypothalamic response to low leptin concentration in cancer patients (5). It has also been indicated that plasma leptin levels decrease after a reduction in adipose tissue mass (19). Considine et al (21) have detected a decrease of 53 % in serum leptin level following a 10 % weight loss.

Factors responsible for the difference in serum leptin levels in individuals having the same body compositions are not well substantiated. Oslund et al (12) suggested that although a small per cent of body fat was lost, plasma leptin levels decreased without balance. Weigle et al (22) have suggested that leptin levels reflected total adipose tissue rather than diet energy content. In our study, while there was a certain amount of decrease in body weight and BMI (mean: 7.49 ± 4.13 % and 7.55 ± 4.19 %, respectively), considerable amount of decrease in serum leptin level was observed (mean: 54.44 ± 19.76 %).

Consequently, serum leptin levels in patients with solid malignant tumors indicated a significant correlation with BMI. Decrease in serum leptin seen with weight loss in patients with solid malignant tumor is more likely to develop due to the decrease in fat mass. But the fact that the decrease in leptin concentration was not found to be related to the decrease in body weight and BMI shows that the effects of some unknown factors, besides fat cell production, in leptin secretion could play a role.

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**Address correspondence**:
Dr.Fuat ERDEM

Atatürk Üniversitesi Tıp Fakültesi
İç Hastalıkları Anabilim Dalı
25240 Erzurum, Turkey
Tel: +90 442 236 12 12-1539
e-posta: fuaterdem@yahoo.com