REVIEW

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The Relationship of Leptin, Obesity, and Exercise: A Systematic Review

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Abstract

Obesity and obesity-related diseases have become a rapidly increasing important health problem. Hormones such as leptin, ghrelin, obestatin, and nesfatin-1 play an important role in fat tissue accumulation and the appetite mechanism. Leptin belongs to a class of hormones known as adipocytokines, which play a role in regulating energy metabolism. This study aimed to investigate the relationships between leptin, obesity, and exercise. This study analyses the relationship of leptin, obesity, and exercise using the Preferred Reporting Items for Systematic Reviews. We conducted this systematic review following the PRISMA 2020 statement. The systematic review used a search to identify studies published in PubMed, Wiley Online Library, EBSCO, Science Direct, and Web of Science databases. In this study, the relationships between leptin, obesity and exercise were investigated. A total of 1022 records were initially scoped in the literature search, 784 of which were duplicates. After screening for eligibility and inclusion criteria, 57 articles were ultimately included in the study. Hormones, which are thought to be the source of obesity, are the focus of current studies. Studies have shown that maintaining certain circulating leptin concentrations is essential. Studies have shown a positive relationship between leptin levels and serum fasting insulin and insulin resistance in obese individuals. It also shows that insulin resistance is associated with leptin and adiponectin. There are studies showing that exercise decreases leptin concentration. The discrepancies in the results of studies examining the effect of exercise on the leptin response may arise from many methodological differences, such as the intensity, duration, frequency, and scope of exercise, the nutritional status of the participants, and the time and frequency of sampling. This review shows that chronic exercise interventions consistently reduce leptin concentrations, mostly mediated by fat mass loss. Acute effects are inconsistent and often delayed. Prolonged strenuous exercise leads to marked decreases. Future research should standardize leptin measurement, incorporate biomarkers such as soluble leptin receptor and adiponectin, and explore leptin-targeted therapies in obesity treatment.

Keywords: Exercise, Leptin, Obesity

Introduction

Obesity and obesity-related diseases have become a rapidly increasing important health problem (1). Obesity, defined as abnormal or excessive fat accumulation in the body to the extent of impairing health, has been revealed by some studies to be caused by many exogenous factors as well as various endogenous factors. In recent studies, it has been reported that hormones such as leptin, ghrelin, obestatin and nesfatin1 play an important role in fat tissue accumulation and appetite mechanism.

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Although obesity occurs as a result of the imbalance between energy intake and use, it has been known for years that obesity is genetic. Regardless of genetics, increased energy intake and decreased movement increase the development of obesity. Etiological factors in the formation of obesity can be classified as energy imbalance, genetic factors and environmental factors. Regulation of energy balance and genetic factors are endogenous factors effective in the formation of obesity. Environmental factors can be shown as exogenous factors in the formation of obesity (2, 3).

The hormone leptin, produced mainly from adipose tissue, affects fatty tissue through negative feedback. There is a positive correlation between free circulating serum leptin concentration and body fat tissues. Although the main determinant of leptin is body fat tissue, insulin, glucocorticoids and prolactin increase leptin synthesis, thyroid hormones, growth hormone, somatostatin, free fatty acids, long-term exposure to cold, catecholamines and exercise have a restrictive effect on leptin. Just as genetic mutation in the formation of leptin or leptin receptors leads to obesity, leptin resistance also causes obesity. Since women have more fat mass than men, serum leptin levels are also higher than men (4).

Leptin belongs to a class of hormones known as adipocytokines, which play a role in regulating energy metabolism (5). Extensive research has revealed that maintaining specific circulating leptin concentrations is essential to prevent imbalance in food intake (6). Leptin deficiency or leptin resistance states result in obesity, diabetes and infertility in humans (7, 8). Leptin exerts its metabolic effects through its unique receptors located in the central nervous system and peripheral tissues (9). Although leptin deficiency and leptin receptor deficiency seem similar, studies have shown that leptin receptor deficiency is more congenital (10). Leptin receptor deficiency is more common than leptin deficiency and is responsible for at least 3% of early-life obesity (11).

It has been shown that factors other than the amount of body fat are important in regulating leptin (12). Nutritional status is important in leptin regulation in the short term and is independent of fat tissue (13). Leptin concentration varies depending on food intake, body weight, energy expenditure and gender (14, 15). Various results have been obtained in studies showing changes in short-c51ycle leptin concentrations following energy intake. While some studies found significant changes, others reported no change (16, 17). A decrease in leptin level has been shown due to the decrease in insulin level and increase in catecholamine levels during fasting (18-21).

Obesity and obesity-related diseases have become a rapidly increasing important health problem. Hormones such as leptin, ghrelin, obestatin and nesfatin1 play an important role in fat tissue accumulation and appetite mechanism. Leptin belongs to a class of hormones known as adipocytokines, which play a role in regulating energy metabolism. In this field, the number of related studies is small, the research direction is relatively concentrated, and a comprehensive analysis and standard evaluation system are lacking. This study aimed to investigate the relationships between leptin, obesity and exercise. This study explores the relationship of leptin, obesity and exercise through a systematic literature review.

Methodology

We conducted this systematic review following the PRISMA 2020 statement. Databases searched: PubMed, Web of Science, ScienceDirect, Wiley, and EBSCO, up to December 2024. All studies evaluating the relationship between leptin, obesity and exercise were eligible for inclusion. The inclusion criteria were (i) publication date between 1996 and 2024, (ii) being an empirical study, (iii) written in English and Turkish languages, (iv) published in a scholarly peer-reviewed journal, and (v) conducted an assessment of the relationship between leptin, obesity and exercise objectively.

In this study, the relationships between leptin, obesity and exercise were investigated. The systematic review used a search to identify studies published from PubMed, Wiley Online Library, EBSCO, Science Direct and Web of Science databases. The relationship between leptin and obesity and leptin exercise has been investigated in detail. Using a combination of the following search terms: “leptin”, “obesity”, and “exercise”.

The Relationship of Leptin and Obesity

As a result of the studies, serum levels of the leptin hormone, which increases energy expenditure and reduces appetite, were found to be higher in obese individuals than in normal individuals. It is believed that this situation is due to the insensitivity of hypothalamic receptors to leptin in obese individuals or to a problem in leptin's passage through the blood-brain barrier. In parallel with this situation, studies conducted found a positive relationship between leptin level and BMI in obese men and women, while this relationship was not observed in individuals with normal body weight (22, 23). In a study, leptin values in women were found to be significantly higher than in men. The reason why

women have more leptin than men is thought to be due to testosterone's suppressive effect on leptin and gender-related fat storage (24).

Söylemez et al. (25), in the study on 87 individuals, examined the individuals in 3 groups as normal weight, overweight and obese. A positive correlation was found between body weight and serum leptin levels and total oxidant levels. In a study conducted on 32 normal weight and 68 obese individuals, it was found that body weight showed a positive correlation with serum insulin and leptin values. Additionally, when the serum leptin values of individuals with positive insulin resistance were compared with those of the group with negative insulin resistance, no significant difference was found in serum leptin levels. This situation has been explained that hyperinsulinemia does not affect serum leptin levels (26). Other studies have shown that serum insulin level or insulin resistance does not affect serum leptin level, but leptin has inhibitory effects on insulin secretion. It is also thought that leptin works like insulin and increases the use of glucose, especially in muscle tissue (27).

There are studies suggest that exercise, as well as diet, has effects on serum leptin in obese individuals. In order to determine the effect of long-term changes in diet and exercise on leptin levels, 186 men were grouped as diet, exercise, both together and control, and serum leptin levels were measured. There was a decrease in plasma leptin level and body fat mass by decreasing food intake and increasing physical activity. It was concluded that long-term low-energy diet intake and increased physical activities reduced leptin levels beyond the expected change in fat mass. Other studies have suggested that chronic exercises instead of acute exercises decrease serum leptin levels due to a decrease in body fat mass (28, 29). Factors that increase and decrease leptin production from adipose tissue are given in Table 1.

There are also studies showing that nutritional differences at an early age have an impact on serum leptin levels. It has been observed that serum leptin levels are higher in babies who were fed with formula in addition to breast milk earlier than in those who received only breast milk. It is reported that excessive food intake in infancy increases the risk of obesity at later ages. Considering that obesity is related to leptin concentration, leptin concentrations of 13-16 year old adolescents who were born prematurely and were fed with enriched formula or breast milk were determined. While the ratio of leptin to fat mass was found to be higher in adolescents who were fed enriched formula in infancy than those who were breastfed, the ratio of leptin concentration to fat mass was found to be lower in adolescence in those who were breastfed. In addition to this, there are also studies arguing that high serum leptin levels and leptin resistance are important causes of early obesity. As a result, it is thought that the effect of nutrition in infancy on obesity at later ages may be related to leptin (30-32).

The Relationship of Leptin and Exercise

It is a known fact that exercise changes energy balance by increasing energy consumption and causes fat mass to decrease. This fact underlies many studies examining the effects of exercise on leptin. It is thought that exercise exerts its effects on leptin through the sympathoadrenergic system (33). Weltman et al. (34) found that 30 minutes of acute exercise did not change serum leptin, regardless of exercise intensity, and stated that studies should be conducted to evaluate the effects of exercise intensity on leptin metabolism, taking into account total energy consumption.

Table 1 Factors that increase and decrease the production of leptin from adipose tissue (30)

Increasers	Decreasers
Food intake	Hunger
Fire	Cold
insulin	Exercise
Glukokortikoid	Noradrenalin
Dexamethasone	Testesteron
α-MPT (Metil-P-Tirosin)	Thiazolidinedion
TNFα	

Exercises lasting less than 60 minutes do not cause or cause little change in serum leptin levels (35-37). The decrease in serum leptin levels in some studies may be attributed to diurnal rhythm or hemoconcentration. In addition, short-term exercises of 41 minutes or less may change serum leptin concentrations if they are depleting (38-40).

Long-term (≥60 minutes) exercises cause a decrease in serum leptin levels. It has been found that with this decrease, free fatty acids increase, insulin decreases, glucose decreases or remains unchanged (35, 41-43). The effects of increased energy consumption during exercise on blood leptin concentration are less than the effects of food restriction (44). The decrease in blood leptin levels caused by exercise can be balanced by nutrition. Gökbel et al. (45) showed that leptin levels decreased 48 hours after strenuous exercise in rats. The physiological significance of the delayed decrease in plasma leptin is unclear. It is suggested that changes in growth hormone, cortisone, insulin (which increase leptin) and testosterone, epinephrine, and norepinephrine (which decrease leptin) that occur during exercise cause delayed leptin decrease.

Short-term training of less than 12 weeks does not affect leptin levels unless it reduces fat mass (46-48). Zheng et al. (49) showed that ob mRNA levels in rat adipose tissue decreased by 30% immediately and 3 hours after acute exercise. Leal-Cerro et al. (50), who reported that strong changes in energy consumption can lead to changes in serum leptin levels, showed that leptin levels decreased after 2800 calories of energy consumption in marathon runners. Dirlewanger et al. (51) found that plasma leptin concentrations did not change with a 30-minute exercise program twice a day for 3 days, although the energy balance was slightly negative. Kraemer et al. (52) showed that serum leptin levels and body fat did not change with a 9-week (3-4 days a week, 20-30 minutes) exercise program. Noland et al. (53) reported that leptin did not decrease at the end of the 9-week exercise program and while there was no change in body composition in men, fat mass decreased in women.

Gomez-Merino et al. (54) found that a 4-week exercise program reduced serum leptin levels without any change in body mass index. However, this study included a heavy military exercise program that resembled a combat course, and daily energy consumption was kept above 5000 kcal. It has been shown that the ob mRNA level in rat adipose tissue decreased by 48% with a four-week exercise program. Long-term (≥12 weeks) exercises reduce leptin levels. This decrease is accompanied by a decrease in fat mass. The decrease in plasma leptin concentration occurring with a 4-16 month exercise program in obese men was found to be associated with a decrease in body fat ratio (55). However, a decrease in leptin values has been reported in sedentary women with a 12-week (4 days a week, 30-45 minutes) exercise program, regardless of fat mass changes (56). Gutin et al. (57) found that plasma leptin concentrations decreased in obese children at the end of a 4-month exercise program (5 days a week, 40 minutes, heart rate average 159/min), even when fat mass loss was taken into account, and leptin levels decreased in the following 4-month period without exercise. Considering the increase in concentration, they stated that leptin reflects changes in energy balance. Ünal et al. (58) found lower leptin levels in professional football players who exercise regularly compared to sedentary players.

A limited number of studies have been conducted on the effects of resistance exercises on leptin concentration. Kanaley et al. (59) found that leptin levels decreased approximately 24 hours after acute resistance exercise in type 2 diabetics, but did not change in normal individuals, and they attributed the decrease in leptin in diabetics to less glucose reaching the fat tissue. The same study showed that chronic resistance exercises were not effective on leptin levels. Nindl et al. (60) reported that leptin concentrations decreased 9 hours after 856 kcal acute resistance exercise. Leptin is one of the most important regulators of energy balance. The fact that different results have been found so far regarding the effects of exercise on leptin suggests that fluctuations in food intake and other factors may be responsible for leptin changes during exercise, and it can be said that exercises at an intensity that will affect energy balance or body fat mass change leptin secretion.

Results

A total of 1022 records were initially scoped in the literature search, 784 of which were duplicates. After screening for eligibility and inclusion criteria, 57 articles were ultimately included in the study (Fig 1).

Using the PRISMA 2020 checklist, the authors combed through the objectives, research methods, survey participants, response rate, index of composition, discussion, and limitations of the 57 selected articles, but found that they may overlap in one or more domains. Risk of bias was generally low to moderate (Table 2). Common concerns included small sample sizes, selection bias, and incomplete reporting. Table 3 shows the list of the 57 analysed manuscripts

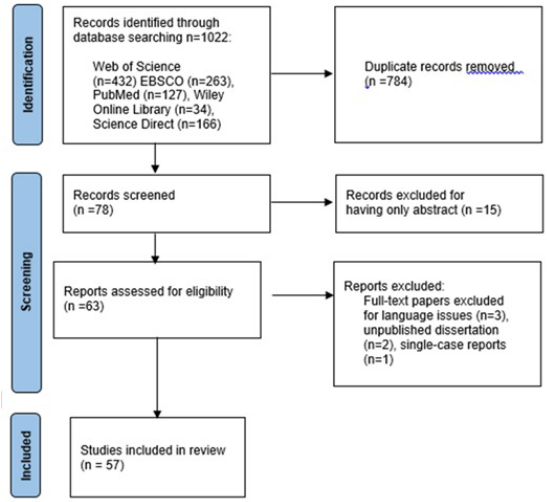

Figure 1
PRISMA flow diagram of paper selection process

Table 2 Risk of Bias Summary (RoB2/ROBINS-I)

Domain	Low Risk	Some Concerns / Moderate	High/Serious Risk
Randomization process	12	3	0
Deviations from interventions	10	5	0
Missing outcome data	11	3	1
Measurement of outcome	12	2	1
Selection of reported results	13	2	0
Confounding (non-RCTs)	5	20	10
Selection of participants	8	15	12
Classification of interventions	6	18	11

focused on the methodological design to evaluate the relationships between leptin, obesity and exercise, the relationships between leptin, obesity and exercisethat have been evaluated and the variables involved in the evaluation by various evaluation methodologies.

Many studies have shown that there is a positive relationship between leptin level and serum fasting insulin and insulin resistance in obese people. It has been stated that the higher the leptin levels, the higher the insulin resistance. Studies show that insulin resistance is associated with leptin and adiponectin. A significant positive correlation was observed between plasma leptin, resistin and adiponectin levels and insulin resistance in obese and normal weight individuals.

Hormones and mediators, which are thought to be the source of obesity, have become the focus of current studies. In recent years, the positive or negative effects of peptide hormones on obesity have not been fully elucidated. Extensive research has revealed that maintaining specific circulating leptin concentrations is essential to prevent an imbalance in food intake. Leptin levels are higher in women than in men, which is thought to be due to testosterone's suppressive effect on leptin and gender-related fat storage.

There are studies showing that exercise decreases leptin concentration. With exercise, fat mass decreases, energy balance changes, hormonal concentrations and metabolites change. All of these changes can alter the leptin response to exercise, depending on many

factors. The discrepancies in the results of studies examining the effect of exercise on the leptin response may also arise from many methodological differences, such as the intensity, duration, frequency and extent of exercise, the nutritional status of the participants, the circadian rhythm of leptin, and the time and frequency of sampling.

Chronic training generally reduced leptin, usually via fat loss. Acute effects were inconsistent, but delayed reductions occurred. Resistance training showed mixed findings. Prolonged exercise consistently reduced leptin. Exercise influences leptin via energy balance and fat mass. Chronic exercise reliably lowers leptin; acute effects are variable. Standardized protocols and novel biomarkers are needed.

Table 3 List of Reviewed Papers

No	Author (Year)	Study type	Population (brief)	Exercise protocol (brief)	Leptin measurement/ timing	Findings (leptin)
1	Leal-Cerro A et al. (1998)	Observational/ Experimental	Marathon athletes	Marathon pre/post	Serum leptin	Leptin decreased after a marathon.
2	Dirlewanger M et al. (1999)	Experimental	Healthy adults	30 min ×2/day ×3 days	Plasma leptin	Leptin unchanged.
3	Kraemer RR et al. (1999)	Experimental	Postmenopausal women (sample)	9-week, 3–4 min/wk, 20–30 min	Serum leptin	No change in leptin and body fat.
4	Noland RC et al. (2001)	Experimental	Male & female swimmers Plasma leptin Overall: leptin unchanged; fat mass decreased in women.	Intensive training, 9-wk	Plazma leptin	Leptin unchanged; fat mass decreased in women.
5	Gomez-Merino D et al. (2002)	Experimental (heavy exercise)	Men (military heavy program)	4-week, heavy/combat-like, EEx >5000 kcal	Serum leptin	Leptin decreased; BMI stable.
6	Gutin B et al. (1999)	Experimental (children)	Obese children	4-month program, 5 min/wk, 40 min, HR≈159/min.	Plasma leptin — end & follow-up	Leptin decreased; the decrease was not due to fat loss.
7	Ünal M et al. (2003)	Paper/ Symposium	Professional football players vs. sedentary	Regular training (professional football)	Serum leptin	Leptin is lower in professional football players.
8	Kanaley JA et al. (2001)	Experimental	Type-2 diabetics & normals	Acute resistance exercise and chronic resistance were also examined	Resting leptin (after acute 24 h)	Leptin decreased after ~24 h in diabetics; unchanged in normals.
9	Nindl BC et al. (2002)	Experimental (resistance)	Men (healthy)	Acute resistance, ≈856 kcal expenditure	Leptin — 9 hours post	Leptin decreased after 9 hours.
10	Weltman A et al. (2000)	Experimental	Young men (trained)	30 min acute exercise; different intensities	Serum leptin	Exercise intensity has no effect on leptin; no change at 30 min.
11	Olive JL et al. (2001)	Experimental	Trained subjects	Maximal vs. moderate-intensity run	Plazma leptin	Different effects of different running types reported (study-specific).
12	Zheng D et al. (1996)	Animal study	Rat adipose tissue	Acute/4-week exercise (animal)	ob mRNA (adipose)	ob mRNA decreased (e.g., 30–48% where reported).
13	Reseland JE et al. (2001)	Experimental (diet+exercise)	Adult males	Diet/exercise interventions (groups)	Plazma leptin	Diet+exercise reduced leptin and fat.
14	Kraemer RR et al. (2001)	Cohort/seasonal	Adolescent female runners	7-week seasonal training Leptin & steroid hormones	Leptin & steroid hormones	Seasonal measurements, leptin, and steroid responses were reported
15	Karamouzis I et al. (2002)	Observational/ marathon swimming	Marathon swimmers	Marathon swimming	Serum leptin & NPY	Effects reported.

Table 3 continued List of Reviewed Papers

No	Author (Year)	Study type	Population (brief)	Exercise protocol (brief)	Leptin measurement/ timing	Findings (leptin)
16	Torjman MC (2001)	Comment/editorial	-	-	-	The delayed leptin effects of exercise are discussed.
17	Svensson J et al. (2005)	Clinical/cross-sectional	GH-deficient adults	-	Adiponectin and leptin measurements.	Leptin association findings were reported.
18	Essig DA et al. (2000)	Experimental Plasma leptin (delayed effects). Delayed leptin effects were observed in some studies.	Healthy individuals	Short/moderate acute exercise	Plasma leptin (delayed effects)	Delayed leptin effects were observed in some studies.
19	Hulver M & Houmard J (2003)	Review	-	-	-	Plasma leptin and exercise: a review (summarized findings).
20	Fan S et al. (2021)	Basic science/ translational	Animal/molecular (neuronal leptin)	-	Neural mechanisms (brain leptin action)	Effects of brain leptin action on diabetes.
21	Poggi AI et al. (2024)	Experimental/real world	Well-trained older men	Repetitive long-term exercise	Men's Liver fat, VAT measurements	Effects of repetitive long-term exercise (prolonged)
22	Gökbel H et al. (2005)	Animal study	Rats (zinc deficiency model)	Strenuous exercise (rats)	Serum leptin (after 48 h)	Leptin decreased after 48 h.
23	Ayvalı Z et al. (2024)	Clinical	Obese patients undergoing sleeve gastrectomy	-	Ghrelin, obestatin, and leptin expression measurements.	Leptin expression is reported.
24	Kraemer RR et al. (2002)	Review/narrative	-	-	-	Review summarizing the relationship between leptin and exercise.
25	Houmard JA et al. (2000)	Experimental	Healthy/obese	Short-term training	Leptin & insulin action	The effects of short-term training on leptin/insulin were reported.
26	Zheng D et al. (1996)	Animal study	Rat adipose	Effect of exercise on ob gene expression	ob mRNA measurements	The ob gene expression decreased.
27	Okazaki T et al. (1999)	Experimental Plasma leptin.	Sedentary women	Light aerobic + hypocaloric diet	Plasma leptin	Light aerobic + diet: a change in leptin was reported
28	Mitoiu BI et al. (2024)	Experimental	Overweight & obese subjects	Resistance & endurance training	Ghrelin & plasma leptin	Impact of resistance and endurance training on plasma leptin levels
29	Reseland JE et al. (2011)	Experimental	Adult men	Long-term diet & exercise	Plasma leptin	Diet + exercise: leptin decreased.
30	Ergün A (1999)	Review / educational	-	-	-	Leptin (ob protein) general information.
31	Lönnerdal B & Havel PJ (2000)	Clinical (infant)	Infants	Diet	Serum leptin	Effects of diet, gender, and adiposity.
32	Singhal A et al. (2002)	Cohort/clinical	Child/feeding	Early feeding	Leptin	Early feeding may affect leptin levels.
33	Torjman MC (2001)	Review	-	-	-	Discussion about the delayed effects of exercise.

Table 3 continued List of Reviewed Papers

No	Author (Year)	Study type	Population (brief)	Exercise protocol (brief)	Leptin measurement/ timing	Findings (leptin)
34	Weltman A et al. (2000)	Experimental Young men (trained) Serum leptin	Young men (trained)	30 min acute exercise	Serum leptin	Intensity change has no effect on leptin; 30 min, no change.
35	Olive JL et al. (2001)	Experimental	Healthy trained subjects	Maximal vs moderate runs	Plasma leptin	Different effects reported.
36	Kraemer RR et al. (1999, Proc Soc Exp Biol Med)	Experimental	Postmenopausal women (HRT/no HRT)	Acute exercise response	Serum leptin	Specific results
37	Torjman MC et al. (1999)	Experimental	Healthy subjects	Maximal incremental & prolonged exercise (recovery)	Serum leptin during recovery	Withdrawal period leptin behaviors reported.
38	Hulver M & Houmard J (2003)	Review	-	-	-	Plasma leptin & exercise.
39	Kraemer RR et al. (2001)	Kohort	Adolescent female runners	7-week season	Leptin & steroid responses	Seasonal follow-up; results reported.
40	Essig DA et al. (2000)	Experimental	Healthy individuals	Various acute/ short protocols	Plasma leptin (delayed)	Delayed decreases were reported.
41	Karamouzis I et al. (2002)	Experimental (marathon swimming)	Marathon swimmers	Marathon swimming	Serum leptin & NPY	Leptin changes were reported.
42	Fan S et al. (2021)	Basic/ translational	Animal models (nöral leptin)	-	Brain leptin action (type-1 dm)	Findings are at the basic science level.
43	Poggi AI et al. (2024)	Experimental / observational	Well-trained older men	Repeated prolonged exercise	Liver fat & VAT measures	Effect of prolonged exercise on liver fat
44	Gökbel H et al. (2005)	Animal study	Rats	Strenuous exercise, zinc deficiency model	Serum leptin	Serum leptin decreases after 48 h.
45	Koch CE et al. (2014)	Animal study (mice)	Leptin-deficient mice, HFD	High-fat diet models	Leptin resistance measures	HFD induces leptin resistance.
46	Bulduk B & Günbatar N (2023)	Animal study	Rats, HFD	Exercise effect	Serum resistin & leptin	The Effect of Exercise on Serum Resistin and Leptin
47	Fried SK et al. (2000)	Review	-	-	-	Regulation of leptin production.
48	Imbeault P et al. (2001)	Experimental	Lean vs obese men	High-fat meal response studies	Leptin response to a meal	Different leptin responses have been reported.
49	Kord HV et al. (2021)	Systematic review/meta-analysis	Humans (fasting/ energy-restricted diets)	Diet interventions	Leptin & adiponectin	Meta-analysis results.
50	Myers MG et al. (2010)	Review	-	-	-	Obesity & leptin resistance.

Table 3 continued List of Reviewed Papers

No	Author (Year)	Study type	Population (brief)	Exercise protocol (brief)	Leptin measurement/ timing	Findings (leptin)
51	Söylemez N et al. (2010)	Cross-sectional Normal/overweight/ obese (3 groups) - Serum leptin & adiponectin	Normal/ overweight/ obese	-	Serum leptin & adiponectin	A positive correlation was found with body weight.
52	Yiğitbaşı T et al. (2010)	Cross-sectional/clinical - GH, leptin, amylin, GLP-1, etc.	Obese patients	-	GH, leptin, amylin, GLP-1, etc.	Relationship Between Leptin and Insulin Resistance
53	Frühbeck G & Salvador J (2000)	Review	-	-	-	Leptin & glucose regulation
54	Üçok K & Gökbel H (2004)	Review/original study abstract - Effects of exercise on leptin levels. Review/study abstracts.	-	-	-	Effects of exercise on leptin levels
55	Reseland JE et al. (2001)	Deneysel (daha önce listelendi)	186-like sample	Diyet & egzersiz arms	Plasma leptin	Diyet+egzersiz leptin azalması.
56	Lönnerdal B & Havel PJ (2000)	Pediatric study: Infants' Diet Effect Serum leptin Effects of diet, gender, and adiposity.	Infants	Diet	Serum leptin	Effects of diet, gender, and adiposity.
57	Singhal A et al. (2002)	Cohort / clinical Child/ early feeding cohort - Leptin in later life.	Child/early feeding	-	Leptin in later life	Early feeding-leptin relationship

Discussion

Obese and overweight people need to be especially evaluated in terms of risk factors. It would be beneficial for obese and overweight people to measure their blood pressure regularly, check their lipid and fasting blood sugar levels, and give advice on healthy nutrition. People of normal weight should also be informed about obesity risks and healthy nutrition. It is important to evaluate the success or failure of weight loss and provide the patient with the necessary motivation and support. Patients should be informed about the mortality and morbidity risks of obesity at every visit. Finally, when the weight loss process is completed, the patient should be advised to maintain a constant weight and should be called for height and weight measurements periodically.

Leptin is a key regulator of energy balance linked to obesity. The effect of exercise on leptin remains debated. The effects of exercise and post-exercise recovery on leptin levels are not fully clarified. Studies demonstrating that exercise reduces leptin concentrations suggest this is due to multiple factors. Physical exercise alters energy balance, reduces fat mass, and alters hormonal concentrations (catecholamines, insulin, cortisol, growth hormone, testosterone, etc.) and metabolites (free fatty acids, lactic acid, triglycerides, etc.). All of these changes can alter the leptin response to exercise, depending on many factors. The discrepancies in research results examining the effect of exercise on leptin responses also stem from methodological differences such as the intensity, duration, frequency, and extent of exercise, the nutritional status of participants, and the timing and frequency of sample collection.

This review shows that chronic exercise interventions consistently reduce leptin concentrations, mostly mediated by fat mass loss. Acute effects are inconsistent and often delayed. Prolonged strenuous exercise leads to marked decreases. Future research should standardize leptin measurement, incorporate biomarkers such as soluble leptin receptor and

adiponectin, and explore leptin-targeted therapies in obesity treatment. More research is needed in this area.

Conflict of Interest Statement
The author declares that no conflict of interest could be perceived as prejudicing the impartiality of the research reported.

Ethical Approval
No ethical clearance was required for this systematic review.

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Artificial Intelligence Statement
The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

References

1. Monica B, Silvia G, Simone R, Alessendro A, Silke M, Federica D, et al. Multi-omics gut microbiome signatures in obese women: role of diet and uncontrolled eating behavior. BMC Med 2022;20(500):1-25.
2. Şahin T, Tozcu D. Leptin, Mikrobiyota ve Obezite İlişkisi. Türkiye Diyabet ve Obezite Dergisi 2022; 6(1):77-84.
3. Barness LA, Opitz, J M, & Gilbert-Barness, E. Obesity: genetic, molecular, and environmental aspects. American journal of medical genetics part A 2007;143(24):3016-3034.
4. Oswal A, Yeo G. Leptin and the Control of Body Weight: A Review of Its Diverse Central Targets, Signaling Mechanisms, and Role in the Pathogenesis of Obesity. Obesity 2010;18:221–229.
5. Khan M, Joseph F. Adipose Tissue and Adipokines: The Association with and Application of Adipokines in Obesity. Science 2014;1:328-592.
6. Genchi VA, D'Oria R, Palma G, Caccioppoli C, Cignarelli A, Natalicchio A, et al. Impaired Leptin Signalling in Obesity: Is Leptin a New Thermolipokine? International Journal of Molecular Sciences 2021; 22(12): 6445.
7. Ayvalı Z, Yakan B, Deniz K. Sleeve Gastrektomi Uygulanmış Obezite Hastalarında Ghrelin, Obestatin, Leptin Ekspreyonları'nın Araştırılması. Sağlık Araştırmaları Dergisi (Tusad) 2024;1(2):80-98.
8. Hekimoğlu A. Leptin ve fizyopatolojik olaylardaki rolü. Dicle Tıp Dergisi 2006;33(4): 259-267.
9. Friedman JM. The Function of Leptin in Nutrition, Weight, and Physiology. Nutrition Reviews 2002; 60(10):1-14.
10. Farooqi IS, Wangensteen T, Collins S. Clinical and molecular genetic spectrum of congenital deficiency of the leptin receptor. N Engl J Med 2007;356:237–247.
11. Calabro P, Limongelli G, Pacileo G, Salvo GD, Golino P, Calabro R. The role of adiposity as a determinant of an inflammatory milieu. J Cardiovasc Med 2007;8:1-11.
12. Bulduk B, Günbatar N. The Effect of Exercise on Serum Resistin and Leptin Values in Rats Fed with a High Fat Diet. Journal of Contemporary Medicine 2023;13(1):82-85.
13. Fried SK, Ricci MR, Russell CD, Laferrère B. Regulation of leptin production in humans. J Nutr 2000;130(12):3127-3131.
14. Erçakır M, Bayram S. Obez Bireylerde Serum Ferritin Düzeyleri, İnsülin Direnci, Metabolik Sendrom ve Beslenme Durumları Arasındaki İlişkinin Retrospektif Analizi. Gazi Sağlık Bilimleri Dergisi 2022;7(2):90-102.
15. Koch CE, Lowe C, Pretz D, Steger J, Williams LM, Tups A. High-fat diet induces leptin resistance in leptin-deficient mice. J Neuroendocrinol 2014; 26(2):58-67.
16. Major GC, Doucet E, Trayhurn P, Astrup A, Tremblay A. Clinical significance of adaptive thermogenesis. International Journal of Obesity 2007;31(2):204-212.
17. Imbeault P, Doucet E, Mauriège P, St-Pierre S, Couillard C, Alméras N, et al. Difference in leptin response to a high-fat meal between lean and obese men. Clin Sci (Lond) 2001;101(4):359-365.
18. Kord HV, Tinsley GM, Santos HO, Zand H, Nazary A, Fatahi S, et al. The influence of fasting and energy-restricted diets on leptin and adiponectin levels in humans: a systematic review and meta-analysis. Clinical Nutrition 2021;40(4):1811-1821.
19. Myers MG, Leibel RL, Seeley RJ, Schwartz MW. Obesity and leptin resistance: distinguishing cause from effect. Trends in Endocrinology and Metabolism 2010;21(11):643-651.
20. Kıvrak EG, Aydın I, Tümentemur G, Altunkaynak BZ, Kaplan S. Effects of leptin on histomorphometry of liver in high-fat diet fed obese rats. Journal of Experimental and Clinical Medicine 2013;30(2):141-145.
21. Pospiech E. Leptin: The Satiety Hormone and its Influence on Obesity. Eukaryon 2010;6:80-83.
22. Özen Ş, Özen G. Leptin Hormonu: Egzersiz ve Obezite ile İlişkisi. New World Sciences Academy 2011;6(2):114-127.
23. Obradovic M. Sudar-Milovanovic E, Soskic S, Essack M, Arya S, Stewart AJ, Isenovic ER. Leptin and obesity: role and clinical implication. Frontiers in endocrinology 2021;12:585887.
24. Gültürk S, Demirkazık A. Leptin ve Diyabet. Cumhuruyet Üniversitesi Tıp Fakültesi Dergisi 2007;29(1):35-40.
25. Söylemez N, Demirbağ R, Sezen Y, Yıldız A, Akpınar O. Vücut kütle indeksine göre leptin ve adiponektin seviyeleri ve bunların oksidatif parametrelerle ilişkisi. Anadolu Kardiyol Derg 2010;10:391-396.
26. Yiğitbaşı T, Baskın Y, Afacan G, Harmanda A. Relationship Between The Levels of Growth Hormone, Leptin, Amylin, Glucagon Like Peptide-1 and Insulin Resistance in Obese Patients. Turk J Biochem 2010;35(3):177–182.
27. Frühbeck G, Salvador J. Relation between leptin and the regulation of glucose metabolism. Diabetologia 2000;43:3-12.
28. Üçok K, Gökbel H. Egzersizin leptin düzeylerine etkileri. Genel Tıp Derg 2004;14(3):121-124.
29. Reseland JE, Anderssen SA, Solvoll K, Hjermann I, Urdal P, Holme I, Drevon CA. Effect of long-term changes in diet and exercise on plasma leptin concentrations. Am J Clin Nutr 2001;73:240–245.
30. Ergün, A. Leptin (ob protein). Turkiye Klinikleri Journal of Medical Sciences 1999; 19(2):130-136.
31. Lönnerdal B, Havel PJ. Serum leptin concentrations in infants: effects of diet, sex, and adiposity. Am J Clin Nutr 2000;72:484–489.
32. Singhal A, Farooqi S, O'Rahilly S, Cole TJ, Fewtrell M, Lucas A. Early nutrition and leptin concentrations in later life. Am J Clin Nutr 2002;75:993–999.
33. Torjman MC. On the delayed effects of exercise on leptin: More questions than answers. Nutrition 2001;17(5):420-422.
34. Weltman A, Pritzlaff CR, Wideman L, Considine RV, Fryburg DA, Gutgesell ME, et al. Intensity of acute exercise does not affect serum leptin concentrations in young men. Med Sci Sports Exerc 2000;32:1556-61.
35. Olive JL, Miller MS, Miller GD. Differential effects of maximal- and moderate- intensity runs on plasma leptin in healthy trained subjects. Nutrition 2001;17:365-9.
36. Kraemer RR, Johnson LG, Haltom R, Kraemer GR, Hebert EP, Gimpel T, et al. Serum leptin concentrations in response to acute

exercise in postmenopausal women with and without hormone replacement therapy. Proc Soc Exp Biol Med 1999;221:171-7.
37. Torjman MC, Zafeiridis A, Paolone AM, Wilkerson C, Considine RV. Serum leptin during recovery following maximal incremental and prolonged exercise. Int J Sports Med 1999;20:444-50.
38. Svensson J, Herlitz H, Lundberg PA, Johannsson G. Adiponectin, leptin, and erythrocyte sodium/lithium countertransport activity, but not resistin, are related to glucose metabolism in growth hormone-deficient adults. The Journal of Clinical Endocrinology Metabolism 2005;90(4):2290-2296.
39. Kraemer RR, Acevedo EO, Synovitz LB, Hebert EP, Gimpel T, Castracane VD. Leptin and steroid hormone responses to exercise in adolescent female runners over a 7-week season. Eur J Appl Physiol 2001;86:85-91.
40. Hulver M, Houmard J. Plasma leptin and exercise: Recent findings. Sports Med 2003;33:473-82.
41. Essig DA, Alderson NL, Ferguson MA, Bartoli WP, Durstine JL. Delayed effects of exercise on the plasma leptin concentration. Metabolism 2000;49:395-9.
42. Karamouzis I, Karamouzis M, Vrabas IS, Christoulas K, Kyriazis N, Giannoulis E, et al. The effects of marathon swimming on serum leptin and plasma neuropeptide Y levels. Clin Chem Lab Med 2002;40:132-6.
43. Fan S, Xu Y, Lu Y, Jiang Z, Li H, Morrill JC, et al. A neural basis for brain leptin action on reducing type 1 diabetic hyperglycemia. Nature communications 2021;12(1):2662.
44. Poggi AI, Andreasen MW, Sahl RE, Hansen MT, et al. Effect of repeated prolonged exercise on liver fat content and visceral adipose tissue in well-trained older men. Scandinavian Journal of Medicine & Science in Sports 2024;34(4):14612.
45. Gökbel H, Baltaci AK., Üçok K. Okudan N, & Moğulkoç R. Changes in serum leptin levels in strenuous exercise and its relation to zinc deficiency in rats. Biological Trace Element Research 2005;106:247-252.
46. Ayvalı Z, Yakan B, Deniz K. Sleeve Gastrektomi Uygulanmış Obezite Hastalarında Ghrelin, Obestatin, Leptin Ekspreyonları'nın Araştırılması. Sağlık Araştırmaları Dergisi 2024;1(2):80-98.
47. Kraemer RR, Chu H, Castracane VD. Leptin and exercise. Exp Biol Med 2002;227:701-8.
48. Houmard JA, Cox JH, MacLean PS, Barakat HA. Effect of short-term exercise training on leptin and insulin action. Metabolism 2000;49:858-61.
49. Zheng D, Wooter MH, Zhou Q, Dohm GL. The effect of exercise on ob gene expression. Biochem Biophys Res Commun 1996;225:747-50.
50. Leal-Cerro A, Garcia-Luna PP, Astorga R, Parejo J, Peino R, Dieguez C, et al. Serum leptin levels in male marathon athletes before and after the marathon run. J Clin Endocrinol Metab 1998;83:2376-9.
51. Dirlewanger M, Di Vetta V, Giusti V, Schneiter P, Jéquier E, Tappy L. Effect of moderate physical activity on plasma leptin concentration in humans. Eur J Appl Physiol 1999;79:331-5.
52. Kraemer RR, Kraemer GR, Acevedo EO, Hebert EP, Tample E, Bates M, et al. Effects of aerobic exercise on serum leptin levels in obese women. Eur J Appl Physiol 1999;80:154-8.
53. Noland RC, Baker JT, Boudreau SR, Kobe RW, Tanner CJ, Hickner RC, et al. Effect of intense training on plasma leptin in male and female swimmers. Med Sci Sports Exerc 2001;33:227-31.
54. Gomez-Merino D, Chennaoui M, Drogou C, Bonneau D, Guezennec CY. Decrease in serum leptin after prolonged physical activity in men. Med Sci Sports Exerc 2002;34:1594-9.
55. Okazaki T, Himeno E, Nanri H, Ogata H, Ikeda M. Effects of mild aerobic exercise and a mild hypocaloric diet on plasma leptin in sedentary women. Clin Exp Pharmacol Physiol 1999;26:415-20.
56. Mitoiu BI, Nartea R, Miclaus RS. Impact of resistance and endurance training on ghrelin and plasma leptin levels in overweight and obese subjects. International Journal of Molecular Sciences 2024;25(15):8067.
57. Gutin B, Ramsey L, Barbeau P, Cannady W, Ferguson,M, Litaker M, & Owens S. Plasma leptin concentrations in obese children: changes during 4-mo periods with and without physical training. The American journal of clinical nutrition 1999;69(3):388-394.
58. Ünal M, Ünal DÖ, Baltacı AK, Moğulkoç R, Yıldız S, Kayserilioğlu A. Erkek profesyonel futbolcular ve sağlıklı sedanter erkeklerde serum leptin seviyelerinin incelenmesi. I. Leptin Sempozyumu. Konya; 20-22 Haziran 2003
59. Kanaley JA, Fenicchia LM, Miller CS, Ploutz-Synder LL, Weinstock RS, Carhard R, et al. Resting leptin responses to acute and chronic resistance training in type 2 diabetic men and women. Int J Obes 2001;25:1474-80.
60. Nindl BC, Kraemer WJ, Arciero PJ, Samatallee N, Leone CD, Mayo MF, et al. Leptin concentrations experience a delayed reduction after resistance exercise in men. Med Sci Sports Exerc 2002;34:608-13.