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The Effect of Exercise Training Combined with Nanocurcumin Supplementation on Metabolic and Liver Function Markers in Post-Bariatric Surgery Patients: A Randomized Controlled Trial

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Abstract

Objective: Obesity is a chronic inflammatory condition associated with metabolic disorders such as cardiovascular disease, diabetes, and non-alcoholic fatty liver disease. This study aimed to investigate the additive effects of nanocurcumin supplementation combined with exercise training on metabolic and liver function markers in patients after bariatric surgery.

Materials and Methods: In this randomized, single-blind, placebo-controlled trial, 60 patients (35-45 years) with a history of bariatric surgery were assigned to two groups: exercise + nanocurcumin or exercise + placebo (n= 30 each). Both groups performed combined aerobic-resistance training (3 sessions/week) for 6 weeks. The intervention group received 40 mg nanocurcumin twice daily. Blood samples were collected before and after the intervention. Data were analyzed using MANCOVA ($P \leq 0.05$).

Results: A significant multivariate effect of group was observed (Wilks' Lambda, $P < 0.001$). Compared with placebo, the intervention group showed significant reductions in LDL, triglycerides ($P = 0.001$), body fat percentage ($P = 0.004$), ALT ($P = .017$), AST ($P = .004$), and ferritin ($P = 0.002$) along with increases in HDL ($P = 0.023$) and albumin ($P = 0.017$).

Conclusion: Nanocurcumin supplementation combined with exercise training may improve lipid profile, liver enzyme levels, and inflammation-related markers in patients after bariatric surgery. However, due to identical exercise protocols in both groups, the findings reflect the additive effect of nanocurcumin rather than its independent effect.

Keywords: Bariatric surgery, Metabolic syndrome, Exercise training, Nanocurcumin, Liver enzymes

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Introduction

Obesity is a major global health concern associated with reduced quality of life and an increased risk of metabolic and cardiovascular diseases. The World Health Organization has identified obesity as one of the most significant health challenges in adults (1). In Iran, its prevalence is higher among women and increases with age, partly due to reduced physical activity and changes in body composition (2).

Obesity is closely linked to metabolic disturbances such as dyslipidemia, insulin resistance, and chronic low-grade inflammation, which contribute to the development of cardiovascular disease, type 2 diabetes, and metabolic syndrome (3). Regular physical activity is a key strategy for the prevention and management of obesity. Both aerobic and resistance training have been shown to improve body composition and lipid profiles (4). Current guidelines recommend at least 150 minutes of moderate-intensity aerobic activity per week to reduce obesity-related risks (5).

Recently, there has been growing interest in natural compounds as complementary therapies for metabolic disorders. Curcumin, the main bioactive component of turmeric, has demonstrated anti-inflammatory and antioxidant properties and may improve lipid profiles and liver function (6). The curcumin supplementation combined with resistance training did not significantly affect lipid profiles in obese women(7), while some studies found no significant changes in metabolic markers following curcumin supplementation in women with polycystic ovary syndrome(8). These discrepancies may be related to differences in study design, dosage, intervention duration, and participant characteristics.

Bariatric surgery is one of the most effective treatments for severe obesity, leading to substantial weight loss and metabolic improvement. Nevertheless, some patients may experience weight regain or recurrence of metabolic complications over time (9).Despite the known benefits of exercise and curcumin, limited evidence exists regarding their combined effects on metabolic and liver function markers in patients after bariatric surgery. Therefore, this study aimed to investigate the effects of exercise training combined with nanocurcumin supplementation on metabolic and hepatic indicators in this population.

Material and methods

This study was a quasi-experimental, randomized, single-blind, placebo-controlled pre-test–post-test clinical trial conducted between April and September 2024 at the Minimally Invasive Surgery Research Center of Iran University of Medical Sciences, Tehran. Participants were recruited using convenience sampling from patients attending their first postoperative follow-up visit one week after bariatric surgery (gastric sleeve or gastric bypass). Eligibility was confirmed by a gastrointestinal surgeon based on predefined inclusion criteria. Sample size was calculated a priori using G*Power software (version 3.1.9.7) for a repeated-measures design with two independent groups. Based on previous studies in post-bariatric surgery populations, which have reported moderate-to-large effects of exercise and nutritional supplementation on metabolic outcomes, an anticipated moderate-to-large effect size (Cohen's $f= 0.30$) was considered appropriate. A statistical power of 80% and a significance level of $\alpha= 0.05$ (two-tailed) were applied. The analysis for a repeated-measures ANOVA / MANCOVA design indicated a minimum required sample size of approximately 50 participants to detect a group × time interaction effect. To account for potential attrition (10-15%), particularly relevant in post-surgical cohorts due to follow-up loss or medical complications, the final sample size was increased to 60 participants (10).Participants were randomly allocated into two equal groups:

Exercise training+ nanocurcumin supplementation (n= 30; 15 males, 15 females)
Exercise training+ placebo (n= 30; 15 males, 15 females)
Randomization was performed using a computer-generated sequence with concealed allocation.
The study was conducted in a single-blind manner, in which participants were unaware of their group assignment. Participants were informed about study procedures, risks, and their right to withdraw at any time.

Inclusion criteria

BMI> 40 ‹Age 35-45 years ‹History of bariatric surgery ‹No structured exercise in the past 6 months ‹No smoking, alcohol consumption, or medications affecting metabolism ‹No major musculoskeletal, renal, hepatic, pulmonary, or gastrointestinal diseases.

Exclusion criteria

Pregnancy ‹Revision (second) bariatric surgery ‹Use of medications affecting metabolism (e.g., metformin, levothyroxine, corticosteroids, topiramate) within 1 month prior to enrollment ‹Missing more than two exercise or supplementation sessions ‹Known hypersensitivity to curcumin ‹Withdrawal of consent.

Training protocol

The exercise intervention lasted 6 weeks with 3 supervised sessions per week on alternate days. Each session included:
Warm-up: 10 minutes (dynamic stretching and slow walking)
Main exercise: combined aerobic and resistance training (details provided in table 1)
Cool-down: 10 minutes (static stretching and deep breathing) (11).
All sessions were supervised by a certified trainer and the researcher.

Supplementation protocol

The intervention supplement was Sina Curcumin (Exir Nano Sina, National ID: 10103994515), a nanotechnology-based formulation approved under Iranian National Standard No. 21145.

Participants in the intervention group received 40 mg nanocurcumin twice daily with meals for 6 weeks (12).The control group received identical placebo capsules. To minimize potential confounding effects, participants were instructed to maintain their usual dietary habits, medication use, sleep patterns, and physical activity levels outside the prescribed training program throughout the study period. Participants with major changes in medication or clinical condition during the intervention were excluded.

Measurements

Anthropometric and biochemical measurements were conducted before and after the intervention. Body weight and height were measured using a Seca medical scale (Germany) with 0.1 kg and 0.1 cm accuracy. Body mass index (BMI) was calculated as Weight /height (kg /m^2)(2) . Body fat percentage was assessed using the in Body 570 analyzer. Blood samples (10 cc) were collected from the antecubital vein between 8:00 and 9:00 a.m. after 12 hours of fasting, 48 hours before and after the intervention. Plasma was separated by centrifugation (4000 rpm, Routine 28, Behdad Co., Iran) and stored at -80°C until analysis.

Biochemical variables were measured using Pars Peyvand kits with the following sensitivities:
Triglycerides: 5 mg/dL - (LDL, HDL, Albumin) : 0.2 mg/dL - (AST, ALT) : 2 U/L
Ferritin: 0.2 ng/mL

Statistical analysis

Data were expressed as mean ± standard deviation. Normality was assessed using the Shapiro–Wilk test. Homogeneity of variance was tested using Levene’s test, and homogeneity of covariance matrices was assessed using Box’s M test. Multicollinearity and homogeneity of regression slopes were also evaluated.

Multivariate analysis of covariance (MANCOVA) was used to assess between-group differences while controlling for baseline values. Results were reported using Wilks' Lambda, Pillai's Trace, Hotelling's Trace, and Roy's Largest Root, along with F values, significance levels, and partial eta squared (η^2) as effect size indicators.Following a significant multivariate effect, univariate ANCOVA analyses were performed for each dependent variable to identify specific group differences. Interpretation was based on both multivariate and univariate results ($P \leq 0.05$). All analyses were performed using SPSS version 22.

Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants. Ethical approval was granted by the Ethics Committee of Islamic Azad University, East Tehran Branch (IR.IAU.ET.REC.1404.003), and the study was registered in the Iranian Registry of Clinical Trials (IRCT20250420065394N1).

Table 1. Training program

week	Resistance training (with body weight)	Aerobicexercise (brisk walking)	Warm-up (10 min)	Cool down (10 min)	Recovery time
1 Saturday	Squats: 2 sets, 8-10 Reps each Glute Bridge: 2 sets, 8-10 reps each. Wall Push-ups: 2 sets, 6-8 reps each	10 minutes (50-60% maximum heart rate	Dynamic stretching + gentle walking	Stretching Static muscles lower body	2-3 minutes between sets
Monday/	Half Crunch: 2 sets, 8 reps each. Glute Bridge: 2 sets, 8-10 reps each Wall Push-ups: 2 sets, 6-8 reps each	10 minutes 50-60% maximum heart rate	Slow walking + arm movement shoulder	Back and hamstring stretch	2-3 minutes between sets
Wednesday	Squats: 2 sets, 8-10 Reps each. Forward Lunges: 2 sets, 6-8 reps each leg Half Crunch: 2 sets, 8 reps each.	15 minutes 50-60% maximum heart rate	Dynamic stretching + gentle walking	Shoulder and chest stretch	2-3 minutes between sets
2 Saturday Monday Wednesday	Same as week 1 + increase exercise repetitions to 10-12	15 minutes 60% maximum heart rate	Same as the first week	Same as the first week	2-3 minutes between sets
3 Saturday	Squats: 2 sets, 8-10 Reps each. Glute Bridge: 3 sets, 10-12 reps each. Wall Push-ups: 3 sets, 8-10 reps each.	20 minutes 60-65% maximum heart rate	Dynamic stretching + gentle walking	Stretching Static Muscles Lower Body	120-90 seconds between set
Monday	Forward Lunges: 2 sets, 6-8 reps per leg. Half Abdominal Crunch: 3 sets, 10-12 reps per set. Hip Bridge: 3 sets, 10-12 reps per set	20 minutes 60-65% maximum heart rate	Full body stretching + slow walking	Lower back and Hamstring stretch	120-90 seconds between set
Wednesday	Squats: 3 sets, 10-12 reps each. Wall Push-ups: 3 sets, 8-10 reps each. Hip Bridges: 3 sets, 10-12 reps each.	25 minutes 60-65% Maximum heart rate	Dynamic stretching	Back and abdominal muscles stretch	90-120 seconds between set
4 Saturday Monday Wednesday	Increase the number of repetitions to 12-15.				90-120 seconds between set
5 Saturday	Squats: 3 sets, 12-15 reps each. Knee Push-Ups: 3 sets, 8-10 reps each. Full Abdominal Crunch: 3 sets, 12-15 reps each.	25 minutes 65-70% Maximum heart rate	Dynamic Stretches + Trunk Rotation	Lower body Stretching and deep breathing	60-90 Seconds between set
Monday/	Forward lunges: 3 sets, 8-10 reps per leg. Hip bridges: 3 sets, 12-15 reps per set. Full abdominal crunches: 3 sets, 12-15 reps per set.	30 minutes 65-70% Maximum heart rate	Dynamic stretching + gentle walking	Abdominal And lower back Muscle stretching	60-90 Seconds between set
Wednesday	Same as the Exercises above, maintaining high intensity.	30 minutes 65-70% Maximum heart rate	As in previous days	Back muscle Stretching and Deep breathing	60-90 Seconds between set
6 Saturday Monday Wednesday	Same as the fifth week				60-90 Seconds between set

Participants were informed about the study objectives, procedures, potential risks, and their right to withdraw at any time without penalty.

Results

A total of 60 patients who had undergone bariatric surgery completed the study and were included in the final analysis. The mean (±SD) age of participants was 40.27 (± 5.0) years, with equal gender distribution (50% male and 50% female). Anthropometric characteristics are presented in table 2.

The results of the Shapiro–Wilk test confirmed normal distribution of all variables ($P > 0.05$). Homogeneity of variances and covariance matrices were verified using Levene's test and Box's M test, respectively, indicating that the assumptions for multivariate analysis were satisfied.

Baseline comparisons between groups showed no significant differences in anthropometric or biochemical variables ($P > 0.05$), confirming successful randomization and group equivalence prior to the intervention.

Follow-up univariate ANCOVA analyses demonstrated significant between-group differences after the intervention. Compared with the placebo group, the exercise + nanocurcumin group showed significant reductions in LDL ($P= 0.001$), triglycerides ($P= 0.001$), body fat percentage ($P= 0.004$), ferritin ($P= 0.002$), ALT ($P= 0.017$), and AST ($P= 0.004$). In contrast, high-density lipoprotein (HDL) ($P= 0.023$) and serum albumin levels ($P= 0.017$) were significantly increased in the intervention group. Changes in biochemical variables are presented in table 3.

Discussion

The present study demonstrated that selected exercise training combined with nanocurcumin supplementation significantly improved metabolic and inflammatory markers in patients after bariatric surgery. Specifically, significant reductions were observed in LDL, triglycerides, body fat percentage, ferritin, and liver enzymes (ALT and AST), along with an increase in HDL and serum albumin.

The improvement in lipid profile is consistent with previous studies reporting beneficial effects of exercise and nutritional interventions following bariatric surgery.

Table 2. Baseline and post-intervention anthropometric characteristics

Variable	Time	Exercise + Placebo	Exercise+ Nano curcumin
Weight (kg)	Pre	117.55 (± 5.72)	119.15 (± 6.89)
	Post	107.99(± 5.75)	105.17 (± 5.59)
Height (cm)	Pre	160(± 2.14)	162(± 4.04)
	Post	160 (± 2.14)	162. (± 4.04)
BMI (kg/m²)	Pre	45.77(± 2.13)	45.34(± 1.72)
	Post	42.21 (± 2.19)	40.19 (± 1.94)

Table3. Changes in biochemical variables (Mean ± SD)

Variable	Time	Nano curcumin + Exercise	Placebo + Exercise	*P*-value	Effect size (η^2)
LDL (mg/dL)	Pre	181.87 (± 5.15)	183.87 (± 6.15)	0.177	0.418
	Post	170.77 (± 4.88)	177.97(± 6.15)	0.001	
HDL (mg/dL)	Pre	50.24(± 4.29)	53.30(± 5.41)	0.403	0.101
	Post	62.37(± 2.93)	61.27(± 5.06)	0.023	
TG (mg/dL)	Pre	266.10 (± 1.34)	268.10(± 1.06)	0.519	0.461
	Post	252.70(± 1.13)	261.23(± 1.03)	0.001	
Body fat (%)	Pre	40.33(± 3.10)	41.08(± 2.47)	0.358	0.160
	Post	34.91 (± 3.34)	37.20(± 2.41)	0.004	
Ferritin (ng/mL)	Pre	37.04 (± 3.41)	37.25(± 3.52)	0.817	0.280
	Post	33.61 (± 3.77)	35.01(± 2.31)	0.002	
Albumin (g/dL)	Pre	4.61(± 0.36)	4.70(± 0.35)	0.742	0.111
	Post	4.99 (± 0.28)	4.81 (± 0.42)	0.017	
ALT (U/L)	Pre	38.92 (± 2.44)	37.61(± 1.37)	0.113	0.111
	Post	31.15(± 3.17)	32.83(± 1.87)	0.017	
AST (U/L)	Pre	39.52 (± 1.84)	40.00(± 2.79)	0.434	0.154
	Post	33.93 (± 2.83)	36.32(± 2.88)	0.004	

For instance, Sabooni et al. (2025) and Rakab et al. (2025) also reported favorable changes in lipid and anthropometric indices following protein and probiotic supplementation(13،14) . These findings collectively suggest that adjunct lifestyle and nutritional strategies may enhance metabolic recovery after bariatric procedures.

From a physiological perspective, the observed lipid improvements may be attributed to exercise-induced activation of lipoprotein lipase (LPL), which facilitates triglyceride breakdown and enhances lipid clearance(15). In addition, regular physical activity promotes fatty acid oxidation and improves mitochondrial function, thereby contributing to improved lipid metabolism and reduced atherogenic lipoproteins(2). Also exercise training may increase angiogenesis and blood supply and reduce hypoxia and associated inflammation in adipose tissue (16).

Nanocurcumin may have further enhanced these effects through its anti-inflammatory and antioxidant properties. By reducing systemic inflammation and oxidative stress, curcumin may positively influence lipid metabolism and metabolic homeostasis (17). Therefore, the combined application of exercise and nanocurcumin may exert synergistic effects on cardiometabolic risk factors.

The reduction in body fat percentage observed in the present study is in line with previous evidence indicating that structured exercise programs after bariatric surgery improve body composition(16,14). These effects are likely mediated by increased energy expenditure, enhanced lipid oxidation, and metabolic adaptations in skeletal muscle (11,15). Meta-analysis studies reported that curcumin consumption can reduce leptin and increase adiponectin levels, thereby modulating appetite and energy homeostasis(6). On the other hand, overproduction of the hormone adiponectin can increase glucose utilization and fatty acid oxidation by activating AMPK, which in turn facilitates weight loss(7).

A significant reduction in serum ferritin was also observed. Since ferritin is both an iron storage protein and an acute-phase inflammatory marker (18), its reduction may reflect improved iron turnover and a decrease in systemic inflammation. Exercise-induced alterations in iron metabolism (intravascular hemolysis), along with the anti-inflammatory effects of curcumin, may have contributed to this outcome.

The increase in serum albumin may be explained by improved protein metabolism, enhanced hepatic synthetic function, and changes in plasma volume distribution associated with physical activity(19). Additionally, the reduction in inflammatory status following weight loss and curcumin supplementation may have supported higher circulating albumin levels.

Furthermore, the reduction in ALT and AST levels suggests improved liver function. This may be related to decrease hepatic fat accumulation, reduced oxidative stress, and attenuation of inflammatory pathways. These findings are consistent with previous studies indicating that combined lifestyle interventions after bariatric surgery can improve liver enzyme profiles (20,21).Some discrepancies with previous studies may be due to differences in exercise protocols, intervention duration, supplement dosage, and participant characteristics, all of which can influence metabolic and inflammatory responses.

One limitation of this study was the lack of separate exercise-only or supplementation-only groups, preventing a full assessment of the independent effects of exercise training and nanocurcumin supplementation; however, the use of identical exercise protocols in both groups allowed for better control of the training effect and enabled the comparison of the additive effect of nanocurcumin**.** Baseline comparability between groups for key anthropometric and biochemical variables was confirmed. However, certain variables such as type of bariatric surgery (sleeve vs. bypass), time since surgery, dietary intake, stress levels, sleep quality, and socioeconomic status were not strictly controlled and reflect real-world clinical conditions.

Conclusion

The present study demonstrates that selected exercise training combined with nanocurcumin supplementation has beneficial effects on lipid profile, body composition, liver enzymes, iron-related markers, and serum albumin in patients after bariatric surgery. These findings suggest that this combined intervention may serve as an effective non-pharmacological strategy to improve cardiometabolic and inflammatory status in this population. Therefore, this combined approach may be recommended as a supportive intervention, provided it is prescribed and monitored by a physician. However further studies with longer follow-up periods and larger sample sizes are recommended to confirm these findings and clarify the long-term effects of this combined intervention.

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Conflict of Interest

The authors declare no conflicts of interest.

Authors' contributions

All authors contributed significantly to the development of this manuscript. MR.G: implemented the exercise protocol and conducted the study on the participants, M.H: designed the study and wrote the manuscript. SH.SHSH: proper administration of the supplement and collected the data as well as supervised interpreting the results. SH.SHSH Contributed to data extraction and provided feedback on the report. Sh.RM: contributed to data analysis. All authors participated in drafting the manuscript, reviewed the final version, and approved it for submission.

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