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Effects of combined GLP-1 receptor agonist therapy and exercise on body composition in individuals with obesity: a systematic review

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Abstract

Background. Obesity management necessitates a multidisciplinary approach. Combining tailored exercise therapy with pharmacotherapy utilizing GLP-1 receptor agonists is emerging as a prominent interventional strategy.

Aim. This systematic review evaluates the efficacy of combining GLP-1 agonists with exercise therapy versus monotherapies. The focus was on maximum weight reduction and the prevention of adverse musculoskeletal effects following treatment cessation, specifically muscle mass loss and reduced bone mineral density (BMD).

Materials and methods. Conducted according to PRISMA 2020 guidelines, the review included English-language randomized controlled trials (RCTs) published after 2016, retrieved from PubMed and PEDro databases.

Results. Three publications based on a single cohort (n=215) were included. Combination therapy was the most effective modality, yielding the greatest weight reduction, most favorable cardiometabolic improvements, and highest subjective quality of life. Furthermore, during a 52-week post-treatment follow-up, it demonstrated the greatest efficacy in mitigating weight regain. Crucially, unlike isolated pharmacotherapy, combination therapy increased BMD in the evaluated regions.

Conclusions. Combination therapy (GLP-1 agonists and exercise) is the most effective long-term obesity treatment. It highlights the necessity of tailored exercise programming integrating resistance and aerobic training to preserve musculoskeletal integrity and sustain beneficial metabolic adaptations.

Keywords: obesity, GLP-1 receptor agonists, exercise therapy, systematic review, bone mineral density (BMD), liraglutide.

Introduction

Obesity, defined by the World Health Organization (WHO) as excessive fat accumulation assessed using the Body Mass Index (BMI) when it equals or exceeds 30 kg/m2 (overweight, according to WHO, falls within the range of 25-29.9 kg/m2) (2), is a problem affecting 1/8 of the global population in 2022, with an upward trend. There are three classes of obesity based on BMI values: 30-34.9 kg/m2 (class I obesity), 35-39.9 kg/m2 (class II obesity), and class III obesity (BMI greater than or equal to 40 kg/m2) (3). Obesity poses a tremendous civilizational threat; its presence increases the risk of developing type 2 diabetes, arterial hypertension, chronic kidney disease, and osteoarthritis. Ultimately, it elevates the risk of premature death and decreases the daily quality of life for patients (4) (5).

Consequently, the treatment of overweight and obesity presents a major challenge for modern medicine, requiring a holistic approach encompassing pharmacology, dietetics, and physiotherapy (6). Appropriately guided physical activity, combined with dietary habit modifications, demonstrates a positive impact on obesity treatment. In December 2025, the WHO issued recommendations regarding the introduction of GLP-1 (glucagon-like peptide-1) receptor agonists in obesity therapy. These drugs are responsible for reducing blood sugar levels

and stimulating insulin secretion, which ultimately has a positive effect on weight reduction by decreasing appetite and increasing the feeling of (4). The administration of GLP-1 medications has been shown to reduce CRP (C-reactive protein) levels, a primary biomarker of systemic inflammation, which results from:

- anti-inflammatory effects on bodily tissues,
- weight reduction during GLP-1RA therapy (7).

The GLP-1 drug class includes the following substances: liraglutide, semaglutide, and dulaglutide (8). The decision to initiate therapy with GLP-1 receptor agonists must be made by a physician and conducted under their continuous supervision to ensure safe dosing, monitor efficacy, and avoid adverse reactions. The main side effects associated with the aforementioned drugs include a decrease in muscle and bone mass, which may adversely affect physical functioning and increase the risk of conditions such as osteoporosis (8). In recent years, clinical studies have demonstrated that GLP-1 receptor agonists (GLP-1RAs) and their analogues can significantly improve bone metabolism in diabetic patients by promoting osteoblast differentiation, thus playing a role in countering diabetic osteoporosis (8). Simultaneously, it should be noted that substantial weight loss also causes a decline in bone mass, leading to an increased risk of fractures due to reduced bone mineral density (BMD) (9). A decrease in the BMD index has been demonstrated not only in studies involving older adults but also in young individuals with obesity (10) and without it (11). This highlights the need for properly planned obesity therapy that focuses not only on short-term effects but also emphasizes the necessity of considering the long-term consequences of treatment, namely a potential significant deterioration in the quality of life if managed inadequately (9).

The use of GLP-1 agonists results in weight loss; however, the most significant impact is achieved through combined therapy utilizing pharmacotherapy alongside appropriately guided physical activity (according to the WHO, 150 minutes/week of physical activity serves a preventive purpose, whereas for weight reduction-focused activity, this increases to approximately 200-300 minutes/week) (12).

To conduct effective obesity physiotherapy, the following conditions must be met: physical activity should consist of general conditioning aerobic exercises aimed at increasing the expenditure of energy stored in adipose tissue. Aerobic physical activity enables the activation of a chain of biochemical processes that utilize fatty acids, leading to a reduction in the amount

of stored adipose tissue (13). Aerobic exercises are characterized by moderate or even low intensity while demonstrating efficient oxygen consumption by the working muscles (including muscles responsible for cardiovascular system function), and the ability to utilize biomechanical chains, engaging large muscle groups in continuous work during prescribed exercises. They facilitate exertion that promotes a therapeutically valuable phenomenon of building cardiopulmonary endurance. This suggests that appropriately utilized aerobic exercises, tailored to the patient's physical capabilities and exercise tolerance, constitute a crucial element determining the efficacy of the therapy (13).

The aim of this systematic review is to address the existing gap in the scientific literature regarding obesity treatment and to evaluate the effectiveness of combined therapy pharmacotherapy integrated with physiotherapy as the most optimal form of obesity management.

Methodology

This systematic review was conducted and reported based on selected PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (14).

Only articles evaluating the efficacy of combined therapy utilizing GLP-1 receptor agonists and physiotherapy in the form of exercise training for obesity management were eligible for inclusion in this systematic review. The inclusion criteria were as follows: controlled trials, randomized controlled trials (RCTs), publications with available full text, articles published in peer-reviewed journals, publications written exclusively in English, and a publication date after 2016. Articles discussing therapies conducted on animal models or pediatric populations were excluded. Furthermore, review articles, conference reports, statistical reviews, and case studies were excluded from the review. The methodological quality of the randomized clinical trials and the timeframe of measurements assessing treatment efficacy (the time from the completion of therapy to the follow-up measurement) did not constitute inclusion criteria for this review.

The following electronic databases were utilized for the literature search: PubMed and PEDro, during the period from May 1, 2026, to June 30, 2026. The retrieved literature was subsequently analyzed.

Search results

Following the application of appropriate keyword-based search queries to the PubMed and PEDro electronic databases, and the implementation of filters regarding language and publication date, a total of 117 articles were retrieved.

The results of the literature search and selection process, conducted in accordance with the PRISMA guidelines, are presented in Figure 1.

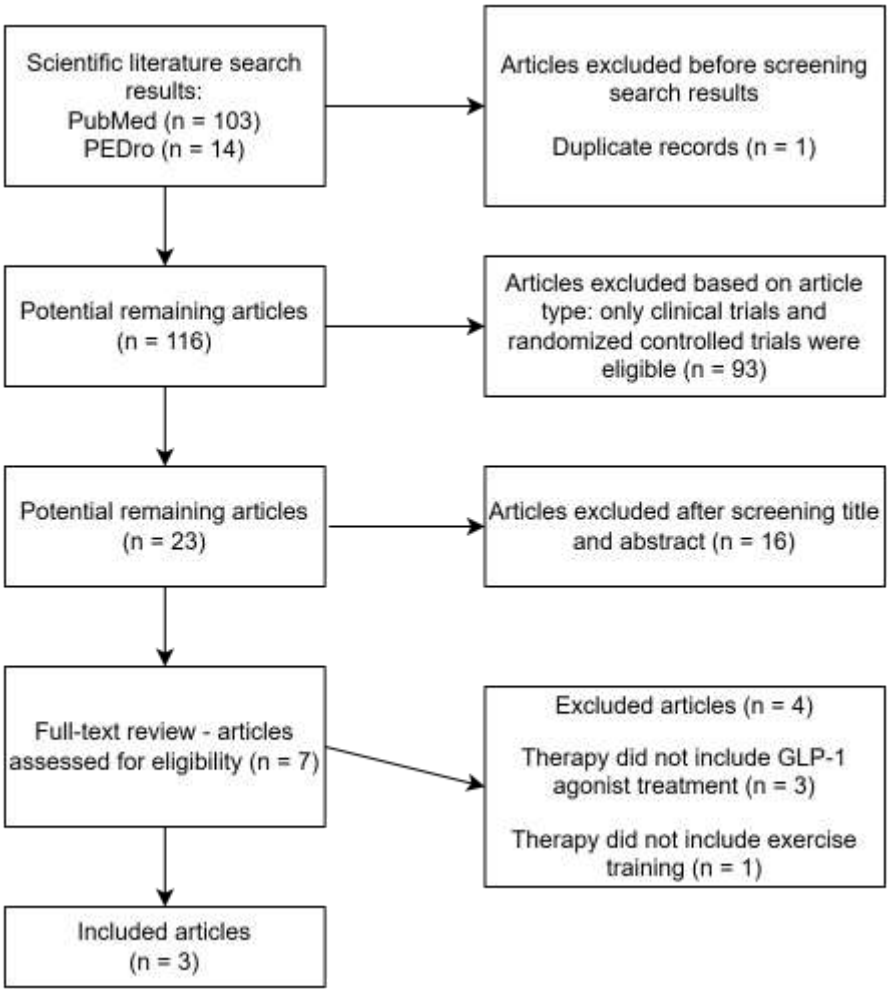

Figure 1. Literature search and selection

Publication	Aim of the study	Materials and Methods	Results	Conclusions
Sandsdal et al., 2023, Denmark (15)	To demonstrate that the combined therapy of regular physical activity and liraglutide treatment is a more effective method for reducing cardiometabolic risk than either of these interventions applied separately.	The study cohort initiated a low-calorie diet (800 kcal/day) (n = 215); age 42±12 years, BMI 37±2.9 kg/m2. Following the completion of the low-calorie diet, the remaining participants (n = 195) were randomly assigned to one of four treatment groups: ● placebo ● moderate-to-vigorous physical activity (> 150 minutes/week of moderate-intensity aerobic exercise or > 75 minutes/week of vigorous-intensity exercise, or an equivalent combination of physical activity forms) ● pharmacotherapy with liraglutide administered at a dose of 3.0 mg/day ● combined therapy of liraglutide and physical activity as described above	Following the completion of the low-calorie diet, the following results were obtained: ● a reduction in the number of individuals with arterial hypertension (n = 63) (33% of subjects) ● a reduction in the number of individuals with prediabetes (n = 30) (15% of subjects) ● a decrease in mean chest circumference by approximately 10.6 cm ● a decrease in mean systolic blood pressure by approximately 10 mmHg ● a decrease in mean diastolic blood pressure by approximately 7 mmHg ● a decrease in HDL level by approximately 0.2 mmol/L ● a decrease in triglyceride level by	It was demonstrated that the combined therapy led to improvements in all analyzed parameters compared to placebo, potentially providing the greatest reduction in the risk of future cardiometabolic diseases in adults with obesity.

		Measurements were obtained from the subjects at the following time points: prior to the initiation of the diet, upon completion of the diet, and 52 weeks post-diet in comparison to the placebo group. Baseline characteristics prior to the intervention were as follows: ● age: 42±12 ● sex: 80 males / 135 females ● number of individuals with arterial hypertension (n = 134) (62% of subjects) ● number of individuals with prediabetes (n = 96) (45% of subjects) ● number of individuals receiving antihypertensive pharmacotherapy (n = 26) ● number of individuals receiving lipid-lowering pharmacotherapy (n = 14) ● mean chest circumference: 110.6±11.3 (cm) ● systolic blood pressure: 132±16 (mmHg)	approximately 0.4 mmol/L ● a decrease in fasting blood glucose level by approximately 0.5 mmol/L ● a decrease in HOMA-IR value by approximately 0.44 ● a decrease in MetS-Z score by approximately 0.52 ● a reduction in body weight by approximately 13.1 kg ● a reduction in BMI by approximately 4.4 kg/m² ● a reduction in total body fat percentage by approximately 2.4 percentage points ● a reduction in android fat percentage by approximately 2.9 percentage points, including: in females by approx. 2.0, in males by approx. 4.6 ● a reduction in gynoid fat percentage by approximately 1.8 percentage points, including: in females by approx. 1.5, in males by approx. 2.3	

		• diastolic blood pressure: 86±9 (mmHg) • HDL level: 1.3±0.3 (mmol/L) • triglyceride level: 1.5±1.0 (mmol/L) • fasting blood glucose level: 5.6±0.6 (mmol/L) • HOMA-IR: 3.9±2.4 • MetS-Z: 0.57±0.59 • body weight: 109.7±14.9 (kg) • body fat percentage: 41.0±6.1 (%) • android fat percentage: 44.3±4.7 (%), including: females – 46.0±4.1, males – 41.3±4.2 • gynoid fat percentage: 40.7±7.3 (%), including: females – 45.0±4.3, males – 32.9±4.6 • android-to-gynoid fat ratio: 1.11±0.16 • hsCRP: 3.8 (range 1.6 to 8.4)	• a decrease in the android-to-gynoid fat ratio by approximately 0.03 • a decrease in hsCRP level by approximately 0.68 Follow-up measurements were conducted after 52 weeks. In the combined therapy group (n = 29), the following changes were observed (compared to the measurements taken upon completion of the low-calorie diet): • a reduction in the number of individuals with arterial hypertension (n = 7) (24% of subjects in the group) • a reduction in the number of individuals with prediabetes (n = 4) (14% of subjects in the group) • a decrease in mean chest circumference by approximately 6.3 cm • an increase in mean systolic blood pressure by approximately 1.2 mmHg • a decrease in mean diastolic blood	

			pressure by approximately 0.1 mmHg ● an increase in HDL level by approximately 0.31 mmol/L ● an increase in triglyceride level by approximately 0.1 mmol/L ● a decrease in fasting blood glucose level by approximately 0.2 mmol/L ● an increase in HOMA-IR value by approximately 1.02 ● a decrease in MetS-Z score by approximately 0.39 ● a reduction in body weight by approximately 6.0 kg ● a reduction in total body fat percentage by approximately 3.7 percentage points ● a reduction in android fat percentage by approximately 6.1 percentage points, including: in females by approx. 6.4, in males by approx. 5.4 ● a reduction in gynoid fat percentage by approximately 3.8 percentage points,	

			including: in females by approx. 3.8, in males by approx. 3.8 ● a decrease in the android-to-gynoid fat ratio by approximately 0.06 ● an increase in hsCRP level by approximately 0.48 This is in comparison to the placebo group, which experienced weight regain (an increase ranging from 3.4 to 8.7 kg) and an increase in body fat percentage (ranging from a 1% decrease to a 1.7% increase—averaging an increase of approx. 0.3%). In the groups subjected to liraglutide monotherapy or exercise training alone, positive changes in body composition parameters were maintained, but not as effectively as in the combined therapy.	
Simon Birk Kjær Jensen et.,	Analysis of bone health at clinically	The study cohort initiated a low-calorie diet (800 kcal/day) (n = 215); age 42±12 years, BMI	The following results were obtained:	It was demonstrated that the combined

2024, Denmark (9)	relevant sites (hip, spine, forearm) following diet-induced weight loss, and subsequently after a one-year pharmacological intervention (liraglutide), exercise training, or a combination of both.	37±2.9 kg/m². Following the completion of the low-calorie diet, the remaining participants (n = 195) were randomly assigned to one of four treatment groups: ● placebo ● moderate-to-vigorous physical activity (> 150 minutes/week of moderate-intensity aerobic exercise or > 75 minutes/week of vigorous-intensity exercise, or an equivalent combination of physical activity forms) ● pharmacotherapy with liraglutide administered at a dose of 3.0 mg/day ● combined therapy of liraglutide and physical activity as described above Bone mineral density (BMD, expressed in grams per square centimeter) measurements were obtained from the subjects. Measurements were performed using densitometry, in a fasting state, separately for the left hip and the lumbar spine	In the comparison of groups following the completion of the therapy, the greatest efficacy in body weight reduction was demonstrated in the combined therapy group (n = 49): a mean decrease of 16.9 kg, compared to 7.0 kg in the placebo group and 13.7 kg in the liraglutide therapy group. It was shown that the introduction of combined therapy provides fracture prevention in vulnerable areas (hip joints and spine). The exclusive use of liraglutide resulted in a decrease in BMD in the hip region. In the group receiving combined therapy, body weight reduction was characterized by a loss of adipose tissue and a concomitant increase in muscle mass, whereas the group receiving exclusive liraglutide therapy exhibited solely a reduction in adipose tissue. The aforementioned data are based on the study by Rasmus M. Sandsdal et al., discussed	therapy of exercise and liraglutide pharmacotherapy enables the greatest reduction in body weight while simultaneously preserving musculoskeletal health.

		(L1–L4). BMD was also evaluated at the distal forearm (1/3 of the radius and ulna length) and the whole body. Changes in bone mineral density (BMD) were calculated for the period from the initiation of the low-calorie diet to one year post-randomization, at the following time points: upon completion of the diet, and at 4, 13, 26, 39, and 52 weeks after the initiation of the randomized therapy.	in the first row.	
Simon Birk Kjær Jensen et., 2024, Denmark (16)	Analysis of changes in body weight and body fat levels in subjects, conducted 104 weeks after the randomized assignment of participants to four forms of obesity therapy, with the aim of demonstrating the	Subjects from the study by Rasmus M. Sandsdal et al. (2023) were utilized. The study cohort initiated a low-calorie diet (800 kcal/day) (n = 215); age 42±12 years, BMI 37±2.9 kg/m². Following the completion of the low-calorie diet, the remaining participants (n = 195) were randomly assigned to one of four treatment groups: ● placebo	The following results were obtained: In subjects who received liraglutide exclusively, a net weight gain (calculated from the weight loss at week 52, i.e., the end of treatment) of 8.7 kg was observed. In subjects undergoing combined therapy, the net weight	It was demonstrated that the combined therapy of pharmacotherapy and supervised physical activity has a greater potential for body weight maintenance and body fat reduction

	most effective long-term treatment.	• moderate-to-vigorous physical activity (> 150 minutes/week of moderate-intensity aerobic exercise or > 75 minutes/week of vigorous-intensity exercise, or an equivalent combination of physical activity forms) • pharmacotherapy with liraglutide administered at a dose of 3.0 mg/day • combined therapy of liraglutide and physical activity as described above Measurements of the following parameters were performed: Body weight, chest and waist circumferences, glucose levels, and blood pressure were measured prior to the initiation of the diet (week -8), at the week of randomization (week 0), and at weeks: 4, 13, 26, 39, 52, as well as one year following the completion of the therapy: week 104. Measurements of body fat content, HbA1c, lipid levels, and subjective quality of life were	gain was 3.5 kg; this result was 5.1 kg lower than in the liraglutide monotherapy group (P = 0.040) and 4.1 kg lower than in the placebo group (P = 0.14). It was demonstrated that participants who had previously engaged exclusively in supervised exercise gained 3.6 kg during the post-treatment phase. Consequently, the post-treatment body weight increase was 6.0 kg (2.1-10.0) greater following liraglutide treatment compared to exercise alone, and 2.5 kg (-1.5 to 6.5) greater compared to the combined treatment.	compared to subjects who received pharmacotherapy exclusively.

		conducted at weeks: -8, 0, 52, and 104.	From randomization to one year post-treatment (weeks 0–104), participants who had previously received combined therapy demonstrated a decrease in body fat percentage of 2.3 percentage points compared to participants who had previously received liraglutide exclusively (P = 0.026). One year following the completion of treatment, participants who had engaged exclusively in physical exercise or utilized it in combination with liraglutide reported the highest levels of moderate-to-vigorous physical activity. Among individuals undergoing exclusive liraglutide therapy without physical activity, the majority demonstrated an absence of any activity: the median was 150 min/week for the placebo group, 240 min/week for the exercise group, 30 min/week for the liraglutide group, and 225 min/week for the combined therapy group,	

			respectively. Physical activity measurements confirmed the previously demonstrated higher levels of physical activity in the exercise groups.	

Following the selection process conducted in accordance with PRISMA guidelines, 3 articles were identified and subjected to detailed analysis. It is important to emphasize that all three articles are based on the same patient cohort (the patient group from the study by Sandsdal et al. (15); however, they discuss different aspects of functioning. The first article investigates the most effective form of therapy aiming to maintain the lowest possible cardiometabolic risk for the organism (15). The second study examines the same patient group (n = 215), analyzing selected therapeutic methods in terms of minimizing the risk of musculoskeletal diseases while simultaneously sustaining patient weight loss (9). The third study investigates the same patient cohort over an additional 52-week period following the completion of the initial therapy, seeking the most effective long-term treatment by evaluating body weight and changes in body fat levels (16).

Each of the aforementioned articles demonstrates that combined therapy (kinesiotherapy combined with liraglutide) is a more effective form of obesity treatment compared to both the placebo group and the groups assigned to monotherapy, successfully preventing weight regain (16). Furthermore, it was shown to maintain bone mineral density (BMD) at the highest level in fracture-prone areas (9) compared to monotherapy, where BMD actually decreased in the case of liraglutide alone (9). In the research conducted by Sandsdal et al., the combined therapy exhibited the most preventive character regarding the risk of cardiometabolic diseases, achieving greater reductions in the examined parameters relative to both the placebo group and the monotherapy groups (15).

Discussion

The analysis confirmed that monotherapy with GLP-1 agonists (e.g., liraglutide) is effective in reducing body weight; however, as a monotherapy, it can lead to additional side effects- namely, the loss of muscle and bone mass, as well as a "rebound" effect upon discontinuation of the medication. The analyzed studies indicate that combined therapy incorporating kinesiotherapy represents the optimally selected obesity treatment program. In addition to preventing the negative consequences of pharmacotherapy alone, it further supports musculoskeletal prophylaxis, demonstrating an improvement in subjective quality of life. The loss of bone mineral density (BMD) observed in the case of monotherapy carries the risk of an increased number of fractures in the areas examined by Jensen (9) (i.e., hip joints, spine, forearm). For

instance, a femoral head fracture may entail prolonged physiotherapeutic management, which should be accessible to the patient, conducted regularly, reliably, and in accordance with current medical knowledge—a standard that is not guaranteed in terms of full availability due to the burdens on the healthcare system (17).

Contemporary medicine offers other forms of obesity treatment besides pharmacotherapy, such as bariatric surgery (e.g., gastric resection, gastric bypass). Although these have been evaluated for efficacy and safety in clinical trials (18), they remain an aggressive form of therapy, carrying potential complications characteristic of other surgical procedures performed in the gastric region, and they impose radical lifestyle changes regarding dietary habits. They naturally remain available treatment options; however, patients must be informed of the potential risks associated with the surgical procedure, and it should be considered one of the final viable options in the management of obesity.

Appropriately conducted physiotherapy will serve as a key element in the prevention of musculoskeletal diseases in individuals with obesity, who are susceptible to numerous overload lesions and fractures in both proximal and peripheral joints (19). To conduct effective obesity physiotherapy, it is necessary to consider previously mentioned data indicating that physical activity should consist of general conditioning aerobic exercises aimed at increasing the expenditure of energy stored in adipose tissue (13). From a physiotherapeutic perspective, the significant role of resistance training in therapy is highlighted. The application of isolated exercises on specialized equipment, preceded by objective diagnostic tests and muscle strength measurements, allows for precise load dosing. This approach enables safe stimulation and muscle strength development while simultaneously offloading critical structures (e.g., by building the strength of postural muscles). During ongoing pharmacological therapy, this ensures the reduction of adipose tissue without concomitant loss of muscle tissue (20).

Obesity prophylaxis should also incorporate social factors, such as family support, the desire for recovery, and the planning of dietary modifications that will be accessible to patients while simultaneously encouraging them to adopt these changes. Although these may not be the primary factors, a holistic approach dictates their inclusion if the goal is to achieve optimal results in obesity prevention (21).

The primary limitation of this systematic review is the small number of included studies, indicating the necessity to expand research efforts regarding the use of GLP-1 analogues. These

medications have become a massive source of patient interest regarding the pharmacological potential for weight reduction, while simultaneously representing a relatively novel topic in contemporary science. Consequently, the conducted systematic review highlights another limitation, as the measurements in all discussed articles were performed on a single patient cohort (n = 215). Although individual studies highlighted different clinically significant parameters, this underscores the need to conduct research on similar forms of obesity therapy across other study groups (diverse populations).

The systematic review also highlights the need for research evaluating and providing a detailed comparison of the efficacy of various forms of kinesiotherapy combined with pharmacotherapy. Such research would aim to establish guidelines for physiotherapeutic management-specifically, whether interventions should be directed more toward resistance training, whether the role of aerobic training should be emphasized, or if there is a greater need to utilize endurance training, which would also provide support in reducing additional adipose tissue.

Conclusions

Combined therapy, integrating pharmacotherapy with GLP-1 receptor agonists and kinesiotherapy, constitutes the most effective and safest form of obesity treatment. It provides subjects with the highest subjective quality of life and positively impacts the reduction of adipose tissue, enabling the preservation or development of muscle mass and the maintenance of bone tissue without deficits. Individually tailored and appropriately guided kinesiotherapy is indicated as the foundation for preventing the adverse effects of GLP-1 agonist monotherapy, particularly concerning the prevention of bone mineral density and muscle mass loss. The need for a holistic physiotherapeutic approach in obesity management is emphasized, incorporating aerobic exercises alongside components of resistance and endurance training. Furthermore, it is necessary to highlight the need for further research involving larger study cohorts to confirm the impact of combined therapy in obesity treatment. There is also a need to develop standardized guidelines for the physiotherapeutic community regarding the management of patients with obesity who are supported by this specific form of weight-reducing pharmacotherapy.

Disclosure

Authors' Contributions Statement:

Conceptualization: Paulina Żuk, Patrycja Pogorzelska, Martyna Saleh, Kacper Kulik, Jakub Tomczyszyn

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Software: Paulina Żuk, Patrycja Pogorzelska, Martyna Saleh, Kacper Kulik, Jakub Tomczyszyn

Check:. Paulina Żuk, Patrycja Pogorzelska, Martyna Saleh, Kacper Kulik, Jakub Tomczyszyn

Formal Analysis: Investigation:. Paulina Żuk, Patrycja Pogorzelska, Martyna Saleh, Kacper Kulik, Jakub Tomczyszyn

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