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Impact of Semaglutide on Body Composition and Muscle Mass Maintenance in Patients Undergoing Semaglutide Induced Weight Loss Therapy: A Systematic Review

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Abstract

Background:

Semaglutide, a glucagon-like peptide-1 receptor agonist (GLP-1 RA), has emerged as an effective pharmacological therapy for obesity and type 2 diabetes mellitus due to its potent effects on weight reduction and metabolic regulation. However, increasing concerns have arisen regarding its influence on body composition, particularly the preservation of skeletal muscle mass during rapid weight loss.

Aim:

This systematic review evaluates the impact of semaglutide and related GLP-1-based therapies on body composition, skeletal muscle preservation, metabolic remodeling, and associated risks of sarcopenia during weight reduction therapy.

Materials and methods:

A systematic analysis of clinical, translational, and mechanistic studies was conducted, focusing on semaglutide-induced changes in fat mass, lean body mass, skeletal muscle function, and molecular pathways associated with muscle metabolism.

Results:

Semaglutide consistently promotes substantial fat mass reduction with proportionally smaller decreases in lean mass, generally preserving muscle functionality and improving body composition quality. Mechanistic studies suggest additional protective roles through modulation of SIRT1, mitochondrial efficiency, inflammatory suppression, and anabolic signaling. Nevertheless, specific

populations, particularly older adults, may remain vulnerable to sarcopenic complications without appropriate nutritional and exercise interventions.

Conclusions:

Semaglutide represents a highly effective therapy for obesity with generally favorable effects on body composition. Optimal therapeutic outcomes require integrated resistance training, nutritional support, and individualized monitoring to maximize fat loss while preserving skeletal muscle integrity.

Keywords:

Semaglutide; GLP-1 receptor agonists; obesity; body composition; skeletal muscle mass; lean body mass; sarcopenia; weight reduction therapy; metabolic remodeling; muscle preservation; adipose tissue; type 2 diabetes mellitus

1. Introduction

Semaglutide is a long-acting glucagon-like peptide-1 (GLP-1) receptor agonist, originally developed for the treatment of type 2 diabetes mellitus and currently widely used in obesity therapy. Its mechanism of action is based on mimicking the effects of the endogenous incretin hormone GLP-1, which regulates glucose and energy homeostasis. Through activation of GLP-1 receptors, semaglutide enhances glucose-dependent insulin secretion, suppresses glucagon release, delays gastric emptying, and affects the central nervous system by increasing satiety and reducing appetite. As a result, this leads to significant caloric restriction and sustained body weight reduction.

Beyond its classical antidiabetic and anorectic effects, semaglutide also demonstrates broad pleiotropic properties, including improved insulin sensitivity, reduction of visceral adipose tissue, attenuation of chronic inflammation, and beneficial effects on cardiovascular and metabolic function. Increasing significance is being attributed to its role in qualitative body composition remodeling, where fat mass reduction may occur alongside relative preservation of skeletal muscle function. Owing to these properties, semaglutide currently represents one of the most important tools in modern pharmacotherapy for obesity and metabolic disorders.

2. Material and Methods

This systematic review was conducted to evaluate the effects of semaglutide and GLP-1 receptor agonists on body composition, skeletal muscle preservation, and metabolic remodeling during weight reduction therapy. Literature sources were identified primarily through PubMed and related biomedical databases, focusing on clinical trials, observational studies, mechanistic animal studies, and review articles.

Inclusion criteria comprised:

Studies involving semaglutide or GLP-1/GLP-1-GIP agonists, Evaluation of body composition outcomes, Assessment of lean mass, skeletal muscle mass, or functional muscle parameters, Published peer-reviewed studies.

Exclusion criteria included:

Non-English publications, Studies lacking body composition analysis, Articles focused solely on glycemic control without weight or muscle outcomes.

Selected studies were categorized into thematic domains:

- Effects on body composition,
- Molecular mechanisms of muscle preservation,
- Risks of sarcopenia and preventive strategies,
- Systemic and organ-protective effects.

3. Effects of Semaglutide and GLP-1 Agonists on Body Composition During Weight Reduction

Semaglutide leads to significant body weight reduction primarily through decreasing fat mass, while loss of lean body mass remains proportionally smaller and does not correspond to disproportionate skeletal muscle wasting. Analysis of body composition changes indicates that a substantial portion of weight reduction also includes decreases in visceral adipose tissue and other metabolically burdensome components rather than selective muscle degradation. Despite a slight decline in absolute muscle mass, the relative proportion of muscle to total body mass and functional parameters remain preserved or may even improve.

The action of semaglutide differs from classical caloric restriction by involving distinct modulation of muscle proteomics, improved tissue metabolic efficiency, and favorable body composition remodeling. Therefore, weight loss primarily reflects selective reduction of pathological excess adipose tissue with relative preservation of muscular function, suggesting that GLP-1 therapy does not directly induce intensified myodegeneration but rather promotes metabolic reconstruction of the organism, enhancing mobility and functional performance. [1]

Semaglutide induces substantial body weight reduction through sustained restriction of energy intake, leading primarily to decreases in total and visceral fat mass, while the decline in lean body mass remains relatively smaller than fat loss. Analysis of body composition changes indicates that despite total weight reduction, there is an improvement in the proportion between adipose tissue and lean mass, suggesting beneficial metabolic remodeling rather than selective skeletal muscle degradation. Preservation of the relative proportion of lost mass in relation to total body weight indicates qualitative improvement in body composition despite overall weight reduction.

The dominant process remains pharmacologically induced energy deficit, resulting in preferential mobilization of pathological fat reserves. The clinical significance of lean mass loss depends on its magnitude, the rate of reduction, and concurrent anabolic support; however, the overall therapeutic effect indicates metabolically beneficial body composition shifts toward reduced adiposity with relative preservation of functionally important structural components. [2]

Semaglutide produces substantial body weight reduction primarily through sustained limitation of energy intake, resulting in dominant fat mass loss alongside proportionally smaller reductions in lean body mass. Analysis of body composition changes indicates that lean mass reduction remains largely a predictable consequence of total weight loss, without evidence of selective, disproportionate skeletal muscle degradation. Simultaneously, the relative proportion of lean mass in relation to total body weight improves, suggesting favorable metabolic and functional remodeling of body composition.

Thus, the mechanism of action primarily involves pharmacologically induced energy deficit with preferential mobilization of pathological fat reserves rather than direct muscular catabolism. The clinical significance of muscle mass loss depends largely on the degree of anabolic support during therapy, while the overall effect of semaglutide indicates qualitative body composition improvement, characterized by adiposity reduction with relative preservation of functionally significant structural components. [3]

Semaglutide in real-world clinical practice leads to significant body weight reduction mainly through selective reduction of total and visceral adipose tissue, with simultaneous relative preservation of muscle mass and skeletal muscle function. Muscle mass loss remains substantially smaller than fat reduction, while parameters such as skeletal muscle index, grip strength, and calf circumference do not significantly deteriorate, indicating favorable body composition remodeling without accelerated functional muscular degradation. [4]

Oral semaglutide administration, accompanied by SNAC enabling effective gastric peptide absorption, leads in clinical settings to early improvement in glycemic control and significant body composition remodeling in patients with type 2 diabetes mellitus. The therapeutic mechanism includes reduction of total and visceral fat mass while preserving lean body mass and skeletal muscle mass, resulting in improved muscle-to-fat ratios and reduced risk of unfavorable muscle tissue loss during weight reduction.

Simultaneously, improvements are observed in body fluid distribution and favorable metabolic parameters associated with hepatic steatosis, including reductions in steatosis indices and liver enzyme activity. These effects indicate that semaglutide's action extends beyond simple weight reduction, producing selective metabolic improvement, enhanced body composition quality, and improved nutritional functional status through preferential limitation of pathological adipose tissue while preserving muscular components. [5]

One study also demonstrated that oral semaglutide administration over 24 weeks leads to significant glycemic improvement alongside selective reduction of adipose tissue mass without significant decreases in total lean body mass or skeletal muscle index. This mechanism indicates that GLP-1 receptor agonism-induced energy deficit results in preferential utilization of fat reserves while simultaneously limiting muscular catabolism, distinguishing this metabolic profile from more nonselective weight reduction interventions.

Observed body composition remodeling suggests favorable metabolic shifts toward reduced adipose tissue while preserving functionally significant muscle tissue, potentially reducing risks of impaired glucose metabolism, sarcopenia, and physical functional decline. Therefore, the therapeutic effect encompasses not only weight reduction but qualitative improvement in body composition through dominant fat loss with relative preservation of muscular components. [6]

Semaglutide, regardless of oral or subcutaneous administration route, has been demonstrated over 24 weeks to produce significant body weight reduction primarily through selective decreases in total and visceral fat mass, with relative preservation of lean body mass, skeletal muscle mass, and stability of the cellular phase angle. This mechanism indicates that the dominant therapeutic effect is preferential mobilization of pathological fat reserves without significant deterioration of cellular integrity or soft tissue quality, thereby promoting favorable body composition remodeling.

Concurrently, improvements occur in glycemic control, reductions in insulin requirements, and favorable lipid profile modifications, reflecting broad enhancement of metabolic homeostasis. Comparable efficacy between both administration routes suggests that metabolic and compositional effects arise primarily from GLP-1 receptor agonism rather than the route of administration itself, leading to qualitative metabolic improvement through fat mass reduction while preserving functionally important body components. [7]

Semaglutide administered once weekly for 12 months in individuals with type 2 diabetes and obesity leads to progressive body composition remodeling, with selective fat mass reduction—particularly visceral fat—being the dominant component, while lean body mass declines proportionally less. The greatest changes occur during the early phase of therapy, when adiposity reduction coincides with improved glycemic control, reduced insulin resistance, and beneficial modulation of metabolic parameters.

The mechanism of action reflects chronic energy intake restriction induced by GLP-1 agonism, leading to preferential mobilization of pathological fat reserves with relative preservation of soft tissue functional quality. Thus, the long-term therapeutic effect includes not only weight reduction but also qualitative improvement of body composition through decreased adipose burden and improved metabolic status without significant structural destabilization of the organism. [8]

In real-world clinical practice, compounded semaglutide therapy leads to significant body weight reduction through chronic limitation of energy intake, resulting in dominant adipose tissue loss with relatively smaller reductions in lean body mass. Changes in body composition indicate favorable shifts in the proportion between fat mass and total body mass, suggesting that weight reduction primarily reflects mobilization of fat reserves rather than selective muscular catabolism.

Mechanistically, the observed remodeling of body composition reflects the metabolic consequences of GLP-1 agonism, including appetite suppression and improved energy regulation, leading to qualitative

enhancement of body composition. Despite partial loss of lean body mass, relative preservation of muscular structures suggests that the dominant effect remains fat mass reduction while maintaining functionally significant bodily components. [9]

4. Molecular Mechanisms of Skeletal Muscle Protection and Remodeling During GLP-1 Therapy

Semaglutide counteracts obesity-induced skeletal muscle atrophy through activation of the SIRT1 pathway, which plays a central role in regulating muscle metabolism, insulin sensitivity, and the balance between anabolic and catabolic processes. Therapy leads to suppression of muscle atrophy markers such as Atrogin-1 and MuRF-1 while simultaneously increasing expression of myogenic factors, including Myogenin and MyoD, thereby promoting regeneration and maintenance of muscle mass. SIRT1 activation also enhances GLUT4 expression, increasing glucose uptake and reducing muscular insulin resistance.

Simultaneously, ectopic lipid accumulation in muscles is reduced, glucose tolerance improves, and lipid disturbances associated with high-fat diets are attenuated. Inhibition of SIRT1 weakens the observed protective effects, confirming its key mechanistic significance. Therefore, GLP-1 agonist activity encompasses not only body weight reduction but also direct structural and metabolic protection of skeletal muscles through modulation of the SIRT1 axis involved in energetic and protein homeostasis. [10]

In one murine study, semaglutide demonstrated pleiotropic metabolic effects extending beyond classical glycemic control and weight reduction through multilevel modulation of inflammatory processes, oxidative stress, mitochondrial function, and tissue homeostasis. Mechanisms include activation of pathways improving insulin sensitivity, attenuation of chronic inflammation, reduction of reactive oxygen species production, and stimulation of mitochondrial biogenesis, thereby supporting improved function of skeletal muscles, adipocytes, and other insulin-sensitive tissues. Concurrently, processes promoting browning of white adipose tissue, increased energy expenditure, and regulation of autophagy were observed, potentially supporting protection against metabolic aging and muscular degeneration.

Semaglutide’s effects also include potential organ protection through improved endothelial function, immune modulation, and reduction of obesity- and diabetes-related complications. Thus, the drug functions as a broad metabolic regulator restoring balance between disrupted energy metabolism,

inflammatory processes, and cellular stress. However, most of these effects are based primarily on preclinical data, indicating the need for further validation in human populations. [11]

Semaglutide induces body weight reduction through limiting energy intake, leading to decreases in both fat mass and lean mass; however, fat mass loss remains the dominant component of total weight reduction. Simultaneously, improvements occur in skeletal muscle mitochondrial performance, including increased oxidative phosphorylation efficiency, improved functional mitochondrial quality, and beneficial remodeling of muscular metabolism. Despite reductions in absolute muscle mass, enhanced muscle bioenergetics suggest increased metabolic quality of muscle tissue rather than nonspecific catabolism.

This mechanism indicates that semaglutide not only reduces adipose tissue but also remodels muscular function through improved mitochondrial efficiency and energetic performance, potentially limiting the metabolic consequences of weight loss. Therefore, the therapeutic effect includes qualitative transformation of body composition, in which fat reduction is accompanied by adaptive improvement in skeletal muscle function at the cellular level. [12]

Semaglutide counteracts skeletal muscle atrophy induced by chronic liver disease under diabetic conditions through multilevel modulation of both systemic and direct cellular mechanisms. Protective effects include limitation of hepatic damage, reduction of oxidative stress, and decreased production of proinflammatory cytokines, leading to suppression of ubiquitin-dependent muscle protein degradation and restoration of mTOR pathway activity disrupted by metabolic stress and amino acid deficiency. Concurrent increases in IGF-1 production support anabolic processes and muscle protein synthesis.

At the muscular level, direct GLP-1 receptor activation initiates cAMP/PKA and AKT pathways, improves mitochondrial biogenesis, reduces reactive oxygen species accumulation, and suppresses NF-κB/myostatin axis activation responsible for proteolysis. Simultaneously, HSF-1 activity is enhanced, supporting myogenesis and muscle fiber regeneration. The cumulative effect includes inhibition of muscle mass and strength loss through simultaneous suppression of catabolism and stimulation of regenerative-anabolic processes within muscle tissue. [13]

Semaglutide-based therapies exert complex effects on skeletal muscle health through simultaneous action of beneficial metabolic mechanisms and potential catabolic effects associated with weight reduction. Improved insulin sensitivity, reduced chronic inflammation, attenuation of oxidative stress,

enhanced mitochondrial function, and decreased myosteatosis may support preservation of muscle quality and metabolic function. Simultaneously, rapid body weight reduction induced by chronic energy deficit may lead to decreased lean body mass, particularly under conditions of insufficient protein intake or lack of resistance activity.

Thus, the therapeutic impact on muscle depends on the balance between direct protective effects and indirect risk of intensified catabolism. Integration of pharmacotherapy with anabolic-supportive interventions such as resistance training, optimized protein intake, and muscle function monitoring is of critical importance. Effective treatment should focus not solely on body weight reduction but on qualitative remodeling of body composition, maximizing fat loss while preserving musculoskeletal integrity. [14]

5. Risk of Muscle Mass Loss, Sarcopenia, and Preventive Strategies During Pharmacological Weight Reduction Therapy

Weight-loss pharmacotherapy based on incretin agonists, including semaglutide, induces substantial body weight loss through profound restriction of energy intake; however, it simultaneously causes rapid and significant declines in lean body mass, primarily involving skeletal muscle. The scale of weight loss may correspond to physiological changes observed over a decade of aging, thereby increasing risks of sarcopenia, functional impairment, and subsequent fat mass regain through reduced resting energy expenditure.

A key mechanism counteracting these effects is implementation of targeted resistance training, which stimulates muscular anabolism, increases strength, and supports preservation or restoration of lean body mass during pharmacological fat reduction. Maintenance of muscle mass may limit secondary declines in energy expenditure and reduce the risk of post-treatment weight regain. Therefore, optimization of therapy requires shifting the therapeutic objective from simple weight reduction toward selective body composition remodeling, maximizing fat loss while protecting musculoskeletal function. [15]

Pharmacological obesity treatment in older adults using semaglutide leads to body weight reduction through chronic appetite suppression, decreased energy intake, improved glucose-insulin homeostasis, and beneficial modulation of adipose tissue distribution. The negative energy balance induced by therapy effectively reduces adipose tissue; however, it may simultaneously lead to loss of lean body

mass, including skeletal muscle and bone tissue, thereby increasing the risk of sarcopenia progression, osteopenia, and frailty syndrome in geriatric patients.

Therefore, in older populations, qualitative control of the weight reduction process is of critical importance, aimed at maximizing fat loss while preserving musculoskeletal function. This is achieved through integration of pharmacotherapy with resistance training, adequate protein intake, and monitoring of body composition and functional performance. Holistic obesity treatment in this group requires balancing the metabolic benefits of fat reduction with the risk of catabolic consequences associated with rapid weight loss, shifting therapeutic goals from simple body weight reduction toward precise body composition remodeling. [16]

Semaglutide therapy induces substantial body weight reduction primarily through limitation of energy intake; however, this process involves not only adipose tissue loss but also significant reductions in muscle mass and lean body mass. Muscle loss results primarily from chronic energy deficit, reduced protein intake, diminished anabolic stimulation, and secondary changes in myokine secretion and skeletal muscle activity. This phenomenon may compromise long-term maintenance of therapeutic effects through reduced resting energy expenditure, increased sarcopenia risk, and weakened muscular metabolic function.

Therefore, considerable importance is attributed to protection of muscle tissue during pharmacological weight reduction through implementation of resistance training, optimization of protein intake, and modulation of anabolic pathways associated with myokines and muscle metabolism. [17]

Sarcopenic obesity develops through coexistence of excessive adipose tissue, chronic inflammation, insulin resistance, mitochondrial dysfunction, and progressive loss of skeletal muscle mass and function associated with aging. Incretin-based therapies, particularly semaglutide, effectively reduce body weight through appetite suppression and reduced energy intake; however, induced weight loss also includes lean mass components, which may exacerbate existing sarcopenia and worsen functional performance in older individuals.

Thus, the key therapeutic objective becomes not only quantitative weight reduction but qualitative body composition remodeling, maximizing fat loss while preserving muscle mass and function. This is achieved through integration of pharmacotherapy with resistance training, increased protein intake, monitoring of muscle function, and development of muscle-protective therapies such as modulation of the myostatin/activin pathway. Therapeutic strategies therefore require balancing the metabolic

benefits of obesity reduction with the necessity of limiting catabolic treatment consequences in order to improve long-term metabolic and functional stability. [18]

Modern anti-obesity pharmacotherapies, particularly semaglutide, induce substantial body weight reduction through profound appetite suppression, decreased energy intake, and improved metabolic glucose regulation; however, a considerable proportion of lost mass also includes lean body mass, including muscle and bone tissue. The magnitude of muscle mass loss varies between therapies, but its contribution may be substantial during intensive weight reduction, increasing the risk of impaired functional performance, decreased energy expenditure, and progression of sarcopenia, particularly in older patients.

In response to these limitations, strategies aimed at selective muscle preservation are being developed, including combining incretin therapies with additional hormonal agonists such as amylin or glucagon, as well as use of myostatin–activin pathway inhibitors, which limit muscular catabolism and support skeletal muscle hypertrophy. Overall therapeutic trends are shifting from models of general weight reduction toward precise body composition modulation, maximizing fat loss while preserving musculoskeletal function, which is critical for long-term metabolic and functional efficacy in obesity treatment. [19]

Long-term semaglutide therapy in older adults with type 2 diabetes mellitus leads to significant body weight reduction but simultaneously accelerates peripheral muscle mass decline and worsens functional muscular parameters, particularly gait speed. This mechanism results from intensified energy deficit induced by GLP-1 agonism, which, combined with geriatric vulnerability, promotes sarcopenia progression through lean body mass loss, especially in individuals with already reduced baseline muscle mass.

Dose-dependent effects have been observed, with higher semaglutide exposure correlating with greater intensification of muscular catabolism. Initial improvements in grip strength may reflect short-term metabolic benefits; however, long-term progression of muscular functional decline predominates. These data indicate that in geriatric populations, treatment requires systematic monitoring of body composition and physical performance as well as concurrent anabolic interventions to limit accelerated muscle loss associated with chronic pharmacological weight reduction. [20]

Optimization of semaglutide therapy requires integration of pharmacotherapy with precisely targeted nutritional and exercise interventions, as pharmacological weight reduction alone is associated with

risks of lean body mass loss, functional impairments, and gastrointestinal adverse effects. Key mechanisms for improving long-term therapeutic outcomes include increased protein intake (>1.2 g/kg/day), balanced amino acid distribution, resistance training, and aerobic activity, all of which support muscle mass preservation, body composition improvement, visceral fat reduction, and limitation of energy expenditure decline.

Simultaneously, therapeutic success depends on active management of gastrointestinal symptoms such as nausea, vomiting, constipation, or reflux, which influence treatment adherence and continuity. Overall, GLP-1 agonist therapy should not be viewed as an isolated pharmacological intervention but rather as a component of a multidisciplinary metabolic strategy aimed at maximizing fat loss while preserving muscular-metabolic function and ensuring durability of clinical outcomes. [21]

6. Pleiotropic Organ Effects of Semaglutide: Cardiac Muscle, Systemic Metabolism, and Long-Term Homeostasis

Semaglutide alleviates high-fat diet-induced myocardial injury through reduction of lipid disturbances, suppression of chronic inflammation, and attenuation of oxidative stress in cardiomyocytes. The mechanism includes downregulation of HSDL2 expression, a protein regulating lipid metabolism whose overactivity under obesity conditions promotes lipid accumulation, increased reactive oxygen species production, and activation of autophagic and apoptotic processes. Suppression of the HSDL2 axis leads to reduced lipid peroxidation, decreased TNF-α, IL-6, IL-1β, and ROS levels, and improved cellular survival.

Simultaneously, semaglutide limits pathological autophagy and structural remodeling of cardiac muscle, improving cellular integrity and cardiac function under metabolic overload conditions. Therefore, the therapeutic effect results from molecular modulation of lipotoxicity and inflammatory-oxidative responses, indicating protective action against obesity-induced cardiomyopathy through stabilization of cardiomyocyte metabolic homeostasis. [22]

Semaglutide counteracts pathological cardiac remodeling induced by chronic pressure overload through optimization of energetic substrate utilization in cardiomyocytes and restoration of mitochondrial homeostasis. Mechanistically, this includes activation of the PI3K/AKT pathway and regulation of the Creb5/NR4A1 transcriptional axis, resulting in reduced NR4A1 expression and limited mitochondrial translocation. This leads to improved mitochondrial integrity, decreased

oxidative damage, reduced lipid accumulation, and increased ATP production through intensified fatty acid oxidation and improved pyruvate incorporation into the tricarboxylic acid cycle.

The resulting metabolic reconstruction suppresses cardiomyocyte hypertrophy, reduces myocardial fibrosis, and improves cardiac contractile function. Therefore, semaglutide's action focuses on energetic metabolic remodeling and mitochondrial protection as key mechanisms limiting progression of heart failure associated with hemodynamic overload. [23]

Semaglutide limits ischemia-reperfusion-induced cardiomyocyte apoptosis through increased GLP-1R expression and activation of the PKG/PKCε/ERK1/2 signaling axis. Activation of this pathway suppresses proapoptotic processes, stabilizes cellular integrity, and limits myocardial injury, resulting in reduced infarct size, decreased markers of cardiac injury, and improved cell survival under ischemia-reperfusion stress.

PKG activation plays a central role, as pharmacological inhibition of this enzyme weakens semaglutide's protective effect, confirming the critical significance of the GLP-1R–PKG/PKCε/ERK1/2 pathway in cardioprotection. Thus, semaglutide exerts molecular enhancement of cellular survival pathways and suppression of reperfusion-induced cell death, indicating therapeutic potential in limiting secondary myocardial damage following ischemic events. [24]

Reduction in dosing frequency of GLP-1 receptor agonists after achieving initial weight reduction may maintain a significant portion of metabolic and compositional treatment effects, provided adequate pharmacological exposure is preserved. Continued therapy under reduced-frequency administration still supports appetite control, stabilization of energy balance, and limitation of secondary fat regain, although efficacy may be somewhat lower than with full standard dosing.

Overall, this suggests that chronic GLP-1 axis activation does not necessarily require maximal exposure intensity to maintain part of the achieved metabolic remodeling but rather consistent neurohormonal modulation of satiety and energetic homeostasis. Therefore, dosing frequency reduction may represent a maintenance strategy capable of lowering costs and potential adverse effects while preserving improvements in body composition and metabolic parameters following the intensive weight reduction phase. [25]

7. Discussion

The collected evidence indicates that semaglutide induces clinically meaningful weight loss primarily through preferential fat mass reduction while generally preserving functional muscle mass. Although some degree of lean mass reduction is expected, current data suggest that this loss is typically proportional to total body mass reduction rather than reflecting disproportionate skeletal muscle catabolism.

Importantly, semaglutide appears to exert broader metabolic effects that may partially protect skeletal muscle through improvements in mitochondrial function, insulin sensitivity, inflammatory regulation, and anabolic signaling pathways such as SIRT1 and mTOR. However, vulnerable populations including elderly patients and individuals with pre-existing sarcopenia may experience increased risks of adverse musculoskeletal outcomes.

These findings underscore the necessity of combining pharmacological therapy with resistance exercise, adequate protein intake, and individualized clinical monitoring to optimize therapeutic efficacy while minimizing long-term functional risks.

8. Conclusion

Semaglutide and related GLP-1-based therapies represent transformative interventions in obesity management, offering substantial metabolic and body composition benefits. Their therapeutic success depends not solely on total weight loss, but on achieving selective adiposity reduction while preserving skeletal muscle mass and functional capacity.

Future therapeutic strategies should prioritize comprehensive metabolic remodeling through multidisciplinary approaches integrating pharmacotherapy, nutrition, exercise, and personalized monitoring. Further long-term human studies are necessary to clarify the full implications of semaglutide on muscle preservation, aging, and functional outcomes.

Disclosure:

Author's contribution:

Conceptualization: DZ, MS

Methodology: JT, DZ

Validation: DZ, PP

Resources: JT, MS

Data curation: KK, PP

Writing- original draft preparation: KK, JK

Writing- review and editing: MS, DZ, JT

Visualization: DZ, JK

Supervision: DZ, MS

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DZ, MS- these authors have contributed equally to this work and share first authorship.

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