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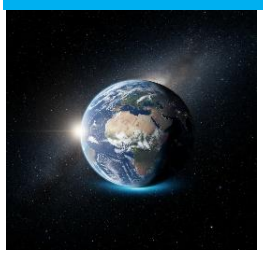

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Impact of GLP-1 Receptor Agonists on Body Composition and Physical Performance in Patients with Obesity: A Comprehensive Review of Current Research

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Abstract

Background.
Glucagon-like peptide-1 receptor agonists (GLP-1RAs) have rapidly become central to the pharmacological management of obesity, producing unprecedented and sustained weight loss in large randomized controlled trials. Their benefits extend beyond weight reduction to include improvements in glycemic control, blood pressure, lipid profile, and cardiovascular outcomes. However, increasing attention has been directed toward their effects on body composition, particularly the balance between fat mass reduction and loss of lean body mass, as well as their potential influence on skeletal muscle function, functional capacity, and physical performance. These outcomes are of high relevance to sports medicine, rehabilitation, and clinical exercise physiology, where preservation of muscle mass and function is fundamental to performance, injury prevention, and long-term health.
Aim.
To comprehensively review and critically appraise current evidence on the impact of GLP-1 receptor agonists on body composition and physical performance in adults with obesity, with particular emphasis on fat mass reduction, lean mass changes, functional outcomes, and populations at risk of adverse muscle-related effects.
Materials and methods.
A narrative review was conducted using 30 PubMed-indexed publications comprising randomized controlled trials, long-term extension studies, DXA substudies, and systematic or narrative reviews published between 2015 and 2026. Studies evaluating liraglutide, semaglutide, and

tirzepatide in adults with overweight or obesity were included. Outcomes of interest were changes in total body weight, fat mass, lean body mass, indices of physical function, exercise tolerance, and health-related physical performance.
Results.
Across the STEP and SURMOUNT trial programs, GLP-1RAs consistently induced large reductions in total body weight and fat mass [1–12]. DXA-based analyses demonstrated that 15–40% of total weight loss was attributable to reductions in lean body mass [13,21,25–28]. Functional outcomes varied by population: in patients with obesity-related functional impairment and heart failure with preserved ejection fraction (HFpEF), semaglutide improved symptoms, physical limitations, and exercise tolerance [15–19]. Conversely, concerns have emerged regarding potential sarcopenic effects in older adults and individuals with low baseline muscle reserves [20,25–28]. Systematic reviews highlight heterogeneity in lean mass responses and underscore the importance of concurrent lifestyle interventions [25–28].
Conclusions.
GLP-1 receptor agonists induce profound fat mass reduction but are accompanied by clinically relevant loss of lean mass in a substantial proportion of patients. Improvements in physical performance are evident in populations with obesity-related functional limitation, whereas preservation of skeletal muscle mass remains a critical therapeutic challenge, particularly in older adults and physically active individuals. Integration of pharmacotherapy with structured exercise and nutritional strategies is essential to optimize body composition and functional outcomes in sports medicine and rehabilitation contexts.
Key words: GLP-1 receptor agonists; obesity; body composition; lean mass; physical performance; functional capacity; sarcopenia.

1. Introduction

Obesity represents one of the most pressing public health challenges worldwide, with rapidly increasing prevalence across all age groups and profound implications for cardiometabolic health, musculoskeletal function, and quality of life. Beyond its well-established association with type 2 diabetes, cardiovascular disease, and premature mortality, obesity is increasingly recognized as a condition characterized by impaired physical performance, reduced exercise tolerance, diminished mobility, and increased risk of musculoskeletal injury. These functional limitations are particularly relevant in the context of sports medicine and rehabilitation, where excess adiposity compromises biomechanical efficiency, increases joint loading, and predisposes individuals to both acute and overuse injuries.

Historically, obesity management has relied on lifestyle modification, including dietary caloric restriction and increased physical activity. Although these interventions remain foundational, their long-term effectiveness is limited by physiological adaptations that favor weight regain and by challenges in sustained adherence. The introduction of glucagon-like peptide-1 receptor agonists (GLP-1RAs) has profoundly altered the therapeutic landscape of obesity management. Large randomized controlled trials within the STEP program demonstrated that once-weekly semaglutide at a dose of 2.4 mg produces mean body weight reductions exceeding 10–15% over 68 weeks, with sustained effects observed in long-term extension studies [1–6]. Comparable and even greater weight reductions have been reported with tirzepatide in the SURMOUNT program, with mean reductions approaching 20–22% in some populations [8–12]. Liraglutide, although associated with more modest weight loss, remains a widely studied GLP-1RA with established efficacy in long-term weight management [22–24].

While total body weight reduction is a clinically meaningful outcome, it represents a crude surrogate for more nuanced changes in body composition. From a functional and performance

perspective, the relative contributions of fat mass and lean body mass to total weight loss are of paramount importance. Fat mass reduction is associated with improved insulin sensitivity, reduced cardiometabolic risk, and decreased mechanical load on weight-bearing joints. In contrast, loss of lean mass—particularly skeletal muscle—may adversely affect muscle strength, power output, metabolic rate, and physical performance. This distinction is especially critical in populations for whom physical capacity is a key determinant of health and quality of life, including older adults, patients undergoing rehabilitation, and physically active individuals seeking to maintain or improve performance.

Emerging evidence from DXA substudies and systematic reviews indicates that GLP-1RA-induced weight loss is accompanied by a measurable reduction in lean body mass, accounting for approximately 15–40% of total weight loss [13,21,25–28]. These findings parallel observations from dietary weight loss interventions but raise important questions regarding the potential for pharmacologically induced weight loss to exacerbate sarcopenic risk, particularly in vulnerable populations. In older adults, age-related declines in muscle mass and strength (sarcopenia) are already prevalent, and additional loss of lean mass may compromise functional independence. Similarly, in physically active individuals and athletes with obesity, reductions in muscle mass may impair training capacity, performance outcomes, and injury resilience.

At the same time, clinical trials in populations with obesity-related functional impairment provide evidence that GLP-1RA therapy may improve physical performance and exercise tolerance. In the STEP-HFpEF trials, semaglutide significantly improved health-related quality of life, physical limitations, and exercise capacity in patients with heart failure with preserved ejection fraction and obesity [15–19]. These findings suggest that reductions in fat mass and improvements in cardiometabolic status may translate into functional benefits, even in the presence of some degree of lean mass loss. This apparent paradox underscores the complexity of interpreting body composition changes in relation to functional outcomes and highlights the need for nuanced, population-specific evaluation.

From a sports medicine perspective, the rapid adoption of GLP-1RAs raises important practical and ethical considerations. Increasing numbers of physically active individuals and recreational athletes are seeking pharmacological assistance for weight management. While reductions in fat mass may improve relative power-to-weight ratio and endurance performance, unintended losses of lean mass could compromise absolute strength and muscular performance. Furthermore, the long-term implications of GLP-1RA use for muscle quality, neuromuscular function, and adaptation to training stimuli remain incompletely understood.

Research Objective.

To synthesize and critically appraise current evidence on the effects of GLP-1 receptor agonists on body composition and physical performance in adults with obesity, with particular emphasis on fat mass reduction, lean mass changes, and functional outcomes relevant to sports medicine and rehabilitation.

Research Problems.

1. What proportion of GLP-1RA-induced weight loss is attributable to fat mass versus lean mass reduction?
2. How do GLP-1RAs influence physical performance and functional capacity in populations with obesity?
3. Which patient subgroups may be at greatest risk of clinically relevant lean mass loss and functional impairment?
4. What are the implications of GLP-1RA-induced body composition changes for sports medicine and rehabilitation practice?

Research Hypotheses.

GLP-1 receptor agonist–induced weight loss is associated with clinically relevant reductions in lean body mass that may have functional implications, particularly in older adults and individuals with low baseline muscle reserves. Improvements in physical performance are most pronounced in populations with obesity-related functional limitation, whereas preservation of skeletal muscle mass remains a critical challenge in physically active populations.

2. Research materials and methods

This narrative review was conducted using the 30 PubMed-indexed publications provided, comprising randomized controlled trials, long-term extension studies, DXA substudies, and systematic or narrative reviews published between 2015 and 2026. The evidence base included large clinical trial programs evaluating semaglutide (STEP trials) [1–7,14–21], tirzepatide (SURMOUNT trials) [8–13], and liraglutide (SCALE trials) [22–24]. Additional sources provided insights into body composition changes, lean mass loss, and functional outcomes through DXA substudies and systematic reviews [21,25–28], as well as observational and real-world syntheses [29,30].

The primary outcomes of interest were:

(1) changes in total body weight and fat mass,

(2) changes in lean body mass assessed by DXA or related methods, and

(3) measures of physical performance and functional capacity, including exercise tolerance, symptom burden, and health-related physical functioning.

Due to heterogeneity in study populations, outcome measures, and study designs, a narrative synthesis approach was applied. Findings were grouped thematically into domains addressing body composition changes, lean mass dynamics, and functional performance outcomes. Emphasis was placed on clinically relevant implications for sports medicine, rehabilitation, and exercise prescription in patients with obesity.

3. Research results

3.1. Effects of GLP-1 receptor agonists on total body weight and fat mass

Large randomized controlled trials consistently demonstrate that GLP-1 receptor agonists induce substantial and sustained reductions in total body weight in adults with overweight and obesity. In the STEP trial program, semaglutide 2.4 mg once weekly resulted in mean body weight reductions ranging from approximately 10% to 15% over 68 weeks, with maintained effects during long-term follow-up [1–6]. In STEP 4, continued treatment with semaglutide was necessary to sustain weight loss, whereas discontinuation led to significant weight regain, highlighting the chronic nature of obesity and the need for ongoing pharmacotherapy [2]. Similar findings were observed when semaglutide was combined with intensive behavioral therapy, indicating that pharmacological and behavioral interventions exert additive effects on weight reduction [3].

The SURMOUNT trial program evaluating tirzepatide reported even greater weight loss, with reductions approaching 20–22% in some populations [8–12]. In SURMOUNT-1, tirzepatide produced dose-dependent weight reductions that exceeded those observed with semaglutide in comparable populations, suggesting enhanced efficacy of dual GIP/GLP-1 receptor agonism [8]. These effects were sustained over time, with extension and maintenance studies confirming the durability of weight loss under continued treatment [11,12]. In SURMOUNT-3, participants who achieved initial weight loss through intensive lifestyle intervention experienced additional and sustained reductions with tirzepatide, indicating that pharmacotherapy can augment lifestyle-induced weight loss [10].

Liraglutide, administered at a daily dose of 3.0 mg, demonstrated clinically meaningful but comparatively smaller weight reductions in the SCALE trials [22–24]. Long-term maintenance of weight loss with liraglutide required continued treatment, reinforcing the chronic nature of pharmacological obesity management.

Reductions in total body weight in these trials were primarily driven by fat mass loss. DXA and imaging substudies demonstrated significant decreases in total fat mass and visceral adipose tissue, a metabolically deleterious fat depot strongly associated with cardiometabolic risk [13,21]. The magnitude of visceral fat reduction observed with GLP-1RAs is clinically relevant, as reductions in central adiposity are associated with improvements in insulin sensitivity, lipid metabolism, and inflammatory markers. Collectively, these findings establish GLP-1RAs as among the most effective pharmacological interventions for fat mass reduction currently available.

3.2. Body composition changes and lean mass dynamics

Despite the favorable reductions in fat mass, body composition analyses indicate that GLP-1RA-induced weight loss is accompanied by measurable loss of lean body mass. DXA substudy data from the SURMOUNT-1 trial revealed that approximately 15–40% of total weight loss achieved with tirzepatide was attributable to lean mass reduction [13]. Comparable proportions of lean mass loss have been reported in semaglutide-treated populations, as summarized in DXA substudies and systematic reviews [21,25–28]. These findings parallel observations from dietary weight loss interventions, suggesting that pharmacologically induced negative energy balance leads to reductions in both fat and lean tissue.

Systematic reviews examining GLP-1RA effects on body composition consistently report heterogeneity in the proportion of lean mass loss relative to total weight loss [25–28]. Factors contributing to this variability include baseline body composition, age, sex, degree of caloric deficit, and concomitant lifestyle interventions. Importantly, individuals with higher baseline fat mass tend to experience greater absolute fat loss, whereas those with lower baseline lean mass reserves may be more vulnerable to clinically significant muscle loss. This has particular relevance for older adults, who may already exhibit age-related sarcopenia.

Evidence from studies in older populations suggests that semaglutide-associated weight loss may be accompanied by declines in muscle mass and potentially muscle function [20]. Although reductions in body weight may improve mobility and reduce joint loading, loss of skeletal muscle mass may compromise strength, balance, and resilience to physical stressors. These concerns are echoed in narrative and systematic reviews emphasizing the potential for GLP-1RA therapy to exacerbate sarcopenic risk in vulnerable populations [25–28].

The clinical significance of lean mass loss during GLP-1RA therapy remains an area of active debate. On one hand, reductions in fat mass may confer substantial functional benefits by decreasing mechanical load and improving metabolic health. On the other hand, loss of muscle mass may reduce absolute strength and power, potentially impairing performance in physically

active individuals and increasing fall risk in older adults. The net functional impact of these opposing effects likely varies by population and baseline functional status.

3.3. Physical performance and functional outcomes in clinical populations

Evidence regarding the impact of GLP-1RAs on physical performance and functional capacity is most robust in populations with obesity-related functional impairment, particularly individuals with heart failure with preserved ejection fraction (HFpEF). In the STEP-HFpEF trials, semaglutide significantly improved symptoms, physical limitations, and health-related quality of life as assessed by validated patient-reported outcome measures [15–19]. Improvements were observed in physical functioning domains, including reduced exertional dyspnea and fatigue, which translated into enhanced exercise tolerance and daily functional capacity.

Prespecified analyses demonstrated that semaglutide treatment was associated with meaningful improvements in functional status across baseline levels of left ventricular ejection fraction and obesity severity [16,18]. These findings suggest that reductions in fat mass and improvements in cardiometabolic status can translate into clinically meaningful functional benefits, even in the presence of some degree of lean mass loss. Furthermore, improvements in exercise capacity observed in HFpEF populations may reflect reductions in body mass and improvements in hemodynamic and metabolic efficiency, thereby reducing the relative energetic cost of movement.

In addition to HFpEF populations, observational studies and narrative syntheses suggest that GLP-1RA-induced weight loss may improve general physical functioning and mobility in adults with obesity [29,30]. Reduced body mass lowers mechanical loading on joints, potentially alleviating pain and facilitating greater participation in physical activity. These changes may create a positive feedback loop, whereby improved mobility enables greater engagement in exercise, further enhancing cardiometabolic health and functional capacity.

However, data directly assessing changes in objective measures of muscle strength, power output, and exercise performance in response to GLP-1RA therapy remain limited. Most large trials have prioritized cardiometabolic endpoints and patient-reported outcomes over direct assessments of muscular performance. Consequently, it remains unclear to what extent improvements in relative performance (e.g., power-to-weight ratio) may be offset by declines in absolute muscle strength due to lean mass loss. This represents a critical knowledge gap with direct implications for sports medicine and rehabilitation practice.

3.4. Subgroup considerations: older adults and individuals with low baseline muscle reserves

Older adults represent a subgroup of particular concern regarding the body composition effects of GLP-1RAs. Age-related declines in muscle mass and strength are well documented, and additional lean mass loss induced by weight loss interventions may exacerbate functional decline. Evidence from studies in older populations indicates that semaglutide-associated weight loss may be accompanied by reductions in muscle mass and potentially muscle strength, raising concerns regarding sarcopenic risk [20]. Systematic reviews further emphasize that older individuals and those with low baseline muscle reserves may be disproportionately affected by lean mass loss during GLP-1RA therapy [25–28].

Similarly, individuals with obesity and pre-existing functional limitations or comorbidities affecting musculoskeletal health may be more vulnerable to adverse muscle-related effects. In such populations, even modest reductions in muscle mass may have clinically meaningful consequences for balance, mobility, and independence. These considerations underscore the importance of individualized risk–benefit assessment when prescribing GLP-1RAs, particularly in older adults and those with baseline sarcopenia or frailty.

3.5. Clinical implications for sports medicine and rehabilitation

From a sports medicine and rehabilitation perspective, the body composition effects of GLP-1RAs present both opportunities and challenges. Reductions in fat mass may improve relative strength-to-weight ratio, aerobic efficiency, and biomechanical loading, potentially enhancing performance in weight-bearing activities. For recreational athletes with obesity, weight loss may facilitate greater participation in training and reduce injury risk associated with excess body mass.

Conversely, unintended loss of lean mass may compromise absolute muscle strength and power, potentially impairing performance in strength- and power-dependent activities. In rehabilitation settings, preservation of muscle mass is critical for recovery from injury and for maintaining functional independence. The available evidence suggests that GLP-1RA therapy should not be implemented in isolation in physically active populations or in patients undergoing rehabilitation. Rather, integration with structured exercise and nutritional interventions is likely necessary to mitigate lean mass loss and optimize functional outcomes.

3.6. Mechanistic interpretation of body composition changes during GLP-1RA therapy

The mechanisms underlying body composition changes observed during GLP-1 receptor agonist therapy are multifactorial and reflect both direct pharmacological effects and indirect

consequences of sustained negative energy balance. GLP-1RAs primarily exert their anti-obesity effects through appetite suppression, delayed gastric emptying, and modulation of central satiety pathways, leading to reduced caloric intake and sustained weight loss [1–12,22–24]. The resulting caloric deficit inevitably induces mobilization of energy stores from both adipose tissue and, to a lesser extent, lean tissue.

DXA substudies and systematic reviews indicate that lean mass loss accounts for approximately 15–40% of total weight reduction during GLP-1RA therapy [13,21,25–28]. This proportion is broadly consistent with observations from dietary weight loss interventions, suggesting that GLP-1RA-induced negative energy balance does not fundamentally alter the partitioning of weight loss between fat and lean compartments. However, the magnitude of absolute lean mass loss may be clinically relevant given the large total weight reductions achieved with semaglutide and tirzepatide [1–12]. Thus, even a similar proportion of lean mass loss translates into greater absolute muscle loss compared with more modest lifestyle-induced weight loss.

Age, baseline body composition, and comorbid conditions likely modulate the extent of lean mass loss during GLP-1RA therapy. Older adults, who typically exhibit reduced anabolic responsiveness and lower baseline muscle mass, may experience disproportionate functional consequences from lean mass loss [20,25–28]. Similarly, individuals with obesity-related comorbidities that impair physical activity participation may experience greater muscle loss due to reduced mechanical loading and activity levels during weight loss.

3.7. Integration of body composition changes with functional outcomes

The functional implications of GLP-1RA-induced body composition changes are complex and context-dependent. On one hand, substantial reductions in fat mass reduce mechanical load on weight-bearing joints, improve cardiometabolic efficiency, and decrease the energetic cost of movement. These changes can translate into meaningful improvements in mobility, exercise tolerance, and perceived physical functioning, as demonstrated in the STEP-HFpEF trials [15–19]. In these populations, improvements in functional capacity likely reflect a combination of reduced body mass, improved cardiovascular and metabolic function, and reduced symptom burden, even in the presence of some lean mass loss.

On the other hand, lean mass loss may compromise absolute muscle strength and power output, which are critical determinants of performance in strength- and power-dependent activities. The limited availability of direct measures of muscle strength and performance in GLP-1RA trials represents a significant gap in the literature. Most large trials have prioritized cardiometabolic endpoints and patient-reported outcomes over objective performance measures, making it difficult to quantify the net impact of GLP-1RA therapy on muscular performance.

In physically active individuals, reductions in body mass may improve relative performance metrics such as power-to-weight ratio and aerobic efficiency. However, if absolute muscle strength declines due to lean mass loss, performance in tasks requiring high force production (e.g., sprinting, jumping, resistance training) may be adversely affected. This trade-off underscores the importance of distinguishing between relative and absolute performance outcomes when evaluating the functional impact of GLP-1RA therapy.

3.8. Implications for training adaptation and exercise capacity

The interaction between GLP-1RA therapy and training adaptation represents an emerging area of interest in sports medicine. Weight loss may facilitate increased participation in physical activity by reducing joint pain and perceived exertion, potentially enhancing adherence to exercise programs. Observational syntheses suggest that improved mobility following GLP-1RA-induced weight loss may create opportunities for greater engagement in physical activity, thereby reinforcing functional improvements [29,30].

However, sustained negative energy balance may impair anabolic responses to training, particularly resistance training, if not accompanied by adequate nutritional support. Although direct evidence from GLP-1RA trials is limited, systematic reviews of body composition changes emphasize the potential for lean mass loss during pharmacologically induced weight loss [25–28]. This raises concerns that training adaptations, particularly hypertrophic responses, may be blunted during GLP-1RA therapy if energy and protein intake are insufficient to support muscle protein synthesis.

In rehabilitation contexts, preservation of lean mass is central to restoring functional capacity following injury or illness. The use of GLP-1RAs in patients undergoing rehabilitation should therefore be carefully considered, with particular attention to maintaining sufficient nutritional intake and incorporating resistance training to counteract potential muscle loss. Failure to address these factors may compromise rehabilitation outcomes, despite improvements in cardiometabolic health and body weight.

3.9. Population-specific considerations: athletes and physically active individuals with obesity

The increasing use of GLP-1RAs among physically active individuals and recreational athletes seeking weight management raises important considerations for sports medicine practice. In such populations, reductions in fat mass may improve biomechanical efficiency and relative performance, particularly in endurance-oriented activities where body mass represents a limiting factor. However, loss of lean mass may compromise maximal strength and power output, potentially impairing performance in sports requiring explosive force production.

The absence of direct evidence evaluating GLP-1RA use in athletic populations represents a critical limitation of the current literature. Extrapolation from clinical trials in sedentary or comorbid populations may not fully capture the performance implications of GLP-1RA therapy in athletes. Nevertheless, the observed patterns of lean mass loss during GLP-1RA-induced weight loss [13,21,25–28] warrant caution in athletic contexts, where preservation of muscle mass is integral to performance and injury resilience.

3.10. Risk–benefit considerations and clinical decision-making

The clinical decision to initiate GLP-1RA therapy in individuals with obesity must balance the substantial benefits of fat mass reduction and cardiometabolic improvement against potential risks related to lean mass loss and functional consequences. In populations with obesity-related functional impairment, such as HFpEF, the net functional benefit appears favorable, with significant improvements in symptoms and physical limitations observed with semaglutide therapy [15–19]. In contrast, in populations where physical performance and muscle strength are primary outcomes of interest, such as athletes and individuals engaged in rehabilitation, the potential for lean mass loss necessitates careful monitoring and supportive interventions.

Systematic reviews emphasize heterogeneity in body composition responses to GLP-1RA therapy and highlight the importance of individualized assessment [25–28]. Factors such as age, baseline muscle mass, comorbidities, and physical activity levels should inform clinical decision-making. The emerging real-world evidence suggests that integration of pharmacotherapy with lifestyle interventions may optimize outcomes and mitigate potential adverse effects on lean mass [29,30].

4. Discussion

The present narrative review synthesizes evidence from large randomized controlled trials, DXA substudies, and systematic reviews to evaluate the impact of GLP-1 receptor agonists on body composition and physical performance in adults with obesity. The findings demonstrate that GLP-1RAs, including semaglutide, tirzepatide, and liraglutide, induce substantial and sustained reductions in total body weight and fat mass [1–12,22–24]. These effects represent a major therapeutic advance in obesity management and are associated with clinically meaningful improvements in cardiometabolic outcomes and, in selected populations, functional status [14–19].

However, the reviewed evidence consistently indicates that GLP-1RA-induced weight loss is accompanied by measurable reductions in lean body mass, accounting for approximately 15–40% of total weight loss [13,21,25–28]. Although this proportion is comparable to that observed with dietary weight loss interventions, the magnitude of absolute lean mass loss may be greater

given the substantial total weight reductions achieved with modern GLP-1RA regimens. This finding has important implications for populations in which preservation of skeletal muscle mass and strength is central to functional capacity, including older adults, patients undergoing rehabilitation, and physically active individuals.

4.1. Interpretation of functional outcomes in the context of body composition changes

Functional outcomes associated with GLP-1RA therapy appear to be population-specific. In patients with obesity-related functional impairment, particularly those with HFpEF, semaglutide therapy resulted in significant improvements in symptoms, physical limitations, and exercise tolerance [15–19]. These benefits likely reflect reductions in fat mass, improvements in cardiometabolic efficiency, and decreased symptom burden, which collectively reduce the energetic cost of physical activity and improve perceived exertion. In such populations, the net functional effect of GLP-1RA therapy appears favorable despite concomitant lean mass loss.

In contrast, in populations where absolute muscle strength and power are key determinants of performance, the potential for lean mass loss raises concerns. The current evidence base lacks direct assessments of objective muscle strength and performance outcomes in response to GLP-1RA therapy. Consequently, it remains unclear whether improvements in relative performance metrics (e.g., power-to-weight ratio) are offset by declines in absolute strength. This gap in the literature highlights a critical need for future trials to incorporate standardized measures of muscle function and performance alongside cardiometabolic endpoints.

4.2. Implications for sports medicine practice

From a sports medicine perspective, the widespread adoption of GLP-1RAs for weight management necessitates careful consideration of their potential impact on muscle mass and performance. Reductions in fat mass may confer advantages in endurance-oriented activities by improving relative efficiency and reducing mechanical load. However, unintended reductions in lean mass may compromise strength and power, potentially impairing performance in sports requiring high force production. The balance between these opposing effects is likely to vary by sport, training status, and individual physiology.

Given the lack of direct evidence in athletic populations, extrapolation from clinical trial data must be undertaken cautiously. Nevertheless, the consistent observation of lean mass loss during GLP-1RA-induced weight loss [13,21,25–28] suggests that athletes and physically active individuals using GLP-1RAs should be closely monitored for changes in muscle mass and performance. Integration of pharmacotherapy with structured resistance training and

appropriate nutritional strategies is likely essential to mitigate potential adverse effects on muscle mass and function.

4.3. Implications for rehabilitation and older adults

In rehabilitation contexts, preservation of skeletal muscle mass is central to restoring functional independence and preventing disability. Older adults represent a particularly vulnerable population, as age-related declines in muscle mass and anabolic responsiveness may exacerbate the functional consequences of lean mass loss during weight loss interventions [20,25–28]. Although reductions in fat mass may improve mobility and reduce joint loading, unintended muscle loss may compromise balance, strength, and resilience to physical stressors, potentially increasing fall risk and delaying rehabilitation progress.

The reviewed evidence underscores the importance of individualized risk–benefit assessment when prescribing GLP-1RAs to older adults and patients undergoing rehabilitation. While the cardiometabolic and functional benefits of weight loss may be substantial, proactive strategies to preserve muscle mass and function are likely necessary to optimize outcomes in these populations.

4.4. Limitations of the current evidence base

Several limitations of the current evidence base should be acknowledged. First, most large GLP-1RA trials prioritize cardiometabolic endpoints and patient-reported outcomes over direct measures of muscle strength, power, and physical performance. As a result, the functional implications of lean mass loss remain incompletely characterized. Second, DXA-based body composition assessments provide estimates of lean mass but do not directly assess muscle quality, neuromuscular function, or intramuscular fat infiltration, all of which may influence performance. Third, the heterogeneity of study populations, intervention durations, and outcome measures complicates direct comparison across trials.

Finally, the absence of data from athletic populations represents a critical gap in the literature. Future studies specifically designed to evaluate the effects of GLP-1RAs on body composition, muscle function, and performance in physically active individuals and athletes are needed to inform evidence-based practice in sports medicine.

4.5. Directions for future research

Future research should prioritize:

1. Incorporation of standardized, objective measures of muscle strength, power, and functional performance into GLP-1RA trials.

2. Longitudinal assessment of muscle quality and neuromuscular function during prolonged GLP-1RA therapy.
3. Evaluation of the combined effects of GLP-1RAs and structured exercise interventions on body composition and performance.
4. Investigation of GLP-1RA effects in athletic and physically active populations.
5. Identification of patient subgroups at greatest risk of clinically meaningful lean mass loss and functional impairment.

5. Conclusions

GLP-1 receptor agonists represent a major advance in the pharmacological management of obesity, producing unprecedented and sustained reductions in body weight and fat mass [1–12,22–24]. However, these benefits are accompanied by clinically relevant reductions in lean body mass in a substantial proportion of patients [13,21,25–28]. Functional improvements are evident in populations with obesity-related functional impairment, such as individuals with HFpEF [15–19], whereas the implications for absolute muscle strength and performance in physically active populations remain uncertain.

In sports medicine and rehabilitation contexts, GLP-1RA therapy should not be implemented in isolation. Preservation of skeletal muscle mass and function is essential to optimize physical performance and functional outcomes. Individualized integration of pharmacotherapy with exercise and nutritional strategies is likely necessary to maximize benefits and mitigate potential adverse effects on lean mass. The growing use of GLP-1RAs in diverse populations underscores the need for evidence-based guidelines that address body composition and functional outcomes alongside traditional cardiometabolic endpoints.

Disclosure:

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The authors declare no conflict of interest.

Declaration of Generative AI and AI-Assisted Technologies

During the preparation of this work, the authors used ChatGPT-5.2 to improve grammar and language clarity. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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