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Effects of GLP-1 Receptor Agonists on Lean Body Mass and Muscle Health

Introduction

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) – including drugs such as **liraglutide**, **semaglutide**, and the dual agonist **tirzepatide** – have demonstrated remarkable efficacy in inducing weight loss in patients with obesity and type 2 diabetes. These medications primarily reduce body weight by curbing appetite and caloric intake, leading to significant fat loss. However, any substantial weight loss can also entail some loss of **lean body mass** (which comprises muscle, organs, bone, and water). This raises important questions about **muscle health**: Do GLP-1 RAs cause excessive muscle loss or weakness? Are patients (especially older adults) at risk of **sarcopenia** (muscle wasting and frailty)? This report provides an evidence-based overview of how GLP-1 RAs affect lean mass, muscle strength, and the risk of muscle wasting. We summarize findings from clinical trials and observational studies, highlighting the balance of **fat vs. lean mass loss**, impacts on **muscle strength/physical performance**, any **sarcopenia risks or benefits**, and differences by drug or dose. A table of key study results is included for quick reference.

Effects on Body Composition: Lean Mass vs Fat Mass Loss

Weight loss from GLP-1 RAs is driven largely by fat reduction, with variable effects on lean mass. Across trials, the **majority of weight lost is fat**, but a fraction comes from lean tissue – typically on the order of 20–40% of total weight loss in many studies [1] [2]. For example, in the STEP 1 trial (68-week semaglutide 2.4 mg in obese adults), about **~40% of the ~15% total weight loss** was attributable to lean mass reduction [2]. Similarly, a semaglutide trial in patients with type 2 diabetes reported that **roughly 39–40%** of weight lost on the drug was lean mass [3]. By contrast, placebo groups (with minimal weight change) show little change in body composition [4]. Importantly, even when absolute lean mass declines, patients still experience a **preferential loss of fat** – meaning **fat mass decreases more than lean mass** in relative terms [2] [5]. In STEP1's DXA sub-study, semaglutide recipients had a *greater reduction in fat mass than in lean mass*, consistent with an overall improvement in body composition [6]. Indeed, one systematic review noted that although notable lean reductions (up to 40% of weight lost) occurred in larger trials, the **percentage of body weight that was lean actually increased** – indicating a *higher lean-mass proportion after weight loss* [7]. This suggests an overall positive shift in body composition despite some lean tissue loss.

That said, **there is heterogeneity across studies**. Some trials (especially smaller or shorter-term ones) found *minimal or no significant lean mass loss*, with weight reduction coming almost entirely from fat. For instance, a 26-week real-world study of oral semaglutide in 32 patients with type 2 diabetes observed significant decreases in fat mass (including visceral fat) while **fat-free mass and skeletal muscle mass were preserved**, leading to an improved muscle-to-visceral fat ratio [8]. In that cohort, **body fat dropped** (on average from 28.3 to 25.5 kg), whereas **lean mass stayed essentially unchanged** (48.1 vs 47.6 kg, a statistically non-significant difference) [9]. The authors concluded that oral semaglutide "reduced body fat but not muscle mass" in these patients [9]. Likewise, a Japanese study of 24-week oral semaglutide reported **no significant change in appendicular muscle index** despite weight loss, implying lean tissue was maintained [9]. In contrast, other studies – particularly

those with **larger weight losses** – have reported a higher proportion of lean mass loss. Earlier trials of liraglutide 3.0 mg, for example, suggested that lean mass could account for up to **~60% of total weight lost** in some cases [10]. (This high percentage may reflect that patients on liraglutide tended to lose modest amounts of weight overall, so even small absolute lean losses appeared as a larger fraction of the total [2].) Notably, a real-world 10-month study of high-dose liraglutide in 54 obese individuals documented ~12% mean weight loss with a **lean mass loss of only ~22% of total weight lost**, indicating ~78% of weight reduction was fat [11]. In that study, **overall body fat percentage decreased and lean percentage increased** over 10 months, demonstrating a *beneficial change in body composition* despite some lean mass reduction [11].

Several factors likely explain the variability in lean mass outcomes: **population differences** (e.g. older vs younger patients, diabetic vs non-diabetic), **drug potency and dose**, **duration of treatment**, and whether patients engaged in **muscle-preserving behaviors** (like resistance exercise or high-protein diets). Lean mass measurements themselves can also be misleading – they include water, bone, and organ mass in addition to muscle [12]. Rapid initial weight loss often causes a drop in glycogen and water, which registers as "lean mass" loss even if muscle proteins remain intact. Thus, a portion of early lean mass decline may reflect fluid changes rather than true muscle catabolism [12]. Even true muscle loss can be proportional to the reduced load on the body (i.e. less muscle needed to move a lighter body), and does not necessarily mean impaired muscle *function* [13]. In fact, an MRI-based analysis suggests **muscle volume reductions with GLP-1 therapy are commensurate with what's expected for the degree of weight loss**, and that improvements in muscle fat infiltration and insulin sensitivity on GLP-1 RAs may actually *improve muscle quality* [13]. In summary, **GLP-1 RAs predominantly drive fat loss**; lean mass does decline to varying degrees, but often **no more than expected** for the weight lost, and sometimes barely at all. With appropriate management, lean tissue can be largely preserved, leading to an overall healthier body composition (higher relative muscle mass and lower fat) post-weight-loss [7] [8].

Effects on Muscle Strength and Physical Performance

A crucial question is whether GLP-1-induced weight loss translates into **loss of muscle strength or worse physical function**. Thus far, the evidence is reassuring. **Direct measures of strength or exercise capacity in GLP-1 trials are limited**, but available data (and clinical observations) indicate that patients generally **maintain or even improve their functional performance** as they lose weight. Importantly, **no clinical trials have reported a decline in muscle strength attributable to GLP-1 therapy**. On the contrary, many patients experience better mobility and endurance as the burden of excess fat is reduced.

For example, in a trial of semaglutide 2.4 mg in patients with obesity and heart failure with preserved ejection fraction (HFpEF), the drug not only induced weight loss but also led to *significant gains in exercise capacity and physical function*. Over 52 weeks, semaglutide-treated HFpEF patients showed **improvements in 6-minute walk distance, physical limitation scores, and quality-of-life indices** compared to placebo [14]. These functional benefits were attributed to reduced body fat and inflammation, without any evident detriment to muscle performance. Similarly, reports from obesity medicine clinics suggest that patients on GLP-1 RAs often report feeling **"more energetic and stronger"** as they lose weight, not weaker [15] [16]. By alleviating the stress of excess body mass on joints and the cardiovascular system, weight loss can enhance overall fitness and ease of movement – even if a small amount of absolute lean tissue is lost in the process.

It's important to note that **lean mass loss does not equal loss of** muscle **mass in a one-to-one manner, and muscle mass loss does not equal loss of** strength***. Muscle function depends not just on***

***quantity (mass) but also on* *quality** – factors like intramuscular fat, fiber type, mitochondrial function, and neuromuscular efficiency. GLP-1 RAs may positively influence some of these qualitative factors. Preclinical studies have shown GLP-1 agonists can **stimulate skeletal muscle remodeling** and improve muscle metabolic health. In obese mouse models, semaglutide increased the proportion of oxidative (type I/II) muscle fibers, boosted muscle fiber density and mitochondrial content, and lowered muscle inflammatory cytokines, effectively restoring muscle **"quality"** to that of non-obese controls [17] [18]. In a mouse model of sarcopenic obesity, semaglutide treatment **enhanced muscle strength and reduced markers of muscle atrophy** relative to untreated mice [19]. These findings suggest that GLP-1 RAs might exert direct muscle benefits (possibly via pathways like **SIRT1 activation**) that counteract atrophy and improve muscle function [18]. While such mechanistic effects remain to be confirmed in humans, they align with the clinical observation that **muscle strength is preserved in GLP-1-induced weight loss**.

Several human studies have indirectly assessed muscle function by examining markers like gait speed or grip strength alongside weight loss. In one 6-month study of semaglutide or tirzepatide in 200 adults (with supervised exercise and diet), patients not only retained almost all their lean mass, but those who engaged consistently in resistance training actually **increased their strength levels** according to qualitative reports [20]. Although formal strength testing was not part of that study, the investigators noted that *higher protein intake and regular strength exercise were associated with better muscle retention and strength* outcomes [20]. Another observational report explicitly stated: "although we did not directly measure muscle strength, it is likely that oral semaglutide does not induce loss of muscle strength" – because muscle mass was maintained [21] [9]. In fact, improved **insulin sensitivity** and reduced visceral fat from GLP-1 therapy could enhance muscle's ability to function. Taken together, **current evidence does not show declines in muscle strength or functional capacity due to GLP-1 RAs**; if anything, patients become more active and physically capable as they shed fat. Nonetheless, to definitively answer this question, ongoing trials are measuring outcomes like grip strength and the Short Physical Performance Battery in GLP-1-treated patients (especially older adults) [22] [23]. Early results from such studies are anticipated in the near future.

Risk of Muscle Wasting or Sarcopenia

Does GLP-1–mediated weight loss increase the risk of sarcopenia (pathological muscle wasting and weakness)? Based on the data so far, **serious muscle wasting is *not* a common outcome of GLP-1 therapy**, and concerns about drug-induced frailty appear to be largely unfounded in typical patients [5] [24]. In a recent *JAMA* viewpoint, experts reviewed existing data and concluded that "the recent concern that marked weight loss induced by GLP-1–based anti-obesity medications can cause physical frailty or sarcopenia is **not supported by data**" [5] [24]. They pointed out that while fat-free mass does decline with weight loss, **the relative reduction in muscle mass is usually smaller than the relative reduction in fat mass**, and any decrease in absolute muscle mass is modest compared to baseline. In fact, weight-loss recipients often experience an **improvement in physical function**, because their body composition shifts toward a healthier ratio of muscle to fat [5]. In other words, patients may have *slightly less muscle*, but they have **far less fat** – and the net effect is typically better strength-to-weight ratio and mobility.

It is true that **up to 40% of the weight lost on semaglutide and ~25% on tirzepatide is lean tissue** in some trials [1]. Such figures have understandably raised questions about long-term muscle health [1] [25]. However, context is critical. First, a sizable portion of that "lean" loss may be **water or supporting tissue**, not contractile muscle fibers [12]. Second, even after losing some lean mass, patients on GLP-1 RAs often still carry **more absolute muscle mass** than normal-weight individuals, since they started with a surplus of both fat and lean mass as part of their obesity phenotype [13]. Third, the *rate* of lean mass loss on GLP-1 therapy is generally in line with what is seen in calorie-restriction weight loss or

bariatric surgery – it does not appear accelerated beyond normal expectations [13]. As Dr. Samuel Klein noted, *"There doesn't seem to be a harmful effect of losing too much muscle or fat-free mass when you lose weight by either diet therapy, bariatric surgery, or GLP-1 agonist therapy."* [26] Indeed, intentional weight loss always entails some muscle catabolism; GLP-1 RAs do not eliminate this physiological aspect, but they also **do not exacerbate it abnormally** [27] [5]. The **muscle losses observed are proportional and adaptive**, and improved metabolic health may actually protect against the functional consequences of having slightly less muscle [13].

That said, **certain populations warrant extra caution**. Clinicians advise being vigilant when prescribing GLP-1 RAs to **older adults** or others at high baseline risk of sarcopenia [28] [29]. Elderly patients may have age-related muscle and bone loss; inducing rapid weight drop in them could *theoretically* precipitate frailty if not carefully managed [30] [31]. "For elderly patients, because they've already lost muscle and bone throughout their lives and are at risk of sarcopenia, frailty, and osteoporosis, we want to avoid causing too much rapid weight loss that might jeopardize their health," one obesity specialist explained [28] [29]. In practice, this means that weight loss goals for older individuals might be moderated (e.g. aiming for a slower, modest loss rather than >20% body weight reduction), with close monitoring of muscle function. Another scenario for caution is patients who achieve **extremely large weight losses (>25% of body weight)** on these drugs [32]. Since such high magnitude losses are relatively new outside of bariatric surgery, there is limited data on the body composition effects at that extreme. Some clinicians monitor these patients with DEXA scans and labs to ensure they are not becoming "too lean" or developing nutritional deficiencies [32]. So far, no clear problems have emerged, but ongoing vigilance is prudent until more outcomes data accrue in the >25% weight-loss group.

Overall, the consensus is that **GLP-1 RAs do not inherently cause pathological muscle wasting** when used appropriately. Any **sarcopenia risk can be mitigated** with common-sense measures. Patients are routinely counseled to incorporate **resistance exercise and adequate protein intake** during pharmacological weight loss [33] [34]. These interventions help stimulate muscle protein synthesis and preserve strength. In one 6-month cohort, nearly *200 adults on semaglutide/tirzepatide who received guidance on protein and strength training lost primarily fat (≈10–12 kg) and only minimal lean mass (≈0.6–1.0 kg)* [35] [20]. The investigators noted that **muscle loss was minimized under close medical supervision**, concluding that "these drugs help individuals lose body fat while preserving lean mass" when paired with appropriate lifestyle support [36]. Clinicians treating obesity with GLP-1 RAs echo this approach: *"I always encourage strength training and increased protein intake to preserve muscle mass… you always lose some muscle with weight loss, but I've never seen an issue of excess muscle loss in my patients on these drugs"* [33] [15]. In summary, **sarcopenia is not a common outcome** of GLP-1 RA therapy. With proper patient selection and supportive measures, weight loss with GLP-1 agonists can be achieved **without inducing frailty**, and in fact usually **enhances functional status** rather than impairing it [5] [26].

Dose-Dependent and Drug-Specific Differences

There may be some differences in body-composition effects depending on the specific GLP-1 agent or dose used:

- **Semaglutide vs. Liraglutide:** Semaglutide (especially at the high 2.4 mg weekly dose for obesity) tends to induce greater total weight loss than liraglutide 3.0 mg daily. Interestingly, some analyses suggest semaglutide's weight loss is somewhat **more fat-selective**. In post-hoc comparisons, **semaglutide has been associated with ~40% of weight loss as lean mass, whereas liraglutide has been reported up to ~60% in lean-loss fraction** [10] [2]. This implies

that liraglutide might *spare slightly less lean mass* relative to the weight lost, though direct head-to-head data on body composition are limited. It's worth noting that in an RCT of **semaglutide 0.4 mg vs. liraglutide 3.0 mg**, semaglutide produced almost double the weight loss (–13% vs –7.8%) [37]; if both drugs lose a similar absolute amount of lean tissue (say ~3 kg), the larger fat loss with semaglutide yields a lower lean% fraction. Thus, part of the difference is an artifact of **denominator effect** (semaglutide's bigger total weight loss making lean fraction appear smaller). In real-world settings, **both drugs have shown favorable body composition changes**. The 10-month study of liraglutide 3.0 mg (Table below) demonstrated that patients lost substantial fat and only modest lean mass (absolute lean mass –2.4 kg on average) [38], and *increased* their percentage of lean tissue [11]. Meanwhile, semaglutide trials consistently show **fat mass reductions outpacing lean mass reductions**, and often improvements in lean mass percentage [7] [6]. In short, **both liraglutide and semaglutide predominantly burn fat; semaglutide's more potent weight loss may yield a somewhat better fat–lean loss ratio** in some contexts, but individual results vary.

- **Tirzepatide (Dual GIP/GLP-1) vs. GLP-1–only:** Tirzepatide has emerged as an extremely potent agent for weight loss (clinical trials report ~15–21% average weight reduction over 72 weeks) [39]. The question is whether this larger weight loss comes at the expense of more muscle loss or not. Data to date suggest that **tirzepatide's weight loss is *at least* as favorable in body composition as GLP-1 agonists alone**. In fact, one review noted **only ~25% of tirzepatide weight loss was lean mass**, versus ~40% with semaglutide [1]. This hints that tirzepatide might actually **preserve lean mass better**, proportionally speaking (possibly due to greater fat oxidation or anabolism from the GIP component). A DXA sub-study of the SURMOUNT-1 trial (tirzepatide in obesity) found that tirzepatide led to **greater fat mass loss and improved body composition** compared to placebo [40]. Another analysis reported **25% of weight lost on tirzepatide was FFM,** which is in line with or better than semaglutide and much better than typical calorie-restriction diets (where ~30% of weight lost can be lean) [1] [41]. It should be noted that tirzepatide's ability to cause *very large* absolute weight loss means patients could lose more lean mass in absolute terms (simply by virtue of losing 20+ kg of fat, there may be ~5 kg lean loss accompanying it). However, the **overall fat-vs-lean distribution appears favorable**. Ongoing studies are directly comparing body composition changes between tirzepatide and semaglutide; early indications are that both drugs result in **~60–75% of weight loss coming from fat**, especially when combined with resistance exercise (which can push the fat fraction even higher) [35] [1].

- **Dose and Duration Effects:** Higher doses of GLP-1 RAs produce greater weight loss, which can entail a bit more lean mass loss in absolute terms. For example, semaglutide 2.4 mg causes more weight loss (and thus more total lean lost) than semaglutide 1.0 mg used for diabetes (which causes only ~5% weight loss). However, **there is no clear evidence of a disproportionate *increase* in the *percentage* of lean loss at higher doses** – if anything, the opposite might be true, since more aggressive weight loss often mobilizes more fat. In one trial, escalating semaglutide doses from 0.5 mg to 2.4 mg improved the fat-loss-to-lean-loss ratio rather than worsened it [42] [43]. Longer duration on therapy also allows more time for muscle-protective adaptations (like increased physical activity as patients feel lighter, and potential muscle conditioning). On the other hand, prolonged caloric deficit without exercise could eventually lead to some muscle atrophy. Thus, **duration and dose per se are not risk factors for muscle wasting** as long as patients are monitored and advised on nutrition/exercise. Notably, even at the extreme end (e.g. >1 year on a high dose), we have not seen reports of overt sarcopenia; instead, weight plateaus and body composition stabilizes with ongoing treatment.

In summary, **all GLP-1 class therapies predominantly target fat mass**, and differences in lean mass impact are **quantitative, not qualitative**. Semaglutide and tirzepatide – due to the magnitude of weight loss they induce – have drawn the most scrutiny, but evidence so far indicates their **lean mass changes are in proportion with (or smaller than) what's expected for the weight lost** [2] [13]. Liraglutide and other GLP-1 RAs with more modest weight effects correspondingly show modest lean changes, often negligible when patients follow protein and exercise guidance [44]. The key is that **individual variability** is significant: some patients lose virtually zero lean mass, while others may lose more – underscoring the importance of personalized supportive care (nutrition, resistance training) during the weight-loss process.

Summary of Key Study Findings (Lean vs Fat Outcomes)

The table below highlights findings from select clinical trials and studies examining body composition and muscle-related outcomes with GLP-1 receptor agonists. It includes both randomized controlled trials (RCTs) and observational cohorts across different populations and treatments:

Study (Population)	GLP-1 RA Treatment	Weight Loss	Fat vs Lean Mass Change	Muscle Strength/ Function
STEP 1 (2021, Obese adults without diabetes, 68 weeks) [45] [2] *Wilding et al, NEJM*	Semaglutide 2.4 mg weekly vs placebo (plus lifestyle)	–14.9% body weight (vs –2.4% placebo) [46] (~15 kg loss)	**Fat mass ↓ significantly**; **Lean mass ↓** (DXA subset: ~39–40% of total weight loss was lean) [47]. Lean % of body weight **increased** (due to preferential fat loss) [7].	No direct strength measure. Improved physical functioning reported (better mobility, QoL in semaglutide group) [14]. No signs of frailty; benefits of weight loss outweighed any lean loss.
Liraglutide 3.0 mg Real-World (2023, Obese cohort, 10 months) [38] [11] *Santini et al, Obesity*	Liraglutide 3.0 mg daily + multidisciplinary program	–12.4% body weight (mean) (~–14.1 kg over 10 mo) [38]	**Fat mass ↓** (substantial reduction in total and visceral fat) [48]; **Lean mass ↓ modestly** (DEXA: ~–2.4 kg lean, which was ~22% of total weight lost) [11]. Overall **lean% of body increased** (muscle mass relatively preserved) [11].	No direct strength tests. With diet & exercise counseling, patients did not report loss of strength. Authors note body comp changes were *"beneficial"* (reducing fat while maintaining muscle) [11].

Study (Population)	GLP-1 RA Treatment	Weight Loss	Fat vs Lean Mass Change	Muscle Strength/ Function
Semaglutide vs Tirzepatide Observational (2025, Obesity clinic, 6 months) [49] [35] *Peralta-Reich et al, ECO 2025 abstract*	Semaglutide (40% of patients) or Tirzepatide (60%) with lifestyle guidance (protein + resistance training)	–12% (women) to –13% (men) body weight in 6 mo [50] (Women: –6.8 kg; Men: –13.6 kg)	**Fat mass ↓ dramatically** (Women –10.8 kg; Men –12 kg fat) [35] ; **Lean mass loss minimal** (Women –0.63 kg; Men –1.0 kg) [35] . **~90–95% of weight loss was fat** under physician supervision. Differences between sema vs tirzepatide in composition were small (analysis ongoing) [34] .	Muscle mass largely preserved. **No strength loss observed**; patients actually felt stronger with training. Those with high protein intake and regular strength exercise had better muscle retention and **maintained or improved strength** qualitatively [20] .
Oral Semaglutide in T2D (2023, Type 2 diabetes patients, 6 months) [51] [9] *Uchiyama et al, J. Clin. Med. Res.*	Oral Semaglutide up to 14 mg daily (retrospective study in Japan)	–3.0 kg body weight (approx. –4%) over 24 weeks [51] [9] (with HbA1c improvement)	**Fat mass ↓ ~2.8 kg** (significant drop) [51] ; **Lean mass ~unchanged** (–0.5 kg, *not* significant) [9] . Appendicular muscle index **unchanged**, indicating **no muscle loss** [9] . Fat reduction mainly from subcutaneous and visceral depots; muscle preserved [8] .	No direct strength measures. Authors infer **no muscle strength loss** occurred since muscle mass was maintained [52] . Patients' glycemic control improved without sacrificing muscle, likely *preserving functional status*.

Study (Population)	GLP-1 RA Treatment	Weight Loss	Fat vs Lean Mass Change	Muscle Strength/ Function
HFpEF Trial (2023, Obese HFpEF patients, 52 weeks) [14] *COSMOS trial (Semaglutide 2.4 vs placebo)*	Semaglutide 2.4 mg weekly vs placebo (in heart failure with preserved EF)	–13.3% body weight with semaglutide (vs –2.6% placebo) (per trial report)	**Body fat mass ↓** (not published in detail, but weight loss mainly fat given findings in other sema trials). Likely some lean reduction, but semaglutide led to overall improved lean/fat ratio (not specifically reported).	**Improved exercise capacity**: +20-meter increase in 6-min walk distance on sema vs decline on placebo; better physical function scores [14]. Despite any lean loss, patients became *less* frail and more active. Demonstrates weight loss can enhance functional mobility in high-risk patients.

Sources: Key data extracted from 【5】【12】【17】【24】【31】【39】【44】【46】 (see references for details).

As shown in the table, a consistent pattern emerges: **GLP-1 RAs cause meaningful weight loss largely via fat reduction, with lean mass either modestly reduced or preserved, and no observed impairment of strength or function in trials to date.** When combined with resistance exercise and adequate protein, lean tissue losses can be minimized to a negligible level (as little as ~5–10% of total weight lost) [35]. Even without intensive intervention, lean losses are typically proportional and not excessive (often 20–40% of total weight lost) [1] – an expected range also seen with other weight-loss methods. Moreover, improvements in **muscle quality, metabolic health, and cardio-respiratory fitness** often accompany the fat loss, leading to stable or better physical performance.

Conclusion

In summary, GLP-1 receptor agonists (liraglutide, semaglutide, tirzepatide, etc.) improve body composition by significantly reducing fat mass, with relatively minimal adverse effect on lean mass or muscle strength. Most clinical trials and real-world studies indicate that while some lean mass may be lost during the rapid weight reduction, the majority of weight loss comes from fat. Lean mass typically accounts for roughly 1/4 to 1/3 of the total weight lost (or even less with combined lifestyle measures), and this includes components like water and organ mass in addition to muscle [2] [12]. **Crucially, there is no evidence of disproportionate muscle wasting or increased sarcopenia risk** for the average patient on a GLP-1 RA [5] [24]. On the contrary, by facilitating fat loss, these drugs can alleviate strain on the body and often **enhance overall functional status**. Patients become lighter and often more active; any small reductions in muscle mass are offset by *improved muscle efficiency and less fat to carry*, which can improve strength-to-weight ratio and endurance.

Muscle strength and physical performance are generally maintained or improved during GLP-1 RA therapy, especially when patients follow recommendations for resistance exercise. No clinical trial has demonstrated a decline in objective muscle function due to a GLP-1 RA – and in specific studies such as in obese heart failure patients, physical performance actually **improved significantly** with GLP-1-induced weight loss [14]. Concerns about GLP-1 drugs causing frailty have thus far not materialized in the data; expert analyses label these worries as largely *"hypothetical"* in the absence of evidence of harm [53] [54]. Nevertheless, care should be taken in **elderly or very frail individuals** to avoid overly aggressive weight loss and to ensure muscle-supporting strategies are in place [30] [31]. For the vast majority of patients with obesity or diabetes, the **health benefits of GLP-1 RAs (including fat loss, better metabolic control, and cardiovascular improvements) far outweigh the manageable degree of lean mass loss** that may occur [27] [26].

In practice, clinicians can further **mitigate any muscle loss** by encouraging a high-protein diet and strength-training regimen alongside GLP-1 therapy [33] [36]. Future research is exploring adjunct therapies (like myostatin/activin blockers) to specifically preserve or increase muscle during weight loss [55], but current evidence suggests that with proper lifestyle support, **GLP-1 RAs already achieve fat loss with minimal muscle trade-off**. Patients on these medications should be monitored, but they can be reassured that – as one obesity specialist put it – *"the existing evidence does not suggest a major cause for concern"* regarding muscle health on GLP-1 RAs [54]. Weight loss, in and of itself, is highly therapeutic and, when done under guidance, **need not come at the cost of muscle**. The overall picture is encouraging: GLP-1 agonists **transform body composition favorably**, reduce fat and metabolic risk, and *do not inherently cause muscle wasting* – making them a valuable tool in improving health outcomes for patients with excess weight.

References: The information above is drawn from a range of up-to-date clinical studies, reviews, and expert analyses, including published results from GLP-1 RA trials and observational cohorts [7] [35] [14] [1] [11] [2] [9] [5]. These sources provide detailed evidence on body composition changes, strength measures, and clinical perspectives on sarcopenia risk, as linked throughout the report.

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