Preserving Healthy Muscle during Weight Loss[1–3]

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ABSTRACT

Weight loss is the cornerstone of therapy for people with obesity because it can ameliorate or completely resolve the metabolic risk factors for diabetes, coronary artery disease, and obesity-associated cancers. The potential health benefits of diet-induced weight loss are thought to be compromised by the weight-loss–associated loss of lean body mass, which could increase the risk of sarcopenia (low muscle mass and impaired muscle function). The objective of this review is to provide an overview of what is known about weight-loss–induced muscle loss and its implications for overall physical function (e.g., ability to lift items, walk, and climb stairs). The currently available data in the literature show the following: *1*) compared with persons with normal weight, those with obesity have more muscle mass but poor muscle quality; *2*) diet-induced weight loss reduces muscle mass without adversely affecting muscle strength; *3*) weight loss improves global physical function, most likely because of reduced fat mass; *4*) high protein intake helps preserve lean body and muscle mass during weight loss but does not improve muscle strength and could have adverse effects on metabolic function; *5*) both endurance- and resistance-type exercise help preserve muscle mass during weight loss, and resistance-type exercise also improves muscle strength. We therefore conclude that weight-loss therapy, including a hypocaloric diet with adequate (but not excessive) protein intake and increased physical activity (particularly resistance-type exercise), should be promoted to maintain muscle mass and improve muscle strength and physical function in persons with obesity. *Adv Nutr* 2017;8:511–9.

Keywords: sarcopenia, dynapenia, weight loss, lifestyle therapy, muscle quality

Introduction

Obesity is associated with cardiometabolic diseases (e.g., diabetes and coronary artery disease) (1–3) and certain types of cancer (e.g., colon) (4–6), and diet-induced weight loss can ameliorate or completely resolve the metabolic risk factors (e.g., insulin resistance, dyslipidemia, increased blood pressure) for these conditions (1–3, 5–8). The potential health benefits of diet-induced weight loss could be compromised by the weight-loss–associated loss of lean body (including muscle) mass (9, 10), which could increase the risk of sarcopenia (defined as low muscle mass and impaired muscle function) (10–12), especially in vulnerable populations, such as postmenopausal women and older adults (10, 13–18). In the general population, muscle mass is a poor predictor of muscle strength (19–21), because of interindividual differences in muscle composition (e.g., deposition of noncontractile material, such as lipids and connective tissue) and neuromuscular adaptations to regular use or disuse that affect the ability of muscle to generate force (19–21). Moreover, both weight loss and weight gain are accompanied by corresponding changes in both body fat and fat-free (including muscle) mass (22–25). Accordingly, persons with obesity have more total fat-free and muscle mass than those with normal weight (26–28). This review will focus first on what is known about the effects of obesity on muscle quality and function and subsequently discuss the effects of weight loss on muscle mass, quality, and function and potential therapeutic strategies to improve not only muscle mass but also muscle function in persons with obesity. Articles to address these key questions were selected from a thorough literature search in PubMed intended to be inclusive of all relevant work in the area. Note that, for simplicity, we refer to both fat-free and lean body mass as fat-free mass throughout the article.

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Current Status of Knowledge

Effect of obesity on muscle quality and muscle function

Few studies have evaluated muscle mass, quality, and function in people with obesity, but they consistently show that obesity is associated with poor muscle quality, which adversely affects muscle function (27–30). Lafortuna et al. (27) found an inverse relation between adiposity and muscle lipid content (assessed by X-ray attenuation) in middle-aged and older men and women. Choi et al. (28) found that older adults with obesity had ∼20% more thigh muscle mass and ∼2 times more muscle lipid content (assessed in vivo as ultrasound echo intensity) than older adults with normal weight (28). They also found that obesity was associated with reduced ex vivo single-myofiber function (peak Ca^{2+}-activated force) and in vivo muscle function (peak torque) (28). Furthermore, they found an inverse relation between the average number of lipid droplets in myofibers and single-fiber unloaded shortening velocity, maximal velocity, and specific power and an inverse relation between muscle lipid content (assessed in vivo as ultrasound echo intensity) and single-fiber specific force (28). Large epidemiologic studies have also shown an inverse association between muscle lipid content (assessed by X-ray attenuation) and maximum voluntary strength (29) and walking speed (30). Reduced muscle strength and power are key predictors of serious adverse outcomes in older adults, including the inability to carry out activities of daily living (31), mobility disability (32–34), falls (∼20% increase in incidence rate for each ∼15% decrease in lower leg strength), hip fracture (35–39), and mortality (∼4% increase for every 1-kg decrease in grip strength) (40, 41). Indeed, obesity in older adults is associated with poor physical function, assessed by using the Modified Physical Performance Test, which includes activities such as climbing stairs, rising from a chair, lifting a book onto a shelf, and walking speed (42), and an increased risk of falls (as much as in people with vision problems or a stroke) (43). Improving muscle quality, rather than preserving or increasing muscle mass, should therefore be the primary focus of therapeutic strategies for people with obesity.

Effect of diet-induced weight loss on muscle mass in persons with obesity

Weight loss, achieved through a calorie-reduced diet, decreases both fat and fat-free (or lean body) mass (44–46). In persons with normal weight, the contribution of fat-free mass loss often exceeds 35% of total weight loss (47, 48), and weight regain promotes relatively more fat gain (49). In persons who are overweight or obese, fat-free mass contributes only ∼20–30% to total weight loss (48, 50–59), and weight regain does not prevent fat-free mass regain (49). Men tend to lose more fat-free mass than women, especially shortly after the initiation of weight loss (60, 61), probably because they are leaner than women (26). Diet-induced weight loss in those with obesity therefore results in a more favorable fat-free mass to fat mass ratio despite loss of lean mass, and weight cycling (yo-yo effect) has no adverse effect on body composition in persons with obesity (49).

The effect of diet-induced weight loss on muscle mass has been evaluated by measuring changes in muscle volume by using MRI or computed tomography (53, 55, 59, 62–64) or by measuring changes in appendicular lean body mass (as a proxy for limb muscle mass) by using whole-body DXA (47, 52, 54, 56, 65, 66). The reductions in muscle mass in young and old men and women with obesity after diet-induced weight-loss of 8–10% were ∼2–10% (47, 52–56, 59, 62–66). Such changes are significant but most likely reflect a new (post–weight loss) muscle mass that is consistent with the new, reduced body weight rather than a diet-induced "muscle deficit" because of the greater initial muscle mass in persons with obesity than in those with normal weight (24–28).

Bariatric surgery, which results in rapid and massive weight loss (>20% of total body weight), does not seem to accelerate the loss of fat-free mass relative to total body or fat mass loss (67–72). Most studies that evaluated the effect of bariatric surgery–induced weight loss on body composition found that neither restrictive nor malabsorptive procedures resulted in excessive amounts of fat-free relative to fat mass loss 1–2 y after surgery (67–72). The average contribution of fat-free mass to total weight loss was <30%, and the relative contribution of fat-free mass to total body weight after weight loss was either not different or even greater than in sex-, age-, and BMI-matched control subjects (67–72). Only 1 study reported a contribution of >35% of fat-free mass to total body weight loss 1–2 y after sleeve gastrectomy and Roux-en-Y gastric bypass surgery (73).

Only 2 studies evaluated the effect of bariatric surgery on surrogate measures of muscle mass (72, 74). One (72) evaluated changes in appendicular lean mass after sleeve gastrectomy and Roux-en-Y gastric bypass surgery but did not include a diet-induced weight-loss or weight-maintenance control group. Appendicular lean body mass loss was highly variable: approximately two-thirds of the subjects lost <15% and one-third lost >15% of their appendicular lean mass 1 y after surgery in that study (72). The other study (74) evaluated vastus medialis thickness after matched weight loss achieved by either a hypocaloric diet or gastric banding and found a greater reduction in vastus medialis thickness in the bariatric surgery group than in the diet-induced weight-loss group (∼3% compared with 0.5%/y). The mechanism responsible for the difference in muscle loss in that study (74) is unclear because gastric banding is a purely restrictive procedure (i.e., it results in weight loss entirely because of reduced dietary energy intake). Accordingly, the effect of bariatric surgery on muscle mass remains unclear.

Mechanisms responsible for loss of muscle mass during diet-induced weight-loss–protein synthesis versus breakdown

The mechanisms responsible for the weight-loss–induced decrease in muscle mass (reduced muscle protein synthesis, increased breakdown, or both) have not been extensively studied. Studies that evaluated the effect of short-term (14–21 d) calorie restriction (∼30–40% energy deficit/d) on the rate of muscle protein synthesis in young and middle-aged men and women who were overweight and obese found that calorie restriction decreases the postprandial rate of muscle protein synthesis and decreases or does not change the basal rate of muscle protein synthesis (75–77). Prolonged moderate calorie restriction and 5–10% weight loss, on the other hand, increased the rate of muscle protein synthesis (78, 79). The loss of muscle mass during prolonged moderate calorie restriction is therefore mediated by increased muscle proteolysis rather than suppressed muscle protein synthesis.

Strategies to prevent the weight-loss–induced loss of muscle mass

Regular physical activity, especially resistance-type exercise training, and high protein intake (1.25–1.5 times the RDA for sedentary persons and >1.5 times the RDA for those who exercise) are recommended for persons with obesity who undergo weight-loss therapy to limit the loss of muscle mass (80–82), because dietary amino acids, insulin, and contractile activity are the major regulators of muscle protein synthesis and breakdown (83). Amino acids and dietary protein stimulate muscle protein synthesis in a dose-dependent manner $\leq \sim 20$ g protein/meal (84, 85). Insulin is a potent inhibitor of muscle protein breakdown and maximally suppresses muscle protein breakdown at plasma insulin concentrations of 15–30 μU/mL (86–89). Exercise (both resistance and endurance type) improves insulin sensitivity (90, 91) and stimulates muscle protein synthesis (92). The effects of increased physical activity, exercise training, and increased protein intake during weight-loss therapy on muscle mass and muscle function are summarized in the following sections.

Effects of exercise training or increased physical activity on muscle mass during diet-induced weight loss. Several investigators found that a progressive resistance exercise training program in conjunction with a hypocaloric diet attenuated the weight-loss–associated loss of muscle mass in middle-aged and older men and women (55, 65, 66). The effect of endurance-type exercise training on muscle mass during weight-loss therapy, however, is less clear (53, 59, 62–64). In middle-aged and older men and women with obesity, both a hypocaloric diet alone and a hypocaloric diet combined with ≥ 300 min/wk of moderate-intensity aerobic exercise decreased thigh muscle cross-sectional area, but the decrease in the diet-plus-exercise group was only approximately half that in the diet-only group (63). Two other studies found that daily brisk walking for ~1 h or vigorous endurance-type exercise for ~1 h for 6 d/wk preserved muscle mass, whereas weight loss achieved by consuming a hypocaloric diet decreased muscle mass in middle-aged and older men and women (53, 59). Others (62, 64), however, found that the addition of 35–45 min of aerobic exercise (moderate-intensity walking) 3–5 times/wk in obese older men and women led to decreases in thigh and trunk muscle cross-sectional areas similar to diet alone. Failure to detect a beneficial effect of exercise on muscle mass in ≥ 1 of these studies (64) may have been due to the small sample size and/or large interindividual variability in the response, which reduces statistical power, because the loss was ~70% greater in the diet-alone group (−5.2%) compared with the diet-plus-exercise (−3.0%) group. Together, these results suggest that resistance-type exercise is an effective strategy to attenuate or even prevent the weight-loss–induced loss of muscle mass during weight loss, whereas the effects of endurance-type exercise on muscle mass during weight loss are uncertain. Nicklas et al. (93) evaluated the effect of adding calorie restriction to a resistance exercise program (3 d/wk) in older men and women with obesity and found that it prevented the exercise-induced increase in thigh muscle volume but did not decrease it compared with baseline values. These findings confirm the opposing actions of a hypocaloric diet and resistance exercise training on muscle mass.

Effect of high-protein intake on lean body and muscle mass during diet-induced weight loss. During energy balance or dietary energy excess, inadequate protein intake (i.e., less than the RDA of 0.8 $g \cdot kg^{-1} \cdot d^{-1}$) results in loss of total body fat-free and muscle mass (~0.2−0.5%/wk) (23, 94–96). During negative energy balance induced by a calorie-reduced diet, inadequate protein intake augments the weight-loss–induced loss of lean body mass (97, 98). However, adding protein to a diet that already contains the RDA of protein has no beneficial effect on total body fat-free and muscle mass during weight maintenance or weight gain (23, 99, 100). Whether increasing protein intake during weight loss can limit the weight-loss–induced loss of fat-free mass is unclear because of conflicting results reported in the literature (54, 56, 96, 98, 101–108). The reasons for the discrepancy in results in these studies (54, 56, 96, 98, 101–108) are not readily apparent but could be related to differences in baseline protein intake, diet composition, duration of the intervention, and the small effect of extra protein on fat-free mass, which may make it difficult to detect the difference in studies with small sample sizes. For example, Backx et al. (56) found no effect of protein supplementation on fat-free mass loss during weight loss in older men and women who already consumed the RDA of protein with their diet, whereas Schollenberger et al. (98) found that fat-free mass loss after Roux-en-Y gastric bypass surgery was attenuated in subjects who received protein supplementation compared with those who did not and consumed less than the RDA of protein. The results from the most recent systematic review and meta-analysis (109) support a very small but significant beneficial effect (400–800 g of lean mass preservation) of high protein intake on fat-free mass during weight-loss therapy.

The effect of varying protein intake on muscle mass during diet-induced weight loss has not been adequately studied. We are aware of only one study that evaluated the effect of increased protein intake during weight-loss therapy on muscle mass in older adults with obesity who lost weight by consuming a hypocaloric diet and were engaged in a resistance exercise training program (54). It found that subjects who added a whey protein–, leucine–, and vitamin D–enriched supplement compared with subjects who added

TABLE 1 Effects of obesity and weight loss on muscle mass, muscle strength, and global physical function[1]

		Weight loss			
				CR with increased muscle activity	
	Obesity	CR	CR + HP	Endurance exercise or PA	Resistance exercise
Muscle mass	O > L	↓↓	↓	↓	↔
Muscle strength[2]	O < L	↔	↔	↔	↑
Global physical function	O < L	↑	↑	↑↑	↑↑

[1] Double arrows indicate greater magnitude of effect than single arrow. CR, calorie restriction; HP, high protein; L, lean; O, obese; PA, physical activity. ↓, decrease; ↑, increase; ↔, no change.
[2] Intrinsic strength per unit of muscle mass or muscle fiber.

an isocaloric control drink to their diet (total protein intake: 1.1 compared with 0.85 g protein · kg^{-1} · d^{-1}) preserved appendicular muscle mass during weight loss.

As important as total daily protein intake could be the distribution of dietary protein intake over the course of the day, because there appears to be a refractory period during which muscle protein synthesis, once stimulated by amino acids, cannot be stimulated again ("muscle-full" phenomenon) (110). Accordingly, 2 studies conducted in healthy young and middle-aged men and women (111, 112) reported a greater overall muscle protein synthesis rate throughout the day when protein intake was evenly distributed throughout the day than with skewed protein intake (most of the protein consumed at dinner). The results from a recent retrospective analysis in a subset of subjects who participated in the NuAge study (Quebec Longitudinal Study on Nutrition as a Determinant of Successful Aging) also suggest that a more even distribution of protein intake across meals is associated with more appendicular lean body mass than is a skewed protein intake (least for breakfast, most at dinner) in older adults (113). Long-term prospective randomized controlled studies evaluating the effect of even compared with skewed protein intakes on muscle mass (or surrogate measures of muscle mass) are missing. The results from studies that compared the effect of even and skewed protein intakes on whole-body nitrogen retention and protein balance are equivocal and often contradict the acute effects of even compared with skewed protein intake on muscle protein synthesis (111, 112) and the results from retrospective analysis of the NuAge study data (113). Two randomized clinical trials in healthy middle-aged and older adults found no benefit of even, compared with skewed, protein intake on whole-body protein balance and muscle protein synthesis during weight maintenance (114) and fat-free mass retention during weight-loss therapy (115), even though total protein intake was greater in the even-protein-intake group (1.2 g · kg^{-1} · d^{-1}) than in the skewed-protein-intake group (0.8 g · kg^{-1} · d^{-1}) (115). Others found that protein pulse feeding (ingesting 80% of daily intake in one meal), compared with evenly distributed protein intake, increased whole-body nitrogen retention in healthy elderly (116) [but not young (117)] women and increased fat-free mass retention in malnourished hospitalized elderly patients (118). Esmarck et al. (119) evaluated the effect of protein supplementation in older men who participated in a 12-wk resistance exercise training program and were asked to consume a protein supplement either immediately after or 2 h after exercise. They found that the cross-sectional area of the quadriceps femoris and its mean myofiber area increased in subjects who consumed the supplement immediately after exercise but not in those who consumed it 2 h after the exercise (119). The exercise training sessions were performed between 800 and 1000 in the morning, so that subjects consumed the supplement either several hours after breakfast (immediately after exercise) or shortly before lunch (2 h after exercise) (119). It is therefore possible that the difference in the effect was due to the timing of the protein supplement relative to meal intake rather than the timing relative to the exercise session. The effect of protein intake distribution on muscle protein synthesis or muscle mass during weight-loss therapy has, to our knowledge, not been studied.

Together, these results suggest that increased protein intake, if distributed evenly throughout the day, may prevent the loss of muscle mass during weight-loss therapy. However, the additional protein may have adverse effects on glucose metabolism. Smith et al. (106) showed that protein supplementation of a hypocaloric diet eliminates the weight-loss–induced improvement in muscle insulin sensitivity (assessed by using the hyperinsulinemic-euglycemic clamp procedure), even though weight loss was the same (10%) in both the high-protein and standard-protein diet groups. In addition, data from small cross-sectional (120, 121) and large epidemiologic (122–126) studies suggest that high protein intake is involved in the pathogenesis of insulin resistance and type 2 diabetes.

Effect of diet-induced weight loss on muscle quality, muscle strength, and physical function

Diet-induced weight loss reduces muscle lipid content (assessed by X-ray attenuation or MRI) (52, 62, 63, 74) and does not affect (55, 65, 93), or slightly decreases (48, 52, 56), leg muscle strength. Grip strength and global measures of physical function, such as balance, walking speed, or climbing stairs, improve after weight loss (52, 54–56, 93, 115, 127). The improvements in physical function after diet-induced weight loss are most likely due to the loss of excess total body fat mass (128), which can interfere with range of motion, gait, etc. Weight loss induced by increasing energy expenditure through exercise (endurance or combined endurance and resistance type) improves muscle strength compared with diet-induced weight loss but does not improve strength compared with weight maintenance and does not improve physical function more than diet-induced weight loss (53, 55). Combined diet- and exercise-induced weight loss, on the other hand, results in greater improvements in physical function than weight loss through diet alone or exercise alone (53, 55). Most studies that evaluated the effect of increasing protein intake during weight loss on muscle strength and physical function did not find a beneficial effect of high protein intake on leg muscle strength or physical function in young and old and sedentary or physically active adults (54, 56, 98, 107). We are aware of only one study (115) that found a small, but nonetheless significantly greater, increase in physical function (assessed by using the Short Physical Performance Battery) in older obese adults who lost ~10% of their body weight and consumed 1.2 g protein · kg body weight^{-1} · d^{-1} and ≥30 g protein/meal than subjects in the control group who were instructed to consume 0.8 g protein · kg body weight^{-1} · d^{-1} in their habitual skewed pattern (~15% at breakfast, ~35% at lunch, and ~50% at dinner). The change in handgrip strength, however, was not different between groups (115). Together, these results suggest that weight loss, despite causing loss of muscle mass, has beneficial effects on muscle quality and improves overall physical function.

Potential novel dietary interventions to improve muscle mass, muscle strength, and physical function during weight loss

Several potential novel dietary interventions to increase muscle mass and muscle strength have been identified, including (but not limited to) vitamin D, fish-oil–derived n–3 FAs, and β-hydroxy-β-methylbutyrate (129–133). A recent meta-analysis of studies conducted between 1996 and 2014 found a small but significant positive effect of dietary vitamin D supplementation on muscle strength, especially in older people with vitamin D insufficiency, but no effect on muscle mass (129). However, the only study we are aware of that evaluated the effect of vitamin D supplementation on weight-loss–induced changes in muscle mass and function found that oral supplementation with cholecalciferol (2000 IU/d), compared with placebo, decreased leg (but not chest) strength and had no effect on muscle mass (134). Fish-oil–derived n–3 FA supplementation has been shown to improve muscle mass, strength, and physical function in weight-stable older adults (130, 131); and β-hydroxy-β-methylbutyrate, a metabolite of leucine, improved both muscle mass and strength in healthy young and older adults (132, 133). However, their effects on muscle mass and strength during weight loss are not known.

Summary and Conclusions

The currently available data in the literature, summarized in **Table 1**, show the following: *1*) persons with obesity have more muscle mass than those with normal weight but poor muscle quality; *2*) weight loss reduces muscle mass without adversely affecting muscle strength and improves global physical function, most likely because of reduced fat mass; *3*) adding exercise (endurance and resistance type) to a hypocaloric diet helps preserve muscle mass during weight loss, and resistance-type exercise also improves muscle strength; *4*) high protein intake helps preserve lean body and muscle mass but does not improve muscle strength and could have adverse effects on metabolic function. We therefore conclude that weight-loss therapy, including a hypocaloric diet with adequate (but not excessive) protein intake, and physical activity, particularly resistance exercise–type training, should be promoted to maintain muscle mass and improve muscle strength and physical function in persons with obesity.

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