REVIEW

OPEN

The impact and utility of very low-calorie diets: the role of exercise and protein in preserving skeletal muscle mass

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Purpose of review
Very low-calorie diets (VLCD) are used as a weight loss intervention, but concerns have been raised about their potential negative impact on lean mass. Here, we review the available evidence regarding the effects of VLCD on lean mass and explore their utility and strategies to mitigate reductions in skeletal muscle.

Recent findings
We observed that VLCD, despite their effects on lean mass, may be suitable in certain populations but have a risk in reducing lean mass. The extent of the reduction in lean mass may depend on various factors, such as the duration and degree of energy deficit of the diet, as well as the individual's starting weight and overall health.

Summary
VLCD may be a viable option in certain populations; however, priority needs to be given to resistance exercise training, and secondarily to adequate protein intake should be part of this dietary regime to mitigate losing muscle mass.

Keywords
energy restriction, muscle mass, resistance exercise training

INTRODUCTION

A very low-calorie diet (VLCD) is a dietary regimen that reduces energy intake to very low levels, usually between 800 and 1200 kcals per day [1]. This level of energy intake is often below an individual's resting metabolic rate. VLCD are often implemented to induce rapid weight loss among individuals with poor metabolic conditions, people with obesity, and have or are at risk of developing type II diabetes (T2D) [2]. A primary utility of a VLCD is to promote rapid weight loss in preparation for patients undergoing, for example, bariatric surgery [3,4]. In addition, VLCDs are often used by athletes who are seeking rapid weight loss for competition (i.e., weight-class specific sports) [5] and individuals who seek very low levels of body fat, such as a bodybuilder or physique athlete during periods of contest-preparation [6]. Although VLCDs have been demonstrated to be effective at reducing body and fat mass and improving metabolic health, they may have potential risks, including a reduction in lean mass, particularly skeletal muscle mass [3,7]. The effects on lean mass will depend on several factors, including an individual's baseline body composition, the magnitude and length of the VLCD, an individual's protein intake, whether they are performing resistance exercise training (RET), their training status (i.e., trained vs. untrained), and other lifestyle factors (i.e., sleep, stress, and so on) [8,9]. Thus, the purpose of this opinion paper is to review the utility of a VLCD and for whom it may be suitable.

The main risk from following a VLCD is the potential loss of muscle mass [7]. Preventing/negating muscle mass loss could result in avoiding

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KEY POINTS

- Rapid weight loss from VLCD may be a suitable option in the short term and may be used in a clinical context to improve health markers.
- To minimize the loss of lean mass during a VLCD, individuals must ensure they consume adequate protein intake (at least 1.2 g/kg) in conjunction with a RET regimen.
- Supplementation with either animal or plant-derived protein powders is advised, provided they are enriched with all nine essential amino acids.
- Older adults at risk of developing sarcopenia should be careful using VLCD; however, type 2 diabetes patients could benefit from VLCD.

declines in physical function and strength [10]. Especially with advancing age, it is important to maintain muscle mass to avoid accelerating sarcopenia [1]. An important distinction to acknowledge is that although muscle mass is a component of lean mass, they are not synonymous with one another. In addition, muscle mass accounts specifically for the weight of skeletal muscle within the body and lean mass typically refers to the total weight of anything that is not fat or bone, see Fig. 1. Although muscle mass is included, lean mass includes organs, connective tissue, and body water [11]. Thus, it is important to note that an increase or decrease in lean mass does not automatically equate to the same for muscle mass and *vice versa*. Indeed, maintaining or increasing muscle mass during periods of energy restriction will help to support metabolic health, improve physical performance and activities of daily living (ADL), and reduce the risk of chronic diseases such as sarcopenia, obesity, T2D, and cancer [12]. Baseline body composition has an important effect on the magnitude of the loss of skeletal muscle mass resulting from a VLCD. For example, well trained individuals with low body fat levels will have significantly less fat to burn than people with obesity; hence, such individuals will be unlikely to adhere to a VLCD long-term, if at all, without losing muscle mass. However, individuals with higher body fat levels could increase the magnitude and duration of a VLCD with a lower risk of atrophy, as they have more energy reserves (i.e., body fat). As energy levels become extremely low, the body will increase net muscle tissue loss to provide amino acid precursors for gluconeogenesis and fuel to match energy demands [13]. Another consideration is that the effect of VLCD on lean tissue may differ among clinical populations. Thus, VLCD are not without their shortcomings, but some strategies to prevent atrophy and maintain or even increase skeletal muscle mass are discussed in greater detail.

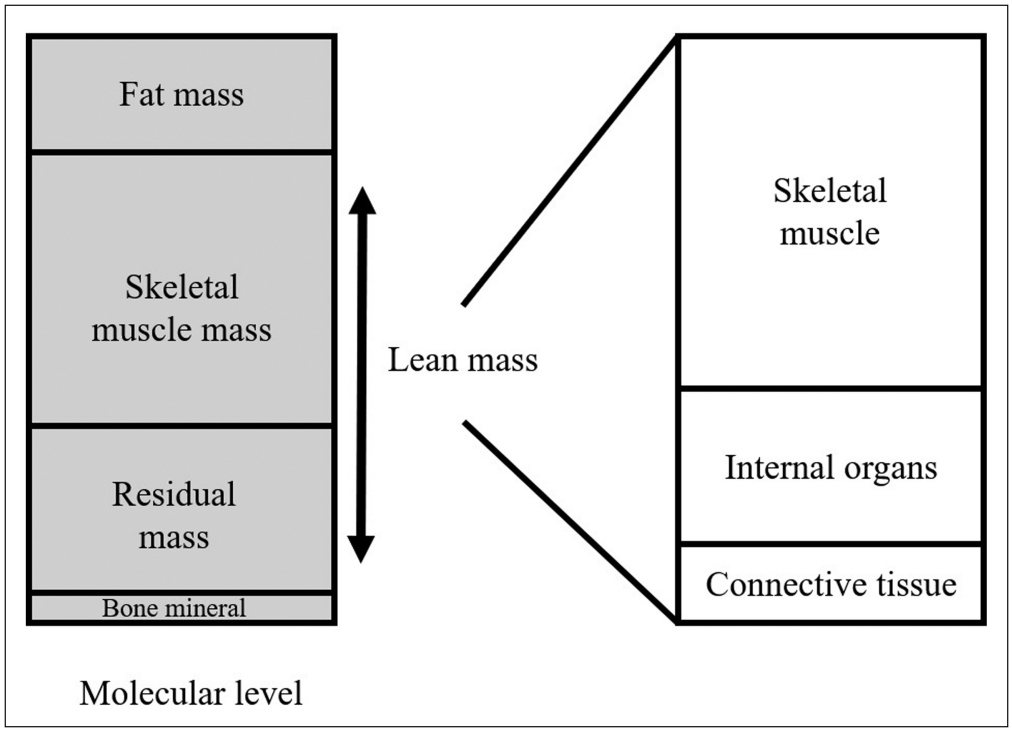

FIGURE 1. A schematic showing how body composition and lean mass are defined.

THE ROLE OF PROTEIN INTAKE

Skeletal muscle mass is regulated by the net balance between muscle protein synthesis (MPS) and muscle protein breakdown (MPB). On average, muscle protein has a daily turnover rate of nearly 1.5% [14]. The two primary stimuli for MPS are ingesting protein-containing food and physical exercise that creates muscle loading (resistance exercise training; RET) [15]. More specifically, protein ingestion increases the concentration of circulating essential amino acids (EAA), increasing MPS rates [16]. During energy restriction, muscle protein balance is shifted to a net negative state, likely through a decrease in MPS and maybe small increases in MPB, so amino acids are released as substrates for gluconeogenesis and as fuel for various tissues [17,18]. To maintain a more positive net muscle protein balance during an energy deficit, MPS must be increased by ingesting adequate amounts of dietary protein, exercising (i.e., RET), or combining the two. As the rate of MPB exceeds MPS, dietary protein becomes important for the maintenance and remodelling of skeletal muscle; however, it appears that RET is the major stimulus for muscle mass retention. Although there are some conflicting views on whether the dietary protein intake can independently preserve lean mass during periods of negative energy balance [9,19,20], multiple studies have demonstrated that lean mass can be maintained in obese/overweight individuals with additional protein ingestion either through their dietary sources or via supplementation [21,22]. Supplementation with whey protein has been shown to attenuate the decline in postprandial MPS following weight loss, which may be an effective strategy for long-term weight loss interventions [23]. It is important that the magnitude of the deficit is not too large, as protein intakes of 52 g/day (35% daily intake) or 77 g/day (40% daily intake) were not sufficient to mitigate reductions in lean mass in overweight or obese individuals following 8 weeks of a daily caloric intake of 600 and 700 kcal/day, respectively [24]. In addition, it may be important that dietary protein intake is evenly spread throughout the day with equivalent intakes at each meal occasion [25]. A retrospective analysis revealed that when ingesting an isolated source of protein, MPS had a ''breakpoint'' at 0.24 [90% confidence interval (90% CI): 0.18–0.30] g/kg and 0.40 (90% CI: 0.21–0.59) g/kg in older adults, respectively [26]. Furthermore, a recent meta-analysis revealed that protein supplementation beyond 1.6 g/kg resulted in no further gains in muscle mass and strength [25]. Thus, per-meal protein feedings should be between 0.30 and 0.59 g/kg (for younger to older adults) throughout the day, targeting a total daily intake of nearly 1.2–1.6 g/kg to stimulate MPS and suppress MPB optimally and support skeletal muscle repair and remodeling [27]. Lastly, recommendations should be tailored to an individual's health and training status in combination with the magnitude and duration of the diet. Future research should determine how different protein intakes affect various energy deficits among diverse populations.

THE ROLE OF EXERCISE

Exercise is usually categorized as aerobic (repetitive, continuous performance of activity to move lower loads or body weight) or resistance (intermittent performance of activity to move higher loads or body weight) [28]. Engaging in RET is the most potent nonpharmacological stimulus to activate MPS [29].

Evidence on the effect of aerobic exercise on skeletal muscle mass preservation is still unclear [1]. Given the compelling evidence, it stands to reason that RET is more effective for maintaining muscle mass during a VLCD due to its ability to stimulate MPS [30]. In addition, aerobic exercise burns significantly more energy and may lead to a lower increase in MPS than resistance exercise. It is important to note that exercise form does not need to be one or the other, as a combination of RET and aerobic exercise is the most effective in improving functional status in older obese adults [31,32▪]. Thus, we recommend that the duration and intensity of physical activity, combined with a VLCD, need a monitored personalized approach. Patients who are in the hospital for a prolonged period of time or have a disease that causes prolonged periods of bed rest should work closely alongside medical professionals (e.g., physicians, dieticians, physiotherapists, and so on) to ensure they improve their health outcome measures while mitigating the loss of muscle mass. Future research should aim to determine the impact of varying intensities and duration of both RET and aerobic exercise on skeletal muscle mass loss following VLCD [33▪▪].

ADEQUATE PROTEIN INTAKE IN COMBINATION WITH RESISTANCE EXERCISE TRAINING

Consuming adequate dietary protein may support lean mass maintenance; however, the anabolic effects of protein ingestion will be largely augmented acutely by prior RET [14,34]. During a caloric deficit, MPB remains constant, leading to the decline in MPS as the primary mechanism for reductions in lean mass [18,35▪]. It has been demonstrated that combining RET with protein intake spread across multiple feedings per day ''rescues'' this

decline in MPS [36]. When adhering to a VLCD, RET will be the most powerful nonpharmacological stimulus for maintaining muscle mass and attenuating muscle atrophy. When RET is combined with a higher protein intake (~1.2 g/kg), they work synergistically to promote lean mass sparing during periods of an energy deficit. Jo *et al.* [40] aimed to investigate the effect of a VLCD with adequate protein (1.1–1.3 g/kg) in conjunction with RET. Eleven obese individuals underwent 12 weeks of a VLCD with supplemental protein (1120 kcal/day), where one group was assigned to a control ($n = 5$) and the other was assigned to RET 3x/week ($n = 6$) [37]. Both groups lost a significant amount of total body and fat mass, with no differences between groups. Notably, the control group lost 4.6 ± 0.8 kg ($P = 0.004$) of lean mass, while the RET group had no changes. Thus, it is clear that RET positively affected weight loss and body composition by preserving lean mass without compromising overall weight or fat loss in obese men and women following a protein-supplemented (~1.1–1.3 g/kg/day) VLCD. In addition, these changes accompanied positive adaptations for resting metabolism and muscular function.

Adding RET to adequate dietary protein intake is also an effective strategy for older adults with metabolic impairments. Amamou *et al.* [21] had 26 overweight older adults (aged 60–75 years, BMI 32.4 ± 3.9 kg/m^2) with at least two factors of the metabolic syndrome and were randomized into two groups: high-protein caloric restriction protein (HP; $n = 12$) and high-protein caloric restriction combined with dynamic-resistance training (HP+RT; $n = 14$). Energy intake was reduced by 500 kcal/day in all participants, and protein intake equated to 25–30% of total calories (~1.4 g/kg/day). The authors reported significant reductions in total and trunk fat mass (FM) and fasting glucose, triglycerides, and total cholesterol levels, with no differences between the groups. However, total and appendicular lean mass significantly decreased only in the high-protein group. The authors concluded that although high-protein energy restriction improves the health profile among obese older adults at a high risk of chronic disease, it needs to be combined with RET to retain lean mass.

Longland *et al.* [38] studied young men adhering to nearly 40% energy deficit, providing 33 ± 1 kcal/kg lean mass, and randomly assigned to consume either a lower-protein (1.2 g/kg/day) (CON) or a higher-protein (2.4 g/kg/day) (PRO) diet. Both groups performed RET combined with high-intensity interval training 6 days per week. Results indicated that lean mass significantly increased in the PRO group (1.2 ± 1.0 kg) and to a greater extent compared with the CON group who maintained their lean mass (0.1 ± 1.0 kg). The PRO group had a greater fat mass loss than the CON group (PRO: -4.8 ± 1.6 kg; CON: -3.5 ± 1.4 kg; $P < 0.05$). Employing higher protein and RET concomitantly can, as shown, even increase muscle mass and reduce fat mass; such a pattern of weight loss has been referred to as high-quality weight loss or body recomposition [39,40]. Although it has been a common belief that untrained and obese populations would experience body recomposition due to the novelty of performing RET, evidence has shown that trained individuals can also experience recomposition [30]. However, the likelihood of experiencing body recomposition will depend on a multitude of factors such as an individual's training status (i.e., trained vs. untrained), the magnitude and length of their calorie deficit, lifestyle (i.e., sleep, stress, etc.), and their training variables (volume, intensity, frequency, etc.). For example, a VLCD may be suitable for someone who has higher levels of body fat and who are untrained/novice. Although feasible, trained individuals with low body fat levels should be cognizant of the potential downsides of a VLCD. Huovinen *et al.* [41] had national-level track and field males diet with either a large deficit (750 kcal deficit; ~24% restriction, $n = 8$) or a small deficit group (300 kcal ~12% energy restriction; $n = 7$). Both groups had higher protein intakes set at 2 g/kg. Although the group adhering to a large deficit lost significant weight (~2 kg) with no significant fat-free mass (FFM) loss, those with body fat below 10% could not preserve FFM. Thus, individuals who already have a lower amount of fat mass should be aware that periods of energy restriction and adherence to a VLCD will likely experience a loss of muscle mass and potentially other negative consequences (i.e., hormonal disturbances, sleep disruption, etc.).

CLINICAL POPULATIONS

Type II diabetes

VLCDs have been demonstrated to positively affect the health of persons with type 2 diabetes (T2D). The improved prognosis is primarily due to the large energy deficit resulting in rapid weight loss leading to improved glycemic control, insulin sensitivity, and reduced cardiovascular risk factors in obese individuals with T2D [2,42▪▪]. A popular form of VLCD is a very low-calorie ketogenic diet (VLCKD), which involves a daily carbohydrate intake below 50 g or less than 10% of an individual's intake [43▪▪]. A recent meta-analysis compared the effects of a VLCKD on glycemic control, body weight, lipid profile, medication use, and dropouts vs. other recommended diets for 12 weeks or longer in people

with T2D [43▪▪]. The authors found that a VLCKD led to reductions in body weight and improved glycemic regulation for up to 6 months in people with obesity and T2D. Furthermore, improvements in triglycerides, high-density lipoprotein (HDL) cholesterol, and a reduction in antidiabetic medications persisted for up to 12 months. However, as weight loss continues, a ketogenic diet may have unfavorable effects on total cholesterol and low-density lipoprotein levels in normal-weight individuals [44▪]. An umbrella review of ketogenic diets found that in overweight adults or people with obesity, a VLCKD was significantly associated with improved anthropometric and cardiometabolic outcomes without worsening muscle mass, LDL-C, and total cholesterol. However, a ketogenic low carbohydrate high fat (KLCHF) diet was associated with reduced body weight and body fat percentage and reduced muscle mass in healthy participants [45▪]. In addition, prolonged low carbohydrate availability will be exacerbated following a VLCKD, which may increase branched-chain amino acid (BCAA) oxidation and impair muscle retention [46▪]. An important caveat is that VLCDs are highly restrictive, which challenge long-term adherence. In addition, metabolic adaptations may reduce energy expenditure, leading to a weight loss plateau [47]. Notably, VLCD also increases the risk of losing skeletal muscle mass and potential weight regain upon resuming normal dietary habits [47]. Thus, VLCD/VLCKD can be used in the short term as an effective rapid weight loss strategy to improve glycemic control and reduce cardiovascular risk factors; however, we recommend that individuals who follow them do so under medical supervision and do not employ them long-term. For long-term success in managing T2D, individuals should work under the supervision of a healthcare professional and adopt a sustainable lifestyle and behavioral change program, including monitoring energy intake, limiting alcohol consumption, engaging in daily physical activity, resistance exercise training, and sufficient protein intake, which will be paramount in maintaining health and limiting skeletal muscle loss.

SARCOPENIA

Sarcopenia is the age-related loss of muscle mass and function that negatively impacts physical function and quality of life [48]. Weight loss in older adults, especially when using a VLCD, can worsen sarcopenia by increasing muscle loss. The loss of muscle mass in adults who are already at risk for sarcopenia can have detrimental effects on their general health. Protein intake becomes critical in regulating skeletal muscle mass and function for middle-aged and older adults who have or are at risk of developing sarcopenia [1]. Protein intakes above the current RDA (~0.8 g/kg/day) may increase MPS in sarcopenic individuals, supporting the contention that the current RDA is too low for sarcopenic individuals [49▪,50]. Overall, the guidelines for protein intake in the general population may not be appropriate for sarcopenic individuals, and additional protein supplementation will be beneficial for lean mass preservation, especially in the context of energy restriction or VLCD.

Therefore, we do not recommend VLCD for individuals at risk for sarcopenia, especially older adults. Of note, postmenopausal women with obesity who followed a severe energy restriction of 65–75% of their estimated energy expenditure reported a 2.5-fold greater loss in hip bone mineral density (BMD) compared with those following a moderate deficit of 25–35% [51]. Thus, a more balanced and moderate approach to weight loss that includes sufficient protein intake and resistance exercise is recommended to preserve muscle mass and function [52]. A healthcare professional can help to determine an appropriate weight loss plan based on an individual's specific needs and goals. It is important to highlight that adopting a VLCD may not be intentional, as older adults may have a lower appetite leading to lower total caloric/protein intake. In this case, we encourage individuals to participate in structured RET and consider supplementation with high-quality protein with a full complement of EAA to help stimulate MPS and preserve skeletal muscle mass.

CONCLUSION AND PRACTICAL APPLICATION

In conclusion, rapid weight loss from VLCD may be a suitable option in the short term and may be used in a clinical context to improve health markers. However, due to their low energy content, largely risking the loss of skeletal muscle mass and their restrictive nature, it is likely not an ideal option for long-term weight loss/maintenance, see Fig. 2. The extent of loss of lean mass can vary depending on many factors, including an individual's beginning body composition, the magnitude of energy deficit and length of the diet, an individual's protein intake, whether they are performing RET, their training status, and other lifestyle factors. To minimize the loss of lean mass during a VLCD, individuals must ensure they consume adequate protein intake in conjunction with a RET regimen. Finally, due to the potential risks and side effects, the authors advise individuals to consult a healthcare professional before choosing to pursue a VLCD.

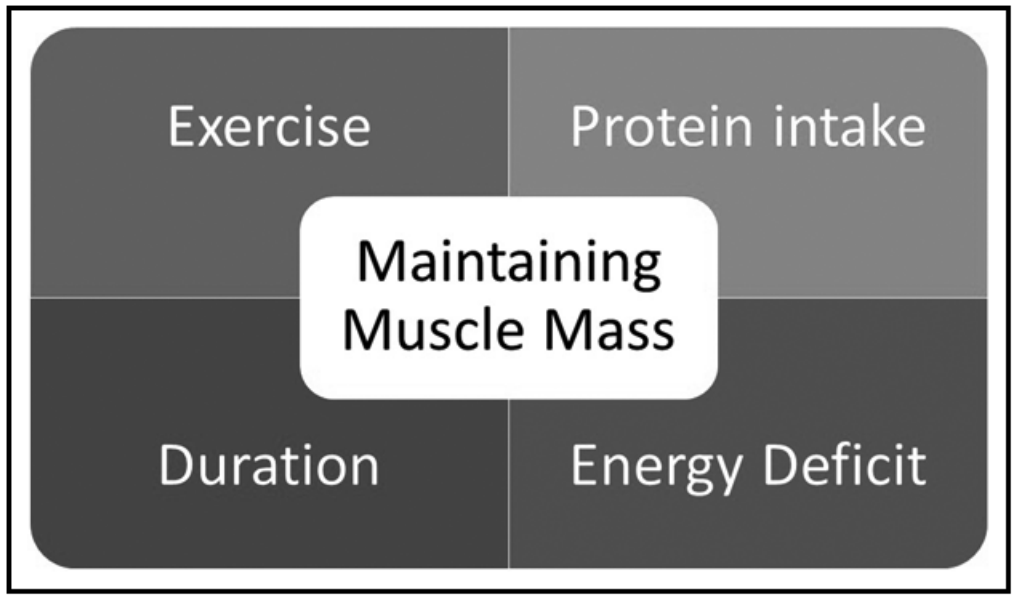

FIGURE 2. Aspects of diet and activity during a very-low calorie diet that could influence muscle mass maintenance. Exercise refers to resistance training specifically, consuming sufficient amounts of dietary protein can help preserve muscle mass, there is an increased risk of losing muscle mass if the duration of the diet is increased, there is an increased risk of losing muscle mass if the energy deficit becomes greater.

The amount of protein required on a VLCD will depend on many factors, including age, training status, body composition, and activity levels. However, at a minimum, it is recommended that individuals on a VLCD consume 1.2–1.5 g/kg/day and limit the magnitude of their energy deficit to help preserve muscle mass. To help meet this intake while adhering to VLCD recommendations, including lean, nutrient-dense sources such as lean meat, fish, tofu, kidney beans, and low-fat dairy products. Supplementation with either animal or plant-derived protein powders is also advised, provided they are enriched with all nine EAAs. In addition, protein intake must be spread relatively evenly throughout multiple daily feedings to stimulate MPS and reduce MPB enhancing muscle mass retention.

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Conflicts of interest

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- ■■ of outstanding interest

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