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Invited Commentary | Nutrition, Obesity, and Exercise

Very Low-Energy Diets—Opportunity for Greater Weight Loss, but Risk of Bone Loss

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Eat less, move more. This may seem like the straightforward solution to the increasing obesity epidemic. But it is not as simple as that. Weight loss and maintenance are challenging.[1] Seimon et al[2] aim to provide some much-needed answers to questions regarding the health effects of very low-energy diets (VLEDs) compared with conventional caloric restriction diets. Postmenopausal women with obesity in the Type of Energy Manipulation for Promoting Optimum Metabolic Health and Body Composition in Obesity (TEMPO) Diet Trial[2] were randomized to a 25% to 35% caloric restriction diet for 1 year (moderate intervention) or a VLED (aiming at 65%-75% caloric restriction) for 16 weeks followed by a 25% to 35% caloric restriction diet (severe intervention). Compared with the moderate intervention, the severe intervention resulted in a greater loss of total body weight, whole-body fat mass, and abdominal subcutaneous and visceral adipose tissue as well as a greater reduction in waist to hip ratio at 1 year. There was also a greater loss of whole-body lean mass and thigh muscle area in the severe intervention group, which was proportional to the greater total body weight reduction. There was no significant difference between interventions in whole-body bone mineral density (BMD) or lumbar spine BMD loss. On the downside, the severe intervention resulted in an approximately 3.3% reduction in total hip BMD compared with an approximately 1.3% reduction in the moderate intervention group, which was not explained by the greater total weight loss in the severe group.[2]

How do these findings compare with previous evidence on caloric restriction, particularly in relation to BMD? And what do these findings mean when considering the long-term risks and benefits of VLEDs as weight loss strategy?

Some loss of whole-body lean mass, the primary outcome in the current study,[2] is expected with weight loss, but excessive loss may be a concern for the risk of sarcopenia.[3] Reassuringly, the greater whole-body lean mass loss in the severe group compared with the moderate group was proportional to the greater total body weight loss,[2] and the reported mean change was within a suggested ratio of 25 to 75 for lean to fat mass loss at 1 year.[4] Handgrip strength was not significantly reduced in either intervention group after 1 year.[2]

Loss of hip BMD and possibly lumbar spine BMD, but not whole-body BMD, have previously been found with caloric restriction–induced weight loss,[5] but little is known about the effect of severity of caloric restriction on bone loss. Seimon et al[2] now advance the literature by providing one of the first direct comparisons of severe vs moderate caloric restriction. The estimated mean hip BMD loss of 0.032 g/cm^2 (95% CI, 0.029-0.045 g/cm^2) in the severe group is substantial, and more than twice that in the moderate group. Moreover, the trend of hip BMD loss continued during the entire 12-month follow-up, well beyond the initial period of VLED use[2] and longer than the additional approximately 4 to 6 months required for bone remodeling.[6] Follow-up data could provide valuable information on whether hip BMD loss following short-term VLEDs is temporary or represents a long-term decline in bone mass.

The reported greater hip BMD loss raises concerns for longer-term bone health because BMD is a risk factor for fractures.[6] While meta-analysis showed no clear association of VLEDs with total fracture risk,[7] there is evidence for association between intentional weight loss and higher risk of hip[8] and frailty[9] fractures. Future research needs to clarify the specific roles of weight loss and caloric

restriction, as well as other related dietary factors, in long-term fracture risk and determine to what extent associations are mediated by BMD.

Notably, the TEMPO Diet Trial included key strategies to minimize whole-body lean mass loss and BMD loss. For instance, physical activity was encouraged in both intervention groups. Given the proposed importance of reduced skeletal loading on BMD loss,[6] it is plausible that the amount and type of exercise (eg, load-bearing and resistance training) required to prevent bone loss could be affected by the rate of weight loss. Dietary protein, calcium, and vitamin D may help attenuate bone loss, particularly in combination, as dietary protein and vitamin D may both counteract the reduced calcium absorption efficiency due to energy restriction.[6] In the TEMPO Diet Trial, the target protein intake was 1 g/kg of body weight in both groups, and VLEDs in the severe group provided 1200 mg of calcium and 15 µg of vitamin D. Unfortunately, physical activity and dietary intake data were not presented.[2] This leaves us to speculate not only about adherence to the intervention diets, but also on how nutrient intake levels compared between groups. Additionally, biomarker data, such as circulating 25-hydroxyvitamin D levels, could have provided valuable information about effects on nutritional status. Too much is unknown about the optimal physical activity and dietary strategies to attenuate bone loss and potential subsequent fracture risk following different rates of weight loss, an issue that large trials with long follow-up may be best placed to investigate.

Thus, the potential greater loss of hip BMD with severe caloric restriction, its long-term clinical implications, and strategies to prevent it warrant further investigation. Nevertheless, these findings need to be considered in the context of an ever-increasing obesity epidemic and the various obesity-related adverse health outcomes, including type 2 diabetes, cardiovascular diseases, and all-cause mortality.[10] Moreover, increasing evidence suggests that greater weight loss can help achieve type 2 diabetes remission.[4] Finding strategies successful at achieving sustained weight loss in individuals with obesity should be an absolute priority in public health research. The TEMPO Diet Trial now adds to accumulating evidence that VLEDs can help achieve greater weight loss than moderate dietary interventions alone, well after the use of VLEDs is ended.[2,4] The estimated mean 15.3 kg (95% CI, 12.5-18.1 kg) reduction in total body weight in the severe group is within the range previously reported with VLEDs,[4] and almost twice that achieved with moderate caloric restriction.[2] The finding that more than 80% of women in the severe group achieved 10% or greater weight loss is encouraging, as this can provide clinically meaningful health benefits.[4]

Eventually, policy makers need to consider whether the risks associated with reported greater hip BMD loss and a potentially associated higher fracture risk exceed the benefits of the greater weight loss[4] achieved with VLEDs compared with moderate caloric restriction. Given the considerable burden of obesity, this seems unlikely at the population level, but may differ between individuals. Importantly, the 21% higher retention in the severe intervention should not be overlooked.[2] Indeed, the rapid weight loss, satiety, and feasibility of VLED use may contribute to improved adherence.[4] Successful weight loss and maintenance with VLEDs is generally reported when VLEDs are accompanied by additional weight loss maintenance support.[4]

Going forward, we need a better understanding of the totality of (positive and negative) health outcomes with different weight loss strategies. Therefore, future studies need to compare the health effects of different weight loss strategies, including VLEDs, moderate caloric restriction, and other weight loss diets head-to-head, as Seimon et al[2] have done in their current study, with a longer follow-up.

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