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THE DANGER OF WEIGHT LOSS IN THE ELDERLY

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Abstract: Aging is generally accompanied by weight loss made up of both fat mass and fat-free mass. As more people, including elderly, are overweight or obese, weight loss is recommended to improve health. Health risks are decreased in overweight children and adults by dieting and exercise, but the health benefits of weight loss in elderly, particularly by calorie restriction, are uncertain. Rapid unintentional weight loss in elderly is usually indicative of underlying disease and accelerates the muscle loss which normally occurs with aging. Intentional weight loss, even when excess fat mass is targeted also includes accelerated muscle loss which has been shown in older persons to correlate negatively with functional capacity for independent living. Sarcopenic obesity, the coexistence of diminished lean mass and increased fat mass, characterizes a population particularly at risk for functional impairment since both sarcopenia (relative deficiency of skeletal muscle mass and strength) and obesity have been shown to predict disability. However, indices of overweight and obesity such as body mass index (BMI) do not correlate as strongly with adverse health outcomes such as cardiovascular disease in elderly as compared to younger individuals. Further, weight loss and low BMI in older persons are associated with mortality in some studies. On the other hand, studies have shown improvement in risk factors after weight loss in overweight/obese elderly. The recent focus on pro-inflammatory factors related to adiposity suggest that fat loss could ameliorate some catabolic conditions of aging since some cytokines may directly impact muscle protein synthesis and breakdown. Simply decreasing weight may also ease mechanical burden on weak joints and muscle, thus improving mobility. However, until a strategy is proven whereby further loss of muscle mass can be prevented, weight loss by caloric restriction in individuals with sarcopenic obesity should likely be avoided.

Healthy body weight is a key focus of guidelines and recommendations to improve quality of life and decrease health risks. The emphasis on weight loss is due, in great part, to the increasing prevalence of obesity in all populations including older adults and the elderly (1). The most recent dietary guidelines (2) recommend that Americans maintain body weight in a healthy range by balancing calories from foods and beverages with calories expended. While diet and exercise are identified as safe and practical means to modify body weight, a definition of what constitutes a "healthy body weight" is not provided. Specific target body weights, based on a substantial literature, are available for adults and children (3) but identification of an ideal body weight is particularly challenging for older persons (>65 years) for multiple reasons. Older people are more likely to be underweight than young adults and are susceptible to rapid weight loss in response to illness, stress, and the aging process itself (4). Additionally, there is evidence to suggest that excess weight does not confer the same risk in elderly compared to younger adults and may even be protective (5 -9). The objective of this paper is to assess the risks and dangers relative to benefits of weight loss that may be attained in this population.

Average body weight gradually increases during most of adulthood and levels off around 60 years of age after which mean body weight tends to decrease. Most notably, lean body mass, predominantly muscle is lost at an accelerated rate with and without intentional weight loss as people age (7). Weight loss is often due to a reduction in food intake which occurs for a variety of reasons, including both physiological and non-physiological causes (10). Thus, it is important to assess if weight loss is intentional or unintentional. Rapid and significant unintentional loss of body weight is indicative of underlying disease. For example, release of cytokines in response to chronic or acute disease can induce anorexia and stimulate lipolysis, muscle protein breakdown, and nitrogen loss (4). Clinical intervention is necessary to identify and address the cause of weight loss and nutritional and physical therapy should be provided to assist in recovery of lost lean body mass. Even in the absence of disease, nutritional frailty and sarcopenia (a loss of muscle mass and strength), occur with advancing age and are estimated to impair functional capacity in 30% of people over the age of 60 and possibly more than 50% of those over 80 (11,12). Weight stable individuals who maintain adult body weight through their 60's and 70's are not necessarily protected from age-related muscle loss (13). A study by Gallagher et al (14) observed a significant shift in body composition marked by progressive skeletal muscle loss over a 5-year period in healthy, ambulatory, weight stable elderly subjects. The authors describe sarcopenia as a silent, progressive phenomenon similar to osteoporosis and emphasize

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the need to consider body composition in determining a healthy body weight for older adults.

While fat free mass is almost universally lost with aging, weight gain is not uncommon in people as they age, particularly in individuals who decrease their level of physical activity (15). Furthermore, the escalating prevalence of obesity in adults age 25-59 will continue to increase the number of overweight and obese elderly individuals as the population ages. The National Center for Health Statistics estimated in 2000 that 33-39% of men and women 65-74 years old are overweight or obese (16). The health implications for this cohort are uncertain and present a challenge to geriatricians, health care providers and policy makers who must interpret and extrapolate data available from adults on body weight and health. In addition to age-related shifts in the proportion of fat mass to fat-free mass, the distribution of fat also changes with aging. Intra-abdominal fat increases to a greater extent than subcutaneous or total fat. This redistribution, along with increases in intramuscular and intrahepatic fat, is associated with adverse health outcomes such as insulin resistance and other components of metabolic syndrome (17, 18). Fat mass is directly correlated with many of the adverse health effects of obesity (19) while fat free mass, in particular muscle and bone, is positively associated with strength, physical function and overall quality of life (20). Assessment of body composition is particularly important in determining if an older individual will benefit from intentional weight loss and if so, which strategies will most effectively target fat loss while maintaining or increasing lean mass.

Direct measures of body composition require significantly greater resources than simple anthropometric measures. Thus, most screening indices and categories of weight status are based on height and weight. Relatively clear cut standards exist to identify adults and children at risk for underweight and overweight/obesity and the associated adverse health consequences. Two commonly used methods of defining "desirable weight" are calculation of body mass index (weight, kg/[height·m^2) (21) and comparison to Metropolitan Life Insurance Tables (22). These tools enable health care providers to educate and instruct adults, adolescents, and children to achieve a body weight appropriate for height and within a range associated with low morbidity and mortality. A serious limitation of these standards is that they do not represent ideal body weights for older adults and the elderly. The Metropolitan Tables are based on populations of men and women ages 25-59 while BMI, an indicator of body fatness defines weight status relative to the relationship between body fat and disease and death for adults 20 years old and older. While BMI is interpreted differently for children and teens (age and sex specific), a similar distinction is not made for older adults although it is recognized that, at the same BMI, older people tend to have more body fat than young adults (7, 23). Although BMI underestimates body fat in older adults, it may overestimate health risks associated with overweight status in the elderly (7, 24). A number of studies (8, 25) observe that minimum mortality occurs at a higher BMI in older subjects compared to younger subjects while some even suggest that high BMI does not predict mortality in persons age 70 and older (6). In fact, several studies report that weight loss, both intentional and unintentional, is predictive of increased all-cause mortality (9, 26-28).

Extremes of both low and high body weight are associated with higher mortality rates in the general population as well as in older adults. Interestingly, in a study of estimated excess deaths across a range of BMI categories, the majority of excess deaths associated with obesity occurred in individuals younger than 70 years whereas the vast majority of excess deaths associated with underweight occurred in those individuals greater than 70 years of age (25). Underweight or "thinness" is defined by a BMI of less than 17 in children and adolescents (29) or lower than 18.5 in adults (3). Less than 2% of the U.S. adult population (25-59 y) fits this criteria whereas ~ 3% of adults 60 y and older are underweight by this definition (25). Analyses of earlier data sets provide higher estimates suggesting that 9-17% of the population is underweight (3). Underweight in children and adults is often indicative of disease or some disorder including eating disorders. Correction of the underlying problem should improve weight status of the individual. Elderly who present with low body weight may have health conditions which contribute to weight loss or they may simply lack appetite due to decreased physical activity, drug interactions, dentition difficulties, and/or decreased sense of taste and smell (4, 11). In any case, consequent nutritional frailty impairs quality of life and increases risk of falls, fracture and mortality (30). Galanos and colleagues (31) examined the relationship between body mass index and the ability to perform activities of daily living in free-living elderly subjects. Functional impairment was significantly greater in those individuals with either a low BMI or a high BMI. In an Italian cohort of hospitalized patients (8) a BMI <22 kg/m^2 predicted dependency in daily activities and shortened survival whereas a BMI >27kg/m^2 was not related to risk of mortality. Frailty in older women, as identified by unintentional weight loss, weakness, self-reported poor energy, slow walking speed, and/or low physical activity, increased the risk of recurrent falls, hip fracture, nonspine fractures and death (26). This relationship persisted even in individuals categorized as frail despite a relatively high BMI (>30 kg/m^2), underscoring the primary need to consider muscle mass in determining a healthy body weight.

Sarcopenic obesity characterizes a unique weight status observed in the elderly in which as unhealthy excess of body fat is accompanied by detrimental loss of muscle and fat free mass including bone (32). Obese individuals in general have more muscle and stronger bones than their lean counterparts and even elderly classified with sarcopenic obesity appear to have more total fat free mass (muscle, bone mineral density). However, the proportion of muscle relative to total weight is low compared to non-obese elderly with or without frailty (33). Furthermore, Villareal and colleagues observed that muscle quality, a nassessment of muscle strength per unit of muscle

mass, is also compromised in obese elderly, which greatly influences functional capacity and quality of life for this group (33). Both sarcopenia and obesity are independently associated with disability but Baumgarten and colleagues (34) showed that sarcopenic obesity was more strongly associated with disability than either body composition type alone. Subjects classified with sarcopenic obesity had a 2.5 to 3.0 fold increased risk for disability in performing Independent Activities of Daily Living (34). The InCHIANTI study, a prospective Italian population based study of older people (35), looked at the role of obesity related inflammatory factors as mediators of muscle weakness and disability. Obese elderly were further classified according to type of obesity, either central or global. Muscle strength and inflammatory markers were measured and found to be related to global obesity and to a greater extent to central obesity. Central obesity was associated with higher circulating levels of pro-inflammatory cytokines which had a direct inverse relationship to muscle strength. The authors speculate that obesity, particularly the type characterized by visceral adiposity, negatively affects muscle strength through upregulation of proinflammatory cytokine production. Cytokines may act on several pathways to induce muscle catabolism. For example, IL-6 may inhibit the anabolic effects of IGF-1 on muscle synthesis and, along with other cytokines, may induce insulin resistance. Cytokines also appear to play a role in apoptosis or "cell death" which has been linked to sarcopenia (36). Exercise appears to exert some anti-inflammatory effects (35), but reversal of inflammation and muscle loss in overweight elderly by decreasing adiposity has not been tested nor has an anabolic effect of pharmacological agents used in treatment of inflammation been demonstrated.

More than sixty-five percent of all young and middle aged adults are overweight or obese. Overweight and obesity are defined by BMI values of >25-29 and > 30kg/m^2 respectively (1). Ample evidence exists documenting the health risks of obesity in these populations. These include cardiovascular disease (CVD), type 2 diabetes, hypertension, arthritis and certain cancer (21, 37). Population studies consistently show increased risk of morbidity and mortality in obese individuals while overweight status is less clearly associated with excess deaths (25, 38, 39). Weight loss in middle-aged adults, as shown in numerous clinical trials, improves or completely normalizes the cluster of metabolic abnormalities linked to obesity (18). Even modest weight loss (5-10%) can improve risk factors associated with coronary heart disease (19). Similar benefits appear to be achievable in obese older persons (40). Lifestyle intervention including diet and exercise therapy improved metabolic syndrome, lipid profile and inflammatory markers in obese adults 65 y and older (18). Two separate trials in overweight post-menopausal women (mean ages 57 and 60 y) improved coronary heart disease risk factors and glucose tolerance via weight loss mediated by hypocaloric diet and low-intensity exercise (41, 42). Weight gain throughout life exacerbated risk of hypertension in predisposed women aged 40-70 years while weight loss significantly lowered the risk (43). Mechanical complications of obesity such as osteoarthritis and respiratory problems improve with weight loss even in the very old (44).

The benefits of weight loss cited above pertain more to obese rather than overweight older adults (18) and must be weighed against unintentional adverse consequences of calorie restriction and weight loss in the elderly (5, 27). Suboptimal nutrient intake or even malnutrition is a very real risk in older people decreasing already limited calories. Requirements for specific nutrients increase in the face of diminishing calorie needs with aging thereby necessitating nutrient dense diets (2). Protein intake, in particular, must be maintained and even increased in older individuals restricting calories. Dietary protein and amino acids represent one of the most effective means to slow or prevent muscle protein catabolism (20). Blunting of the anabolic response in elderly due to changes in digestion, gastric emptying, splanchnic uptake and peripheral utilization can be overcome by strategically timing the ingestion of appropriate amounts of protein or amino acid supplements (12). Protein also protects against age-related loss of bone mineral density as do vitamin D and calcium. Decreased ability to synthesize vitamin D and potential issues with lactose intolerance often lead to compromised status of these nutrients (45). Animal protein intake often decreases with aging due to dentition issues, satiety induced by these foods, and issues related to cost and convenience (12). Consequently, nutrients at risk include iron, zinc and vitamin B12. In many elderly individuals, vitamin B12 status is further compromised by food-bound malabsorption (46). Nutritional supplements may be the only means to meet nutritional needs in older adults restricting their calorie intake. Weight loss inevitably includes loss of muscle and bone mass which appears to be proportionately similar in young and old but may have a more profound impact on body composition of older adults already experiencing loss of lean tissue. Newman (47) reported on percentage changes in lean and fat compartments with weight loss and weight gain in 70-79 y old adults. Lean mass compared to fat mass represented a significantly greater percentage of weight loss whereas weight gain was predominantly represented by fat mass. The implications of this trade-off are serious, particularly if weight is cyclically lost and regained in the aging person.

The key issue in determining the balance between potential beneficial effects as opposed to detrimental effects of weight loss in elderly revolves around maintenance of the muscle mass. The importance of muscle mass, strength, and metabolic function in the performance of exercise, as well as the activities of daily living (ADL),is obvious (48). Perhaps less well recognized, muscle plays a central role in whole-body protein metabolism that is particularly important in the response to stress (20). In the post-absorptive state essential tissues and organs such as brain, skin and liver rely on a steady supply of amino acids via the blood to serve as precursors for the synthesis of new proteins to balance the persistent rate of protein breakdown that occurs in all tissues. In the absence of

nutrient intake (such as occurs between meals), muscle protein serves as the principal reservoir to replace blood amino acid taken up by other tissues (49). The stressed state, such as in sepsis, advanced cancer, and following traumatic injury, imposes greater demands for amino acids from muscle protein breakdown than fasting (50). Physiological responses necessary for recovery may include accelerated synthesis of acute phase proteins in the liver, synthesis of proteins involved in immune function, and synthesis of proteins involved in wound healing. Net breakdown of muscle protein is stimulated to provide abundant amino acids to meet these increased demands. This response is not readily reversed, even by aggressive nutritional support (50). Not surprisingly, individuals with limited reserves of muscle mass respond poorly to stress. For example, loss of muscle mass is known to be detrimental to survival from cancer (51).

In addition to the physiological role of muscle in the response to serious illness and stress, abundant evidence points to a key role of altered muscle metabolism in the genesis, and therefore prevention, of many common pathological conditions and chronic diseases. Both cardiac failure and cancer are often associated with rapid and extensive loss of muscle mass, strength, and metabolic function (cachexia). In the case of both cardiac and cancer cachexia, the loss of muscle mass is an important determinant of survival (51, 52). Correlations between grip strength and bone area, bone mineral content and bone mineral density in both healthy athletes (53) and stroke patients (54) support the notion that muscle contractions play a significant role in bone strength and mass. Muscle mass, and the concomitant energy cost of associated muscle protein turnover, can have a significant impact on energy balance (20). Finally, muscle disuse can lead to insulin resistance and type II diabetes, which is fundamentally a disease of muscle (55).

The above discussion of the importance of muscle leads to the conclusion that if the clinical diagnosis of an elderly individual warrants weight loss because of clear detrimental effects of continued obesity, weight loss should be undertaken in a manner that maintains muscle mass to whatever extent possible. In this regard, physical activity beneficially influences energy balance and provides multiple benefits beyond weight management. Studies in young and middle-aged adults found that adding endurance or resistance exercise training to weight loss programs helped to preserve muscle (56). Limited trials in obese older subjects also suggest that regular exercise attenuates the percentage of lean mass that is lost during dieting (18). Increased physical activity also stimulates muscle protein synthesis, increases strength and endurance, improves balance, combats depression, and may prevent deterioration below functional thresholds enabling activities of daily living (17). Chronic disabilities and disease obviously limit the capacity for physical activity but appropriate supervision and gradual progression to higher intensity, duration, and frequency should enable even very old and frail persons to participate (48).

In conclusion, the potential detrimental effects of weight loss in elderly individuals must be weighed against real or perceived beneficial effects. The risk:benefit ratio may be considered a function of the interaction between age and severity of obesity. For example, an overweight, elderly person (70-80 y) would likely experience comparatively greater risk and marginal benefit from weight loss compared to a severely obese (BMI >35) individual between 50-60 years of age. There will be circumstances in which weight loss is desirable, such as when body weight significantly limits mobility and independence. In any circumstance in which clinical examination results in the recommendation for weight loss, attention must be paid to attempting to maintain muscle mass. The successful therapeutic approach will achieve this goal and minimize adverse outcomes by inclusion of physical activity and optimal protein intake, as well as maintenance of micronutrient intakes at adequate levels.

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