

Involuntary Weight Loss in the Elderly

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CME ARTICLE

Educational Objectives

1. To recognize the importance of involuntary weight loss in the elderly
2. To understand the factors associated with unintentional weight loss in the elderly
3. To be able to investigate and manage weight loss in the elderly in a logical way, avoiding unnecessary investigations
4. To understand the importance of psychosocial factors and a multi-disciplinary approach in the management of unintentional weight loss in the elderly

Involuntary weight loss is a common complaint in the elderly. Prevalence estimates of weight loss among older persons vary tremendously and are as high as 27% in high-risk populations, such as free-living frail elderly receiving community services.¹ Increasing age, disability, coexisting medical illnesses, previous admission to the hospital, low education level, presence of cognitive impairment, smoking, loss of a spouse, and low baseline body weight have all been associated with a higher likelihood of weight

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loss.² Although there is no clear consensus, the most well-accepted definition of clinically important weight loss is 5% over a period of 6-12 months. This is based on the finding that weight loss of 4-5% over a 1-year period identified subjects whose weight loss was associated with increased mortality.³ A 4% weight loss at 1 year had a sensitivity of 75% and specificity of 61% for predicting subsequent 2-year mortality. In this study, the annual incidence of 4% weight loss was 13% with a relative risk of 2-year mortality at 2.43 (95% confidence interval [CI], 1.23-4.41). These findings have been confirmed in other studies.⁴ The relationship of weight and subsequent mortality was examined in the Framingham Heart Study. The relative risk of death in persons over age 65 who are at the lower extreme of body mass index was found to be twice that of other individuals.⁵ In another study in elderly patients admitted for elective surgery, significantly higher mortality rates were found in those with weight loss of more than 10 pounds in 6 months compared to those with weight loss of less than 10 pounds.⁶ Weight loss also predicts mortality in nursing home patients. In a retrospective study, residents losing 10% or more of their body weight over a period of 6 months to 3 years had a 62% mortality rate over 3 years, compared with 42% among residents with stable weight.⁷ In addition, weight loss was associated with decreased functional ability and transfer to a higher level of nursing home care. In another retrospective study, long-term care residents with a 5% weight loss over 1 month were 4.6 times more likely to die within 1 year compared to those with stable weight.⁸

Unintentional weight loss is also associated with an increased risk of in-hospital complications, a decline in activities of daily living or physical function, higher rates of admission to an institution, and poorer quality

of life.^{9,10} Elderly patients recently admitted to the hospital are particularly susceptible to increased mortality.

Many elderly patients with unintentional weight loss have concomitant malnutrition. Cachexia is associated with a disproportionate loss of skeletal muscle rather than of body fat. Excessive loss of lean body mass results in skeletal and cardiac muscle wasting, loss of visceral protein, and alterations in physiologic functions.¹¹ Loss of more than 10% of body weight is associated with significant losses of visceral protein, resulting in impairment of many physiologic functions. Cachexia is associated with a systemic inflammatory response, increased cytokine concentrations, and impaired immunity—all of which are believed to contribute to adverse outcomes, including early death. Protein-energy malnutrition impairs both cell-mediated and humoral immunity, and increased rates of infection are found in elderly patients who have lost a significant amount of weight.¹² Weight loss in excess of 20% is associated with pronounced organ dysfunction.

NORMAL AGING AND WEIGHT

Both lean body mass and body fat contribute to weight. Patients with higher body fat content lose more fat compared to lean body mass. Lean body mass declines at a rate of 0.3 kg per year, beginning in the third decade. At the same time there is an increase in body fat, which continues up to age 70 years. As a result, the total body weight tends to peak in the fifth to sixth decade, remains stable until age 65-70 years, and then slowly decreases. Normal aging is associated with only very small decrements in weight (0.1-0.2 kg/year).

Numerous studies have confirmed that in humans there is a decline in food intake over the lifespan. Between the ages of 20 and 99 years, there is an aver-

age decline in energy intake of 25% over 30 years.¹³ Another study of persons age 64-91 years reported a decrease of 19.3 kcal per day per year in women and 25.1 kcal per day in men during a 7-year follow-up.¹⁴

Aging is associated with changes in gastrointestinal function, which may contribute to weight loss. For example, delayed gastric emptying in elderly subjects may cause distension of the stomach and contribute to lack of appetite. In older individuals there is a reduction in the ability of the gastric fundus of the stomach to show adaptive relaxation. This results in more rapid antral filling and earlier satiation. Cholecystokinin (CCK) may play a part in early satiation in the elderly, as it directly modulates antral stretch. Most studies have shown that plasma CCK concentrations are higher in healthy older persons than in young adult subjects.¹⁵ Sensitivity to satiating effects of CCK also increases with age.¹⁶ These changes are associated with both early satiety and a decline in appetite; collectively they contribute to the “anorexia of aging.”

Endogenous opioids, primarily dynorphin, but also beta-endorphin and the enkephalins, play an important role in mediating the short-term sensory reward response to food. Elderly patients suffering from idiopathic senile anorexia exhibit reduced plasma and cerebrospinal fluid concentrations of beta-endorphin, as compared to normal weight, age-matched controls.¹⁷ Leptin levels increase with age in men. The increase is correlated with age-related decline in testosterone levels. The elevated levels of leptin in older men may be partly responsible for the greater degree of anorexia seen in older men compared to older women, in whom leptin levels decline.¹⁸

Altered taste and olfactory deficits due to age-related chemosensory losses might play a role in the anorexia observed in older persons. Some studies have found that age reduced olfactory sensitivity more than

taste sensitivity.¹⁹ Age-related alterations in senses of taste and smell may influence the type of food eaten and thus contribute to weight loss. Medical conditions and their treatments can have more dramatic effects on taste and smell and may increase the risk of malnutrition. Drugs commonly implicated in altered taste sensation include antihistamines, captopril, carbamazepine, allopurinol, levodopa, and lithium.

CAUSES OF WEIGHT LOSS IN THE ELDERLY

Weight loss may occur over relatively short periods of time in association with acute illness or, more indolently, in association with chronic illnesses. It may be affiliated with normal appetite (hyperthyroidism, diabetes mellitus, or malabsorption) or reduced appetite (cancer, chronic infections, cardiovascular, pulmonary, or renal disease).

Cancer is the most frequently cited cause of involuntary weight loss, and accounts for about one-third of all patients presenting with unintentional weight loss. Weight loss may be a presenting feature of malignancy before other symptoms emerge. Malignancies of gastrointestinal, hepatobiliary, hematologic, lung, breast, genitourinary, ovarian, and prostate are relatively common causes of weight loss. Cancer anorexia is multifactorial in its pathogenesis, and most of the hypothalamic neuronal signaling pathways modulating energy intake are likely to be involved. Hormones (leptin), neuropeptides (neuropeptide Y), cytokines (interleukin-1, interleukin-6, tumor necrosis factor, and interferon gamma), and neurotransmitters (serotonin and dopamine) have been implicated in the pathogenesis of cancer cachexia.²⁰

Depression in the elderly is frequently associated with weight loss. It has been shown that almost 15% of older persons living in the community have depressive symptoms, and 3.6% have major depres-

sive disorder.²¹ The incidence of depression is even higher in institutionalized elderly. Depression was the most prevalent underlying diagnosis in several studies of patients with unintentional weight loss.²² Bereavement is also associated with significant weight loss, more commonly among men than women. Alcoholism, frequently overlooked in the elderly, may also cause weight loss.

Patients with dementia are at high risk for development of nutrition-related problems. Unintentional weight loss has been reported in as many as 50% of institutionalized patients with dementia, and up to 30% of noninstitutionalized patients with mild-to-moderate Alzheimer's disease.²³ It may precede the diagnosis of mild-to-moderate dementia. The pathogenesis of weight loss in dementia is not well understood. A combination of factors may all play a part, including forgetting to purchase groceries or prepare meals, apraxia, agnosia, anosmia, paranoid ideas about food, and increased caloric needs due to movement disturbances.

Drugs are a common cause of anorexia and weight loss in the elderly population. They may act centrally or peripherally to decrease appetite. Centrally acting drugs that reduce appetite include catecholaminergics, dopaminergics, serotoninerics, and endorphin modulators such as naloxone. Peripherally acting agents include those that inhibit gastric emptying and bulking agents. Other commonly implicated drugs include antibiotics, digoxin, potassium and iron supplements, and anti-inflammatory drugs.

Gastrointestinal disorders are the most common nonmalignant, organic causes of unintentional weight loss. These include peptic ulcer disease, inflammatory bowel disease, dysmotility syndromes, chronic pancreatitis, celiac disease, and mesenteric ischemia. Malabsorption in the elderly usually pres-

ents with weight loss. Although diarrhea is common, only one-third of patients with diarrhea have malabsorption. Most common causes of malabsorption in the elderly are bacterial overgrowth, pancreatic exocrine deficiency, and celiac sprue.

Oral, dental, and swallowing problems may result in consumption of insufficient calories, and thus cause weight loss. One study found that the number of oral and dental problems was the most important predictor of weight loss over 1 year.²⁴ Drugs with anticholinergic effects may cause xerostomia, and thus contribute to eating problems. Swallowing disorders are common in older adults; they may occur because of a wide variety of structural or functional conditions, including stroke, cancer, neurologic disease, and gastroesophageal reflux disease.

Cachexia is a frequent complication of severe congestive cardiac failure. While the exact pathophysiology of cardiac cachexia is unknown, increased metabolic demand and decreased appetite and caloric intake contribute. Serum leptin levels have been found to be high, indicating a role of leptin in the catabolic state leading to the development of cardiac cachexia in the course of congestive cardiac failure.²⁵ A low-grade chronic inflammatory process may be relevant in the development of tissue wasting in these patients, and has also been linked to raised plasma levels of inflammatory cytokines, such as tumor necrosis factor alpha.

Weight loss is a common finding in patients with chronic obstructive pulmonary disease (COPD), affecting up to 71% of patients.²⁶ Although a number of factors have been shown to contribute, no single mechanism has clearly been identified as a primary cause for weight loss in patients with severe COPD. Increased metabolic rate, energy imbalance, elevated levels of cytokines, tissue hypoxia, and drugs all play a role, either singly or in combination. Malnutrition, in

Causes of Weight Loss in the Elderly

Malignant	Gastrointestinal Hepatobiliary Hematologic Lung	Breast Genitourinary Ovarian Prostate
Psychiatric	Depression Alcoholism	Dementia Bereavement
Neurologic	Stroke Parkinson's disease	Multiple sclerosis Motor neuron disease
Drugs	Catecholaminergics Dopaminergics Serotonergics Naloxone Antibiotics	Digoxin Potassium supplements Iron supplements Anti-inflammatory drugs
Gastrointestinal	Peptic ulcer disease Inflammatory bowel disease Dysmotility syndromes Chronic pancreatitis	Celiac disease Mesenteric ischemia Bacterial overgrowth
Cardiac	Congestive cardiac failure	Subacute bacterial endocarditis
Pulmonary	Chronic obstructive pulmonary disease	
Endocrine	Diabetes mellitus Hypothyroidism Hyperparathyroidism Hypopituitarism	Hyperthyroidism Adrenal insufficiency Pheochromocytoma
Renal	Uremia	Nephrotic syndrome
Infectious	Bacterial Tuberculous	Fungal Parasitic
Deficiency States	Thiamine deficiency Vitamin B ₁₂ deficiency	Vitamin C deficiency Zinc deficiency
Eating Disorders	Anorexia tardive (Anorexia of aging)	Idiopathic senile anorexia
Socioeconomic	Poverty Social isolation	Loneliness
Functional	Visual impairment Ill-fitting dentures	Poor dentition Swallowing problems

turn, can further compromise respiratory function by weakening the diaphragm, diminishing the ventilatory drive, and altering the surfactant film in the lungs.

Diabetes mellitus, hyperthyroidism, and hypothyroidism are the most common endocrine diseases that cause unintentional weight loss. Less common causes are adrenal insufficiency, hyperparathyroidism, pheochromocytoma, and hypopituitarism. Uremia often produces anorexia, nausea, and vomiting. Protein loss in the urine leads to a negative caloric balance. Hemodialysis is accompanied by swings in metabolic balance and is associated with weight loss. Increased synthesis of serotonin due to high tryptophan load and transport across the brain barrier has been proposed as a mechanism for anorexia in end-stage renal disease.²⁷

Infectious processes cause anorexia and hypophagia. In addition, they also produce a catabolic state with negative nitrogen balance that may last for several weeks afterward. The nutritional requirements exceed by 50% above maintenance to compensate for this negative nitrogen balance.

Anorexia nervosa has been reported in the elderly. In some cases it is the recurrence of a pre-existing diagnosis, but in others it is diagnosed first in later life, and is then termed *anorexia tardive*.²⁸ There is a female preponderance, and the clinical features include self-starvation, weight loss, fear of fatness, distorted body image, laxative abuse, and self-induced vomiting. The disorder is associated with depressive features.

Other causes of weight loss in elderly are deficiencies in thiamine, vitamin C, vitamin B₁₂, and zinc. Prevalence of atrophic gastritis and gastric atrophy increases with age, leading to achlorhydria, which may result in malabsorption of vitamin B₁₂, folate, and iron. Reduced food intake may lead to inadequate intake of required nutrients, further increasing anorexia. Thus, anorexia is one of the most frequent-

ly observed symptoms of thiamine deficiency.²⁹ Megaloblastic anemia due to a deficiency in folate, vitamin B₁₂, or vitamin C may also cause loss of appetite. Similarly, zinc deficiency has been associated with anorexia in laboratory animals.³⁰ Visual impairment from ophthalmic or central nervous system disorders can limit a patient's ability to prepare or eat meals. Physical factors, such as poor dentition and ill-fitting dentures, may influence food choice and quantity of food eaten by older persons.

No cause of weight loss was found in 24% of patients in one study of 45 elderly ambulatory patients after at least 24 months of clinical investigation and observation.²² Individuals with no known cause of weight loss generally have a better prognosis than those with known causes. Depression was found in 18% of patients, whereas cancer was found in 16% of patients. Cancer of the lung, colon, pancreas, breast, and prostate were the most common malignancies. Other causes included gastrointestinal disease, medication, Alzheimer's disease, and cerebrovascular disease. In another study involving 154 patients, no definitive diagnosis was found in 23% of patients, despite extensive investigations and a prolonged follow-up.³¹ Of these patients, 36% were found to have cancer, predominantly involving the gastrointestinal tract. Benign gastrointestinal disease, including peptic ulcer disease, motility disorders, cholelithiasis, and inflammatory bowel disease, was found in 17% of patients. Psychiatric disorders were found in 10% of patients, and endocrine causes of weight loss such as diabetes mellitus and hyperthyroidism were found in 3.8% of patients. In another study involving 91 patients with involuntary weight loss, no cause was found in 35% of cases, despite extensive investigation and prolonged follow-up.³² However, 19% were found to have cancer, predomi-

nantly of the lung and gastrointestinal tract, and 14% had benign gastrointestinal disease.

DIAGNOSTIC EVALUATION

Despite its frequency, there are no clear guidelines on how to evaluate weight loss in the elderly. Losses of more than 5% or more of body weight over 6-12 months should prompt clinical evaluation. Weight loss should be verified by reviewing medical records and a change in the fit of clothes, etc. Elderly persons may not be aware of weight loss or may attribute it to a normal process of aging. Body mass index (BMI) can be calculated by dividing the patient's weight in kilograms by the square of the patient's height in meters. Optimal BMI in the elderly is 24-29 kg/m. Thorough nutritional assessment of elderly individuals includes evaluation of clinical, dietary, anthropometric, hematologic, biochemical, and immunologic factors. Assessment of body weight and weight loss is one of the most sensitive indicators of malnutrition.

A careful history and physical examination with particular attention to pharmacologic and psychosocial factors should be obtained. Standard tools for detecting dementia and depression are invaluable. Assessment of caloric intake, functional impairments, assistance needs, and access to food are important parts of a diagnostic work-up. Evaluation of sight and functional assessment of activities of daily living may identify functional impairments.

Basic screening tests such as urinalysis, complete blood count, electrolytes, liver and renal function tests, calcium, glucose, thyroid function tests, stool occult blood, and a chest radiograph will detect the cause or direct to further investigations in most cases. Additional tests such as computed tomography (CT) scanning may be required, but this has low diagnostic yield. Upper and lower gastrointestinal endo-

scopies and barium studies have high diagnostic yields, and may be required depending on signs and symptoms or the results of the initial screening tests.

Three scoring systems have been developed to help clinicians identify which patient with weight loss is likely to have a physical or malignant cause, as opposed to a psychological or unknown cause.^{33,34} None of these scoring systems has been validated in independent populations presenting with weight loss.

TREATMENT

Older persons do not fully regain weight loss that may occur due to acute stressful events. Therefore, early detection and attention to nutrition during periods of acute illness are important. Specific treatment depends on the identification of the underlying cause. It is important to review all medication and make necessary adjustments. Referral to a dietician and nutritional supplements are also important steps in the management of involuntary weight loss. Although use of oral nutritional supplements has been associated with short-term weight gain and improvements in biochemical, anthropometric, and quality-of-life parameters in a number of trials, long-term beneficial effects on health, ability to function, and survival in undernourished elderly have not been demonstrated.³⁵ Providing supplements between meals may result in less compensatory decrease in food intake at meal times. Total daily caloric requirements average 30-35 kcal/kg for ambulatory elderly and 40 kcal/kg for malnourished elderly. Elderly patients with involuntary weight loss may be deficient in micronutrients, and mineral and vitamin supplements may be required.

Attention to psychological and oral health, including dental care, is invaluable. Optimal management often requires multidisciplinary assessment. Speech, physical, and occupational therapists may have an

important role, depending on the factors contributing to weight loss. Social circumstances of the patient should be assessed and provisions made for Meals on Wheels, day care, home health aides, assisted living, or nursing/residential home, depending on the assessments of the therapists. Treatment of depression often leads to rapid improvements in appetite and intake. Tricyclic antidepressants improve appetite and may be preferable over serotonin reuptake inhibitors, which suppress appetite (with the exception of mirtazapine). When possible, physical exercise should be encouraged because increased activity has been shown to promote appetite and food intake.

In a significant proportion of patients, no cause is found despite extensive investigations; a policy of “watchful waiting” may be appropriate in these patients. The role of appetite stimulants in anorexia is not clear. The evidence supporting any pharmacologic agent for the treatment of weight loss is limited to mostly small, uncontrolled studies, and benefits are generally restricted to a small gain in weight without evidence of decreased morbidity and mortality or improved function and quality of life. Most of these agents have significant side effects, particularly in frail elderly, which limit their usefulness.

Although appetite stimulants—including megestrol acetate, dronabinol, and cyproheptadine—may improve oral intake and promote weight gain in patients with cancer or AIDS, and in young patients with anorexia, these agents have not been studied in the elderly population. Megestrol, a progestational agent, is the most widely used among them, but evidence for its use with elderly persons is limited. It is a relatively potent appetite stimulant; however, no effect on survival has been demonstrated, although some improvements in the quality-of-life measures have been noted.³⁶ Cyproheptadine and dronabinol have

only modest effects on appetite and weight. There are no randomized trials of either cyproheptadine or dronabinol in elderly with weight loss, although dronabinol has been studied in one trial involving patients with dementia who were refusing food.³⁷ Both medications are associated with significant side effects, particularly central nervous system toxicity, which may preclude their use in elderly patients. Among anabolic agents, a 4-week randomized trial of human growth hormone in 20 undernourished elderly demonstrated slightly faster weight gain and improved walking time in those receiving the hormone, but after 4 weeks, differences in weight were no longer statistically significant.³⁸ Use of human growth hormone in other settings has been associated with increased mortality.³⁹ Several small clinical studies or crossover trials of androgenic agents have not shown that they lead to weight gain. Other pharmacologic approaches, such as anticytokine therapies, antileptin therapies, and anti-inflammatory medications, are being investigated. A small proportion of patients may need tube feeding, although there are no robust data to indicate that it improves survival or quality of life. If long-term therapy is desired, a percutaneous feeding tube may be considered. Tube feeding is not without risks, and a decision to tube feed should be made after carefully considering the needs and desires of the patient.

FUTURE DIRECTIONS

Cytokines such as interleukins, interferons, and tumor-necrosis factor alpha play prominent roles in the anorexia/cachexia syndrome often seen in chronic disease states. Experimental and human data suggest that hypothalamic monoaminergic neurotransmission, particularly serotonergic activity, plays a major role in the pathogenesis of anorexia. Interfering pharmacologically with cytokine expression or

hypothalamic monoaminergic neurotransmission may be an effective therapeutic strategy in patients with anorexia.⁴⁰ In addition, antagonists of CCK, analogues of neuropeptide Y, and cannabinoids are other exciting research areas. Research on the feeding-associated gene products is likely to enhance our understanding of mechanisms of anorexia and lead to newer and more effective therapeutic strategies.

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