Sarcopenia, Cachexia, and Starvation

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As a population, we are extremely concerned about weight. Whether it is the epidemic of overweight children developing very adult problems due to obesity or the rail thin models splashed across the pages of the latest fashion magazines, weight is a hot topic of conversation. As wound care clinicians, we, too, should be very concerned with weight. Instinctively, we understand that patients who are losing body weight may heal slowly or develop chronic wounds. Scientifically, we know when the amount of nutritional substrate is inadequate to meet all the body’s physiologic needs, a competition for the limited available nutrients ensues. Often the wound loses this competition because the body, by necessity, must keep the vital organs functioning; this is a higher priority than wound healing.

Ideally, each patient should meet 100% of his nutritional needs daily but realistically, this often does not happen. As practitioners, we see the end result manifest itself as weight loss. Even more frustrating is seeing weight loss occur despite a seemingly optimal diet. Until recently, all weight loss has been lumped into a single category but this is not the complete picture. Declines in body weight may be the result of loss of lean body mass, loss of fat mass, loss of bone, and/or a change in fluid volume. This article discusses three causes of weight loss—sarcopenia, cachexia, and starvation.

Sarcopenia

Sarcopenia often is defined as an age-related shift in body composition, specifically the loss of muscle mass. The word sarcopenia has Greek origins and literally means “poverty of flesh.” As we age, we naturally lose muscle mass and replace it with fat—anyone over the age of 45 can tell you how the body changes. Nearly 3.6 million people in the United States have sarcopenia, putting them at increased risk for physical disability and frailty. People who are obese also can suffer this loss of muscle mass. In this case, we term it sarcopenic obesity. Although sarcopenia is seen mostly in physically inactive individuals, it is also evident in individuals who remain physically active throughout their lives. This finding suggests that physical inactivity is not the only contributing factor to sarcopenia. Current research is finding that the development of sarcopenia is a multifactorial process generally attributed to three factors: motor unit restructuring, protein deficiency, and changes in hormone concentrations.

Motor unit restructuring. Motor units are the motor neurons and the muscle fibers they control. There are two types of motor neurons: fast twitch (FT) and slow twitch (ST). FT motor neurons die sooner than ST. When this occurs, the muscle fibers commanded by the FT neuron can deteriorate and die as well, a process we commonly call atrophy. To prevent atrophy, when a FT neuron dies, a ST neuron situated nearby will attach itself to the muscle fibers the dead neuron commanded in order to innervate it and keep it alive. This change in command is known as motor unit restructuring. This process is imperfect because ST neurons act with much less precision than FT neurons. We can easily see this process with the naked eye when we look at our aging faces in the mirror. An entire cosmeceutical industry is devoted to minimizing the sagging (atrophy) of our faces. Skin sags and droops because it has lost the muscle fiber underneath due to natural aging.

Protein deficiency. Protein deficiency also is thought to play a role in sarcopenia. The recommended dietary allowance (RDA) for protein, set by the Food and Nutrition Board of the United States National Academy of Science, is 0.8 g protein/kg body weight/day for adults regardless of age. The issue of the adequacy of the protein RDA, especially for elderly, is currently being debated in order to set future RDAs. The observation that older people lose fat-free mass when they habitually consume diets that provide the RDA of 0.8 g protein/kg, even when they are resistance training, suggests this amount of protein results in subtle metabolic and physiologic accommodation responses and may not be adequate. It appears that an intake of 1.5 g protein/kg/day, or about 15% to 20% of total caloric intake, is a reasonable target for elderly individuals wishing to optimize protein intake in terms of health and function. Additional research is examining the timing and distribution of protein throughout the day to maximize protein synthesis.

Hormones. The third cause of sarcopenia is hormonal. Aging is associated with several changes in hormone levels, including a decrease in the concentrations of growth hormone (GH), testosterone, and insulin-like growth factor (IGF-1). A decrease in the concentrations of these hormones may be linked to the development of sarcopenia. It also has been suggested that changes in female estrogen levels may play a role in the development of sarcopenia during menopause. Hormone replacement has been studied but mainly concentrates on GH with no consensus on whether GH can effectively maintain and rebuild muscle mass in the elderly.

Wounds. For patients with wounds, sarcopenia means losing independence and strength, thereby increasing immobility...
and frailty. It is important to recognize this loss of muscle mass and suggest interventions. Progressive resistance exercise is the number one strategy to keep muscle neurons firing. Although exercise cannot totally prevent sarcopenia, a lack of exercise surely accelerates it. Resistance training can be as simple as using exercise bands while watching television. Provision of adequate amounts of high-quality protein also should be stressed. Protein shakes and protein powders can be utilized to fulfill the necessary amounts. Amino acids also may be used to act synergistically with exercise to increase muscle strength—specifically, arginine, glutamine, and leucine activate mammalian target of rapamycin (mTOR), a protein kinase that functions as a central element in signaling pathways involved in cell growth and proliferation.

**Cachexia**

Cachexia is physical wasting with loss of weight and muscle mass caused by disease. According to Morley et al., “Cachexia is a complex metabolic syndrome associated with underlying illness and characterized by loss of muscle with or without loss of fat mass. The prominent clinical feature of cachexia is weight loss in adults (corrected for fluid retention) or growth failure in children (excluding endocrine disorders). Anorexia, inflammation, insulin resistance, and increased muscle protein breakdown are frequently associated with wasting disease. Wasting disease is distinct from starvation, age-related loss of muscle mass, primary depression, malabsorption, and hyperthyroidism and is associated with increased morbidity.”

Cachexia often is driven by a stress response. When the body is under stress, either physical or psychological, the fight-flight reaction is amplified. The initial insult leads to local and generalized inflammation and an increase in the level of the stress hormones, particularly catecholamines and cortisol. At the same time, levels of anabolic hormones (human growth hormone and testosterone) decrease. This hormonal imbalance leads to a catabolic and hypermetabolic state. A catabolic state is one in which the body breaks down components in order to release energy to meet increased demands. Imagine the body working much harder and faster than usual to fight off the stressor and regain homeostasis. Working harder and faster means an increase in the metabolic rate and an increase in body temperature. To keep up this pace, the body needs an increased supply of glucose, which may come from gluconeogenesis or by rapidly breaking down sufficient energy and nutritional substrate from which to build new tissue to heal a wound. In order to build new tissue, protein must be available to fuel an anabolic process. A stressed, catabolic patient will not have this protein available because a portion of it will be shuttled away from the normal pathway to be used as energy.

Often the initial response to unintended weight loss is to provide a hypercaloric diet. The cachetic patient often does not respond to additional calories alone because the metabolic machinery is affected. For example, many cancer patients consume sufficient calories but continue to lose weight due to cancer cachexia. Diet intervention should focus on providing 55% to 60% of total calories as complex carbohydrates, 20% to 25% of total calories as protein, and 20% to 25% of calories as fat. Fat should not exceed 2 g/kg of body weight per day because amounts above this may affect lipid levels. Studies have investigated a number of pharmaceutical treatments including megestrol acetate, dronabinol, corticosteroids, thalidomide, and the anabolic agent oxandrolone.

### Table 1: Complications relative to loss of lean body mass?

<table>
<thead>
<tr>
<th>Lean body mass (% loss of total)</th>
<th>Complications (related to lost lean mass)</th>
<th>Associated mortality, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Impaired immunity, increased infection</td>
<td>10</td>
</tr>
<tr>
<td>20</td>
<td>Decreased healing, weakness, infection, thinning of skin</td>
<td>30</td>
</tr>
<tr>
<td>30</td>
<td>Too weak to sit, pressure ulcers develop, pneumonia, no healing</td>
<td>50</td>
</tr>
<tr>
<td>40</td>
<td>Death, usually from pneumonia</td>
<td>100</td>
</tr>
</tbody>
</table>

* Assuming no pre-existing loss

Sufficient energy as a means to get more energy.

If this cycle continues for an extended period of time, a patient will lose weight and more importantly, suffer a loss of lean body mass. Table 1 describes the effects of continued loss of lean body mass. If a patient shows a steady downward trend in body weight, it is unlikely the body will have a
coupled with complaints of nausea, vomiting, poor dental status, depression, or a number of other reasons that cause secondary anorexia. Again, the result is unintended weight loss with loss of muscle mass, which can impede wound healing.

Interventions for starvation and anorexia focus on removing barriers to proper nutritional consumption. This requires looking for the root cause and then addressing it. For example, if depression or loneliness is affecting meal intake, these situations must be handled. If taste sensation is a problem, food can be made more appealing by adding spices and flavorings. Small meals served throughout the day may be more tolerable to some patients who do not feel like eating. Cultural and comfort foods eaten during childhood are sometimes appealing. Finding the proper solution for each individual patient requires a thorough nutritional interview and follow-up with the appropriate medical team members. What works for one patient may not work for another.

Practice Points

- Unintended weight loss deserves a closer look because if left unchecked it may lead to a decline in the rate of wound healing and exacerbate chronic wounds.
- Several mechanisms drive weight loss; it is important to recognize each one so you may prescribe the appropriate treatment.
- Loss of lean body has progressively worsening consequences.

- Unique approaches to treat sarcopenia, cachexia, and starvation/anorexia include food, medical nutritional supplements, vitamins, targeted amino acids, appetite stimulants, anabolic agents, and other approaches still under investigation.
- Effective treatment often employs more than one approach. Trial and periodically monitor various management options until you find the combination that works for each individual patient.

Coming next month: Understanding hepatic protein laboratory data

References