

Cachexia: a nutritional syndrome?

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Abstract

Cachexia leads to nutritional deficits including anorexia and loss of fat and muscle mass. In persons with precachexia or early cachexia, e.g., old persons with weight loss and COPD, there is strong evidence that nutritional support improves outcomes. Limited evidence suggests this may be true for heart failure and chronic kidney disease. The evidence for nutritional support in refractory cachexia is, not surprisingly, less dramatic. It would appear that early in the cachectic process, nutrition, coupled with exercise, may be an important therapeutic approach.

Cachexia has been defined as a loss of lean tissue mass.^{1–5} This is often associated with anorexia and a loss of fat mass. This appears to be predominantly due to an increase in proinflammatory cytokines, but may also be due to other factors such as hypoxia through hypoxia inducible factor-1 and a variety of agents produced by tumours.^{6,7} Cachexia can occur in most major diseases including infections, cancer, heart disease, chronic kidney disease, chronic obstructive pulmonary disease, and stroke.^{8–13} While the primary etiologic factors in cachexia induce catabolism, to reverse cachexia, there is a need for nutritional building blocks, that is, protein and calories. In addition, the anorectic component represents a nutritional disorder. For these reasons, we strongly support the concept that cachexia is a nutritional syndrome.

In the case of sarcopenia, a condition which focuses on muscle loss,^{14–16} there is good evidence that protein supplementation together with exercise can reverse the muscle loss.^{17–19} In the case of cachexia, the evidence in support of nutritional benefits is less clear. In malnourished older persons, the Cochrane meta-analysis has now clearly demonstrated that nutritional support leads to a decrease in mortality.²⁰ Cachexia induced weight loss in older persons represents a combination of low level cytokine excess and anorexia.^{21–24} In chronic obstructive pulmonary disease (COPD), nutritional support leads to weight gain, an increase in fat-free mass, increase in 6-min walk distance, increased respiratory muscle strength and an improvement in quality of life as measured by the St. George's Respiratory Questionnaire.²⁵ The combination of nutrition with exercise has an even greater improvement in COPD outcomes.²⁶ Both of these situations involved the treatment of persons with precachexia and early

cachexia, whereas in studies in other areas, the studies have often been undertaken in well advanced or refractory cachexia.

Poor nutrition is clearly associated with poor survival in cancer cachexia.^{27,28} At present, neither dietary counselling nor enteral supplementation has been clearly shown to improve outcomes in cancer cachexia.^{29,30} These studies have included persons with refractory cachexia. There is some evidence to support nutritional support in persons with head and neck cancer.^{31,32} No adequate studies exist in persons receiving palliative care.³³ Megestrol acetate increased appetite and weight gain but did not improve mortality.³⁴ In persons with AIDS, nutritional support increased weight but did not have other positive outcomes.³⁵

In heart failure cachexia, there are limited studies. Rozenyrt *et al.*³⁶ found that a high calorie, high protein supplement increased weight, 6-min walking distance and quality of life. An amino acid supplement improved exercise capacity in heart failure patients.³⁷ Rizo³⁸ reported a survival benefit after approximately 3 years in a small group of heart failure patients given L-carnitine compared with controls. An increased survival and decreased hospitalization were found by the GISSI-HF investigators in the group of heart failure patients receiving polyunsaturated fatty acids.³⁹ More studies are needed to confirm these benefits of nutritional support in patients with heart failure.^{40,41}

In persons on hemodialysis there is an association between under-nutrition and mortality.⁴² Exercise can reverse muscle mass loss in renal failure.^{43,44} Protein supplementation during dialysis reduced inflammation and enhanced physical function and quality of life.^{45,46} This approach has also been shown to reduce mortality.⁴⁷

Overall, there is tantalizing evidence that early nutrition intervention during the pre-cachexia and early cachexia stage, especially in illnesses with prolonged survival, can play an important role in improving outcomes and quality of life in persons with cachexia. There is a need for large, well-controlled studies to determine the most appropriate approaches. There is a small amount of evidence that anabolic therapies (e.g. exercise and testosterone), when combined with caloric/protein supplement, have enhanced outcomes.^{48–51}

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Acknowledgement

The authors of this manuscript certify that they comply with the principles of ethical publishing in the Journal of Cachexia Sarcopenia and Muscle 2010;1:7–8 (von Haehling S, Morley JE, Coats AJ and Anker SD).

Conflict of interest

The authors declare no conflict of interest.

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