

# Cancer Cachexia: It Takes a Team to Fix the Complex Machinery

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Cachexia is one of the most common metabolic syndromes in patients with advanced cancer and is associated with decreased physical function, suboptimal treatment outcomes, compromised quality of life, and increased mortality. Bruggeman et al<sup>1</sup> provided an excellent update on the management of cachexia. At the moment, the treatment options for cachexia remain suboptimal—megestrol acetate is associated with increased thromboembolic risk and mortality, cannabinoids can have significant psychotropic effects, and corticosteroids can be immunosuppressive.<sup>2</sup> Moreover, these agents have not been demonstrated to increase skeletal muscle mass. Novel interventions such as selective androgen receptor modulators and grehlin mimetics have a positive effect on lean body mass but not function, and thus have not yet been approved for clinical use. The situation looks grim, but hope is around the corner.

Over the past few decades, much progress has been made in understanding the physiologic processes that regulate nutrition and metabolism by mapping out parts of a highly complex machinery. Cachexia occurs when multiple parts of this machinery break down, and the goal of treatment is to repair the different components by using a team approach. Effective treatment requires us to concurrently target the cancer, inflammation, primary anorexia, nutrition impact symptoms, muscle loss, functional impact, and the emotional factors associated with cachexia. As highlighted by Bruggeman et al<sup>1</sup>, this necessitates a close collaboration among oncologists, palliative care teams, physiotherapists, dieticians, psychologists, dentists,

and specialists in other disciplines. This interdisciplinary approach represents a paradigm shift from the traditional approach that focused on fixing one issue at a time and explains why randomized trials investigating single modalities for cachexia often have mixed, if not negative, findings.

## Nutrition Impact Symptoms

Several aspects of cachexia management warrant further discussion because of their therapeutic implications. Nutrition impact symptoms, such as early satiety, constipation, mucositis, abdominal pain, chronic nausea, and dental issues, often contribute to a decrease in oral intake, which compounds the weight loss already happening with cachexia through the starvation mechanism. Nutrition impact symptoms are important symptoms in their own right, and they have a significant impact on quality of life.<sup>3</sup> Proactive management of these very treatable symptoms is thus essential in patients at all stages of cachexia. For instance, early satiety may be treated with a prokinetic agent such as metoclopramide, constipation can be managed with laxatives, and chronic nausea can be controlled with scheduled antiemetics. Referral to a palliative care team would allow nutrition impact symptoms to be addressed comprehensively. In a study of 151 patients with cancer seen at a cachexia clinic provided by a palliative care team, the median number of nutrition impact symptoms was 3 (interquartile range, 2 to 4), with early satiety (62%), constipation (52%), and nausea (44%) being the most common. At

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follow-up, appetite significantly improved from 7 of 10 to 5 of 10 on a 0-to-10 numeric rating scale ( $P = .001$ ) in which 0 indicates best appetite and 10 indicates worst appetite; 31 (34%) of 92 patients experienced weight gain despite a history of progressive weight loss.<sup>4</sup> Further research is needed to explore treatment options for more challenging nutrition impact symptoms such as dysgeusia.

### Psychological Care

It is also important to address the psychological aspects of cachexia.<sup>5</sup> Depression may lead to anorexia and weight loss. In turn, changes in body image, the lack of interest in food, and the pressure to “eat more and get better” might contribute to depressed mood and decreased quality of life. Thus, longitudinal patient and caregiver education, dietary advice, and emotional counseling are essential components of a cachexia intervention. Psychotropic agents such as olanzapine and mirtazapine may modulate mood while stimulating appetite and need to be further studied in adequately powered randomized trials.<sup>6,7</sup>

### Timely Interdisciplinary Care

Interdisciplinary cachexia clinics are being established to address the multidimensional needs of patients with cancer along the cachexia spectrum. A recent survey of the European Society for Medical Oncology Designated Centers of Integrated Oncology and Palliative Care revealed that 53 (35%) of 152 centers operated such clinics.<sup>8</sup> However, only a few groups have published their experience in regard to the structure, processes, and outcomes of these multimodal interventions.<sup>4,9,10</sup> More research is necessary to standardize the clinic assessments and interventions.

In addition to teamwork, timely intervention is key to the management of many symptoms including cachexia. Taking the machinery analogy one step further, it is essential to provide routine maintenance, to grease the cogwheels regularly, and to troubleshoot any issues early before the machinery breaks down. Thus, timely referral of patients at risk for cachexia to interdisciplinary cachexia clinics and/or palliative care teams

may complement oncology practice. At the refractory cachexia state, the machinery may be beyond repair.

In summary, we have made significant advances in defining cachexia, assessing it, and mapping the pathophysiologic changes. These discoveries have led to the development of multiple promising therapies. Going forward, more teamwork is needed to devise the multimodal interventions, conduct the practice-changing trials, and develop the interprofessional cachexia clinics. In the case of cancer cachexia, together we thrive. **JOP**

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**AUTHOR'S DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST****Cancer Cachexia: It Takes a Team to Fix the Complex Machinery**

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