EDITORIAL

Journal of Cachexia, Sarcopenia and Muscle 2018; **9**: 1189–1191
Published online in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/jcsm.12388

Cachexia as a common characteristic in multiple chronic disease

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Keywords cachexia; cancer; chronic diseases; muscle wasting

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Cachexia, or body wasting,[1] is a serious complication and frequently occurs at advanced stage of the variety of chronic diseases, including cancer, multiple inflammatory organ-specific disease, and cardiovascular disease. Cachexia affects the life quality and survival of the patients.[2,3] The prevalence of cachexia depends on the underlying disease and widely ranges between 15 and 90%.[4] Patients with cancer are most commonly affected by cachexia that often occurs as a late-stage complication. In cancer, the prevalence of cachexia[5] may vary between 50 and 90% depending on the type of cancer,[6] where a clinical course of gastrointestinal or lung cancers is most frequently associated with the development of cachexia.[7,8] The multifactorial pathogenesis of cachexia, including anorexia, inflammatory activation, and impaired metabolic turnover of both structural and energy metabolism, lead to a decrease of adipose and lean tissue mass and low muscle strength.[9]

The discussion is ongoing whether cachexia in various chronic diseases should be viewed as a common final metabolic pathway regardless of the underlying disease or if it is disease specific, and distinct pathophysiological mechanisms exist in different diseases. A recent retrospective clinical study described different phenotypes of cachexia in patients with advanced pancreatic ductal adenocarcinoma (PDAC) undergoing chemotherapy.[10] The assessment of longitudinal changes of body composition by computed tomography (CT) revealed three phenotypes of body wasting in these patients: patients who lost skeletal muscle and fat tissue, patients who only lost fat tissue, and patients without wasting who had a significantly improved survival. Several other studies investigated patients with different types of gastrointestinal cancer and reported either a loss of muscle tissue[11,12] or a loss of both skeletal muscle and adipose tissue mass.[13] In addition, loss of cardiac muscle tissue in cancer cachexia (CC) has been shown in clinical and experimental studies.[14–16]

It is known that cachexia is characterized by body wasting that involves all compartments of body tissue (i.e. muscle, adipose, and bone tissues).[9,17,18] From all of these compartments, the loss of muscle tissue is considered the key pathophysiological mechanism to explain reduced physical capacity, increased frailty, susceptibility to disease progression, increased hospitalization rate, and, consequently, increased mortality. A major hurdle for the research on loss of muscle tissue, or sarcopenia,[19,20] is a lack of the reference standard for determination of skeletal muscle mass.[21,22] A number of clinical diagnostic methods are available ranging from easy applicable, such as bioelectrical impedance analysis (BIA),[23,24] to highly complex, challenging, and costly techniques, such as magnetic resonance imaging (MRI) or CT.[25,26] The setting of the research question and specific study design define the appropriate method to be used for the given context. Importantly, apart from the assessment of muscle bulk, functional and metabolic characteristics of the skeletal muscle tissue might have a role in the determination of functional capacity and symptomatic severity of muscle wasting and hence may have an impact on clinical outcome.[27–30]

As previously mentioned, cachexia is usually reported as a complication of chronic diseases, including chronic obstructive pulmonary disease (COPD),[31,32] rheumatoid arthritis,[33,34] chronic hepatitis and cirrhosis,[35,36] diabetes mellitus,[37] chronic kidney disease (CKD),[38] and chronic heart failure (CHF).[39–41] A hypothesis has been proposed that independent of the individual chronic disease, the wasting process follows a common final metabolic pattern. This metabolic pattern

usually relates to an advanced stage of the underlying disease and can best be summarized as an increased catabolic turnover and anabolic blunting.

Nevertheless, cachexia has not been sufficiently investigated in many other pathological conditions, including stroke. Body weight loss after neurological stroke is frequently observed in clinical and experimental settings and associated with adverse clinical outcome.[42,43] The consequences of ischaemic stroke on myocardium have been investigated in an experimental study by Veltkamp *et al*.,[44] which showed a transient myocardial dysfunction and atrophy of cardiomyocytes following the brain ischaemia. Further clinical studies investigating cachexia and muscle wasting in patients with stroke are warranted.

Despite intensified research in the field, no medical therapy has emerged for a wider clinical application to prevent or even reverse the development of cachexia and muscle wasting. The medical treatment of cachexia includes a dietary supplementation of proteins, vitamins, or minerals.[45–48] Multiple attempts have been made to identify and validate treatment options to counteract the development of muscle wasting. The efficacy of physical exercise training has been confirmed in clinical and experimental studies, and it is regarded as the most promising treatment approach to delay or prevent progression of muscle wasting.[49–53] However, there is an urgent need for the development of clinical practice guidelines for treatment patients with cachexia.[54] Additional clinical studies are highly warranted to explore further the mechanisms of tissue wasting in chronic illnesses and to discover novel drug therapies to prevent or reverse the development of cachexia regarded as a severe complication of a variety of end-stage chronic disease.

Acknowledgements

We acknowledge support from the German Research Foundation (DFG) and the Open Access Publication Fund of Charité – Universitätsmedizin Berlin.

The authors certify that they comply with the ethical guidelines for publishing in the *Journal of Cachexia, Sarcopenia and Muscle: Update 2017*.[55]

Conflict of interest

None declared.

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