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The need for a specific definition of cardiac cachexia

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Cachexia is a complex and multifactorial wasting syndrome, associated with several chronic illnesses; including cancer, renal disease, chronic obstructive pulmonary disease, stroke and heart failure. Cachexia results in severe weight loss over time, either through loss of muscle or both muscle and fat. The exact pathophysiology of the syndrome, and its association with chronic illnesses, is not fully understood; though it is known to ultimately lead to catabolic dominance and tissue wasting. More easily understood, is the syndrome’s high prevalence and debilitating nature, with sufferers experiencing increased frailty, poor quality of life and a greater risk of premature death. For example, one study showed that out of 297 patients with chronic atrial fibrillation, there was 24.6% mortality in two years for those with a normal BMI (who were most likely to be classed as cachexic), 15.4% for those classed as overweight and 7.8% for obese individuals. Similar effects are also reported in other work - with an estimated 1-year mortality rate of 20-40%. Such a wide approximation of mortality is indicative of the relatively low evidence-base surrounding the syndrome, with the majority of research to date focused on cancer. This is further compounded by the lack of a specific definition in cardiac disease, meaning that clinical recognition of the syndrome and research into areas such as its prevalence and clinical implications remain poor. As such, it is challenging for nurses to identify cardiac cachexia and effectively care for those with the syndrome; a situation which is made worse by the current lack of guidelines/interventions to improve quality of and life and outcomes for this patient population.

Historical definitions of cachexia focused on the extent of weight loss over periods ranging from six to twelve months. Various cut-off values were suggested for this weight loss, such as a body mass index (BMI) of between 18.5 and 23 kg/m² or a certain degree of percentage weight loss. For example, in 2006, it was suggested that cardiac cachexia should be defined as weight loss of more than 6% over a period of at least six months, in a non-oedematous state. However, using these definitions patients with simple starvation would also be classed as cachexic, whilst those who are naturally thin or have a higher BMI could be misdiagnosed. As such, a more detailed consensus definition was formed in 2008 by Evans et al., that incorporated a number of additional indicators to define the syndrome. According to the definition by Evans et al. (4), cachexia is present when the patient has a weight loss of at least 5% in ≤ 12 months or BMI < 20 kg/m², plus three of the following five criteria: 1) Decreased
muscle strength; 2) Fatigue; 3) Anorexia; 4) Lean tissue depletion; 5) Abnormal biochemistry: anaemia [haemoglobin < 120 g/L]; low serum albumin [< 32 g/L] and increased inflammatory markers [C-reactive protein, interleukin-6].

With its comprehensive criteria, the 2008 consensus definition appears to be a useful tool for nurses and other clinicians to identify cachexia. However, an important limitation is that it is not specific to any chronic condition, which is concerning as each varies greatly in their aetiology and progression. For example, considering cardiac cachexia it is important to only use determinations of non-oedematous weight loss, as changes in fluid retention that many patients with heart failure can experience may lead to misdiagnosis. Additionally, there is an urgent need for the identification of an effective biomarker, because levels of currently suggested markers like albumin and C-reactive protein are impacted by common co-morbidities in this population other than cachexia. Furthermore, over half of patients with heart failure are anaemic and on some form of iron therapy, meaning haemoglobin may not always be a reliable indicator for cachexia in these individuals. As such, the 2008 consensus definition requires disease specific refinement for use by cardiac nurses and should be applied with these limitations in mind.

The ideal biomarker(s) should be specific to cardiac cachexia and not overly influenced by heart failure alone or other comorbidities. More importantly, it should serve as a prognostic indicator – allowing the early identification of the syndrome and improved therapeutic strategies. Biomarkers such as C-terminal agrin fragment (CAF) and tumour necrosis factor alpha (TNF-α) have shown promise in identifying cardiac cachexia, though neither meets the criteria of an ideal biomarker – as neither is specific to cardiac cachexia. Efforts to identify an ideal single marker are challenging, given the polysymptomatic nature of cachexia and its complex pathophysiology; as well as that of heart failure. Furthermore, other factors such as age-related sarcopenia also need to be considered. As such, it has been suggested that a combination of multiple markers should be used, such as products from proteases, to better reflect the multi-faceted processes involved in the syndrome.

In addition to biomarkers, the other criteria used in the 2008 consensus definition, such as muscle strength and fatigue, can be influenced by confounding factors. Taking muscle strength as an example, obese individuals are known to have greater muscle strength than non-obese persons – though when normalised to body mass they are actually weaker. As such, it is important that the muscle strength of patients with heart failure, who often have a relatively high BMI, is normalised to body mass. Furthermore, muscle strength, fatigue, anorexia and low muscle mass may be influenced by changes in biochemistry, whilst symptoms such as anorexia and fatigue may be present in individuals without cachexia; such as those with age-related sarcopenia. It is therefore important that nurses consider
these confounding factors when identifying patients with cachexia; whilst further research is needed to enable a consensus definition and improved understanding/management of the syndrome. The first step in this is to recognise that we do not fully understand the impact cachexia has on the daily lives of patients with heart failure and their carers. Such work has been completed in the field of cancer cachexia by Fearon et al.\textsuperscript{12} and others,\textsuperscript{13} leading to improved and earlier identification of the syndrome. It is now thought that cancer cachexia develops after pre-cachexia – currently defined as weight loss less than 5% of body weight with anorexia and inflammation. Similar work in the field of cardiac cachexia could improve nurses understanding of the syndrome; allowing for its earlier identification and the development of care which recognises and responses to the needs of this client cohort - targeting improved quality of life, experience and outcomes. It is therefore imperative that work to better elucidate the mechanisms and clinical implications of the syndrome is conducted; which, given its prevalence and debilitating nature, should a priority in both research and clinical environments.

Implications for practice

- Cardiac cachexia remains an understudied syndrome, lacking a disease specific definition; hampering treatment efforts and its identification by healthcare professionals.
- Work to identify effective biomarkers for cardiac cachexia should be a priority, as well as investigations into cut-off values that may allow for its early identification.
- Further research in other areas, such as the syndromes clinical implications and effect on the daily lives of patients and carers, is also urgently required - to improve understanding of the syndrome and patient outcomes.

References


