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Original article

Use of routinely available clinical, nutritional, and functional criteria to classify cachexia in advanced cancer patients

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SUMMARY

Background: Cachexia is a highly prevalent syndrome in cancer and chronic diseases. However, due to the heterogeneous features of cancer cachexia, its identification and classification challenge clinical practitioners.
Objective: To determine the clinical relevance of a cancer cachexia classification system in advanced cancer patients.
Design: Beginning with the four-stage classification system proposed for cachexia [non-cachexia (NCa), pre-cachexia (PCa), cachexia (Ca) and refractory cachexia (RCa)], we allocated patients in the cachexia stages according to five classification criteria available in clinical practice: 1) biochemistry (high C-reactive protein or leukocytes, or hypoalbuminemia, or anemia), 2) food intake (normal/decreased), weight loss: 3) moderate (≤5%) or 4) significant (>5%/past six months) and 5) performance status (Eastern Cooperative Oncology Group Performance Status ≥ 3). Thereafter, we determined if symptoms severity, body composition changes, functional levels, hospitalizations and survival rates varied significantly across patients according to the cachexia stages.
Results: Two-hundred and ninety-seven advanced cancer patients with primary gastrointestinal and lung tumors were included. Patients were classified into Ca (36%), PCa and RCa (21%, respectively) and NCa (15%). Significant ($p < 0.05$) differences were observed among the cachexia stages for most of the outcomes (symptoms, body composition, handgrip strength, emergency room visits and length of hospital stays) according to the severity of cachexia. Survival analysis showed differences among all stages except between PCa and Ca.

Abbreviations: aPG-SGA, abridged Patient-Generated Subjective Global Assessment; ASM, appendicular skeletal mass; ASMI, appendicular skeletal muscle index; BMI, body mass index; BW, body weight; Ca, cachexia/cachectic patient; CASCO, cachexia score; CRP, C-reactive protein; DXA, dual-energy X-ray absorptiometry; ER, emergency room; ESAS, Edmonton Symptom Assessment System; FM, fat mass; LBM, lean body mass; LBMI, lean body mass index; LMI, lean mass index; LOS, length of hospital stay; MNUPAL, McGill Nutrition and Performance Laboratory; MUHC, McGill University Health Centre; NCa, non-cachexia/non-cachectic patient; PG-SGA, Patient-Generated Subjective Global Assessment; QoL, quality of life; PCa, pre-cachexia/pre-cachectic patient; RCa, refractory cachexia/refractory cachectic patient; WL, weight loss.

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Conclusion: The five criteria that we tested in this study can be used to identify the cachexia stages and predict important clinical, nutritional and functional outcomes. The lack of statistical difference between PCa and Ca in all the clinical outcomes examined may suggest either the PCa group include patients already affected by early cachexia or that more precise criteria need to be used to differentiate PCa vs. Ca patients. More studies are required to validate these findings.

1. Introduction

Because of its complex pathophysiology and multiple phenotypes, it has proven difficult to classify cancer cachexia into stages that are clinically useful for planning treatment or predicting outcome. Proposed classification systems vary in the number of cachexia stages [1–5] and in the criteria used for classification [6–8]. This study was inspired by previous research conducted by Fearon et al. [4], Evans et al. [1], Fearon et al. [3] and Vigano et al. [8]. Fearon et al. [4] measured the absence or presence of cachexia but did not propose specific clinical criteria to classify patients into different stages of cachexia. Evans et al. [1] proposed several criteria that could be used to define cachexia. Fearon et al. [3] designed a very basic classification system that used a limited number of criteria. As a result of these three landmark studies, Vigano et al. [8] proposed a system with four stages and seven criteria: abnormal biochemistry, anorexia or decreased appetite, weight loss (WL) with and without muscle wasting, reduction in strength, and decreased function. Although this study provided a comprehensive assessment using a variety of different criteria, some of the diagnostic criteria called for tools not routinely available to clinicians, such as dual-energy X-ray absorptiometry (DXA) to quantify muscle wasting. Since our goal was to develop a classification system more useful to clinicians, our objective was to select a subset of the original seven classification criteria to predict clinical outcomes such as symptom severity, body composition, function, hospitalizations and survival across the cancer cachexia stages.

2. Subjects and methods

2.1. Subjects

All patients who were referred to and evaluated by the Cancer Cachexia Clinic of the McGill University Health Centre (MUHC), a tertiary care hospital, between May 2004 and March 2014 were included in the study, and had a histologically confirmed diagnosis of advanced (stages III or IV) cancer, and had a life expectancy greater than three months. Many of these patients also had a specialized nutritional and functional assessment at the McGill Nutrition and Performance Laboratory (MNUPAL), a state-of-the-art facility devoted to specialized nutritional and functional assessment of patients with advanced or terminal chronic diseases [9]. The study was approved by the McGill University Institutional Review Board and is in accordance with the Declaration of Helsinki governing ethical principles involving subjects in medical research.

3. Data collection

All patients completed two self-administered questionnaires: the abridged Patient-Generated Subjective Global Assessment (aPG-SGA; appendix A) and the Edmonton Symptom Assessment System (ESAS; Appendix B). The aPG-SGA is a condensed version of the Patient-Generated Subjective Global Assessment (PG-SGA) [10], recommended for use with cancer patients by the Oncology Nutrition Dietetic Practice Group of the American Dietetic Association and the Oncology Nursing Society [11] and is derived from the initial Subjective Global Assessment [12]. The abbreviated version has similar sensitivity and specificity as the PG-SGA [13] and has been used for detecting and characterizing cachexia [8]. From the aPG-SGA, we have used three self-reported measures to classify our patients: 1) WL, 2) change in food intake, and 3) performance. Patients were attributed either moderate (≤5%) or significant WL (>5%) over the past six months (see Appendix A, box 1). Variation in weight was determined as the difference between the measured actual weight and with that estimated six months earlier. This difference was used to calculate the percentage of WL (or weight gain) within the past six months. Patients reported the change in food intake in the past month compared to usual (see Appendix A, box 2). Patients also rated their limitations on usual activities over the past month (see Appendix A, box 4). The ESAS questionnaire (see Appendix B) was developed to assess common symptoms in palliative care [14] and has been found valid and reliable [11].

All patients had a routine blood analysis performed at the hospital, either at their clinic visit or within the preceding 2 weeks. A single non-fasting 20 mL venous blood sample was drawn and analyzed at the hospital, for C-reactive protein (CRP), albumin and complete blood cell count for leucocytes (WBC) and hemoglobin.

As the MNUPAL is located away from the hospital, not all the patients consented to an additional laboratory evaluation to quantify body composition and handgrip strength. Whole body composition was assessed by DXA (Lunar Densitometer, GE Healthcare, Madison, WI, USA). The precision of this DXA machine as measured by the percent coefficient of variation was previously determined as 1.56% for fat mass and 0.72% for fat free mass in advanced cancer patients [15]. The following measures were recorded: fat mass (FM), lean body mass (LBM), lean body mass index (LBMI) as calculated by dividing LBM by the square of patients' height, appendicular skeletal mass (ASM) and appendicular skeletal muscle index as calculated by dividing ASM by the square of patients' height. The ASMI provided the measures to determine the presence/absence of sarcopenia according to the criteria proposed by Baumgartner et al. [16].

Handgrip strength was measured on the dominant hand using the Jamar dynamometer (Sammons Preston, Bolingbrook, IL, USA). This non-invasive, easy to conduct test is a surrogate for upper body strength [17], has been used to measure change over time [18] and predicts mortality [19]. In advanced cancer patients, this test has been demonstrated to be consistent [15] valid and reliable [20]. The dynamometer was set in the standard position (position number three) as recommended by the American Society of Hand Therapists [21]. The maximum of three repetitions was recorded.

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