

The Abridged Patient-Generated Subjective Global Assessment Is a Useful Tool for Early Detection and Characterization of Cancer Cachexia

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ABSTRACT

Cancer cachexia (CC) is a syndrome characterized by wasting of lean body mass and fat, often driven by decreased food intake, hypermetabolism, and inflammation resulting in decreased lifespan and quality of life. Classification of cancer cachexia has improved, but few clinically relevant diagnostic tools exist for its early identification and characterization. The abridged Patient-Generated Subjective Global Assessment (aPG-SGA) is a modification of the original Patient-Generated Subjective Global Assessment, and consists of a four-part questionnaire that scores patients' weight history, food intake, appetite, and performance status. The purpose of this study was to determine whether the aPG-SGA is associated with both features and clinical sequelae of cancer cachexia. In this prospective cohort study, 207 advanced lung and gastrointestinal cancer patients completed the following tests: aPG-SGA, Edmonton Symptom Assessment System, handgrip strength, a complete blood count, albumin, apolipoprotein A and B, and C-reactive protein. Ninety-four participants with good performance status as assessed by the Eastern Cooperative Oncology Group Performance Status completed additional questionnaires and underwent body composition testing. Of these, 68 patients tested for quadriceps strength and completed a 3-day food recall. Multivariable regression models revealed that higher aPG-SGA scores (≥ 9 vs 0 to 1) are significantly associated ($P < 0.05$) with the following: unfavorable biological markers of cancer cachexia, such as higher white blood cell counts (10.0 vs $6.7 \times 10^9/L$); lower hemoglobin (115.6 vs 127.7 g/L), elevated C-reactive protein (42.7 vs 18.2 mg/L [406.7 vs 173.3 nmol/L]); decreased anthropometric and physical measures, such as body mass index (22.5 vs 27.1); fat mass (14.4 vs 26.0 kg), handgrip (24.7 vs 34.9 kg) and leg strength; an average 12% greater length of hospital stay; a dose reduction in chemotherapy; and increased mortality. Given its association with the main features of cancer cachexia and its ease of use, the aPG-SGA appears to be a useful tool for detecting and predicting outcomes of cancer cachexia. Additional research is required to determine what impact the aPG-SGA has on quality of care when used in the clinical setting.

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THE MAJORITY OF PATIENTS WITH ADVANCED CANCER experience malnutrition with progressive weight loss, anorexia, asthenia, anemia, and suppression of immune function, which reflects a syndrome known as cancer cachexia (CC).¹ Recently, experts have agreed on the following clinical phenotypes, underlying physiological mechanisms, and diagnostic stages for cancer cachexia²⁻⁴: progressive loss of both fat and lean body mass; reduced food intake due to anorexia as well as a series of disease- and treatment-related symptoms; changes in metabolism possibly attributable to tumor metabolism, inflammation, increased proteolysis and lipolysis, and the presence of comorbid conditions that exacerbate these changes; and progression over time through clinical stages, beginning with precachexia (<5% weight loss), evolving to cachexia (>5%

weight loss) and ultimately refractory cachexia (extreme loss of physical function), which is often irreversible. Cancer cachexia is associated with decreased quality of life, enhanced treatment toxicity, and reduced survival.⁵ Despite increasingly well-documented causes, symptoms, and progression of cancer cachexia, there is still no clinically useful screening tool that rapidly identifies patients with cancer cachexia and allows for early medical and nutritional intervention.⁶

Involuntary weight loss in advanced cancer patients has long been associated with decreased survival,⁷ performance status, and quality of life,⁸ yet weight loss alone does not fully identify the clinical correlates of cachexia.⁹ The Oncology Nutrition Dietetic Practice Group of the American Dietetic Association and Oncology Nursing Society recommend the

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use of the Patient-Generated Subjective Global Assessment (PG-SGA) as a more robust tool for assessing nutritional status in cancer patients.^{10,11} The PG-SGA contains a self-assessment questionnaire about a patient's weight, food intake, symptoms, and functional ability, along with a physician-administered physical examination and scoring of metabolic abnormalities. An abridged form of the PG-SGA questionnaire (aPG-SGA)¹² exists and contains only the self-assessment component (Figure 1) related to symptoms of cancer cachexia⁴ and allows the tool to be completed in a routine and prompt manner. The purpose of this study was to evaluate which features and outcomes of cancer cachexia are significantly associated with the aPG-SGA.

METHODS

Subjects and Methods

This prospective study received ethical approval from the McGill University Institutional Review Board and is in accordance with the Declaration of Helsinki. Patients 18 years of age and older diagnosed within the previous 6 months with locally advanced, metastatic, or recurrent non-small cell lung or gastrointestinal cancers were eligible for this study. A consecutive cohort of 245 patients who were either admitted or attending the oncology clinics at the McGill University Health Centre (Montreal General Hospital and Royal Victoria Hospital) were approached by their oncologists about the study. Two hundred seven patients provided written informed consent and were all assessed at the hospital bedside. A subset of this sample (n=94) was assessed at the McGill Nutrition and Performance Laboratory, an outpatient facility for evaluating human nutritional and functional status. Of those who went to McGill Nutrition and Performance Laboratory, 68 patients completed all specialized tests (see Laboratory Assessments at McGill Nutrition and Performance Laboratory). Patient recruitment and data collection took place between March 2006 and November 2007.

Bedside Evaluations

Each patient completed the aPG-SGA and an Edmonton Symptom Assessment System (ESAS) for symptom profiling. Patients' handgrip strength was assessed using Jamar Dynamometry (Sammons Preston). A single intravenous blood sample was obtained for the following: complete blood count and differential count, albumin, apolipoproteins A and B, and C-reactive protein (CRP). Patients also completed the Eastern Cooperative Oncology Group Performance Status (ECOG).

aPG-SGA. The aPG-SGA reports patient-identified nutritional, symptom, and functional problems as measured by the following four box scores: box 1 focuses on weight and weight changes with a maximum score of 5, box 2 on food intake with a maximum score of 4, box 3 on symptom profiling with a maximum score of 24, and box 4 on functional status with a maximum score of 3. Scores are then totaled to obtain an overall score between 0 (no problems) and 36 (worst problems).¹² Based on the distribution of cases, clinical relevance, and nutritional triage recommendations,¹³ the aPG-SGA scores were categorized into the following triage ranges: 0 to 1, patients with no particular nutritional problems and in no need of intervention; 2 to 8, patients with increasing nutritional problems who might benefit from but

are not in critical need of interventions by a registered dietitian nutritionist (RDN) or other clinician; and ≥ 9 , patients with a critical need for improved symptom management and/or nutrition-intervention options.

ESAS. The ESAS is a valid test composed of nine questions assessing symptom severity on a scale of 0 (no symptoms) to 10 (worst symptoms).¹⁴ Symptoms include pain, tiredness, drowsiness, nausea, lack of appetite, shortness of breath, depression, anxiety, and well being.

Handgrip Dynamometry. Use of the Jamar handgrip dynamometer has been shown to be valid and highly reliable¹⁵ in advanced cancer patients for measuring hand strength.¹⁶ This measure of upper limb strength is a good surrogate of generalized muscle strength, as it correlates with lower limb strength in this patient population and healthy adults.¹⁷

ECOG. The ECOG is a tool used to measure what impact a patient's disease has on activities of daily living and quality of life with the aim of determining prognosis and appropriate treatments.¹⁸ Scores range from 0 (no impairment) to 5 (death). It was developed by the Eastern Cooperative Oncology Group¹⁸ to facilitate and standardize clinical trials worldwide.

Laboratory Assessments at McGill Nutrition and Performance Laboratory

The 94 patients who consented and were able to travel to McGill Nutrition and Performance Laboratory completed the following tests within 1 week of their bedside assessment: the Brief Fatigue Inventory, the McGill Quality of Life Questionnaire (MQoL), and body composition via dual-energy x-ray absorptiometry (DXA). Of these 94 patients, 68 were able to provide full data and completed three 24-hour food recalls, the sit-to-stand test, and quadriceps strength using Biodex isokinetic dynamometry. Although these tests provide clinically useful information regarding patients' functional and psychological status, they can be impractical to complete on a routine basis in a clinic or hospital setting.

Brief Fatigue Inventory. The Brief Fatigue Inventory assesses level of fatigue and its impact on activities of daily living with nine questions.^{19,20} Three questions assess patients' fatigue during the immediate waking hours and six questions address how fatigue has interfered in the patients' lives during the previous 24 hours. Each question uses a scale from 0 (no fatigue) to 10 (unimaginable fatigue) for a total of 90 points.

MQoL. The MQoL assesses psychological, physical, support, and existential status on a scale of 0 (worst status) to 10 (best status).²¹

24-Hour Recalls. An RDN with previous clinical and research experience performed three 24-hour recalls with each patient, with 1 day being a weekend day. The RDN completed the first recall in a face-to-face interview and the second and third interviews over the phone. During the face-to-face interview, the RDN gave each patient identical measured utensils and dishes to help patients accurately report portion size, which she referred to when conducting the 24-hour

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