

Health professionals' attitudes toward the detection and management of cancer-related anorexia-cachexia syndrome, and a proposal for standardized assessment

Egidio Del Fabbro, MD,^a Aminah Jatoi, MD,^b Mellar Davis, MD, FCCP, FAAHPM,^c Kenneth Fearon, MBCh Hons, MD, FRCPS, FRCS,^d Jonathan di Tomasso, BS^{ce} and Antonio Vigano, MD, MS^{ce}

^aMassey Cancer Center, Virginia Commonwealth University, Richmond, Virginia; ^bMayo Clinic, Rochester, Minnesota; ^cCleveland Clinic Lerner College of Medicine, Case Western Reserve University, Cleveland, Ohio; ^dWestern General Hospital, Edinburgh, Scotland, UK; and ^eMcGill University Health Centre, Montreal, Quebec, Canada

Background The identification and management of patients with cancer anorexia-cachexia syndrome (CACS) can be a challenge despite recent international consensus on the definition of the condition.

Objectives To describe the current views and practice patterns of community oncologists and oncology nurses in regard to CACS and to propose a standardized, pragmatic assessment of CACS for oncological practice.

Methods and materials Responses from 151 community oncologists and nurses obtained across 5 surveys were analyzed. Questions addressed CACS in general and in patients with non-small-cell lung cancer (NSCLC). Surveys 1-3 were directed at physicians, and surveys 4 and 5 were directed at nurses. Surveys 1, 2, 4, and 5 focused on the recognition and monitoring of CACS, and Survey 3 on symptom management.

Results 67% of medical oncologists in Survey 3 selected weight loss as the most important criterion for diagnosing CACS and cited declining appetite and performance status (PS) as the most bothersome effects for patients and families. Weight maintenance/gain was the primary treatment objective for oncologists. Respondents to surveys 1 and 2 acknowledged the risk for CACS is high (60%) in NSCLC but considered the risk much lower (4%) in patients completing a first course of therapy with good PS. 91% of oncologists in Survey 3 reported that symptoms that had an impact on calorie intake were important/very important, and 73% were willing to consider a symptom assessment instrument that included appetite. Nurses in surveys 4 and 5 reported weight loss and appetite were most commonly used to identify cachexia. They considered responsibility for the initial assessment of cachexia was the oncologist's (32%), followed by the nurse practitioner (28%), and the nurse (16%).

Conclusion Most oncologists and nurses recognize the core criteria for the CACS, although there may be under-recognition of the condition's prevalence, particularly earlier in the course of treatment. There is considerable interest in adopting a brief assessment tool for screening, management, and referral of patient who are affected by or at-risk of CACS.

Despite the concerns about of cancer-related loss of appetite and weight among patients and their families,¹ cancer anorexia-cachexia syndrome (CACS) is underrecognized by medical providers and professional organizations. A recent review found that only 2.2% of guidelines – from 6 of 275 international oncological societies – provide physician recommendations for the management of CACS.² The seemingly low priority given to this condition also contrasts with many important advances in the field, including progress in understanding the mechanisms of CACS and the development of promising pharma-

logic and supportive-care interventions. More than 900 scientific papers have been published on CACS in the last 5 years, based on a PubMed search, and a new journal focusing on cachexia, sarcopenia, and muscle wasting was launched in 2010.

Furthermore, specialized clinics devoted to the management of CACS are a rarity, and when they do exist, they are in a few selected academic centers.³⁻⁵ As such, oncologists and nurses likely are responsible for the initial assessment and management of most patients with this condition. A recent report from the Institute of Medicine drew atten-

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tion to the anticipated increase in palliative care burden as populations age and emphasized opportunities for inter-professional education and the integration of palliative care services into oncology practices.⁶ However, in reality, time and resource limitations present challenging barriers for even the most basic assessment of nutritional or CACS symptom status in the busy clinical oncology practice.

Given those constraints, it is critical that oncologists are provided with brief, meaningful assessment tools to measure nutritional impact symptoms and other relevant CACS outcomes. The American Society for Clinical Oncology's Quality Oncology Practice Initiative (QOPI) has adopted some individual symptom measures such as pain, constipation, and chemotherapy-induced nausea and vomiting but does not include specific questions about appetite or other symptoms.⁷

The goals of the present study were to assess the attitudes of oncologists and nurses toward the detection and management of CACS, particularly in patients being treated for non-small-cell lung cancer (NSCLC), and to propose assessment techniques for CACS in daily oncology practice.

Methods and materials

From July 1, 2013–December 31, 2013, a series of 5 unique pilot surveys were undertaken. All of the questions were formulated by the authors of this paper and each survey was limited to 5 multiple-choice or open-response questions to encourage reply. The surveys were administered electronically to a cross-section of US-based, self-identified community medical oncologists and nurses from 30 different states and who had experience in the diagnosis and management of CACS in NSCLC patient populations.

Survey dissemination was directed to active members of the Sermo research database with the use of a proprietary MedPulse tool designed to achieve a random geographic distribution of respondents through a staged query-response process. This protocol sends small survey batches to a target list of health care providers and collects answers electronically. Subsequent batches are then directed to health care providers from geographic regions that are underrepresented in the accumulating database. The process continues until the prespecified number of complete

responses has been collected and compiled. Response rates are not monitored with this technology. The Sermo database for the United States comprises more than 275,000 active physicians, including 5,160 practicing oncologists and more than 150,000 specialty nursing health care providers, all of whom were invited to join and prequalified through telephone or online screening before entering the database. Surveys 1–3 were directed at physicians and surveys 4 and 5 were directed at nurses (Table). Surveys 1, 2, 4, and 5 were designed to gain insight into the recognition and monitoring of CACS, and Survey 3 focused on considerations around symptom management (see online material for the survey questions). In all, there were 151 respondents, including 101 oncologists and 50 nurses. Each respondent answered only one survey.

Results

Perceived frequency of CACS in NSCLC

When community oncologists were asked in Survey 1 about the likelihood of a patient with NSCLC developing CACS during therapy, 60% (15 of 25) indicated that this was inevitable or highly likely, and 4% (1 of 25) indicated that the likelihood was low (Figure 1). The same community oncologists were asked about the likelihood of CACS developing in a patient who had completed a course of therapy and maintained good PS. In that scenario, most of the respondents indicated that CACS was somewhat less likely or unlikely to occur, and 4% (1 respondent) described CACS as very likely, and none thought it was inevitable.

Assessment and diagnosis

To understand current practices around the initial detection of CACS, we asked which personnel were most likely to identify the condition in patients with NSCLC (Survey 1). Sixty-nine percent of community oncologists (n = 25) identified themselves as filling that role, and 15% said nurses filled the role. A small proportion (8%) indicated that CACS is identified when chemotherapy doses are recalculated based on weight loss between office visits. In Survey 4, oncology nurses indicated that CACS is detected primarily by the practicing oncologist (32% of responses), the nurse practitioner/physician assistant (PA/NP; 28%), nursing staff (16%), or family members (16%).

TABLE Summary of survey target audience and date (N = 151)^a

	Oncologists (date, 2013)			Oncology nurses (date, 2013)	
	Survey 1 (July 13)	Survey 2 (July 13)	Survey 3 (Oct 27)	Survey 4 (Dec 5)	Survey 5 (Dec 5)
Respondents, n	25	25	51	25	25

^aEach respondent answered only one survey.

In Survey 3, most of the community oncologists (67%) identified patient weight loss as the most important criterion for diagnosing CACS in daily practice. This was followed by muscle loss, poor appetite, low body mass index, and declining physical function (Figure 2). The same oncologists identified declining physical function (41%) and poor appetite (24%) as the most important CACS-related concerns in patients and their families. Oncology nurses (Survey 4) relied on appetite loss reported either by the patient or a family member (84% of respondents) and weight loss (72%) to identify CACS, followed closely by diminished muscle strength (64%), quality of life (QoL) (64%), and activities of daily living (60%).

In Survey 3, the oncologists ranked the management of symptoms that affect appetite (ie, nausea, early satiety, pain, depression, constipation) Very Important (58.8% of respondents), Important (31.4%), or Somewhat Important (7.8%), with only 9.8% of respondents indicating current use of a formal tool to evaluate these symptoms. Just under half of the respondents (47%) reported they would consider incorporating a short (10-item) survey into their practice for ongoing patient assessment, and another 26% indicated that they would incorporate such a questionnaire depending on the usefulness of the information elicited. Eighteen percent indicated that they would not consider incorporating an instrument for this purpose.

In addition to clinical signs and symptoms, 94% of community oncologists indicated that albumin levels could provide additional insights into the assessment of weight loss. Levels of thyroid-stimulating hormone (TSH) and C-reactive protein (CRP) are used less often, by 19.6% and 13.7%, respectively.

Management strategies for CACS

In Survey 1, community oncologists identified weight stabilization (56%) and improving tolerance for chemotherapy (20%) as important treatment goals. In Survey 2, the most common management strategies included nutritional intervention plus pharmacologic appetite stimulants (64%) or nutritional intervention plus pharmacologic appetite stimulants along with an exercise program (24%).

In Survey 4, 16% of oncology nurses indicated that internal cachexia management teams oversee CACS care in their practice settings, 8% said they refer patients to an external palliative care specialist, and 4% refer to an external nutritionist. In survey 5, nurses said that oversight respon-

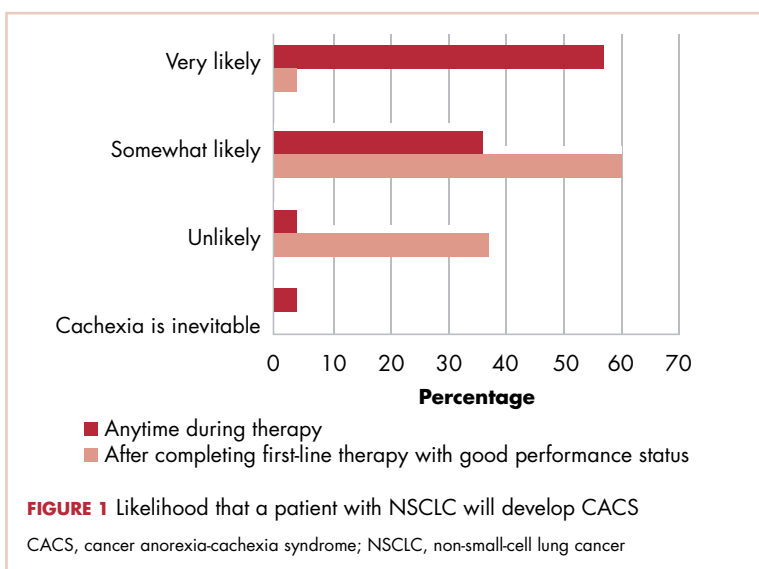


FIGURE 1 Likelihood that a patient with NSCLC will develop CACS
CACS, cancer anorexia-cachexia syndrome; NSCLC, non-small-cell lung cancer

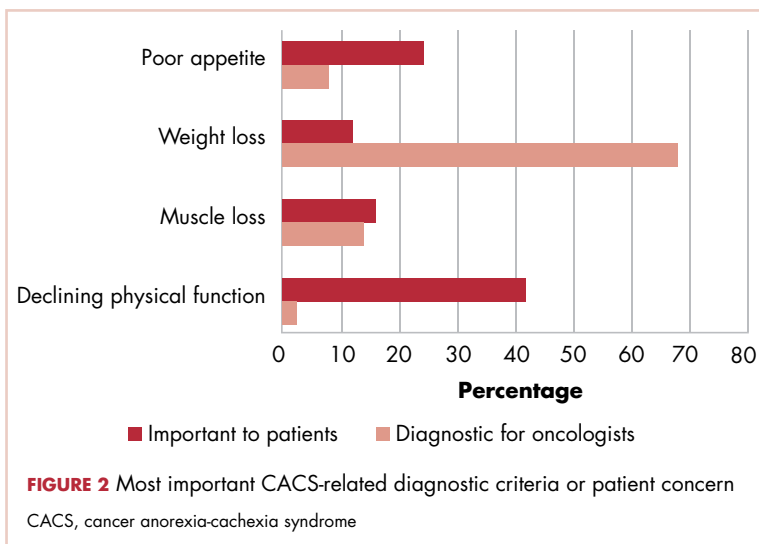


FIGURE 2 Most important CACS-related diagnostic criteria or patient concern
CACS, cancer anorexia-cachexia syndrome

sibilities for supportive/palliative care fell to the oncologist (36%), a designated team within the practice (28%), or the collective efforts of physicians and staff (20%). Although no pharmacologic agent is approved currently for the treatment of CACS, most of the nurse respondents in Survey 4 described the initiation of drug management, either by the oncologist (48%) or NP/PA (32%) for patients with the condition.

Discussion

The results of these pilot surveys provide insight into the detection and management of CACS by community oncology practitioners and underscore an urgent unmet need for standardized symptom assessment. An interesting perception of lower risk for CACS in NSCLC emerged for patients who maintain good PS during their

first course of treatment (Figure 1). However, findings in a recent retrospective study of 425 patients found that a minority (40%) gained weight during concurrent chemoradiotherapy for stage III B NSCLC, and weight loss was associated with inferior survival.⁸ There is also other evidence that various chemotherapies,⁹ including cisplatin,¹⁰ can exacerbate muscle wasting. Weight loss is the core criterion for diagnosing CACS and is associated with a host of negative outcomes such as increased side-effect burden during chemotherapy and poor prognosis,¹¹ so the identification of nutritional impact symptoms such as nausea, depression, and constipation is important because they can be managed in many patients and result in improved oral intake and attenuate weight loss.⁴ The community oncologists who were surveyed reported considerable interest in adopting a brief symptom assessment tool to improve their ability to screen for affected or at-risk patients and to manage symptoms that negatively affect appetite. Their key intervention goals for CACS included weight stabilization or gain and improved tolerance for chemotherapy.

Weight loss and laboratory parameters

This study confirms that weight loss is viewed as the most important clinical sign of CACS among health care providers. In general, the detection of CACS centers on evidence for involuntary weight loss.^{3,12,13} A recent international consensus provides additional structure around the diagnosis and staging of CACS, recognizing that weight loss of more than 5% of baseline body weight over 6 months (or 2% when there is evidence of sarcopenia is present) is a key criterion for CACS.^{12,14,15}

An emphasis on total body weight or BMI also belies an insidious clinical challenge. Given the high prevalence of obesity in the general population, few patients are considered underweight at diagnosis, even if they have lost significant muscle mass. Indeed, at the time of diagnosis, when body composition is assessed by dual-energy x-ray absorptiometry scan or computed-tomography (CT) scan, many patients with NSCLC and an elevated BMI are found to be sarcopenic. The condition, known as sarcopenic obesity, is a particularly poor prognostic indicator for various solid tumor types including NSCLC.¹⁶ At least 50% of patients with cancer are older than 65 years of age, so sarcopenia of aging may compound the muscle loss related to CACS. Although CT imaging is emerging as a useful measure of body composition¹⁷ and could influence clinical decision making and chemotherapy dosing in future,^{18,19} quantification of lean body mass or fat is not yet conducted in daily clinical practice.

In addition to total body weight loss, recently developed staging criteria for the identification of pre-cachexia, cachexia and refractory cachexia, incorporate diminished caloric intake

and PS, as well as markers of inflammation.^{3,12,13} In research settings, laboratory assessment of serum albumin, CRP, TSH, vitamin D, and testosterone levels can offer insight into the underlying mechanisms that may contribute to CACS.²⁰ The Glasgow Prognostic Score is a simple, objective, systemic inflammation based approach using assessment of CRP and albumin levels²¹ that has prognostic value independent of tumor stage, performance status, and treatment (active or palliative), in a variety of advanced common solid tumors.²² Findings from preliminary studies have reported a high prevalence of vitamin D deficiency in patients with cancer cachexia²³ and have shown that testosterone replacement improves some symptoms.²⁴

Patient-reported outcomes

The physician and patient concerns in this study (Figure 2) draw attention to the importance of incorporating patient-reported outcome (PRO) assessments in routine clinical practice. Oncologists depend on patient-volunteered symptoms, however, without systematic inquiry, it is likely that symptoms such as anorexia are more prevalent than identified by oncologists, because patients volunteer few symptoms relative to their total symptom experience.¹⁰ There are currently no specific questions about appetite in QOPI, or in some validated nutrition screening assessments such as the Malnutrition Universal Screening Tool (MUST).²⁵ A systematic review has found that even single-item symptom measures of appetite, fatigue, or pain are important indicators—separately or in combination—for survival.²⁶ Appetite scores also have been shown to provide important prognostic information independent of demographic (age, sex) and clinical variables (PS, distant metastases).²⁷

Although PROs increasingly are recognized as key outcomes, oncologists' views and attitudes about their clinical utility are important when considering the incorporation of assessment tools in daily practice. Recently, a small qualitative study found that oncologists are familiar with PROs and believe that symptoms such as poor appetite, depression, fatigue, insomnia, nausea, and pain are universal across cancer types and potentially could be measured by a single instrument.²⁸

There is no international consensus on the use of a tool for routine clinical assessment of PROs in CACS.²⁹ In North America, Europe, and Africa, the 10-item Edmonton Symptom Assessment Scale (ESAS) is used most frequently in palliative care practice and research.³⁰ In a standardized population-wide investigation, the ESAS detected a high prevalence of multiple symptoms in ambulatory cancer patients, similar to those reported in palliative care populations.³¹ High symptom scores also precipitated clinical action on the part of health care providers.³² Although the ESAS has the advantage of being able to assess symptom severity and includes appetite, it

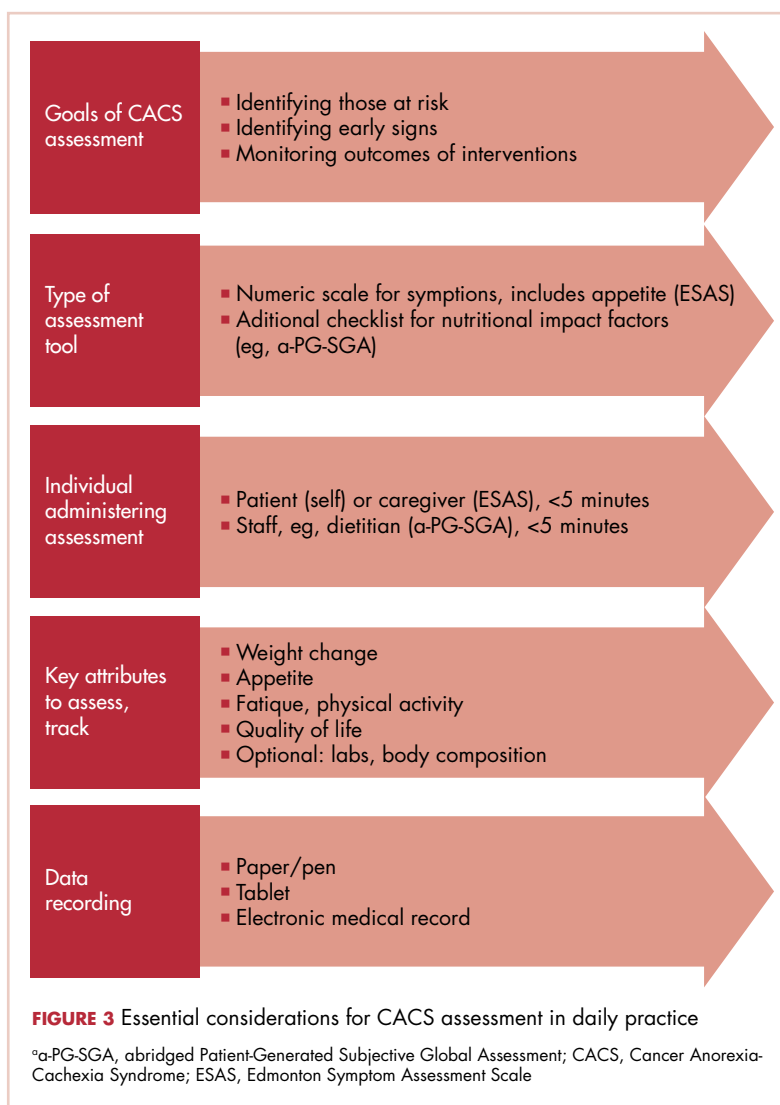
does not include other pertinent CACS symptoms such as constipation, early satiety, or dysgeusia. A more comprehensive evaluation of CACS would require an additional nutritional assessment measure such as the Patient-Generated Subjective Global Assessment (PG-SGA), a validated tool endorsed by the American Dietetic Society that identifies reversible factors contributing to poor oral intake (eg, nausea or severe from oral mucositis).³³ More recently, a brief or abridged (a-PG-SGA) version of the PG-SGA was validated and shown to provide additional diagnostic and prognostic value in evaluating patients with cancer.³³ The a-PG-SGA can be completed by patients in less than 5 minutes, and includes information about the severity and rate of weight loss, food intake, nutritional symptoms and functional status. The a-PG-SGA also correlated with CACS features such as increased markers of inflammation, higher severity of symptoms, decreased muscle strength, loss of fat mass, increased hospitalization, decreased chemotherapy tolerance and shorter life expectancy.

The Mini Nutritional Assessment is simple, validated in the elderly, has independent prognostic value³⁴ and is relatively easy for a nontrained person to administer, but has lower specificity for identifying malnutrition than the a-PG-SGA.³⁵

Proposed standardized assessment

Our survey results suggest that the identification and treatment of CACS may occur late in the disease trajectory, because most respondents described performing these tasks and referring to a palliative specialist team when they identified uncontrolled symptoms. Such a delay could result in patients entering the late, refractory stage of cachexia and missing their anabolic opportunity to reverse muscle wasting and weight loss. In a recent study of 368 patients, fewer than 5% of patients gained skeletal muscle within 90 days of their deaths, based on body composition imaging using a CT scan.³⁶ This suggests that the window of anabolic potential and opportunity for intervention exists in the early phases of the disease trajectory. Given this result and the poor sensitivity and specificity of physician and nurse evaluations of patient supportive care needs and symptoms,³⁷ the incorporation of a standard assessment system in clinical practice is essential.

A brief standardized assessment – including items that measure nutritional impact symptoms such as nausea, depression, and pain – should be extended to all oncology patients who are at risk for CACS. This would provide the opportunity to improve clinical care by identifying and managing symptoms that affect nutritional intake earlier in the CACS disease course. The ESAS questions



about appetite and fatigue would identify 2 of the cardinal symptoms of CACS along with other symptoms that could affect caloric intake, such as depression, nausea, and pain. This symptom assessment, along with a history of weight loss of 5% or more during the previous 6 months, would identify many patients with CACS. Finally, an additional nutritional assessment for these patients, such as the a-PG-SGA, could be easily implemented in oncology practices with sufficient personnel resources. Thus, some of the evaluations currently done in a specialized cachexia clinic could be adopted readily in daily oncological practice. A checklist of practice considerations involved in the evaluation and implementation of assessment tools is summarized in Figure 3.

Multimodal management

The implementation of standardized assessments has impor-

tant clinical implications. CACS responds, in part, to symptom management,⁴ nutritional counseling,³⁸ and multimodality therapy³⁹ even though no single medication is approved for its treatment. Early- and late-phase trials of single agents such as ghrelin,⁴⁰ ghrelin mimetic/receptor agonists,⁴¹ myostatin inhibitors,⁴² and selective androgen-receptor modulators⁴³ have shown promise in improving clinical outcomes such as appetite, caloric intake, lean body mass, and physical function. Soon clinicians may have access to effective pharmacological agents that can be incorporated into a multimodal anticachexia strategy that includes symptom management, nutritional counseling, and exercise.

Study limitations

Several limitations should be considered when interpreting these study findings. These include the use of a nonvalidated questionnaire; though one needs to bear in mind that there is no questionnaire available that would have met the objectives of this study. The small number of respondents to each survey limits generalizability to all community practice settings, and given the limited number of questions per survey, we could not explore other barriers to the management of CACS.

Conclusions

This study suggests that community oncologists recognize the core criteria for the diagnosis of CACS, although the prevalence of this condition may be under recognized. There is considerable interest in adopting a brief symptom assessment tool for screening, management, and referral of affected or at-risk patients. A validated brief assessment tool could be incorporated into daily practice and accomplish the dual purpose of improved health care quality and early identification of patients with the CACS.

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