Original Article

Validation of a Simplified Anorexia Questionnaire

Mellar P. Davis, MD, FCCP, Tugba Yavuzsen, MD, Jordanka Kirkova, MD, Declan Walsh, MSc, FACP, Matthew Karafa, PhD, Susan LeGrand, MD, FACP, and Ruth Lagman, MD, MPH

The Harry R. Horvitz Center for Palliative Medicine (M.P.D., T.Y., J.K., D.W., S.L., R.L.), Taussig Cancer Institute; Section of Palliative Medicine and Supportive Oncology (M.P.D., D.W., S.L., R.L.), and Department of Quantitative Health Sciences (M.K.), The Cleveland Clinic, Cleveland, Ohio, USA

Abstract

Context. Anorexia is a common symptom in cancer and is usually assessed by multiple questions and multidimensional questionnaires. A simplified questionnaire would be less burdensome to patients and abbreviate the process.

Objectives. We compared the reliability at one point in time, sensitivity to change over time, and prognostic accuracy of a two-item questionnaire with the Functional Assessment of Anorexia and Cachexia Therapy shortened 12-question version (A/CS-12).

Methods. Individuals with cancer, who were cognitively intact and verbally agreed to participate, completed a two-item questionnaire and A/CS-12 in random order and again seven days later. We compared the direction of response to the summated two-item questionnaire to the validated A/CS-12 score at a single point in time, then intra-patient changes over a seven-day period of time. Scores of both questionnaires were divided into poor, moderate and good appetite and compared to survival using Kaplan-Meyer curves. Bootstrapping was used to construct confidence intervals for estimated probability agreement. Survival analysis also used hazard ratios from a Cox Proportional Hazards model.

Results. One hundred seventeen individuals from a single institution participated, who were either admitted to an inpatient palliative unit or seen in an outpatient/palliative medicine unit. Median age was 58.8 (range 10.7–87.1 years). Agreement at one point in time was 0.64 (95% confidence interval [CI] 0.63 – 0.66). Agreement over time was 0.53 (CI 0.41 – 0.64). The A/CS-12 predicted survival based on scores on Days 1 and 7 ($P < 0.001$), ($P = 0.003$) (HR 0.97 day 1, HR 0.95 day 7), whereas the simplified questionnaire failed to predict survival.

Conclusions. A simplified questionnaire has moderate correlation with the A/CS-12 at one point in time but loses sensitivity over time, and lacks the ability to predict survival. A change in the questionnaire may improve reliability. Changing

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Web site: www.clevelandclinic.org/palliative.

Address correspondence to: Mellar P. Davis, MD, FCCP, Cleveland Clinic Foundation, 9500 Euclid Avenue, R35, Cleveland, OH 44195, USA. E-mail: mdavis6@ccf.org

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question 2 of the simplified questionnaire to a neutral form (better, same or worse appetite) may improve sensitivity and prognostic capability. *J Pain Symptom Manage 2009;38:691–697.* *© 2009 U.S. Cancer Pain Relief Committee. Published by Elsevier Inc. All rights reserved.*

Key Words
Questionnaire, assessment, anorexia, survival, prognosis

Introduction

Anorexia is a common and important symptom experienced by most with advanced cancer.[1–3] The development of validated scales to accurately measure the course of anorexia is important to research and clinical management. Patient-reported outcomes are an important part of gauging the benefits to anticancer therapy and symptom management. The validation of new assessment tools requires a comparison to instruments that already have been validated, if this is possible.

The Functional Assessment of Anorexia and Cachexia Therapy (FAACT) is a modification of the Functional Assessment of Cancer Therapy—General, which in its original form contained 18 additional questions regarding anorexia and cachexia. This has been shortened to 12 questions (A/CS-12) (Fig. 1) and has been validated as a reliable nutritional

During the past 7 days:

0= Not at all

1= A little bit

2= Somewhat

3= Quite a bit

4= Very much

1. I have a good appetite.	0	1	2	3	4
2. The amount I eat is sufficient to meet my needs.	0	1	2	3	4
3. I am worried about my weight.	0	1	2	3	4
4. Most food tastes unpleasant to me.	0	1	2	3	4
5. I am concerned about how thin I look.	0	1	2	3	4
6. My interest in food drops as soon as I try to eat.	0	1	2	3	4
7. I have difficulty eating rich or "heavy" foods.	0	1	2	3	4
8. My family or friends are pressuring me to eat.	0	1	2	3	4
9. I have been vomiting.	0	1	2	3	4
10. When I eat, I seem to get full quickly.	0	1	2	3	4
11. I have pain in my stomach area.	0	1	2	3	4
12. My general health is improving.	0	1	2	3	4

Fig. 1. The Functional Assessment of Anorexia/Cachexia Cancer Therapy (ACS-12).

assessment tool.[4] This instrument is sensitive to changes in appetite over time.[5]

Several other questionnaires that assess anorexia have been validated but are more burdensome than the A/CS-12.[6–8] The FAACT has been used in large treatment trials for anorexia and thus is reasonable to use as a standard to validate a simplified anorexia questionnaire.[9]

The length of the A/CS-12 also may be burdensome to severely ill patients with advanced cancer who are undergoing palliative therapies. Individuals in acute inpatient palliative units or who are outpatients have multiple symptoms, in addition to anorexia, which require additional assessment, adding to the burden of questions.[5] Brevity without the loss of accuracy or precision would be an important element to assessing anorexia in these settings. A simplified questionnaire would hopefully detect the presence of anorexia with a reasonable degree of reliability and would detect a change in appetite over time with the same sensitivity as the A/CS-12.[10,11]

We developed a two-item questionnaire as a step toward establishing the utility of a simplified questionnaire in treatment trials (Fig. 2). The primary purpose of this study was to perform initial validation of the two-item anorexia questionnaire by comparing it with the A/CS-12 of the FAACT at a single point of time and to determine agreement between the two questionnaires over time. The secondary objective was to compare the ability of the A/CS-12 and simplified questionnaire to predict survival in advanced cancer.

Methods and Materials

This prospective comparison study was approved by the Cleveland Clinic Institutional Review Board. All participants verbally agreed to answer both questionnaires at study entry and one week later. Individuals were recruited from the inpatient acute palliative medicine unit. To prevent the order of the questionnaires from biasing results, the instruments were administered in random order at each interview, using computerized randomization, which was provided by the Department of Quantitative Health Sciences of the Cleveland Clinic. The order was concealed from the interviewers. Questionnaires were completed in person or by telephone (predominantly in the second interview) to minimize attrition. A standardized script and form was used in the administration of the questionnaires, to reduce interrater variability. Patient inclusion criteria were 1) cancer diagnosis; 2) cognitively intact, as defined by a score of less than 2 on a Bedside Delirium Scale; 3) at least 18 years old; 4) verbal consent; and 5) the ability to speak and understand English.

In addition to the two questionnaires, demographics, cancer stage at the time of entrance into the study, Eastern Cooperative Oncology Group (ECOG) performance score, and survival data were collected. Laboratory studies were not collected. Survival was measured from study entrance to death.

An initial pilot phase was performed, followed by the prospective study. The purposes of the pilot phase were to refine and maximize the sensitivity of the simplified questionnaire, test the feasibility of the study design, and identify and resolve any practical or logistical problems. The findings from the pilot phase of the study suggested that the simplified questionnaire was promising enough to warrant a full-scale prospective study and that the study was feasible. Both pilot and study data were combined in the analysis because the study design and methods did not change.

1. On a 0 to 10 scale, where 0 is the complete lack of appetite and 10 normal appetite, my appetite in the last seven days has been

0 1 2 3 4 5 6 7 8 9 10

2. If you have lost your appetite, is the loss of your appetite over the last 7 days mild, moderate or severe?

Fig. 2. The simplified anorexia questionnaire.

Biostatistical Considerations

To determine interpatient comparisons, we ordered the direction of responses to the simplified questionnaire in the same direction as the A/CS-12. This provided a measure of agreement that compared different patients at a single time point. For intrapatient comparisons over time, we categorized appetite as increased, decreased, or the same and then determined if the simplified questionnaire responses were in the same direction as the A/CS-12. This provided a measure of sensitivity to changes in appetite over time using the simplified questionnaire, against the A/CS-12 as the standard. We selected a one-week period for agreement to avoid significant attrition from the study. We did not consider test-retest reliability because anorexia changes over time and there is no consensus on time frames (for reliability). Bootstrapping was used to construct confidence intervals (CIs) for estimated probability of agreement.

We performed two types of analyses to determine sensitivity of the questionnaires to predicting survival. In the first analysis, we used the total score (an aggregation of questions that reflect unidirectional change of appetite, i.e., improvement or worsening). The A/CS-12 was summated using the standard methods (e.g., reversing all but Q_1, Q_2, and Q_{12}; higher scores equal a positive response) to match the direction of appetite change on the simplified questionnaire. The total score for the simplified questionnaire was the sum $Q_1 + Q_2$ and then reversing the scale to match the direction of change found with the A/CS-12. The simplified questionnaire had an aggregated total score, which could range from 0 to 13. For the A/CS-12, the total score could range from −36 to +12. Higher scores were associated with better appetite. There are no recommendations for the division of aggregated ACS-12 scores in reflecting poor, moderate, or good appetite. The clinically meaningful change in appetite on a 0−10 scale has not been defined. We divided the aggregate scores of both questionnaires based on clinical utility to compare patient survival at different levels of anorexia. We used a three-level categorization of appetite loss (Table 1) to compare survival based on the Kaplan-Meier curve. For the second survival analysis, a Cox proportional hazards model was used for univariate and multivariate analyses of survival.

Table 1
Categorization of Anorexia by Division of the Aggregated Appetite Score on the Two Questionnaires

Code Appetite	Simplified Questionnaire	ACS-12
1. Poor	0−3	−36 to −20
2. Moderate	4−7	−19 to −4
3. Good	8−13	−3 to +12
Total score range	0−13	−36 to +12

Results

One hundred eighty-five consecutive individuals were screened, 75 were ineligible, 16 were inevaluable, 13 refused participation, and two were mistakenly asked to participate twice. Twenty-one completed the pilot phase and an additional 79 completed the prospective study. Median age was 59 years (range 18−87), and 69 were female. The median ECOG performance score was 2 (0−4). Eighteen had breast cancer, 17 lung cancer, 14 gastrointestinal malignancies, and 12 had multiple myeloma; the remainder had other types of cancers. Seventy-six percent had metastatic cancer. The median time between the first and the second set of questionnaires was seven days (range 6−12 days). The median A/CS-12 score on Day 1 was −9 (range −31 to +9), and the median on Day 7 was 5 (range −23 to +12). The median score for the simplified questionnaire was 6 (range 0−12) on Day 1, and the median on Day 7 was 7 (range 0−12). Overall, of the 117 individuals who completed the questionnaire on Day 1, 100 completed the A/CS-12 and 89 completed the simplified questionnaire on Day 7. There were no demographic differences between those who completed the study and those who did not. Individuals who completed Day 1 only, however, had worse appetite measured by single questions from the A/CS-12 (Q_4 [$P < 0.001$], Q_6 [$P = 0.002$], and Q_{11} [$P = 0.037$]) and worse appetite summated by the A/CS-12 score ($P = 0.012$). Deaths had occurred in 95 of 117 individuals by the time the study was completed. Those who did not complete the study had shorter survival compared with the rest of 100 individuals (Wilcoxon matched-pairs signed rank test = 0.013).

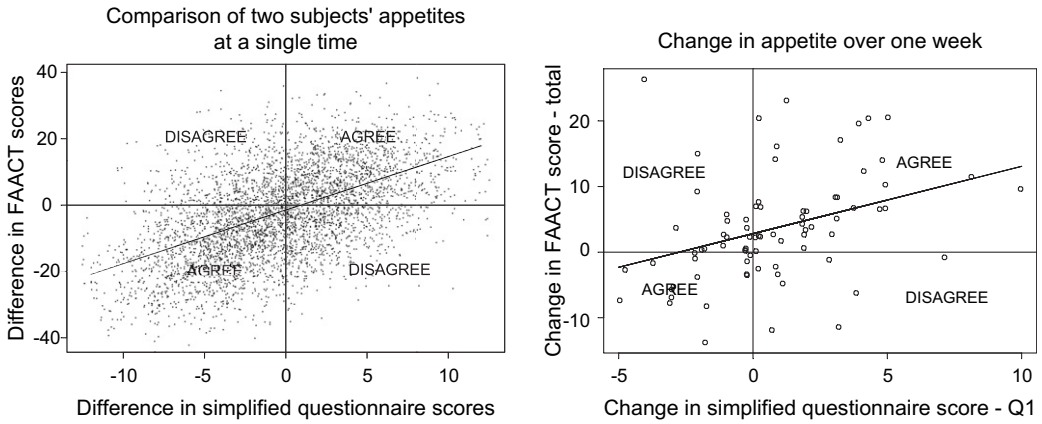


Fig. 3. Agreement between the two questionnaires at a single point in time and over time.

Agreement between the simplified questionnaire and the A/CS-12 at a single point in time, based on 4,278 usable pairs for bootstrapping, was 0.64 (95% CI 0.63 and 0.66) (Fig. 3). Agreement between the simplified questionnaire and the A/CS-12 over time, based on 70 usable subjects, was 0.53 (95% CI 0.41–0.64) (Fig. 3).

Patient survival was a median of 2.8 (range 1.2–17.7) months (25th, 75th percentiles). The total score on A/CS-12 predicted survival better than the simplified questionnaire (Fig. 4). However, the simplified questionnaire was able to discriminate the survival of patients with poor appetite from those with moderate to good appetite, whereas the A/CS-12 could discriminate survival between those with poor, moderate, and good appetite (Fig. 4). The total A/CS-12 score on Day 1 ($P < 0.001$) and Day 7 ($P = 0.003$) predicted survival. As the A/CS-12 score increased, mortality decreased. For Day 1, the hazard ratio (HR) was 0.97 (0.95–0.99, $P = 0.01$), and for Day 7, the HR was 0.96 (0.94–0.99, $P = 0.001$). For the simplified questionnaire, the point estimates were in the same direction, but due to increased variability in score, these results were not significant either on Day 1 ($P = 0.074$) or on Day 2 ($P = 0.43$). The HR for the simplified questionnaire was 0.91 (0.87–1.01) on Day 1 and 0.96 (0.88–1.05) on Day 7. For both the A/CS-12 and the simplified questionnaires, changes in appetite over seven days did not predict survival. In multivariate modeling adjusting for ECOG performance score, the total A/CS-12 score on Day 1 ($P = 0.002$) and Day 2 ($P = 0.005$) predicted survival, whereas the simplified questionnaire did not predict survival (Table 2).

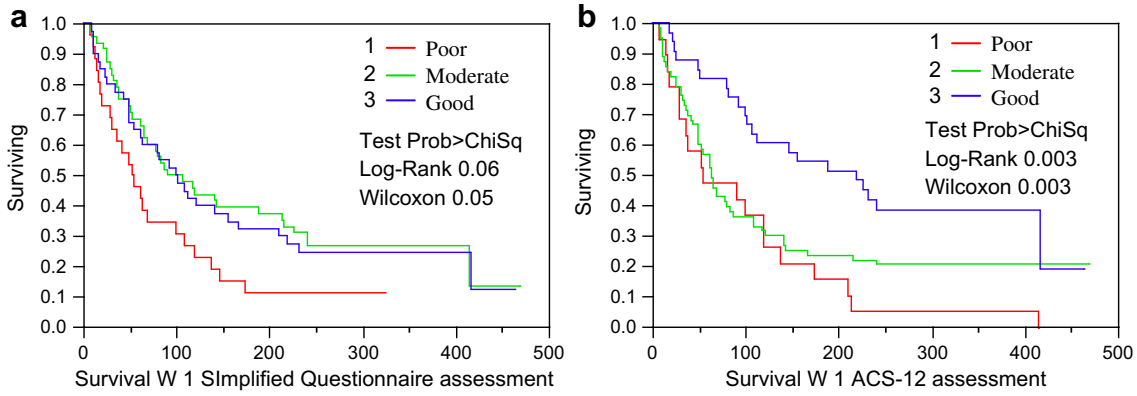


Fig. 4. Survival by Kaplan-Meier curves using appetite severity measured on the two questionnaires: a) survival by the simplified questionnaire, b) survival by the ACS-12.

Table 2
Aggregated Appetite Scores on the Two Questionnaires by Baseline ECOG Level

	Simplified Questionnaire	ACS-12
ECOG Level	Mean (SD)	Mean (SD)
0 ($n=6$)	6.7 (2.4)	−7.0 (9.31)
1 ($n=37$)	7.4 (3.2)	−7.4 (9.59)
2 ($n=38$)	5.9 (3.7)	−10.5 (10.59)
3 ($n=26$)	4.6 (3.2)	−10.7 (7.59)
4 ($n=10$)	6.5 (3.5)	−10.3 (11.8)
Total score range	0−13	−36 to +12

Discussion

Anorexia is frequently accompanied by multiple gastrointestinal symptoms, such as dry mouth, constipation, and early satiety.[12] Early satiety is prognostic in cancer but is not assessed by this simplified questionnaire.[13,14] An abbreviated questionnaire, for this reason, is not recommended as a screening tool.

Multidimensional instruments that assess nutrition, such as the Patient-Generated Subjective Global Assessment (PG-SGA), have a sensitivity greater than 90% and a specificity greater than 80% in detecting malnourished individuals.[14] Median length of hospitalization is longer in individuals deemed malnourished by the PG-SGA; the PG-SGA does not predict short-term (30-day) mortality but does account for 25% of the variance in quality of life.[7,14–16]

Another instrument, the Bristol-Myers Anorexia/Cachexia Recovery Instrument (BACRI) score, correlates with objective weight and lean body mass changes after treatment with megestrol.[7] However, it is not known if the change in BACRI score over time predicts survival.

The A/CS-12 correlates with anorexia measured on a four-point categorical scale found on the Memorial Symptom Assessment Scale. Both questionnaires predict survival.[16]

The simplified questionnaire had a modest positive correlation with the A/CS-12 at a single point in time but reduced sensitivity to change over time. The A/CS-12 predicted survival at a single point in time, whereas changes over time did not predict survival. The simplified questionnaire was not predictive of survival either at a single point in time or with changes over time.

There are limitations to this study. The patient population was derived from very ill inpatients, and outpatients, questionnaires were completed by an interview that was scripted. Patient self-assessment without an interviewer could potentially lead to different answers and a greater number of incomplete questionnaires. This study may not be generalizable to healthier cancer outpatients and earlier stages of cancer. The time frame between assessments may have been too short to adequately gauge change in appetite over time, although symptoms in this population deteriorate fast. It is also possible that an interval of more than seven days will be needed to determine if a change of appetite over time correlates with survival. Due to the short survival of this group of inpatients, we considered the time frame inappropriate to determine test-retest reliability. Those who did not complete the questionnaires on Day 7 had similar demographics to those completing the study, but worse appetite and shorter survival compared with those completing the study. This would reduce the generalizability of the results. The presence or absence of anorexia and its severity are prognostic.[17,18] However, the association of prognosis with appetite changes over time may be less significant or at least not as well established.[17,18]

The simplified questionnaire may be improved through modifications. Question 2 is unidirectional and assumes appetite loss over time. Modification to include the potential for improved appetite would increase clinical utility and perhaps sensitivity to change over time. The question should perhaps be changed to "Has your appetite improved, remained the same, or worsened over the last 7 days?" A relief scale, such as "Is your appetite much better, a little better, the same, a little worse, much worse over 7 days?" may also be better to use in clinical trials and perhaps improve its survival predictability. The anchors of Question 1 may be changed to "No appetite" and "Best possible appetite," to reduce the ceiling effect of "Normal appetite." "Best possible appetite" will allow measuring improvement over the normal appetite. This modification of the simplified questionnaire can be used to screen people without anorexia and follow them longitudinally.

Outcomes based on symptom assessment not only should include reliability and sensitivity to change in symptom severity but should

also be correlated with objective patient-related outcomes, such as weight gain or loss, lean body mass, and/or survival (for those with symptoms that are known to be prognostic).

Conclusions

This study is an initial validation of a short instrument for cancer anorexia that was compared with a standard anorexia tool and to the objective outcome of survival. A simplified two-item questionnaire moderately correlates with the A/CS-12 questionnaire at one point in time, correlates less well with change over time, and loses the ability to predict survival in advanced cancer. If survival is one of the outcomes to anorexia treatment, then the A/CS-12 instrument should be used in assessment. Future studies should evaluate modifications in a simplified questionnaire, focus in detail on other validity and reliability measures, instrument stability over a short time frame, and clinically important differences in subjective and objective outcomes.

References

1. Inui A. Cancer anorexia-cachexia syndrome: current issues in research and management. CA Cancer J Clin 2002;52:72–91.

2. Sarhill N, Mahmoud F, Walsh D, et al. Evaluation of nutritional status in advanced metastatic cancer. Support Care Cancer 2003;11:652–659.

3. Davis MP, Dreicer R, Walsh D, Lagman R, LeGrand SB. Appetite and cancer-associated anorexia: a review. J Clin Oncol 2004;22:1510–1517.

4. Ribaudo J, Hahn E, Lloyd S, et al. Re-validation and shortening of the functional assessment of anorexia/cachexia therapy (FAACT) questionnaire. Qual Life Res 2001;9:1137–1146.

5. Homsi J, Walsh D, Rivera N, et al. Symptom evaluation in palliative medicine: patient report vs. systematic assessment. Support Care Cancer 2006;14: 444–453.

6. Cella D, Leslie W, Von Roenn J, et al. Quality of life and nutritional well-being: measurement and relationship. Oncology 1993;7:105–111.

7. Cella DF, Von Roenn J, Lloyd S, Browder HP. The Bristol-Myers Anorexia/Cachexia Recovery Instrument (BACRI): a brief assessment of patients' subjective response to treatment for anorexia/cachexia. Qual Life Res 1995;4:221–231.

8. Thoresen L, Fjeldstad I, Krogstad K, Kaasa S, Falkmer UG. Nutritional status of patients with advanced cancer: the value of using the subjective global assessment of nutritional status as a screening tool. Palliat Med 2002;16:33–42.

9. Jatoi A, Windschitl HE, Loprinzi CL, et al. Dronabinol versus megestrol acetate versus combination therapy for cancer-associated anorexia: a North Central Cancer Treatment Group Study. J Clin Oncol 2002;20:567–573.

10. Guyatt G, Walter S, Norman G. Measuring change over time: assessing the usefulness of evaluative instruments. J Chronic Dis 1987;40:171–178.

11. Chang VT, Xia Q, Kasimis B. The functional assessment of anorexia/cachexia therapy (FAACT) appetite scale in veteran cancer patients. J Support Oncol 2005;3:377–382.

12. Andrew I, Kirkpatrick G, Holden K, Hawkins C. Audit of symptoms and prescribing in patients with the anorexia-cachexia syndrome. Pharm World Sci 2008;30:489–496.

13. Davis MP, Walsh D, Lagman R, Yauvzsen T. Early satiety in cancer patients: a common and important but under recognized symptom. Support Care Cancer 2006;14:693–698.

14. Komurcu S, Nelson KA, Walsh D, Ford RB, Rybicki LA. Gastrointestinal symptoms among inpatients with advanced cancer. Am J Hosp Palliat Care 2002;19:351–355.

15. Bauer J, Capra S, Ferguson M. Use of the scored Patient-Generated Subjective Global Assessment (PG-SGA) as a nutrition assessment tool in patients with cancer, assessment (PG-SGA) as a nutrition assessment tool in patients with cancer. Eur J Clin Nutr 2002;56:779–785.

16. Isenring E, Bauer J, Capra S. The scored Patient-Generated Subjective Global Assessment (PG-SGA) and its association with quality of life in ambulatory patients receiving radiotherapy. Eur J Clin Nutr 2003;57:305–309.

17. Barbot AC, Mussault P, Ingrand P, Tourani JM. Assessing 2-month clinical prognosis in hospitalized patients with advanced solid tumors. J Clin Oncol 2008;26:2538–2542.

18. Glare P, Sinclair C, Downing M, et al. Predicting survival in patients with advanced disease. Eur J Cancer 2008;44:1146–1156.