

Original Article

Evaluating Cognitive, Emotional, and Physical Fatigue Domains in Daily Practice by Single-Item Questions in Patients With Advanced Cancer: A Cross-Sectional Pragmatic Study

Florian Strasser, MD, Iris Müller-Käser, MD, and Daniel Dietrich, PhD

Oncological Palliative Medicine (F.S.), Division of Oncology/Hematology (F.S., I.M.-K.), Department of Internal Medicine, Cantonal Hospital, St. Gallen, Switzerland; and Statistics Section (D.D.), Swiss Group for Clinical Cancer Research (SAKK), Bern, Switzerland

Abstract

To assess cancer-related fatigue (CRF), multidimensional questionnaires are required. The aim of this study was to evaluate single-item fatigue (SIF) screening questions—one for global fatigue and three for the fatigue domains (cognitive, emotional, and physical)—for their immediate use in daily oncology practice. Sixty-one fatigued patients with advanced cancer completed SIF assessments (visual analog scales for global fatigue and for fatigue in the cognitive, emotional, and physical domains, respectively), and the Brief Fatigue Inventory (BFI), the Fatigue Assessment Questionnaire (FAQ), the Hospital Anxiety and Depression Scale (HADS), and the European Organization for Research and Treatment of Cancer (EORTC) Quality-of-Life-C30 (QLQ-C30). SIF-global correlated with BFI ($r = 0.51$), and the domain-SIFs correlated with their respective FAQ domains (cognitive $r = 0.59$; affective $r = 0.45$; physical $r = 0.33$) and functional EORTC QLQ-C30 subscales ($r = 0.62$; $r = 0.42$; $r = 0.34$). The SIF-emotional also correlated with HADS-Anxiety ($r = 0.43$) and HADS-Depression ($r = 0.62$). Principal component analysis (domain-SIF; respective FAQ and functional EORTC QLQ-C30 subscales) revealed three clusters and a two-factor model (cognitive/emotional, physical), explaining 74% of variability. Patients with one predominant SIF domain had more domain-tailored fatigue interventions than had patients with mixed SIFs. These data suggest that three simple SIF questions permit rapid assessment of the physical and cognitive and probably the emotional domains of CRF in patients with advanced cancer. J Pain Symptom Manage 2009;38:505–514. © 2009 U.S. Cancer Pain Relief Committee. Published by Elsevier Inc. All rights reserved.

Key Words

Fatigue, assessment, single-item assessment, symptom control, quality of life

Address correspondence to: Florian Strasser, MD, Oncological Palliative Medicine, Division of Oncology/Hematology, Department of Internal Medicine and Palliative Care Centre, Cantonal Hospital, Rorschacherstrasse, 9007 St. Gallen, Switzerland. E-mail: Florian.Strasser@kssg.ch

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Introduction

Fatigue is one of the main symptoms affecting patients with advanced cancer. Its detection in clinical practice is challenging because it is a rarely volunteered, or silent, symptom.¹ Most patients with advanced cancer

present with several concurrent causes of fatigue.² The limited availability of therapeutic options with reasonably rapid success rates tempers clinicians' efforts to diagnose and differentiate fatigue.³

Cancer-related fatigue (CRF) affects patients with advanced cancer,⁴ patients undergoing anti-neoplastic treatment,⁵ and cancer survivors.⁶ In advanced cancer, the main factors contributing to fatigue, such as dyspnea,⁴ loss of appetite,⁷ cachexia,⁷ dehydration,⁸ and opioid-associated (cognitive) fatigue,⁹ seem to differ from those of cancer survivors' fatigue, where cognitive factors prevail.⁶

To screen patients with cancer for CRF, diagnostic criteria from the International Classification of Diseases-10th Revision (ICD-10) for CRF have been proposed,¹⁰ in addition to single symptom questions.¹¹ The ICD-10 CRF criteria were compared with instruments measuring fatigue intensity and patients' perceptions of functional impairment and interference due to fatigue, such as the Brief Fatigue Inventory (BFI, 10 items),¹² the Fatigue Symptom Inventory (13 items),¹³ and the Functional Assessment of Cancer Therapy.¹⁴ Even though these instruments are psychometrically very well validated, they are usually not applied in daily clinical care to assist immediate clinical decision making for fatigue treatment.¹⁵

To approach the complex syndrome(s) of CRF, several groups have proposed to break it down into different domains¹⁶ and have developed multidimensional assessment questionnaires. From most of these instruments,^{17–21} three different main domains can be characterized: cognitive^{17,20} (or mental^{18,19} and sensory¹⁷), emotional²⁰ (or affective meaning,¹⁷ motivational,¹⁹ and mood¹⁷), and physical²⁰ (or functional, reduced activity¹⁹). As additional domains (subdomains), some instruments assess vigor¹⁸ or sleep problems.²⁰ These assessment instruments are applied mainly in specialized clinics or as outcome instruments for studies; but for routine daily oncology practice, these questionnaires are too long, ranging from 20 to 83 items,^{18,19} to guide real-time CRF management. Increasingly, clinicians demand that clinical practice questionnaires and prompt sheets include items relevant for the individual patient in order to inform decisions directly.^{22,23}

There is a need for simple instruments that can rapidly assess the main fatigue domains in

daily clinical care. A pragmatic single-item assessment approach has been reported for the analysis of various aspects of health-related quality of life (HRQOL), complex syndromes,^{36,38} and also single symptoms.⁴⁰

The aim of this study was to evaluate single-item screening questions—one for global fatigue and three for the fatigue domains (cognitive, emotional, and physical)—for their immediate use in daily oncology practice.

Patients and Methods

Patients with advanced cancer who were outpatients in a Swiss oncology center were investigated. The study was approved by the local ethics committee, and informed consent was obtained.

Study Design

This prospective cross-sectional study of practice-guiding screening questions for fatigue domains took place in the advanced cancer outpatient setting.

Patient Inclusion/Exclusion Criteria

Patients were eligible if they had advanced incurable cancer, were cognitively able to complete reliably the routinely applied symptom screening (Edmonton Symptom Assessment Scale [ESAS]: 0 = best, 10 = worst),³⁹ and gave informed consent. To be eligible, on the day of the oncologist's consultation or a few days before, patients had to have a symptom fatigue score of 4 or more on the ESAS; this threshold is used in several symptom assessment studies applying the ESAS to discriminate the absence or presence of a symptom.⁹ Patients were excluded if their language or cognition did not permit them to understand the evaluation instruments or if the oncologist judged them to be emotionally too distressed or physically too ill to participate.

Sampling Process

During the oncologist's consultation, eligible patients were prospectively assessed by using the four single-item fatigue (SIF) questions, amending the information from ESAS. The oncologist prescribed the usual interventions for symptom control; the study did not include distribution of recommendations for the various possible treatments of fatigue.

After the consultation, the patients completed the evaluation instruments in the outpatient section of the oncology clinic; they could ask assistance from an oncology nurse not involved in the study. After completion, they returned the questionnaires to the nurse. In exceptional cases, patients were allowed to complete the questionnaires at home on the same day and return them by prepaid mail.

Sample Size

This pragmatic study was designed to allow an exploratory factor analysis of nine factors, requiring a minimum of 45 patients.²⁴

SIF Questions

The questions were asked orally in Swiss German. No written form was shown to patients. Patients made indications on a visual analog scale usually used to assess pain, which constituted a 10 cm straight line anchored by a smiling and a crying face at each end of the scale. The word "pain" was changed to "fatigue," and the procedure was explained to patients orally with no written explanations or questions to answer. The backside of the scale contained the numbers 0–10 (0 = no fatigue; 10 = maximal fatigue) that were not seen by the patient.

The SIF questions were developed based on the assumption that three main fatigue domains can be characterized.^{17–20} In the pretest phase with 15 patients, the understandability and acceptance of the SIF questions were tested. The wording was refined to eliminate misunderstandings or specific meanings in our language and culture. The word "energy" was not used because we noticed that patients associated lack of energy with different domains and because multidimensional instruments assign energy to domains in various ways, either to affective fatigue²⁰ or to a separate subdomain (vigor).¹⁸

The SIF instrument had four questions. First, global fatigue was measured with an open question adopted from the BFI (German version²⁵): "How much fatigue (weariness, tiredness) did you feel during the past 24 hours?" For cognitive fatigue, we asked, "How fatigued do you feel because of 'fatigue in the head,' namely, because you have problems with concentration, thinking, or attention?" Sometimes the question was further

explained that "fatigue in the head" may include concrete changes in concentration (e.g., *attentiveness* while reading newspapers). Regarding emotional fatigue, we asked, "How fatigued do you feel because you feel no joy, no motivation or pleasure or because nothing makes sense to you?" For a few patients, the question was further explained by including cheerlessness, listlessness, or paralyzing fear. We assessed physical fatigue by asking, "How fatigued do you feel because you feel no strength, because your body is weak, or your muscles feel weak?"

Assessing SIF during the consultation took an average period of two minutes, as the oncologist observed and remembered the time spent.

Evaluation Instruments for Fatigue Domains and Emotional, Cognitive, and Physical Symptoms

The evaluation instruments were chosen as established instruments for assessing the severity and impact of fatigue domains and cognitive, emotional, or physical symptoms.

To assess fatigue severity and impact, we used the German translation of the BFI.²⁵ It contains nine items and is well validated in the patient population considered for this study.

To assess fatigue domains, the Fatigue Assessment Questionnaire (FAQ) in the original German version was used.²⁰ It was developed based on thorough interviews by applying a 20-item instrument in a four-category answer format and it was validated in 592 patients with cancer in German-speaking Switzerland. Its multidimensional structure (physical [FAQ-Phys: items 1–11], cognitive [FAQ-Cogn: items 12–14], and affective [FAQ-Emot: items 15–19] domains) was recently confirmed in a general (German) population.²⁶ The presence of fatigue can be defined as having an FAQ item score of 2 (moderate) or 3 (severe),²⁰ in contrast to 0 (none) and 1 (mild).

To assess physical, emotional, and cognitive functioning, the three comparable subscales of the EORTC QLQ-C30³⁴ were applied: physical functioning includes five items (1–5); emotional functioning, four items (21–24); and cognitive functioning, two items (20 and 25). This questionnaire is widely used with advanced cancer patients, and its subscales are well validated.²⁷

To assess emotional aspects, we used the Hospital Anxiety and Depression Scale (HADS),²⁸ a 14-item scale (with seven items each for HADS-Anxiety [HADS-A] and for HADS-Depression [HADS-D]) with a four-category response format widely used and validated in patients with advanced cancer.

For physical symptoms, we used the German language ad hoc module EORTC QLQ-C30 anorexia/cachexia, which is a 14-item questionnaire with a four-category response format. It was translated from the Functional Assessment of Anorexia/Cachexia Therapy questionnaire²⁹ and validated in patients with advanced cancer in the context of a clinical trial.³³

Patients needed about 10–20 minutes to complete the questionnaire. Most patients completed it immediately in the outpatient clinic, but a few took it home and sent it back the next day in a pre-addressed, prepaid envelope.

Symptom Control Interventions for Fatigue Domains in the Routine Outpatient Clinic

As an additional exploratory objective, we asked whether the use of the four SIF questions in daily practice would influence the symptom control interventions prescribed by the oncologists. A chart review was performed independently by two investigators by using a checklist; disagreements were discussed and adapted until consensus was reached.

For each fatigue domain, the symptom control interventions most likely to be prescribed mainly for one of the three fatigue domains were defined. Because the SIF questions might have influenced physicians to order blood tests to determine whether to prescribe symptom control interventions for fatigue (e.g., after blood transfusions), charts were analyzed both on the SIF screening day and one week afterward.

An opioid rotation, a prescription for methyphenidate, hydration, or treatment of hypercalcemia was considered an intervention for cognitive fatigue. The order of a psycho-oncological consult or the prescription of antidepressant medication (usually a selective serotonin reuptake inhibitor) was considered an intervention for emotional fatigue. The initiation of nutritional assessments and counseling or the prescription of nutritional supplements, prokinetic agents, megestrol

acetate, or corticosteroids; transfusions of red blood cells; or treatment with erythropoietins or intravenous iron were considered interventions for physical fatigue.

Other interventions, such as unspecific patient education on how to cope with fatigue (saving energy, regular physical exercise, sleeping rhythm, and doing something good and positive for themselves from time to time) or interventions (such as oxygen) that were difficult to classify (per domain) were not assigned to fatigue domains.

Statistical Analysis

Patients' characteristics and questionnaire scores were analyzed with descriptive statistics. Spearman correlations were used to test associations between SIF questions and items of established instruments for assessment of fatigue: the SIF question of overall fatigue (SIF-global) was compared with the BFI-severity and BFI-impact, the EORTC QLQ-C30 fatigue subscale, and the ESAS question 2 (tired). In addition, the correlations of the three SIF questions cognitive, emotional, and physical with SIF-global were explored. Further tested were the correlations of the three cognitive, emotional, and physical SIF questions with the three domains of the FAQ and with the three EORTC QLQ-C30 subscales of physical, emotional, and cognitive function, respectively.

The three FAQ domains were explored by factor analysis, with principal components as initial solution and varimax rotation. The Kaiser's Measure of Sampling Adequacy was applied; >0.5 was assumed as sufficient and >0.8 as good. The goal was to see if the factor analysis could find the three domains. Then, the three EORTC QLQ-C30 subscales (physical, emotional, and cognitive function) were added with the same question. The three domain-SIFs were then added to a factor analysis of nine variables to explore whether the items assumed to belong to a certain domain loaded on the corresponding factor. Cronbach's alpha was used to check the reliability of each factor extracted by the assumed three-factor solution and other emerging solutions, namely, a two-factor solution. For each of the three SIF questions, item-total correlation with the other items in the domain was calculated.

In addition, we explored the question whether domain-SIF assessments can be helpful in clinical practice to detect patients with one predominant fatigue domain (DoFaDo), in contrast to patients with mixed fatigue syndromes (i.e., having fatigue without one of the domains being dominant). This subgroup (DoFaDo) included patients having only one FAQ domain above the threshold or vice versa. The number of patients having the corresponding domain-SIF higher (more than half of overall domain-SIF standard deviation [SD]³⁰) than the other domain-SIFs was calculated to estimate sensitivity, and a comparable calculation was performed for specificity.

The comparison of corresponding SIF with interventions for cognitive, emotional, or physical fatigue was done with Mann-Whitney tests.

Results

Sixty-one patients with advanced, incurable, mostly metastatic cancer of any type were included (Table 1).

Global Fatigue

The global SIF correlated significantly with BFI-intensity ($r = 0.51$, $P < 0.001$), BFI-impact ($r = 0.45$, $P < 0.001$), and ESAS question 2 on fatigue ($r = 0.50$, $P < 0.001$). The global SIF correlated with SIF-cognitive ($r = 0.40$, $P = 0.002$), SIF-emotional ($r = 0.53$, $P < 0.001$), and SIF-physical ($r = 0.47$, $P < 0.001$).

Fatigue Assessment Questionnaire

The principal component factor analysis with varimax rotation with three factors (physical, cognitive, and emotional) explained 65% of the variability of the FAQ. FAQ items 2–11 load on the physical factor as expected, whereas FAQ item 1 unexpectedly loads on the cognitive factor—as do FAQ items 12–14—as expected. FAQ 16 and 19 load on the emotional factor as expected, but FAQ 15, 17, and 19 load on the cognitive factor.

Fatigue Domains

The mean values of the three SIF domains cognitive, emotional, and physical were 3.4 (SD 2.6), 3.6 (3), and 4.8 (2.8), respectively.

Table 1
Demographics of Patients With Advanced Cancer in an Evaluation of Cognitive, Emotional, and Physical Fatigue Domains by Single-Item Questions

Demographic	n	
Age, yrs (n = 61)		
Median (min, max)	68 (36, 85)	
Gender		
Female, male	16, 45	
Cancer type		
Gastrointestinal, pancreatic	27	
Lung, mesothelioma, head and neck	13	
Kidney, prostate cancer	8	
Hematological	4	
Other	9	
Chemotherapy		
5-FU, capecitabine	4	
CPT-11, oxaliplatin	7	
Paclitaxel, docetaxel	9	
Carboplatin	2	
Gemcitabine	7	
Other	9	
None	23	
Hemoglobin, g/dL (n = 59)		
Median (min, max)	120 (75, 155)	
BFI (0 = best, 10 = worst)		
Median (min, max)		
Fatigue now	n = 61	5.0 (1, 10)
Usual, average fatigue	n = 61	5.0 (1, 10)
Worst fatigue	n = 60	6.0 (1, 10)
Impact of fatigue on		
Activity overall	n = 61	5.0 (0, 10)
Mood	n = 59	3.0 (0, 10)
Ability to walk	n = 61	5.0 (0, 10)
Usual work	n = 59	6.0 (0, 10)
Relationships to other people	n = 60	2.0 (0, 10)
Quality of life	n = 60	3.0 (0, 10)
ESAS (0 = best, 10 = worst)		
Median (min, max)		
Pain	n = 57	4 (0, 8)
Fatigue	n = 57	6 (2, 10)
Nausea	n = 55	0 (0, 8)
Depression	n = 57	0 (0, 8)
Anxiety	n = 57	1 (0, 10)
Dizziness	n = 57	1 (0, 8)
Appetite	n = 57	4 (0, 10)
Overall well-being	n = 57	5 (0, 8)
Dyspnea	n = 57	1 (0, 10)
HADS (0 = best, 21 = worst)		
Median (min, max)		
HADS-A	n = 61	5 (0, 17)
HADS-D	n = 61	7 (0, 21)

5-FU = 5-Fluorouracil.

For single-item cognitive fatigue, we found a significant correlation with the cognitive domain of FAQ ($r = 0.59$, $P < 0.001$) and with the cognitive subscale of EORTC QLQ-C30 ($r = 62$, $P < 0.001$) (Table 2).

For single-item emotional fatigue, substantial correlations were seen with the affective subtype of FAQ ($r = 0.45$, $P < 0.001$), HADS-A

($r = 0.43$, $P < 0.001$), HADS-D ($r = 0.62$, $P < 0.001$) and the emotional subscales of the EORTC QLQ-C30 ($r = 0.42$, $P = 0.0008$).

For single-item physical fatigue, a significant correlation with the physical domain of FAQ was found ($r = 0.33$, $P = 0.009$) with the physical subscale of the EORTC QLQ-C30 ($r = 0.34$, $P = 0.007$) and the overall score of the EORTC QLQ-C30 ad hoc module on anorexia/cachexia ($r = 0.29$, $P = 0.025$).

Principal Component Analysis With Varimax Rotation

For principal component analysis (PCA), the following nine variables were used: the three SIFs (single-item physical fatigue, single-item cognitive fatigue, and single-item emotional fatigue), the three FAQ domains (FAQCogn, FAQEmot, and FAQPhys), and the three EORTC QLQ-C30 subscales (physical, emotional, and cognitive function); the overall Kaiser's Measure of Sampling Adequacy was 0.81.

A factor analysis using the principal components method as an initial factor solution revealed three clusters (Fig. 1) and suggested a model with two factors by the eigenvalue criteria (eigenvalues > 1). Two factors (cognitive and physical) explained 65% of the variability. The rotated factor pattern is shown in Table 3, and the position of the nine factors is depicted in Fig. 1.

The reliability of the two-factor solution was tested by Cronbach's alpha and item-total correlation. For cognitive/emotional fatigue (including both the emotional and cognitive variables of SIF, FAQ, and EORTC QLQ-C30 subscales), the Cronbach's coefficient alpha (standardized) was 0.88. The item-total correlation (standardized variables) for SIF-cognitive was 0.75, and for SIF-emotional, it was 0.51.

A choice of three factors for the varimax rotation (Table 4) resulted in a model explaining 76% of the variability, but only the cognitive factor appeared clearly (FAQ cognitive: 0.87 in factor 1, 0.22 in factor 2, and 0.03 in factor 3; EORTC cognitive: 0.83, 0.19, 0.01; and SIF-cognitive: 0.78, -0.02 , 0.45, respectively). The FAQ physical loads mostly on factor 2 (0.79) compared with factor 1 (0.33) or factor 3 (0.19), as does EORTC physical (0.85, 0.09, 0.10) but not SIF-physical (0.38, -0.08 , 0.77), which loads more on factor 3. Both FAQ affective and EORTC emotional load more on

Table 2
Correlation of SIF Items With the FAQ and EORTC Scales (Spearman Correlation Coefficients, $n = 61$)

	SIFCogn	SIFEmot	SIFPhys
FAQcogn	0.589	0.343	0.123
FAQemot	0.546	0.451	0.274
FAQphys	0.295	0.358	0.334
EORTCcogn	0.622	0.277	0.120
EORTCemot	0.536	0.417	0.242
EORTCphys	0.236	0.245	0.341

Notes: SIF: one item for emotional (SIFemot), cognitive (SIFcogn), physical (SIFphys) (0 = none, 10 = worst). FAQ: three domains including physical (FAQphys: items 1–11), cognitive (FAQcogn: items 12–14), and affective (FAQemot: items 15–19) (0 = none, 3 = much). EORTC QLQ-C30: three subscales including physical functioning with five items (EORTCphys: items 1–5), emotional functioning with four items (EORTCemot: items 21–24), and cognitive functioning with two items (EORTCcogn: items 20 and 25) (1 = not at all, 4 = very much).

factor 1 than on factor 2 or factor 3 (0.60, 0.51, 0.27; 0.67, 0.50, 0.25), whereas SIF-emotional loads most on factor 3 (0.38, 0.05, 0.79). In the three-factor model, Cronbach's coefficient alpha (standardized) was 0.86 for cognitive fatigue, 0.81 for emotional fatigue, and 0.71 for physical fatigue; the item-total correlation (standardized variables) for SIF-cognitive was 0.67, for SIF-emotional 0.48, and for SIF-physical 0.42.

Domain-SIF to Detect Patients Having a Predominant Fatigue Domain

Thirty-nine patients had predominant FAQ fatigue domains, 19 physical fatigue higher than the other two, seven lower cognitive, and 13 lower emotional fatigue. Interestingly, no patient with one predominant FAQ fatigue domain had high emotional or cognitive fatigue or negative physical fatigue.

The sensitivity of SIF-physical to detect predominant (lower or higher) physical fatigue was 68% (25/37); the analogous sensitivity for cognitive and emotional fatigue was 52% (11/21) and 39% (11/28), respectively. The specificity was 45% (22/49), 55% (36/65), and 62% (36/58), respectively.

Interventions

Symptom control interventions, as defined in the checklist for one of the three fatigue domains, were provided during 38 of 57 (67%) consultations (three interventions in one consultation, two interventions in six consultations, and one intervention in 23 consultations).

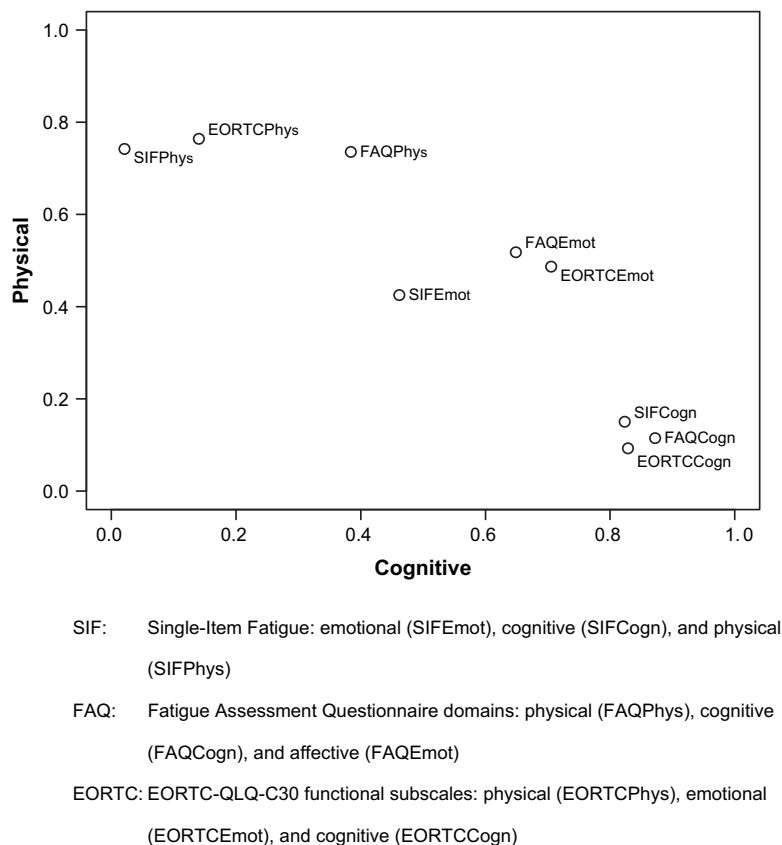


Fig. 1. Two-factor model of physical and cognitive fatigue: rotated factor plot with positions of domain-SIFs and corresponding functional subscales of EORTC QLQ-C30 and FAQ. SIF: single-item fatigue: emotional (SIFEmot), cognitive (SIFcogn), and physical (SIFphys). FAQ: Fatigue Assessment Questionnaire domains: physical (FAQphys), cognitive (FAQcogn), and affective (FAQemot). EORTC: EORTC QLQ-C30 functional subscales: physical (EORTCphys), emotional (EORTCemot), and cognitive (EORTCcogn).

Patients who received a predefined symptom control intervention for cognitive fatigue had a median value of SIF-cognitive of 3.8 ($n = 10$); for patients without such an intervention, that value was 2.6 ($n = 47$; $P =$ not significant). Correspondingly, patients receiving symptom control interventions for emotional fatigue had an SIF-emotional of 6.75 ($n = 8$), and those without had 2.5 ($n = 49$) ($P = 0.017$). Those having had symptom control interventions for physical fatigue had an SIF-physical of 6 ($n = 20$), and those without had 4 ($n = 37$) ($P = 0.12$).

Discussion

This report of single-item screening for cognitive, emotional, and physical fatigue domains is the first report of a pragmatic diagnostic approach that assesses the three key fatigue

domains in patients with advanced cancer and is usable for oncologists in daily care.

We found, as expected, a high correlation of the SIF questions with other measures of patient-reported CRF. This supports the screening concept. The SIF domains depict well the domains of the FAQ²⁰ that were derived from a large number of patients ($n = 592$) from the same region as our study having a cancer epidemiology comparable to other Western countries. It is, therefore, likely that the SIF domains represent the main domains occurring in patients with advanced cancer. As the main multidimensional questionnaires,^{17–19} including the FAQ,²⁰ are only partially validated in various countries, cultures, and languages, the pragmatic SIF domain approach requires careful adaptation when crossing language and cultural borders.

The PCA including the three SIF domains; the three FAQ domains;²⁰ and the cognitive,

Table 3
PCA With Varimax Rotation Resulting in a Two-Factor Model

Rotated Factor Pattern	Factor 1: Cognitive	Factor 2: Physical
SIF		
Cognitive ^a	0.83^d	0.15
Emotional ^a	<i>0.46</i>	<i>0.43</i>
Physical ^a	0.02	0.74
Fatigue Assessment Questionnaire		
Cognitive domain ^b	0.97	0.11
Affective domain ^b	<i>0.65</i>	<i>0.52</i>
Physical domain ^b	0.38	0.74
EORTC QLQ-C30		
Cognitive subscale ^c	0.83	0.09
Emotional subscale ^c	<i>0.71</i>	<i>0.49</i>
Physical subscale ^c	0.14	0.76

^aSIF: one item for emotional, cognitive, and physical (0 = none, 10 = worst).

^bFatigue assessment questionnaire: three domains including physical (items 1–11), cognitive (items 12–14), and affective (items 15–19) (0 = none, 3 = much).

^cEORTC QLQ-C30: three subscales including physical functioning with five items (items 1–5), emotional functioning with four items (items 21–24), and cognitive functioning with two items (items 20 and 25) (1 = not at all, 4 = very much).

^dKaiser's Measure of Sampling Adequacy: bold: > 0.725; italic: > 0.15 and < 0.725.

emotional, and physical functional subscales of EORTC QLQ-C30 shows a dominance of two rather than three domains: The cognitive and emotional domains seem to be less separable from each other than from the physical domain. These findings are consistent with observations of other fatigue assessment instruments showing a proximity of cognitive and emotional domains. The Piper Fatigue

Table 4
Factor Analysis Table With the Nine Variables Included in the Analysis

Rotated Factor Pattern	Factor 1	Factor 2	Factor 3
SIF			
Cognitive ^a	0.78	−0.02	0.45
Emotional ^a	0.38	0.05	0.79
Physical ^a	−0.08	0.38	0.77
FAQ			
Cognitive domain ^b	0.87	0.22	0.03
Affective domain ^b	0.60	0.51	0.27
Physical domain ^b	0.33	0.79	0.19
EORTC QLQ-C30			
Cognitive subscale ^c	0.83	0.19	0.01
Emotional subscale ^c	0.66	0.50	0.25
Physical subscale ^c	0.09	0.85	0.10

^aSIF: one item for emotional, cognitive, and physical (0 = none, 10 = worst).

^bFAQ: three domains including physical (items 1–11), cognitive (items 12–14), and affective (items 15–19) (0 = none, 3 = much).

^cEORTC QLQ-C30: three subscales including physical functioning with five items (items 1–5), emotional functioning with four items (items 21–24), and cognitive functioning with two items (items 20 and 25) (1 = not at all, 4 = very much).

Scale lists a combined cognitive/mood module, in addition to a behavioral/severity, affective meaning, and sensory module.¹⁷ In a study with the Memorial Symptom Assessment Scale and the Piper Fatigue Scale, comparing advanced cancer patients and noncancer patients near end of life, the PCA revealed a psychological and a physical domain.³¹

The choice of instruments to assess cognitive, emotional, and physical aspects of HRQOL may have contributed to the observed combined cognitive/emotional domain. Patients' subjective perception of impaired cognition—measured by EORTC QLQ-C30—may be of limited value in diagnosing cognitive impairment, which would require objective tests.³² The HADS and the emotional subscale of EORTC QLQ-C30 seem to depict reliably the presence of anxiety and depression. For physical causes of fatigue, we used the EORTC QLQ-C30 ad hoc module on anorexia/cachexia³³ and the physical function domain of the EORTC QLQ-C30;³⁴ however, we did not apply objective physical activity or muscle function measures.

We did not observe a significantly higher frequency of domain-specific treatments in patients with the respective prominent SIF domain. However, these therapies were applied in daily practice and did not follow specific recommendations from a study protocol.

This prospective, cross-sectional, pragmatic study did not intend to—nor is it able to—provide information on the epidemiology of various fatigue domains. Other limitations are the lack of objective tests for cognitive impairment and physical activity; the single-center, language, and culture setting;³⁵ and the possible bias inherent in dependence on well-trained physicians applying SIF questions in practice. The small sample size may have prevented the appearance of a clear three-factor model, as many multidimensional fatigue assessments separate three domains.³⁵ The patient population chosen for our study was a sample of patients with various cancers in the advanced, incurable, and symptomatic stage, and the representativeness of our sample may not be extended to patients earlier in the trajectory of their cancer disease. Our study was not designed to perform a full factor analysis of all items of the FAQ; our data revealed, as previously documented, the three-factor solution but not all items loaded on the factors as expected.

Our pragmatic work may encourage clinicians to use and explore simple symptom assessment instruments, such as the three SIF questions, in their daily practice to help guide treatments and decisions. Such simple questions may reduce the need to use longer scales to assess key domains of fatigue in clinical practice. Such a use of single-item questions to screen for key domains of HRQOL was reported for overall quality of life^{36,38} and for individual symptoms^{39,40} but not yet for fatigue domains.

These data suggest that the three SIF domain questions may be useful to distinguish patients with cognitive fatigue from those with mainly physical fatigue; however, our results also suggest that, in our sample, one-third of the patients present with mixed fatigue syndromes and lack a dominant fatigue domain. Patients with mainly emotional fatigue may be detected in clinical practice by simple screening instruments for depression.⁴¹

Our results from the pilot data presented here seem sufficiently promising to further evaluate single-item measures of fatigue domains to guide clinical care. Future research must address the development of a generalizable paper-based instrument that is currently validated and the testing of the hypothesis that fatigue-domain screening can reliably guide fatigue-domain-specific treatments in clinical practice,³⁷ facilitate interdisciplinary management, and improve fatigue-related outcomes.

In conclusion, the SIF domain approach is a novel pragmatic strategy for daily practice care of complex patients with advanced cancer. Extrapolating from this work, studies will explore the potential to decrease the patient and proxy burden of CRF.

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