Assessment of Fatigue in Cancer Patients

Paul B. Jacobsen

Increased recognition of the problem of fatigue in cancer patients can be attributed, in part, to the development of measures that have provided researchers with the tools necessary for quantifying and characterizing fatigue and exploring its etiology and treatment. Although a consensus regarding the definition of fatigue is lacking, there is general agreement that it is a subjective and multidimensional phenomenon whose assessment requires the use of self-report methods. Consistent with this view, several multidimensional measures of fatigue have been developed and validated for use with cancer patients. These measures differ considerably in their format and content and, as with the definition of fatigue, there is no consensus at the present time regarding the dimensional structure of fatigue. In addition to measuring fatigue on a continuum along one or more dimensions, it may also be possible to assess a clinical syndrome of cancer-related fatigue. Criteria for assessing fatigue in this manner have been proposed and are currently undergoing evaluation. Despite the progress that has been made, there are several important unresolved issues in the assessment of fatigue in cancer patients. These include how to distinguish fatigue from depression, how to use self-reports of fatigue in clinical decision-making, how to capture temporal changes in fatigue, and how best to address the continuing lack of consensus regarding the conceptualization and measurement of fatigue. [J Natl Cancer Inst Monogr 2004;32:93–7]

During the last decade, there has been a growing recognition of the high prevalence of fatigue among cancer patients, its adverse effect on their quality of life, and the need to develop effective interventions to prevent or relieve it (1, 2). This increased attention can be attributed, in part, to the development of instruments for the assessment of fatigue and their validation with cancer patients. These instruments have provided researchers with the tools necessary for quantifying and characterizing fatigue and exploring its etiology and treatment. The objective of this report is to provide a brief review of developments in the assessment of fatigue in cancer patients. The most notable development, and the focus of the review, is the creation of several multidimensional measures of fatigue designed specifically for use with cancer patients. These measures differ considerably in their format and content and, thus, present researchers with several issues to consider in selecting among them. In addition to offering suggestions for choosing among available multidimensional measures, this review describes a recently developed clinical syndrome approach to assessing cancer-related fatigue that is currently under evaluation. The review concludes with a discussion of several unresolved issues in the assessment of fatigue that merit further study.

**DEFINING FATIGUE**

The assessment of fatigue in cancer patients is beset by a number of methodological challenges. The lack of a commonly agreed on definition of fatigue is perhaps the greatest challenge. A definition proposed by Cella and colleagues (3) captures several of the more commonly described features of fatigue. They define fatigue as, “a subjective state of overwhelming and sustained exhaustion and decreased capacity for physical and mental work that is not relieved by rest.” With regard to assessment, three features of this definition are worth noting. First, it identifies fatigue as a subjective phenomenon, implying that it can best be measured via self-report methods. Second, it offers several ways in which fatigue may be distinguished from “normal” tiredness. These include its severity and chronicity (“overwhelming and sustained exhaustion”) and its imperviousness to actions that typically provide relief from tiredness (“not relieved by rest”). Third, there is an implication as to the clinical significance of this phenomenon and its multidimensional qualities (“decreased capacity for physical and mental work”).

**UNIDIMENSIONAL AND MULTIDIMENSIONAL MEASURES OF FATIGUE**

In the absence of a commonly agreed on definition of fatigue, it is not surprising that there is a lack of consensus about the optimal approach to assessing fatigue in cancer patients. Although the importance of obtaining patient self-reports is widely acknowledged, a variety of self-report instruments are currently in use. Much of the time, fatigue is assessed using a single item embedded in a symptom checklist such as the Symptom Distress Scale (4) or the Rotterdam Symptom Checklist (5). Single-item visual analog scales and Likert-type scales are also often used to assess fatigue. Because of their single-item format, these measures have limited reliability and provide only the most perfunctory information about patients’ experiences with fatigue. Fatigue is also often assessed using multi-item measures such as the Fatigue Scale of the Profile of Mood States (6). Although these multi-item measures generally possess better psychometric properties than single-item measures, most are limited in that they provide information only about a patient’s general level of fatigue severity.

In a more comprehensive approach, several investigators have developed and validated multidimensional measures of fatigue for use with cancer patients. Such measures include the Brief Fatigue Inventory (7), the Revised Piper Fatigue Scale (8), the Cancer Fatigue Scale (9), the Revised Schwartz Cancer Fatigue Scale (10), the Multidimensional Fatigue Inventory (11), and the Multidimensional Fatigue Symptom Inventory (12). A recent publication provides information about the format of these and other measures and summarizes their psychometric properties (13). Inspection of these measures indicates that there is little consensus at this time about the dimensional structure of...
fatigue in cancer patients (see Table 1). For example, one measure characterizes fatigue in terms of general, mental, and physical dimensions (11), whereas another measure characterizes it in terms of behavioral/severity, affective meaning, sensory, and cognitive/mood dimensions (8).

The Fatigue Symptom Inventory (FSI), a measure developed by our research group (14), will be used to illustrate in greater detail one approach to the multidimensional assessment of fatigue. The FSI is a 14-item measure that assesses the severity, frequency, and diurnal variation of fatigue, as well as its perceived interference with quality of life (Fig. 1). Severity is measured using four separate items that assess most, least, and average fatigue in the past week as well as current fatigue. Frequency is measured using two separate items that assess the number of days in the past week that respondents felt fatigued as well as the portion of each day on average they felt fatigued. Diurnal variation is measured using a single item that provides descriptive information about daily patterns of fatigue. Perceived interference is measured using seven separate items that assess the degree to which fatigue in the past week was judged to interfere with general level of activity, ability to bathe and dress, normal work activity, ability to concentrate, relations with others, enjoyment of life, and mood. The interference ratings can also be summed to yield a total interference score. Preliminary evidence of the reliability and validity of the FSI has been reported for women with breast cancer (14) and for men and women with a variety of cancer diagnoses (15).

**SELECTION OF A FATIGUE MEASURE FOR RESEARCH USE**

Given the number and variety of multidimensional measures of fatigue currently available for use with cancer patients, selecting which measure to use in a research study can be a challenge. Several issues can be identified that may aid researchers in selecting among these measures.

**Table 1.** Examples of multidimensional measures of fatigue

<table>
<thead>
<tr>
<th>Measure</th>
<th>Ref</th>
<th>Dimensions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brief Fatigue Inventory</td>
<td>7</td>
<td>Severity, Interference</td>
</tr>
<tr>
<td>Cancer Fatigue Scale</td>
<td>9</td>
<td>Physical, Cognitive, Affective</td>
</tr>
<tr>
<td>Fatigue Symptom Inventory</td>
<td>14</td>
<td>Severity, Frequency, Diurnal variation</td>
</tr>
<tr>
<td>Multidimensional Fatigue Inventory</td>
<td>11</td>
<td>General, Physical, Mental, Reduced activity</td>
</tr>
<tr>
<td>Multidimensional Fatigue Symptom Inventory</td>
<td>12</td>
<td>General, Physical, Emotional, Mental, Vigor</td>
</tr>
<tr>
<td>Revised Piper Fatigue Scale</td>
<td>8</td>
<td>Behavioral/severity, Affective meaning, Sensory</td>
</tr>
<tr>
<td>Revised Schwartz Cancer Fatigue Scale</td>
<td>10</td>
<td>Physical, Perceptual</td>
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**Fatigue Symptom Inventory**

For each of the following, circle the one number that best indicates how that item applies to you:

1. Rate your level of fatigue on the day you felt most fatigued during the past week:
   - 0 Not at all fatigued
   - 1 As fatigued as I could be

2. Rate your level of fatigue on the day you felt least fatigued during the past week:
   - 0 Not at all fatigued
   - 1 As fatigued as I could be

3. Rate your level of fatigue on the average during the past week:
   - 0 Not at all fatigued
   - 1 As fatigued as I could be

4. Rate your level of fatigue right now:
   - 0 Not at all fatigued
   - 1 As fatigued as I could be

5. Rate how much, in the past week, fatigue interfered with your general level of activity:
   - 0 No interference
   - 1 Extreme interference

6. Rate how much, in the past week, fatigue interfered with your ability to bathe and dress yourself:
   - 0 No interference
   - 1 Extreme interference

7. Rate how much, in the past week, fatigue interfered with your normal work activity (includes both work outside the home and housework):
   - 0 No interference
   - 1 Extreme interference

8. Rate how much, in the past week, fatigue interfered with your ability to concentrate
   - 0 No interference
   - 1 Extreme interference

9. Rate how much, in the past week, fatigue interfered with your relations with other people:
   - 0 No interference
   - 1 Extreme interference

10. Rate how much, in the past week, fatigue interfered with your enjoyment of life:
    - 0 No interference
    - 1 Extreme interference

11. Rate how much, in the past week, fatigue interfered with your mood:
    - 0 Not at all fatigued
    - 1 Not consistent daily pattern of fatigue

12. Indicate how many days, in the past week, you felt fatigued for any part of the day:
    - 0 None of the day
    - 1 The entire day

13. Rate how much of the day, on average, you felt fatigued in the past week:
    - 0 None of the day
    - 1 The entire day

14. Indicate which of the following best describes the daily pattern of your fatigue in the past week:
    - 0 Not at all fatigued
    - 1 Usually worse in the morning
    - 2 Usually worse in the afternoon
    - 3 Usually worse in the evening
    - 4 Usually no consistent daily pattern of fatigue

Fig. 1. Fatigue Symptom Inventory, Moffitt Cancer Center and University of South Florida, Tampa, FL. ©1998.
One issue to consider is whether or not the individuals to be assessed are experiencing fatigue. Some measures, such as the Revised Piper Fatigue Scale, are worded such that they are only appropriate for use with individuals currently experiencing fatigue. Other measures, such as the FSI and the Brief Fatigue Inventory, are suitable for use with individuals who may or may not currently be experiencing fatigue.

A second issue is the time frame covered by the assessment. Some measures, such as the FSI, are keyed primarily to the past week, whereas others, such as the Brief Fatigue Inventory, are keyed primarily to the last 24 hours. Researchers should consider how well these different time frames correspond to the periods they wish to assess. For example, in a study of fatigue during radiotherapy that featured multiple assessments per week, a measure keyed to the past 24 hours would be preferable to a measure keyed to the past week in which the time intervals covered by the assessments would overlap.

A third issue to consider is the measure’s psychometric properties. In choosing a measure, researchers should consider the strength of the evidence for the measure’s reliability and validity and the quality of the methods used to derive the measure’s multidimensional format. A related issue involves consideration of the population on which the psychometric data are based. For example, some measures, such as the Revised Piper Fatigue Scale, have been validated primarily on women with breast cancer. This feature would be an advantage for a study of fatigue in breast cancer patients but may be a potential disadvantage for a study of fatigue in other patient populations.

A fourth issue to consider is the correspondence between the various multidimensional measures and the research questions being asked. For example, a study focusing on possible cognitive manifestations of fatigue (e.g., perceived problems with memory and attention) should consider use of a measure that includes a mental or cognitive scale such as the Multidimensional Fatigue Inventory or the Multidimensional Fatigue Symptom Inventory.

**Clinical Syndrome Approach to Assessing Fatigue**

All the approaches to measuring fatigue described previously share a common feature. That is, they yield continuous measures of fatigue along one or more dimensions. In addition to assessing fatigue along a continuum, it may be possible to identify a set of diagnostic criteria that can be used to assess the presence or absence of a clinical syndrome of cancer-related fatigue. An analogy can be drawn to the assessment of depression along a continuum, it is possible to identify the presence of a clinical syndrome of major depression using standard criteria adopted by the American Psychiatric Association (16). On the basis of this model, a group of researchers have proposed criteria for the diagnosis of a clinical syndrome of cancer-related fatigue (see Table 2) and developed an interview guide to facilitate and standardize the diagnostic process (3,17).

Two recent studies have explored the use of these criteria. One study (18) evaluated the use of the A and B criteria on 379 individuals with a variety of cancer diagnoses previously treated with chemotherapy or with without radiotherapy. Seventeen percent of patients met the criteria of having six symptoms, including significant fatigue every day or nearly every day in a recent 2-week period (criterion A), and having symptoms that caused clinically significant distress or impairment (criterion B). The researchers found that varying the number of additional symptoms experienced in addition to significant fatigue required to meet criterion A resulted in modest differences in prevalence rates. For example, requiring either four or six additional symptoms rather than five resulted in a 2% higher or a 3% lower prevalence rate, respectively. The authors acknowledge that the number of fatigue symptoms currently stipulated in the diagnostic criteria is arbitrary and that further study is needed to identify a clinically meaningful threshold number.

The other study (17) evaluated the full set of diagnostic criteria with 51 patients who underwent blood or marrow transplantation an average of 6.9 months previously. Twenty-one percent of patients met the full diagnostic criteria. Compared with patients who did not meet the criteria, those who met the criteria reported fatigue that was significantly greater in severity, duration, and interference with quality of life as measured by the FSI. According to the authors, this pattern of results indicates that the current criteria can be used to identify a subset of cancer patients experiencing worse fatigue. Although promising, additional research is needed to determine whether use of this clinical syndrome approach improves our understanding of the etiology and treatment of fatigue in cancer patients.

**Unresolved Assessment Issues**

Several issues can be identified that remain unresolved in the assessment of fatigue in cancer patients and that merit further study. One major issue involves the ability of existing assessment approaches to distinguish fatigue from depression. Continuous measures of fatigue and depression administered concurrently to cancer patients generally yield high positive correlations (19), indicating possible problems with discriminant validity. With the advent of diagnostic criteria for a clinical syndrome of cancer-related fatigue, there is a need for research in which clinical syndrome measures of fatigue and depression are administered concurrently to cancer patients. The results of

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**Table 2. Proposed criteria for clinical syndrome of cancer-related fatigue**

<table>
<thead>
<tr>
<th>A. Six (or more) of the following symptoms have been present every day or nearly every day during the same 2-week period in the past month, and at least one of the symptoms is (1) significant fatigue.</th>
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<tbody>
<tr>
<td>1. Significant fatigue, diminished energy, or increased need to rest, disproportionate to any recent change in activity level</td>
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<td>2. Complaints of generalized weakness of limb heaviness</td>
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<tr>
<td>3. Diminished concentration or attention</td>
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<td>4. Decreased motivation or interest to engage in usual activities</td>
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<td>5. Insomnia or hypersomnia</td>
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<td>6. Experience of sleep as unrefreshing or nonrestorative</td>
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<tr>
<td>7. Perceived need to struggle to overcome inactivity</td>
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<tr>
<td>8. Marked emotional reactivity (e.g., sadness, frustration, or irritability) to feeling fatigued</td>
</tr>
<tr>
<td>9. Difficulty completing daily tasks attributed to feeling fatigued</td>
</tr>
<tr>
<td>10. Perceived problems with short-term memory</td>
</tr>
<tr>
<td>11. Post-exertional malaise lasting several hours</td>
</tr>
</tbody>
</table>

| B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. |
| C. There is evidence from the history, physical examination, or laboratory findings that the symptoms are a consequence of cancer or cancer therapy. |
| D. The symptoms are not primarily a consequence of co-morbid psychiatric disorders such as major depression, somatization disorder, somatoform disorder, or delirium. |

Reprinted with permission Cella et al. (3).
this research would indicate the extent to which it is possible to distinguish fatigue associated with cancer and its treatment from fatigue associated with a mood disorder. Likewise, this research would indicate the extent to which it is possible to distinguish whether certain symptoms common to both clinical syndromes (e.g., loss of concentration) are a reflection of an underlying mood disorder or are part of a cancer-related fatigue syndrome. The ability to distinguish fatigue from depression is a particularly important issue for the design of clinical trials that seek to determine the efficacy of antidepressant medications in relieving fatigue in cancer patients.

A second issue concerns the use of self-reports of fatigue in clinical decision making. Specifically, how should these self-reports be used to make clinical decisions about initiation of treatments effective in relieving fatigue? Clinical guidelines for management of cancer-related fatigue exist that include recommendations for intervening based on patient self-reports of fatigue severity. For example, guidelines developed by the National Comprehensive Cancer Network (20) recommend that fatigue severity be rated on a 0–10 scale and that patients reporting “moderate” or “severe” fatigue (identiﬁed as 4–6 and 7–10, respectively), but not “mild” fatigue (identiﬁed as 1–3), receive further evaluation and treatment. Questions arise as to whether these cutoff scores, intended as aids to clinical decision making, are supported by empirical data. Research by Mendoza and colleagues (7) examined the correspondence between ratings of worst fatigue and fatigue interference as one possible means of distinguishing gradations of fatigue severity. In testing several possible boundary models, they consistently found a cutoff point for “severe” fatigue that was between 6 and 7 but noted that a distinction between “mild” and “moderate” fatigue was less well deﬁned. The use of fatigue self-reports in clinical decision making is an important issue that clearly merits further study. In particular, there is a need for research demonstrating that screening for fatigue and intervening based on identified cut-off scores leads to better clinical outcomes for patients.

A third issue concerns the ability to detect temporal changes in fatigue. Fatigue appears to be a variable phenomenon that can fluctuate considerably over time. Temporal variability in fatigue severity may be particularly acute in patients undergoing chemotherapy or radiotherapy treatment. In this context, there may be important changes in the experience of fatigue on a daily or even hourly basis following each treatment administration. Study designs in which patients provide self-reports of fatigue only when they return to the clinic may fail to capture much of this intertreatment variability in fatigue. Problems in detecting temporal changes are likely compounded by the administration of fatigue measures keyed to the past week or even longer periods of time. These obstacles to assessing temporal change could be successfully addressed by the use of a methodology increasingly used in symptom research, known as ecological momentary assessment (EMA) (21). EMA involves assessing the subjective phenomenon of interest in the setting in which it occurs at the time at which it is occurring. As applied to fatigue assessment, this approach would involve having patients provide ratings of their current fatigue on a frequent basis in the interval between clinic visits. Two studies in which patients used diary forms to provide daily ratings of fatigue in the intervals between chemotherapy administrations demonstrate the feasibility of this approach (22,23). Moreover, these studies demonstrate the utility of this approach. In each study, frequent assessment revealed a “rollercoaster” pattern in which fatigue increased in severity sharply during the first week after treatment and then gradually declined before the next cycle of treatment. The advent of handheld computer technology that can be used to prompt patients to rate their symptoms and record their responses (24) is likely to facilitate and further enhance this method of data collection.

One additional unresolved issue concerns the continuing lack of consensus regarding the conceptualization and optimal measurement of fatigue in cancer patients. With the rapid accumulation of research findings in this area, there is an opportunity to conduct qualitative and quantitative reviews of the literature that seek to evaluate the construct validity of current measurement approaches. A critical and systematic review of existing multi-dimensional measures could lead to refinements in the conceptualization of fatigue by identifying those dimensions whose usefulness can be demonstrated repeatedly across applications. Likewise, accumulation and evaluation of findings across studies can serve to identify measures or particular items or scales within measures that provide the most useful information about fatigue. As this line of research matures, it seems likely that the strengths and weaknesses of the various measurement approaches will become increasingly apparent and that empirical evidence will produce a growing consensus as to the optimal means of assessing fatigue in cancer patients.

REFERENCES


