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Validation of the Modified Brief Fatigue Inventory in Head and Neck Cancer Patients

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Abstract

Objective. The aim of this study is to validate the Modified Brief Fatigue Inventory (MBFI). This is the first instrument designed to measure intensity and frequency of fatigue specifically in head and neck cancer patients, potentially allowing objective measurement in addressing this common symptom in a concise yet thorough fashion.

Study Design. Survey validation.

Setting. Academic tertiary medical center.

Subjects and Methods. The 9-item MBFI was administered to 52 consecutive cancer patients and 57 consecutive controls. Demographics, comorbidities, cancer site, and cancer stage were recorded. Psychometric properties and predictors of the MBFI were analyzed.

Results. The MBFI 1-week test-retest reliability was excellent ($r = 0.800$, $P < .001$). Internal consistency was also excellent (Cronbach's $\alpha = 0.938$). Construct validity of the MBFI compared with the previously validated Multidimensional Fatigue Symptom Inventory–Short Form was excellent ($r = 0.814$, $P < .001$). Discriminant validity of cancer patients vs controls was significant ($P = .027$). Predictors of increased MBFI score included American Society of Anesthesiologists (comorbidity) score (bivariate analysis, $r = 0.287$, $P = .039$), cancer stage (analysis of variance, $P = .007$), and adjuvant radiotherapy (t test, $P = .016$). Cancer stage and comorbidity were further correlated with a multiple regression linear model. No significant relationship was found with age, sex, marital status, education, ethnicity, feeding tube, tracheostomy, or laryngectomy.

Conclusion. The MBFI is a reliable and valid tool for measuring fatigue levels in head and neck cancer patients. In the context of initial assessment or posttreatment trending, this brief survey can be rapidly administered, providing valuable objective data on a very common and potentially debilitating symptom.

Keywords

head and neck cancer, fatigue, quality of life, survey validation

Cancer-related fatigue is now recognized as an increasingly significant component in the compromised quality of life within the growing population of patients suffering from various malignancies.¹ Among the most common symptoms reported by cancer patients, fatigue is the most frequent and, in turn, associated with the most interference with quality of life.^{2–4} This cancer-related fatigue has been observed upon presentation, during treatment, and months to years following treatment.^{3,4}

Considerable effort and attention have been focused on systematically assessing and quantifying fatigue, with the ultimate goal of identifying and treating potential causative or related factors.^{5–9} Although several high-quality screening forms for fatigue have been developed and validated in the general cancer population, these surveys have yet to be applied solely to those with head and neck cancer. In fact, very few (if any) head and neck cancer patients have been included in these studies.^{5–9} The National Comprehensive Cancer Network (NCCN) has adopted a validated survey, the Brief Fatigue Inventory (BFI), in rapidly assessing fatigue in cancer patients within the routine clinical setting.⁵ Validation of the BFI has been based on correlations with more comprehensive and lengthy scales that are less practical for routine clinical application, including the Multidimensional Fatigue Symptom Inventory (MFSI), Multidimensional Fatigue Symptom Inventory–Short Form (MFSI-SF), and Fatigue Symptom Inventory (FSI).^{6–9} It is also important to note that

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the BFI itself is limited by only measuring fatigue within a narrow time window of 24 hours.

Given the complex anatomic and functional relationships, patients with head and neck cancer endure distinct limitations to their quality of life, including but not limited to struggles with speech, swallowing, and crucial sensory-motor capabilities. Considering the potentially unique manifestations of fatigue and quality of life within this population, we feel that further investigation of the aforementioned screening tools in those afflicted by head and neck malignancies will afford valuable opportunities in paving a new road toward understanding the pathophysiology and management of fatigue and quality of life in this population.

The MFSI, FSI, MSFI-SF, and BFI all measure multiple facets of fatigue. Although shorter than the MSFI and FSI, the 30-item MSFI-SF may still be tedious and burdensome in the clinical setting. Although the 9-item BFI was developed to address this issue, the narrow intake period of 24 hours limits the sensitivity. As alluded to earlier, none of the aforementioned instruments were validated with solid head and neck tumor patients. This need for a comprehensive yet concise instrument for this unique population led to development of the Modified Brief Fatigue Inventory (MBFI) in head and neck cancer patients.

Methods

The BFI is a 9-item questionnaire, with each item measured on a 0 to 10 numeric rating scale. The time period being assessed is within the past 24 hours. Enhancements to the BFI in developing the MBFI include a more straightforward 0 to 7 numeric scale. Although a 10-point scale is acceptable, the benefit of the few extra response options is offset by the greater complexity, particularly in the context of assembling a more concise instrument.¹⁰ In addition, the narrow time period of 24 hours for symptom assessment was expanded to the past week. An increase to 7 days improves sensitivity for relevant fatigue events while avoiding confounding factors associated with longer recall periods.^{11,12}

The MBFI (**Figure 1**) is a 9-item survey measuring the core facets of functioning and quality of life related to fatigue: general, physical, emotional, and mental. Item 1 measures fatigue at the present moment, with a response of 1 denoting “no fatigue” and 7 being “as bad as you can imagine.” Item 2 asks the same question but in the context of over the past 7 days. Items 3 through 9 measure the frequency that fatigue has interfered with the following aspects of life: general activity, mood, walking ability, normal work, relations with other people, and overall enjoyment of life. Items 3 through 9 are on a 1 to 7 scale, with 1 representing “none of the time” and 7 representing “all of the time.” The overall score is simply the arithmetic mean of the 9 items.

Following approval from the State University of New York Downstate Medical Center University Hospital of Brooklyn at Long Island College Hospital Institutional Review Board, the MBFI was verbally administered to 52

consecutive patients at the outpatient head and neck cancer clinic who were at least 3 months posttreatment. This survey was also given to 57 consecutive age-matched controls without cancer from the general otolaryngology clinic. Cancer patients also received the MSFI-SF during the same visit to ascertain construct validity. The MBFI was administered 1 week later to establish test-retest reliability. A single representative administered all the surveys verbally to ensure a consistent response environment. This approach also allowed for the avoidance of partial or incomplete surveys, while addressing any potential misinterpretation. Exclusion criteria for both cancer patients and controls included age younger than 18 years and psychological and cognitive disabilities precluding adequate completion of the questionnaires. Additional demographic and disease-specific data were collected from the participants. Most notably, cancer stage, site, comorbidity status, laboratory values, and symptom complaints were recorded. Comorbidity status was measured using the American Society of Anesthesiologists (ASA) classification.¹³ The ASA class 1 represents a healthy patient with mild systemic disease, ASA class 2 denotes patients with moderate or severe systemic disease that *does not limit activity*, ASA class 3 denotes patients with severe systemic disease that *limits activity but is not incapacitating*, and ASA classes 4 and 5 represent *incapacitating conditions* that are a constant threat to life or moribund patients, respectively. The level of overall functioning was measured with the Eastern Cooperative Oncology Group (ECOG) performance status.¹⁴ This scale ranges from grade 0 to 5, with grade 0 being fully active and able to carry on with all predisease performance without restriction and grade 5 being deceased.

Psychometric analysis of the survey results included internal validity and test-retest reliability of MBFI scores. The MBFI and MSFI-SF were compared to ascertain construct validity. The MFSI-SF was selected as the comparator because of the value it holds as a more extensive (but lengthy) instrument. A main objective of this study was to demonstrate an acceptable correlation of our more brief and practical survey with an accepted comprehensive counterpart. The final component of the psychometric analysis included determination of discriminant validity by comparing cancer and control MBFI scores controlled for age and comorbidities. In addition, regression models were completed to identify any patient factors significantly predictive of fatigue on the MBFI. Testing of the multiple regressions was completed as well.

Results

Demographic data, along with MBFI results, ECOG grades, and ASA classifications of cancer and control patients, are shown in **Table 1**. There were no significant differences noted between cancer and control groups for age, relationship status, and distribution of ethnicity and sex. There was a significantly higher number of college graduates among noncancer controls. Cancer patients demonstrated significantly higher ECOG grades. Control patients showed lower levels of fatigue on the

Modified Brief Fatigue Inventory

Subject Number: _____ **Date:** _____ **Time:** _____

Throughout our lives, most of us have times when we feel very tired or fatigued. Have you felt unusually tired or fatigued in the last 7 days?

__ Yes __ No

1. Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your fatigue right NOW.

1	2	3	4	5	6	7
No fatigue						As bad as you can imagine

2. Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your WORST level of fatigue during the past 7 days.

1	2	3	4	5	6	7
No fatigue						As bad as you can imagine

3. Circle the one number that describes how often, during the past 7 days, fatigue has interfered with your:

A. General activity						
1	2	3	4	5	6	7
None of the time	Hardly any of the time	A small part of the time	Some of the time	A good part of the time	Most of the time	All of the time
B. Mood						
1	2	3	4	5	6	7
None of the time	Hardly any of the time	A small part of the time	Some of the time	A good part of the time	Most of the time	All of the time
C. Walking ability						
1	2	3	4	5	6	7
None of the time	Hardly any of the time	A small part of the time	Some of the time	A good part of the time	Most of the time	All of the time
D. Normal work (includes both work outside the home and daily chores)						
1	2	3	4	5	6	7
None of the time	Hardly any of the time	A small part of the time	Some of the time	A good part of the time	Most of the time	All of the time
E. Relations with other people						
1	2	3	4	5	6	7
None of the time	Hardly any of the time	A small part of the time	Some of the time	A good part of the time	Most of the time	All of the time
F. Enjoyment of life						
1	2	3	4	5	6	7
None of the time	Hardly any of the time	A small part of the time	Some of the time	A good part of the time	Most of the time	All of the time

4. Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your OVERALL level of fatigue over the past 7 days.

1	2	3	4	5	6	7
No fatigue						As bad as you can imagine

Figure 1. Modified Brief Fatigue Inventory.

MBFI despite having higher comorbidity levels based on ASA classification. Primary cancer site distribution is demonstrated in **Figure 2**, with oral tongue, thyroid, and glottis representing the most common sites.

Psychometric analysis of the MBFI yielded encouraging results. An analysis of initial MBFI responses along with test-retest reliability from cancer subjects is shown in **Table 2**. The mean overall score was 3.14 (out of 7), with an

Table 1. Descriptive Statistics of Cancer and Control Subjects

Descriptor	Cancer (n = 52)	Control (n = 57)	Total (n = 109)	P Value
Male sex	27 (52)	22 (39)	49 (45)	.162 ^a
Age, y				
Mean	60.8 (12.5)	58.8 (13.0)	59.2 (12.8)	.213 ^b
Range	26-86	34-86	26-86	
Ethnicity				
Black	25 (48)	33 (58)	58 (53)	.764 ^a
White	13 (25)	11 (19)	24 (22)	
Latino	9 (17)	9 (16)	18 (17)	
Other	5 (10)	4 (7)	9 (8)	
Education				
College graduate	9 (17)	21 (37)	21 (28)	.023 ^a
Relationship status				
Single	8 (15)	17 (30)	25 (23)	.497 ^a
Married	30 (58)	27 (47)	57 (52)	
Divorced	3 (6)	2 (4)	5 (5)	
Widowed	9 (17)	9 (16)	18 (16)	
Long-term relationship	2 (4)	2 (4)	4 (4)	
ECOG grade, mean (SD)	0.90 (0.80)	0.37 (0.49)	0.62 (0.70)	.002 ^b
ASA class, mean (SD)	1.67 (0.71)	2.11 (0.62)	1.90 (0.69)	.015 ^b
MBFI score, mean (SD)	3.14 (1.46)	2.38 (1.13)	2.75 (1.35)	.027 ^b
MBFI difference (95% CI)			0.76 (0.27, 1.25)	

Values are presented as No. (%) unless otherwise indicated. Abbreviations: ASA, American Society of Anesthesiologists; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; MBFI, Modified Brief Fatigue Inventory.

^a χ^2 test.

^b*t* test.

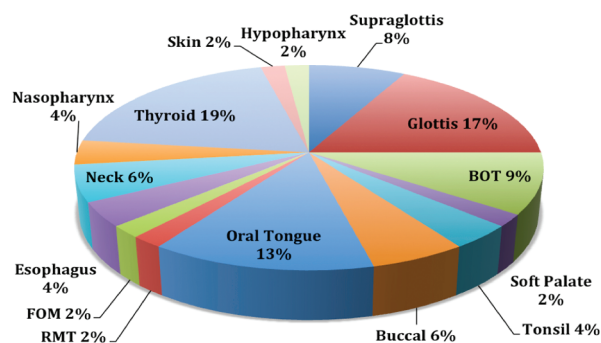


Figure 2. Distribution of primary cancer sites among survey subjects. BOT, base of tongue; FOM, floor of mouth; RMT, retromolar trigone.

excellent test-retest reliability Spearman rank coefficient (r) of 0.800 ($P < .001$). The test-retest interval ranged from 6 to 11 days with a mean (SD) of 8.1 (1.3) days. Forty-four of the 52 subjects (85%) reported no unusual fatigue-related events during the testing period. The internal consistency revealed a significant Cronbach's α of 0.938. Construct validity based on comparisons between MBFI and MFSI-SF showed a Spearman rank coefficient of 0.814 ($P < .001$). Discriminant validity was obtained by comparing cancer vs

control subject results on the MBFI. This was significant based on an initial unadjusted *t* test ($P = .027$). Adjusted discriminant validity for ASA classification using analysis of covariance (ANCOVA) was also significant ($P < .001$). Discriminant validity was also adjusted for ECOG with ANCOVA, which was significant as well ($P < .001$).

Bivariate analysis was performed to identify potential predictive patient factors on MBFI score. Factors with a P value < 0.10 would go on to be included in a multivariate regression model. Comorbidity status or ASA classification ($P = .039$), cancer stage ($P = .008$), prior radiation therapy ($P = .016$), and presence of tracheostomy or laryngectomy ($P = .065$) were eventually analyzed in our multivariate model. There was no significant relationship on bivariate analysis for age, sex, relationship status, education level, ethnicity, presence of a feeding tube, time elapsed after treatment (surgery, radiation, chemotherapy, and/or radioactive iodine), decreased appetite, notable weight loss (greater than 10% body weight), or hemoglobin, albumin, and creatinine levels (measured within the past 30 days). There were too many tumor types in the study to test the specific subsite as a predictive factor. This aforementioned multiple regression linear model (**Table 3**) revealed a significant correlation for comorbidity and cancer stage with MBFI score but not for prior radiation therapy. Assumptions of the multiple regression were tested as well. The

Table 2. Analysis of Cancer Subject Modified Brief Fatigue Inventory Responses

Response Number	MBFI-I Responses (n = 52)			Test-Retest Spearman Rank	
	Category	Mean Value (SD)	Range	r Value	P Value
1	Fatigue now	3.15 (1.75)	1-7	0.924	<.001
2	Worst fatigue	4.33 (2.00)	1-7	0.890	<.001
3	General activity	3.06 (1.58)	1-7	0.890	<.001
4	Mood	2.98 (1.75)	1-7	0.843	<.001
5	Walking ability	3.04 (2.00)	1-7	0.957	<.001
6	Normal work	2.77 (1.75)	1-7	0.884	<.001
7	Relations	2.67 (1.67)	1-6	0.893	<.001
8	Enjoyment of life	2.88 (1.91)	1-7	0.879	<.001
9	Overall fatigue	3.40 (1.62)	1-7	0.913	<.001
	Total score	3.14 (1.46)	1-6.1	0.973	<.001

Abbreviation: MBFI-I, initial Modified Brief Fatigue Inventory administered to cancer subjects.

Table 3. Multiple Regression Linear Model for Further Analysis of Modified Brief Fatigue Inventory Predictive Factors

Multiple Regression Linear Model $R^2 = 0.331$, $P = .001$					
	β (Standard Error)	95% CI	t Score	P Value	
Constant	2.48 (1.47)	-0.47 to 5.43	1.692	.097	
ASA	0.72 (0.25)	0.22 to 1.22	2.898	.006	
Cancer stage	0.43 (0.020)	0.03 to 0.82	2.187	.034	
Radiation therapy	-0.52 (0.39)	-1.30 to 0.26	-1.340	.187	
Presence of tracheostomy or laryngectomy	-0.28 (0.33)	-0.94 to 0.37	-0.871	.388	

Abbreviations: ASA, American Society of Anesthesiologists classification; CI, confidence interval.

relationships were roughly linear with variances approximately equal. There was no significant cross-correlation of the independent variable.

Discussion

The objective of this study was to establish a validated instrument in measuring the intensity and frequency of fatigue in head and neck cancer patients. The 9-item MBFI has been shown to be valid based on psychometric tests of internal consistency, test-retest reliability, discriminant validity, and construct validity. In addition, patient comorbidity and cancer stage have been shown to be significant predictive correlates of MBFI scores.

The MBFI scores were highly correlated with patient performance on the 30-item MSFI-SF ($r = 0.814$). The latter survey assesses multiple facets of fatigue, including general, physical, emotional, mental, and vigor.⁹ Similarly, the MBFI accounts for general, physical, interpersonal relations, and mood. Although both instruments can provide accurate assessments of fatigue levels, the MBFI is much shorter with simple designations of fatigue severity and frequency. The comprehensive yet simple design is ideal for the clinical setting in the context of initial assessment in addition to posttreatment

surveillance. Longer and more descriptive tests such as the MFSI and FSI may be more practically suited for an academic research setting, where time can be allotted for proper assessment and completion.

As with any survey, the risk of bias from both administrators and respondents exists in this study. Modification of a previously validated questionnaire that was simple and clear aided in minimizing confusion and misinterpretation.^{12,15} Furthermore, using the same representative to verbally administer all tests provided consistency and clarity. Sensitivity for detecting fatigue events was augmented by increasing the recall period from 24 hours to 7 days.^{11,12} Subconscious bias may be another issue, where subjects provide extreme answers or affirmative answers to please testers.^{12,15,16} This is a potential concern with verbal questionnaires such as ours. Particularly within a posttreatment setting, patients may fear disappointing their physician by acknowledging any undesired symptoms, including fatigue. In addition, certain patients may underreport their fatigue levels out of a subconscious (or conscious) fear of undergoing additional tests or procedures. These issues were addressed by thoroughly explaining to all subjects the confidential nature of all responses, with no direct clinical implications. Although most patients in this study were unemployed

or retired prior to their cancer treatment, premorbid occupation and activity status may also have a bearing on relative impressions of fatigue and likelihood of returning to a functional state. These factors should be considered in clinical applications and future studies with the MBFI. The final limitation of this study is the few laboratory tests (hematocrit, creatinine, and albumin) completed within 30 days of survey administration. Only 2 patients had these results available, precluding any meaningful assessments of these potentially valuable results. Notably, these tests were available in the majority of cancer subjects and, in turn, successfully correlated to incremental levels of fatigue when validating the original BFI.⁵

Patients with head and neck cancer suffer from specific deficits in breathing, swallowing, speech, and neurosensory functioning. Given the complex and unique anatomic relations within the pathophysiology of these malignancies, a validated instrument is essential in gauging the frequent yet ill-defined complaint of fatigue. This study not only provides a practical tool for assessing fatigue levels in this population but also sheds light on cancer stage and comorbidities as predictive factors.

The availability of a simple scale for ascertaining fatigue levels will pave the way for advancing clinical care by enabling further epidemiologic studies and clinical trials in addition to facilitating communication among care providers. Looking beyond this cross-sectional study, future endeavors should work toward establishing prospective correlations between fatigue level scores with certain objective clinical findings.

Author Contributions

Behrad B. Aynehchi, conception and design, acquisition of data, analysis and interpretation of data, drafting the article, final approval of the version to be published; **Chelsea Obourn**, conception and design, acquisition of data, analysis and interpretation of data, drafting the article, final approval of the version to be published; **Krishnamurthi Sundaram**, conception and design, acquisition of data, analysis and interpretation of data, drafting the article, final approval of the version to be published; **Boris L. Bentsianov**, conception and design, acquisition of data, analysis and interpretation of data, drafting the article, final approval of the version to be published; **Richard M. Rosenfeld**, conception and design, acquisition of data, analysis and interpretation of data, drafting the article, final approval of the version to be published.

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References

1. Horneber M, Fischer I, Dimeo F, Rüffer JU, Weis J. Cancer related fatigue: epidemiology, pathogenesis, diagnosis, and treatment. *Dtsch Arztebl Int*. 2012;109:161-171.
2. Glaus A, Crow R, Hammond S. A qualitative study to explore the concept of fatigue/tiredness in cancer patients and in healthy individuals. *Support Care Cancer*. 1996;4:82-96.
3. Richardson A. Fatigue in cancer patients: a review of the literature. *Eur J Cancer Care*. 1995;4:20-32.
4. Weis J. Cancer-related fatigue: prevalence, assessment and treatment strategies. *Expert Rev Pharmacoecon Outcomes Res*. 2011;11:441-446.
5. Mendoza TR, Wang XS, Cleeland CS, et al. The rapid assessment of fatigue severity in cancer patients: use of the Brief Fatigue Inventory. *Cancer*. 1999;85:1186-1196.
6. Hann DM, Denniston MM, Baker F. Measurement of fatigue in cancer patients: further validation of the Fatigue Symptom Inventory. *Qual Life Res*. 2000;9:847-854.
7. Hann DM, Jacobsen PB, Azzarello LM, et al. Measurement of fatigue in cancer patients: development and validation of the Fatigue Symptom Inventory. *Qual Life Res*. 1998;7:301-310.
8. Stein KD, Martin SC, Hann DM, Jacobsen PB. A multidimensional measure of fatigue for use with cancer patients. *Cancer Pract*. 1998;6:143-152.
9. Stein KD, Jacobsen PB, Blanchard CM, Thors C. Further validation of the Multidimensional Fatigue Symptom Inventory–Short Form. *J Pain Symptom Manage*. 2004;27:14-23.
10. Steiner DL, Norman GR. *Health Measurement Scales: A Practical Guide to the Development and Use*. 4th ed. Oxford, UK: Oxford University Press; 2008.
11. Means B; US National Center for Health Statistics. *Autobiographical Memory for Health-Related Events*. Hyattsville, MD: US Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Center for Health Statistics; 1989.
12. Slattery EL, Voelker CC, Nussenbaum B, Rich JT, Paniello RC, Neely JG. A practical guide to surveys and questionnaires. *Otolaryngol Head Neck Surg*. 2011;144:831-837.
13. Haynes SR, Lawler PG. An assessment of the consistency of ASA physical status classification allocation. *Anaesthesia*. 1995;50:195-199.
14. Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol*. 1982;5:649-655.
15. Fink A. *The Survey Kit*. 2nd ed. Thousand Oaks, CA: Sage; 2003.
16. Choi BC, Pak AW. A catalog of biases in questionnaires. *Prev Chronic Dis*. 2005;2:A13.