DOI: 10.14744/DAJPNS.2026.00322
Dusunen Adam J Psychiatr Neurol Sci
2026;39:90-100

RESEARCH ARTICLE

Distinct fatigue profiles and psychological mechanisms among breast cancer survivors: A latent profile and mediation analysis

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ABSTRACT

Objective: Cancer-related fatigue (CRF) is highly prevalent among breast cancer survivors. This study aimed to identify CRF subgroups in breast cancer survivors using latent profile analysis (LPA) and to examine the effects of rumination on CRF through anxiety, depression, and fear of cancer recurrence.

Method: A total of 201 women diagnosed with early-stage breast cancer completed standardized assessments of fear of cancer recurrence, rumination, anxiety, depression, and cancer-related fatigue. Latent profile analysis was conducted to identify distinct CRF profiles, and differences in psychological variables across groups were examined. Mediation analyses were performed using the PROCESS macro with bootstrapping (5,000 samples) to test indirect effects.

Results: LPA identified three distinct profiles: low (50.2%), moderate (37.3%), and high (12.4%). The model demonstrated excellent classification quality (entropy=0.80; average posterior probabilities=0.89–0.93). Participants in the high-CRF group reported significantly higher levels of rumination, anxiety, depression, and fear of recurrence than those in the other two groups (all $p<0.001$, $\eta^2=0.10–0.30$). Multinomial regression analysis showed that depression, anxiety, and fear of cancer recurrence significantly predicted membership in the high-CRF group. Mediation analyses indicated that rumination predicted CRF indirectly through depression (b=0.07, 95% confidence interval (CI) [0.01, 0.15]), anxiety (b=0.20, 95% CI [0.05, 0.34]), and fear of recurrence (b=0.17, 95% CI [0.04, 0.30]), jointly accounting for 32.6% of the total effect.

Conclusion: The findings suggest that fear of recurrence, anxiety, and depression may increase vulnerability to CRF. The results also underscore the importance of targeting transdiagnostic processes such as rumination in psychological interventions for breast cancer survivors.

Keywords: Breast cancer survivors, cancer-related fatigue, fear of recurrence, latent profile analysis, mediation, rumination

INTRODUCTION

Breast cancer is one of the most prevalent cancers among women worldwide, and advances in early detection and treatment have led to a growing population of long-term survivors (1). However, both survivors and patients undergoing treatment continue to face numerous physical and psychological

How to cite this article: Turkel NN, Turkel A, Ekmekci I, Dogan M. Distinct fatigue profiles and psychological mechanisms among breast cancer survivors: A latent profile and mediation analysis. Dusunen Adam J Psychiatr Neurol Sci 2026;39:90-100.

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Received: December 01, 2025; **Revised:** May 05, 2026; **Accepted:** May 06, 2026

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challenges. Among these, cancer-related fatigue (CRF) is one of the most common and distressing symptoms. CRF often persists after treatment completion, and approximately 66% of breast cancer survivors experience fatigue to some degree (2). A meta-analysis including 84 studies reported an overall CRF prevalence of 52% across all cancer types. (3) CRF is broadly defined as a sense of physical, emotional, and cognitive exhaustion that impairs functioning and is disproportionate to recent activity (4). Numerous factors have been associated with CRF. In addition to physical factors such as chemoradiotherapy, female sex, pain, neurotic personality traits, sleep disorders, and depression have all been identified as potential risk factors (3). However, the mechanisms through which psychological factors contribute to fatigue severity remain incompletely understood.

One approach that may improve understanding of CRF heterogeneity is the use of person-centered statistical methods. CRF is a multidimensional phenomenon encompassing cognitive, emotional, and physical components, and patients may experience fatigue in qualitatively different ways. Latent profile analysis (LPA) is a person-centered statistical approach used to identify subgroups of individuals based on shared patterns of psychological characteristics (5). By identifying distinct fatigue profiles, LPA may provide clinically meaningful insights into symptom heterogeneity and help guide the development of more tailored supportive interventions.

In addition to symptom heterogeneity, cognitive processes may play an important role in the development and maintenance of cancer-related fatigue. Rumination, broadly defined as repetitive thinking about past losses and failures or anticipated future threats, has been identified as a transdiagnostic cognitive process associated with both depression and anxiety (6). In the context of cancer, intrusive rumination may emerge following diagnosis and treatment and has been associated with greater psychological distress and poorer adjustment among cancer survivors (7). Such repetitive cognitive processing may amplify emotional distress and heighten attention to bodily sensations, thereby contributing to the perception and persistence of fatigue.

The current study had two primary objectives. First, we aimed to identify distinct CRF profiles among early-stage breast cancer survivors using latent profile analysis. Second, we investigated whether rumination predicts CRF and whether anxiety, depression, and fear of cancer recurrence mediate or contribute to this relationship. By integrating person-centered and process-focused approaches, this study seeks to improve understanding of CRF and its underlying mechanisms and to inform the development of more tailored psycho-oncological interventions.

METHODS

Study Design and Participants

This cross-sectional study was conducted in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines. A convenience sampling method was used to recruit patients with early-stage breast cancer, defined in this study as stage I–III non-metastatic disease in remission, who attended outpatient follow-up visits at the Medical Oncology Department of Dr. Abdurrahman Yurtaslan Ankara Oncology Research and Training Hospital between March and July 2024. Inclusion criteria were: (1) age 18 years or older; (2) sufficient Turkish literacy to complete self-report questionnaires; (3) diagnosis of early-stage breast cancer and remission status; and (4) absence of severe neurological or psychiatric disorders. Patients with stage IV breast cancer or those receiving active chemotherapy or radiotherapy at the time of the study were excluded. Eligible participants who provided written informed consent completed a set of standardized self-report questionnaires. Of the 210 patients invited to participate, 201 provided valid responses and were included in the final analysis, yielding a response rate of 95.7%.

Measures

Sociodemographic and Disease-Related Variables

Sociodemographic data were collected using a structured questionnaire developed by the researchers. Participants reported their age, marital status, educational level, employment status, family history of cancer, previous cancer diagnoses, and the presence of psychiatric or physical comorbidities. Clinical data, including time since diagnosis, cancer stage, and history of chemotherapy, radiotherapy, and hormone therapy, were obtained from hospital medical records.

Fear of Cancer Recurrence Inventory–Short Form (FCR-SF)

Fear of cancer recurrence (FCR) was assessed using the 9-item Fear of Cancer Recurrence Inventory–Short Form, a 5-point Likert-type scale that evaluates the severity of recurrence-related concerns among cancer

patients. The FCRI-SF is derived from the "Severity" subscale of the original 42-item multidimensional Fear of Cancer Recurrence Inventory (FCRI) developed by Simard et al. (8), which consists of seven subscales. Higher scores indicate greater fear of recurrence (8). The Turkish version of the scale has demonstrated good validity and reliability in cancer populations (9). In the present study, the Cronbach's alpha for the scale was 0.840.

Hospital Anxiety and Depression Scale (HADS)

The Hospital Anxiety and Depression Scale, developed by Zigmond and Snaith, is a 14-item, 4-point Likert-type scale designed to assess symptoms and severity of anxiety and depression. Odd-numbered items assess anxiety, whereas even-numbered items assess depression (10). The Turkish validity and reliability study conducted by Aydemir et al. demonstrated that the scale is appropriate for use in medically ill populations (11). In the current study, Cronbach's alpha coefficients were 0.766 for the depression subscale and 0.799 for the anxiety subscale.

Cancer Fatigue Scale (CFS)

The Cancer Fatigue Scale was developed to assess fatigue in patients with cancer, particularly breast cancer patients. The scale evaluates three dimensions of fatigue: physical, affective, and cognitive. Each item is rated on a 5-point Likert scale (12). The Turkish validity and reliability study of the scale was conducted by Şahin et al. (13) In the present study, the Cronbach's alpha coefficient for the scale was 0.807.

Event-Related Rumination Inventory (ERRI)

The Event-Related Rumination Inventory, developed by Cann et al., assesses repetitive thoughts related to stressful events. The scale consists of 20 self-report items rated on a 4-point Likert scale and includes two subscales: intrusive/involuntary rumination and deliberate rumination. (14) The Turkish version of the ERRI has demonstrated adequate validity and reliability. Only the intrusive/involuntary rumination subscale was used in the present study (15). Cronbach's alpha for this subscale was 0.936.

Statistical Analysis

Descriptive statistical analyses were conducted using SPSS version 25.0. Frequencies and percentages were calculated for categorical sociodemographic and clinical variables, whereas means and standard deviations were calculated for continuous variables. LPA was performed to identify subgroups of early-stage breast cancer survivors based on levels of CRF. Model fit was evaluated using the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and entropy values. Lower AIC and BIC values and entropy values greater than 0.80 were considered indicative of better model fit. The Bootstrap Likelihood Ratio Test (BLRT) was also used to compare successive models (k vs. k–1 classes), consistent with the recommendations of Nylund et al. (16), who identified BLRT and BIC among the most reliable indicators for class enumeration. Four models were tested, and the optimal number of latent classes was determined based on a combination of statistical fit indices and theoretical interpretability. LPA was conducted using the "tidyLPA" package in R. After selecting the final model, chi-square tests and univariate analyses were conducted to compare demographic, clinical, and psychological variables across the identified latent profiles. A p-value <0.05 was considered statistically significant.

To further examine predictors of class membership, multinomial logistic regression analyses were conducted using the "nnet" package in R. Because multinomial logistic regression treats CRF as a categorical outcome, potential indirect effects among variables may not be fully captured. Therefore, complementary mediation analyses were conducted using PROCESS version 4.2, treating CRF as a continuous variable, to examine the mediating roles of depression, anxiety, and fear of cancer recurrence in the relationship between rumination and CRF.

RESULTS

Demographic and Clinical Characteristics

The study initially enrolled 210 female patients diagnosed with early-stage breast cancer. Of these, 201 provided valid responses and were included in the final analyses, resulting in a response rate of 95.7%. Most participants were married (78.1%), and 35.8% had completed a university education. All participants had undergone breast surgery, and 22.4% had been diagnosed with stage III breast cancer. The mean age of the sample was 51.88 years (standard deviation [SD]=9.40), and the mean time since diagnosis was 5.45 years (SD=4.75). Detailed demographic and clinical characteristics of the participants are presented in Table 1.

Latent Profile Analysis

Table 2 summarizes the fit indices for the models generated using the "tidyLPA" package based on

Table 1: Demographic and clinical characteristics of participants (n=201)

Variables	n	%	Variables	n	%
Age group (years)			Psychiatric comorbidity		
<45	56	27.9	Yes	13	6.5
45–65	130	64.7	No	188	93.5
>65	15	7.5	Physical comorbidity		
Marital status			Yes	37	18.4
Unmarried	44	21.9	No	164	81.6
Married	157	78.1	Cancer stage		
Educational level			Stage I	45	22.4
Secondary school	74	38.8	Stage II	111	55.2
High school	55	27.4	Stage III	45	22.4
University	72	35.8	Time since diagnosis		
Employment status			<5 years	134	66.7
Employed	51	25.4	5–10 years	39	19.4
Unemployed	108	53.7	>10 years	28	13.9
Retired	42	20.9	Chemotherapy history		
Family history of cancer			Yes	177	84.3
Yes	63	31.3	No	34	15.7
No	138	68.7	Radiotherapy history		
Previous cancer diagnosis			Yes	153	77.2
Yes	49	24.4	No	48	22.8
No	152	75.6	Hormone therapy history		
Time since diagnosis, mean (SD)	5.45 (4.75)		Yes	172	86.8
Age, mean (SD)	51.88 (9.40)		No	29	13.2

SD: Standard deviation.

Table 2: Fit indices for latent profile models

Variables	AIC	BIC	Entropy	BLRT	BLRT-p	Smallest Class %	Largest Class %
1-Class	1720.23	1740.05	NA	NA	NA	1	1
2-Class	1587.81	1620.84	0.79	140.43	0.001	0.29	0.71
3-Class	1534.66	1580.91	0.80	61.15	0.001	0.12	0.50
4-Class	1532.11	1591.57	0.78	10.55	0.10	0.05	0.53
5-Class	1516.08	1588.76	0.80	24.02	0.001	0.05	0.50
6-Class	1500.25	1586.14	0.81	23.83	0.001	0.05	0.43

AIC: Akaike Information Criterion; BIC: Bayesian Information Criterion; BLRT: Bootstrap Likelihood Ratio Test; NA: Not applicable; Entropy: Classification accuracy index. Lower AIC and BIC values and higher entropy values (>0.80) indicate better model fit.

dimensions of the Cancer Fatigue Scale among early-stage breast cancer survivors. Model fit improved with the addition of each class, as reflected by decreasing AIC and BIC values. Entropy values remained high across models, indicating good classification quality. The three-class model demonstrated the best fit according to the Bayesian Information Criterion (BIC=1580.91) and showed satisfactory entropy value (0.80), indicating clear separation among latent groups. The Bootstrap Likelihood Ratio Test was significant (p=0.01) when comparing the three-class model with the two-class model, further supporting selection of the three-class solution as the optimal model. Models with four or more classes did not improve model fit and resulted in very small latent groups (n<5%).

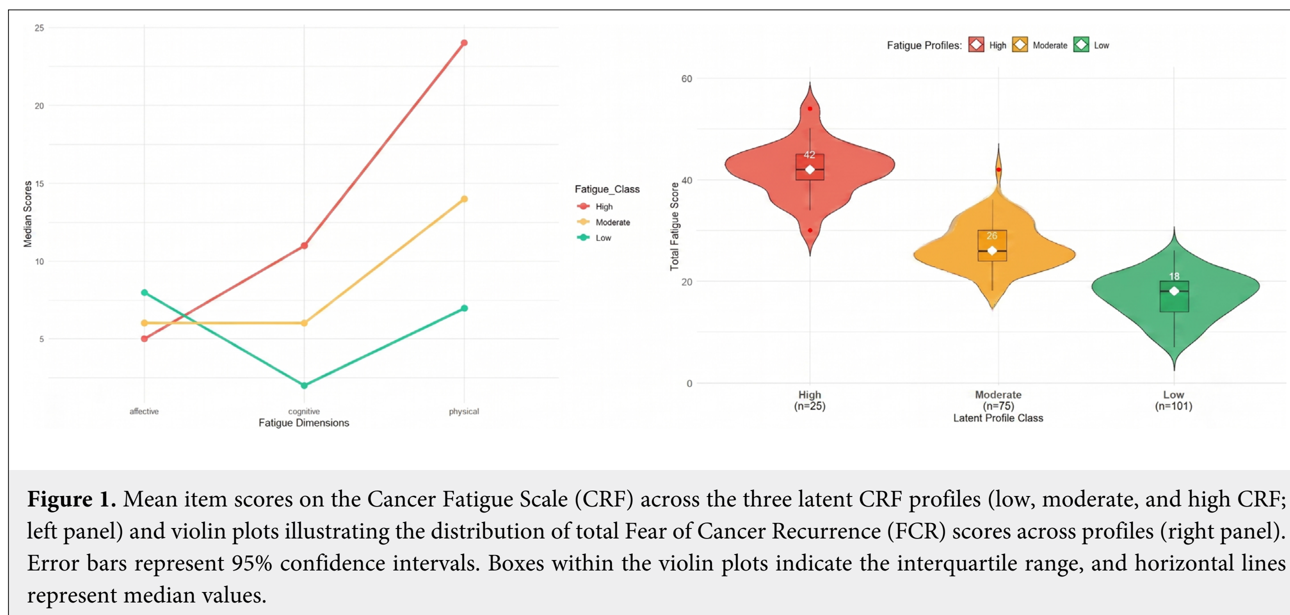

Figure 1. Mean item scores on the Cancer Fatigue Scale (CRF) across the three latent CRF profiles (low, moderate, and high CRF; left panel) and violin plots illustrating the distribution of total Fear of Cancer Recurrence (FCR) scores across profiles (right panel). Error bars represent 95% confidence intervals. Boxes within the violin plots indicate the interquartile range, and horizontal lines represent median values.

Classification quality was high (entropy=0.80). Class-specific average posterior probabilities (APPs) indicated adequate-to-excellent classification accuracy, with values of 0.94, 0.89, and 0.90 for the High, Moderate, and Low fatigue profiles, respectively. The overall classification correctness (OCC) was 0.91, further supporting the robustness of the class assignments.

The identified classes were labeled according to severity of cancer-related fatigue: High Fatigue (12.4%, n=25), Moderate Fatigue (37.3%, n=75), and Low Fatigue (50.2%, n=101). Mean Cancer Fatigue Scale scores across the profiles are presented in Figure 1, demonstrating a clear gradient in symptom severity among the three latent profiles.

Differences in Demographic and Clinical Characteristics Among the Latent Profiles

Table 3 presents comparisons of sociodemographic and clinical characteristics across the cancer-related fatigue profiles. χ^2 tests were used for categorical variables, whereas the Kruskal–Wallis test was used for continuous variables. No significant differences were observed among the profiles with respect to marital status, educational level, occupational status, disease stage, or the presence of additional psychiatric or physical illnesses. However, rank-based analysis of variance revealed significant between-profile differences in fear of cancer recurrence, rumination, anxiety, depression, and cancer-related fatigue scores. Post hoc analyses demonstrated that patients in the High-CRF group scored significantly higher than those in the Moderate- and Low-CRF groups across all measures. Effect sizes were moderate to large (η^2=0.10–0.30), indicating clinically meaningful differences between profiles. Given the exploratory nature of these analyses, p values were interpreted cautiously and were not adjusted for multiple comparisons.

Continuous variables are presented as median (Q1–Q3) values and were compared using the Kruskal–Wallis test followed by Dunn–Bonferroni post hoc analyses. Categorical variables were analyzed using chi-square tests, and Fisher's exact test was applied when expected cell counts were below five.

Multinomial Logistic Regression Analysis

Sociodemographic and clinical variables that differed significantly across latent profiles in the univariate analyses (Table 4) were included in the multinomial logistic regression model.

The final regression model demonstrated acceptable fit indices (AIC=314.06; McFadden's pseudo R^2=0.2481), indicating good overall model fit for multinomial logistic regression. The model correctly classified 63.2% of cases overall, with particularly high accuracy for the Low-Risk Group (80.2%), moderate accuracy for the High-Risk Group (44.0%), and lower accuracy for the Moderate-Risk Group (46.7%).

In the moderate- versus low-risk comparison, depression emerged as a significant independent predictor (odds ratio [OR]=1.159, 95% confidence interval [CI]: 11.032–1.302, p=0.013), indicating that each one-point increase in depression scores was associated with a 15.9% greater likelihood of belonging to the moderate-risk group.

Table 3: Differences in demographic and clinical characteristics across latent profiles (n=201)

Variables	High CFS n (%)	Moderate CFS n (%)	Low CFS n (%)	Test statistic	p
Marital status				2.5515	0.2792
Unmarried	7 (15.9)	12 (27.2)	25 (56.8)		
Married	18 (11.5)	63 (40.1)	76 (48.4)		
Educational level				6.975	0.1432
Secondary school	15 (20.3)	27 (36.5)	32 (43.2)		
High school	4 (7.27)	21 (38.2)	30 (54.5)		
University	6 (8.33)	27 (37.5)	39 (54.2)		
Family history of cancer				12.668	0.5278
Yes	9 (14.3)	20 (31.7)	34 (54.0)		
No	16 (11.6)	55 (39.9)	67 (48.6)		
Previous cancer diagnosis				4.8363	0.08167
Yes	7 (14.3)	24 (49.0)	18 (36.7)		
No	18 (11.8)	51 (33.6)	83 (54.6)		
Psychiatric comorbidity				4.3252	0.07292
Yes	3 (23.1)	7 (53.8)	3 (23.1)		
No	22 (11.7)	68 (36.2)	98 (52.2)		
Physical comorbidity				1.7562	0.45551
Yes	3 (8.11)	17 (45.9)	17 (45.9)		
No	22 (13.4)	58 (35.4)	84 (51.2)		
Cancer stage				5.7944	0.1926
Stage I	7 (16.7)	10 (23.8)	25 (59.5)		
Stage II	12 (10.5)	44 (38.6)	58 (50.9)		
Stage III	6 (13.3)	21 (46.7)	18 (40.0)		
Age, M (Q_1, Q_3)	52 (45–57)	49 (44–56)	52 (46–60)	5.66	0.059
Time since diagnosis, M (Q_1, Q_3)	5 (3–8)	4 (2–6)	5 (2–8)	1.59	0.451
Cognitive fatigue, M (Q_1, Q_3)	11 (9–14)	6 (4–8)	2 (1–4)	119.0	**<0.001**
Emotional fatigue, M (Q_1, Q_3)	5 (4–8)	6 (5–8)	8 (6–10)	26.7	**<0.001**
Physical fatigue, M (Q_1, Q_3)	24 (23–28)	14 (12–16)	7 (4–8)	153.0	**<0.001**
FCR, M (Q_1, Q_3)	24 (21–28)	17 (13.5–22)	15 (9–22)	36.9	**<0.001**
Anxiety, M (Q_1, Q_3)	14 (10–16)	8 (6–10)	5 (2–8)	61.4	**<0.001**
Depression, M (Q_1, Q_3)	10 (7–11)	6 (4–9)	3 (1–5)	49.5	**<0.001**
Rumination, M (Q_1, Q_3)	22 (16–28)	17 (10–20)	12 (6–19)	21.2	**<0.001**

CFS: Cancer Fatigue Scale; FCR: Fear of Cancer Recurrence.

In the high- versus low-risk comparison, anxiety demonstrated the strongest predictive value (OR=1.538, 95% CI: 1.231–1.922, p<0.001), indicating that each one-point increase in anxiety scores was associated with a 53.8% greater likelihood of membership in the high-risk group. FCR also emerged as a significant predictor (OR=1.196, 95% CI: 1.040–1.372, p=0.010), with each unit increase associated with a 19.6% greater likelihood of high-risk classification.

Mediation Analysis

Because multinomial logistic regression treats CRF as a categorical outcome, this approach may obscure the continuous nature of fatigue severity. To address this limitation and further examine potential indirect pathways, a mediation analysis (PROCESS Model 4) was conducted treating CRF as a continuous variable. Rumination was entered as the independent variable (X), anxiety, depression,

Table 4: Predictors of latent profile membership

Predictor	β	SE	Wald	p	OR	95% CI
Moderate CRF vs. Low CRF						
Intercept	-2.188	0.493	19.68	<0.001	0.112	0.043–0.295
Anxiety	0.119	0.069	3.07	0.086	1.126	0.983–1.290
Depression	0.148	0.059	6.20	0.013	1.159	1.032–1.302
FCR	0.018	0.034	0.30	0.587	1.126	0.983–2.090
Rumination	0.005	0.030	0.03	0.867	1.005	0.948–1.065
High CRF vs. Low CRF						
Intercept	-9.809	1.691	33.63	<0.001	0.000	0.000–0.002
Anxiety	0.430	0.114	14.25	<0.001	1.538	1.231–1.922
Depression	0.141	0.099	2.03	0.154	1.152	0.948–1.399
FCR	0.170	0.070	6.58	0.010	1.196	1.040–1.372
Rumination	-0.004	0.056	0.00	0.946	0.996	0.893–1.111

Reference category=Low-CRF group; SE: Standard error; OR: Odds ratio; CI: Confidence interval; CRF: Cancer-related fatigue; FCR: Fear of cancer recurrence.

Table 5: Parallel mediation model regression coefficients predicting cancer-related fatigue scale (CFS)

Dependent variable	Independent variable	β	SE	t	p	R^2
Anxiety	Rumination	0.29	0.03	8.63	<0.001	0.27
Depression	Rumination	0.18	0.04	5.22	<0.001	0.12
FCR	Rumination	0.59	0.05	12.20	<0.001	0.43
CFS	Rumination	-0.05	0.10	-0.56	0.58	
CFS	Anxiety	0.69	0.20	3.38	<0.001	
CFS	Depression	0.39	0.18	2.12	0.03	
CFS	FCR	0.29	0.11	2.60	0.01	

SE: Standard error; FCR: Fear of cancer recurrence.

and fear of cancer recurrence as parallel mediators (M_1, M_2, M_3), and total CRF score as the dependent variable (Y) (Table 5).

The direct effect of rumination on fatigue was not statistically significant (b=−0.05, p=0.58). Therefore, indirect pathways through depression, anxiety, and fear of cancer recurrence were examined.

The total indirect effect was significant (b=0.44, 95% CI [0.26, 0.61]). Each mediator contributed a significant indirect effect:

- Through depression: b=0.07, 95% CI [0.01, 0.15];
- Through anxiety: b=0.20, 95% CI [0.05, 0.34];
- Through fear of cancer recurrence: b=0.17, 95% CI [0.04, 0.30].

Together, the mediators explained 32.6% of the variance in fatigue severity.

These findings suggest that higher levels of rumination are associated with greater depression, anxiety, and fear of cancer recurrence, which in turn contribute to increased fatigue severity. Among the mediators, anxiety exerted the strongest indirect effect, followed by FCR and depression.

DISCUSSION

This study highlights the heterogeneous nature of cancer-related fatigue among patients with early-stage breast cancer in remission by identifying distinct fatigue subgroups—low, moderate, and high CRF—and examining differences between these profiles. Additionally, CRF was conceptualized as a continuous construct to investigate its relationship with rumination and the potential mediating roles of depression, anxiety, and fear of cancer recurrence.

Latent profile analysis revealed that 50.2% of participants belonged to the low-CRF group, 37.3% to the moderate-CRF group, and 12.4% to the high-CRF group. As expected, the high-CRF profile demonstrated the highest CFS scores, whereas the low-CRF profile showed the lowest scores. These proportions are comparable to findings from previous studies. In a study of colorectal cancer survivors, Thong et al. (17) identified three distinct CRF classes: a no fatigue/no distress group (n=644, 56%), a low fatigue/moderate distress group (n=256, 22%), and a high fatigue/moderate distress

group (n=256, 22%). Similarly, Li et al. (18) identified three CRF profiles among patients with hepatocellular carcinoma: "Physical balance–Low fatigue" (20.1%), "Physical imbalance–Moderate fatigue" (69.6%), and "Physical prominent–High fatigue" (10.2%). In the present study, the combined prevalence of moderate and high CRF was 49.7%, consistent with the findings of a systematic review by Ruiz-Casado et al. (19). Collectively, these findings support previous literature indicating that CRF remains a highly prevalent and clinically significant concern among breast cancer survivors.

Progression from minimal to severe CRF was significantly associated with several baseline clinical characteristics. Although previous studies have suggested that younger breast cancer survivors tend to experience higher fatigue levels, findings regarding age remain inconsistent (19). In the present study, age did not significantly differentiate fatigue profiles. One possible explanation is that the sample consisted predominantly of middle-aged participants with relatively homogeneous age distributions, limiting variability across groups. Furthermore, fatigue in breast cancer survivors may be influenced more strongly by psychological and behavioral factors than by demographic variables alone. Consistent with previous research, no significant association was found between cancer stage and CRF severity (19). This finding may reflect the possibility that fatigue is more strongly influenced by long-term treatment effects and psychological adjustment processes than by disease severity itself. Similarly, although social support has been identified as a protective factor against CRF and married individuals are often reported to experience lower fatigue levels, marital status was not associated with fatigue profiles in the present study (20). A possible explanation is that marital status alone may not adequately reflect the quality or availability of social support, which may be a more relevant factor influencing fatigue experiences.

Rank-based analysis of variance (Kruskal–Wallis ANOVA) indicated that individuals with high CRF exhibited elevated levels of fear of cancer recurrence, depression, rumination, and anxiety. Multinomial logistic regression analyses identified depression as the sole significant predictor of transition from the low-CRF group to the moderate-CRF group (OR=1.16, 95% CI: 1.03–1.30, p=0.013). These findings are consistent with recent evidence from a large sample of breast cancer survivors demonstrating that individuals reporting both depression and fatigue experience greater fatigue severity than those reporting fatigue alone (21). Moreover, studies investigating predictors of fatigue have consistently shown that higher fatigue levels are associated with depression (22, 23) Depression and fatigue are strongly correlated, and each symptom may function both as a cause and a consequence of the other (24). Additionally, both conditions may arise through shared pathophysiological mechanisms, or fatigue may develop as a secondary response to the adaptive demands of CRF or post-treatment stress (25, 26). These shared mechanisms include elevated pro-inflammatory cytokines and dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis (27, 28). Increased inflammatory activity has been associated with fatigue, insomnia, and depression among breast cancer survivors (29). In recent years, depression has increasingly been conceptualized as a maladaptive response to impaired interoception (30). From this perspective, individuals with depression may engage in dysfunctional bodily self-focus, potentially interpreting somatic sensations in ways that amplify perceptions of fatigue. Consequently, depression may not only intensify the subjective experience of fatigue but also impair physiological energy regulation, thereby contributing to the persistence of cancer-related fatigue.

A markedly different pattern emerged for the transition to the high-CFR profile, in which FCR (OR=1.20, 95% CI: 1.04–1.37, p=0.010) and anxiety (OR=1.54, 95% CI: 1.23–1.92, p<0.001) emerged as significant predictors, whereas depression was no longer significant. A recent meta-analysis including 34 studies reported significant associations between fear of cancer recurrence and cancer-related fatigue (31). Although FCR and CRF are both prevalent concerns among cancer survivors, their relationship is multifaceted. Pre-treatment anxiety, which is strongly associated with FCR, has been shown to predict CRF both before and after treatment (32). Furthermore, individuals with high levels of FCR often demonstrate heightened anxiety sensitivity and catastrophizing tendencies, which may contribute to the misinterpretation of bodily sensations and thereby intensify fatigue experiences (3, 33). Supporting this interpretation, a meta-analysis of mindfulness-based interventions in cancer patients demonstrated that improvements in mindfulness skills were associated with reductions in both CRF and FCR (34). Conversely, physical symptoms may be misinterpreted as signs of cancer recurrence, while cancer-related fatigue itself may contribute to more negative illness perceptions and intensify concerns that cancer will not be cured, thereby perpetuating FCR (35, 36). Consistent with this interpretation, findings from a recent longitudinal study demonstrated that higher CRF levels significantly predicted increases in FCR over time (36).

Contrary to our hypotheses, intrusive rumination did not significantly predict fatigue transitions in the multivariate model. One possible explanation is that the effects of rumination are fully mediated through depression and anxiety, leaving no remaining unique predictive variance once these variables are statistically controlled. Indeed, when CRF was modeled as a continuous variable, mediation analyses demonstrated that depression, anxiety, and cancer-related fatigue fully mediated the relationship between rumination and CRF. In the parallel mediation model, rumination exerted only indirect effects on CRF, whereas the direct effect remained non-significant.

The cancer diagnosis and treatment process constitutes a highly challenging and potentially traumatic experience that may give rise to intrusive rumination. (37) Previous research has indicated that rumination may exacerbate anxiety and depression by interfering with effective problem-solving and reducing engagement in mood-enhancing or distracting activities (6, 38). From a Bayesian perspective, repetitive thoughts about the self and past experiences may increase expectations of future threat (39). Although FCR is conceptually distinct from anxiety and depression, it is particularly closely associated with anxiety-related processes (40, 41). Dugas et al. proposed that rumination represents a cognitive response to uncertainty and the inability to control ambiguous life situations. (42) In this context, and consistent with Leventhal's Common-Sense Model and Mishel's Uncertainty in Illness Theory, the unpredictable nature of cancer may increase sensitivity to somatic experiences such as fatigue. The present findings are consistent with previous research demonstrating associations between intrusive rumination and cancer-related fatigue among cancer survivors (7).

Our findings support a multidimensional threshold model of cancer-related fatigue development. Rather than representing a simple continuum in which the same factors operate across all severity levels, different psychological mechanisms appear to govern progression through distinct fatigue stages. This perspective challenges linear conceptualizations of fatigue and supports the view that fatigue profiles may represent qualitatively distinct syndromes with different etiological pathways.

The non-overlapping predictive patterns observed for depression versus FCR/anxiety further suggest that these factors may operate through distinct mechanisms. Depression's association with moderate fatigue may reflect its established links with motivational systems and neuroimmune pathways, whereas the specific relationship between FCR/anxiety and severe fatigue may involve heightened threat perception and sustained cognitive-emotional arousal (36, 43). Regarding rumination, our findings suggest that it functions as a transdiagnostic process that operates across fatigue levels but exerts its effects indirectly through other psychological mechanisms. Rather than serving as a direct predictor of specific fatigue transitions, rumination may create a cognitive vulnerability that amplifies both depressive symptoms (relevant to moderate fatigue) and anxiety/FCR (relevant to severe fatigue). This pattern aligns with the conceptualization of rumination as a cognitive style that cuts across diagnostic categories and exacerbates multiple forms of psychological distress.

This study has several limitations. First, the cross-sectional design precludes conclusions regarding the temporal progression of cancer-related fatigue among breast cancer survivors. Future studies should employ longitudinal designs to better capture the dynamic nature of CRF and its psychological correlates over time. Second, the study was conducted in a single tertiary care center in Turkiye, which may limit the generalizability of the findings to other healthcare settings or cultural contexts. Third, all data were derived from self-report measures, which may be influenced by recall bias and social desirability effects. Additionally, the relatively small size of the high-CRF group (n=25) may have limited statistical power for subgroup comparisons. Future studies should incorporate clinician-rated assessments and objective clinical indicators to improve validity.

CONCLUSION

This study provides evidence for distinct fatigue profiles among breast cancer survivors, with differential psychological predictors. The finding that depression predicts moderate fatigue, whereas FCR and anxiety predict severe fatigue, represents a significant advance in understanding the heterogeneous nature of cancer-related fatigue. These results have important implications for both theoretical models of fatigue development and clinical approaches to fatigue management.

The identification of profile-specific risk factors supports moving beyond one-size-fits-all approaches toward personalized interventions targeting the specific psychological mechanisms underlying different fatigue presentations. Clinically, these findings support the implementation of stratified assessment protocols and tailored interventions addressing depression in moderate fatigue and FCR/anxiety in severe fatigue. From a research perspective, these findings underscore the importance of considering fatigue heterogeneity in future study design and analysis.

Ethical Approval: The Gazi University Research Ethics Committee granted approval for this study (date: 13.02.2024, number: 2024–248/03).

Informed Consent: All participants confirmed their understanding of the study procedures by signing an informed consent form.

Conflict of Interest: The authors declare that there is no conflict of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

Use of AI for Writing Assistance: The authors declared that artificial intelligence was not used in the study.

Contribution Categories		Author Initials
Category 1	Concept/Design	N.N.T.
	Data acquisition	A.T.
	Data analysis/Interpretation	N.N.T.
Category 2	Drafting manuscript	N.N.T.
	Critical revision of manuscript	I.E.
Category 3	Final approval and accountability	I.E., M.D.
Other	Supervision	M.D.

Peer-review: Externally peer-reviewed.

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