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Comprehensive evaluation of anxiety, depression, and quality of life in cancer patients: clinical, sociodemographic, and psychosocial influences

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ABSTRACT

Aims: It was aimed to evaluate the prevalence of anxiety and depression among cancer patients, and examine their association with quality of life (QoL).

Methods: A cross-sectional study was conducted, including 750 adult cancer patients at a tertiary oncology outpatient clinic. Anxiety and depression status were measured using the Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI), respectively, while QoL was assessed with the EORTC QLQ-C30. Sociodemographic and clinical data were collected through structured forms. Comparative, correlation, and subgroup analyses were performed, with $p<0.05$ considered statistically significant.

Results: The prevalence of anxiety and depression was 46.5% and 42.4%, respectively, Anxiety was more common among females, widowed individuals, and those living in non-traditional arrangements, and was highest in patients with gynecological cancers. Depression showed no significant association with demographic or clinical factors. Anxiety was negatively correlated with emotional, cognitive, and social functioning, whereas depression was selectively linked to emotional functioning. Patients with comorbid anxiety–depression demonstrated the most significant impairment in emotional functioning.

Conclusion: Anxiety and depression are highly prevalent in cancer patients and exert distinct but overlapping effects on QoL, with anxiety impacting multiple functional domains. Female sex, widowhood, and limited social support emerged as key risk factors, whereas cancer type, metastasis, and comorbidity had a minor influence. These findings underscore the need for universal distress screening and integrated psychosocial support in routine oncology care.

Keywords: Anxiety, depression, quality of life, cancer, psychosocial comorbidity

INTRODUCTION

Many individuals diagnosed with cancer experience ongoing emotional distress, facing psychological challenges from the moment of diagnosis throughout the treatment process. This psychological burden adversely affects the patient's overall health status and quality of life (QoL).[1,2] Depression and anxiety are among the most common mental health issues encountered by cancer patients, significantly influencing treatment adherence, general QoL, and even disease prognosis.[3] Research indicates that untreated anxiety and depression in cancer patients are associated with increased mortality, impaired physical activity, and decreased adherence to treatment. These findings emphasize the importance of continuous psychological assessment, the implementation of supportive interventions, and the integration of mental health care into oncological therapies.[3,4] Moreover, aggressive treatment protocols, financial burdens, and changes in physical functioning may lead to anxiety and depression, common psychiatric comorbidities that can severely impact QoL and hinder treatment outcomes.[5,6] Gaining a deeper understanding of the relationship between anxiety, depression, and cancer, along with developing effective interventions, is essential for improving overall patient well-being.

The frequency of anxiety disorders varies depending on cancer type, disease stage, and individual factors. Psychological effects often begin at the time of diagnosis, with over 50% of depression cases identified within the first three months.[7,8]

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Acute stress related to receiving a cancer diagnosis, making rapid treatment decisions, and concerns about disease progression significantly contribute to heightened anxiety levels. Studies show that these psychological effects can persist for years, with some individuals experiencing high anxiety levels even after achieving remission.[7]

Family support and coping strategies play a crucial role in mitigating the psychological effects of cancer. Studies indicate that patients with strong family and social support systems experience lower levels of anxiety and depression compared to those with limited support networks.[10] Positive psychological traits such as hope, optimism, and a sense of control over one's life serve as protective factors against anxiety and depression. However, despite these protective factors, mental health issues often go unrecognized and untreated, underscoring the importance of routine mental health screenings in cancer care.[9] Anxiety in cancer patients affects multiple aspects of life, including QoL, physical function, social relationships, and emotional well-being.[10] Research shows that high anxiety levels lead patients to seek frequent healthcare visits for psychological relief.[11] Anxiety not only diminishes QoL but also complicates adherence to treatment plans, resulting in poorer health outcomes and faster disease progression.[12] Gender, existing health conditions, and cancer stage significantly influence the likelihood of experiencing anxiety and depression.[12,13] Patients undergoing chemotherapy are particularly vulnerable to fear of death, highlighting the need for targeted psychological interventions in this population.[14]

While numerous studies have investigated mental health in oncology populations, most have concentrated on single dimensions or disease-specific cohorts, leaving a critical gap in understanding how sociodemographic, clinical, and economic factors interact to shape psychological outcomes in real-world practice. Thus, to ensure successful oncological management, it is also essential to assess the physiological and quality-of-life status of cancer patients and take appropriate precautions. In this current study, the aim was aimed to evaluate the prevalence of anxiety and depression among cancer patients and examine their association with QoL.

METHODS

Ethical approval for this research was obtained from the Scientific Researches Ethics Committee of Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital (Date: 17.04.2024, Decision No: 2024/127). The study was conducted in accordance with the principles of the Declaration of Helsinki (2013 revision) and institutional research ethics standards.

This descriptive, cross-sectional study was conducted at the Oncology Clinic of Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital, İstanbul, Turkiye, between May 2024 and December 2024. The study population consisted of cancer patients who were actively receiving treatment during the specified period and met the predefined inclusion criteria.

Written informed consent was obtained from all participants before enrollment. Patient confidentiality and data security were strictly maintained through anonymization and limited access to collected data.

In this study, the Beck Depression Inventory (BDI) and the Beck Anxiety Inventory (BAI) scores were evaluated using binary classification rather than the commonly used multilevel categorization. Specifically, scores of 17 or above on the BDI were considered "clinically significant depression," and scores of 16 or above on the BAI were considered "high anxiety." This approach was chosen to facilitate statistical analyses (e.g., group comparisons) and to focus on the clinically relevant risk group.

Participants

Initially, 750 patients were screened for eligibility. After excluding individuals with incomplete questionnaire data, missing clinical information, or failure to meet inclusion criteria, 703 patients were included in the final analysis. Eligibility criteria included age ≥18 years and a histologically confirmed cancer diagnosis. Patients undergoing active cancer treatment or under routine oncological follow-up were eligible to participate. Exclusion criteria comprised intellectual disability, severe psychopathology (e.g., psychotic disorders, bipolar disorder), and neurological or cognitive impairments that could interfere with questionnaire completion. The participant selection process is summarized in **Figure**.

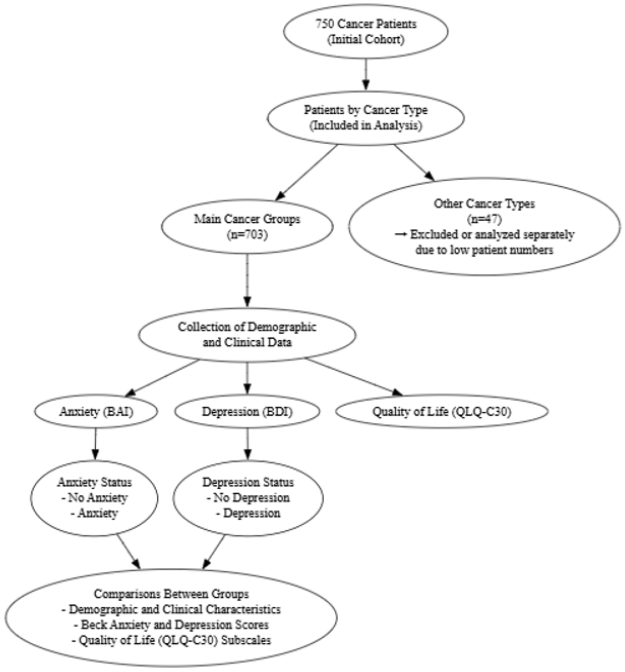

Figure. Flowchart of the study: analysis of anxiety, depression, and quality of life in cancer patients

Data Collection

Data were collected through face-to-face interviews conducted by trained healthcare professionals. A structured information form was developed to gather sociodemographic and clinical characteristics. Participants completed validated questionnaires assessing demographic information, clinical history, and psychological well-being. All data were collected in Turkish to ensure participants could fully understand and

accurately respond to the questionnaires. The BDI, BAI, and EORTC QLQ-C30 scales used in the study have validated and reliable Turkish versions.

Measurement Tools

- **Beck Depression Inventory (BDI):** This 21-item scale evaluates depressive symptoms, with each item scored from 0 to 3. A score above 17 was considered indicative of clinically significant depression.
- **Beck Anxiety Inventory (BAI):** This 21-item scale assessed anxiety levels, with each item scored from 0 to 3. Scores above 16 indicated high anxiety levels.
- **EORTC QLQ-C30:** The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (QLQ-C30), a 30-item tool designed for cancer patients, assessed the QoL across multiple domains, including functional status and symptom burden.

Statistical Analysis

The data analyses were conducted using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was evaluated using both the Shapiro-Wilk and Kolmogorov-Smirnov tests. A variable was considered normally distributed only if both tests yielded p-values >0.05. Normally distributed continuous variables were expressed as means±standard deviations (SD), while non-normally distributed variables were presented as medians with interquartile ranges (IQR). Categorical variables were summarized using frequencies and percentages.

For comparisons of continuous variables between two groups, the Independent Samples t-test was used for normally distributed variables, while the Mann-Whitney U Test was applied for variables that did not follow a normal distribution. The relationships between demographic/clinical variables and anxiety and depression scores were evaluated using Spearman's rank correlation coefficient. Chi-square tests were applied to examine associations between categorical variables. A p-value <0.05 was considered statistically significant.

Statistical Power Analysis

A post-hoc power analysis was conducted using G*power (version 3.1.9.7) to evaluate the statistical power of the study based on the actual sample sizes of the comparison groups: no anxiety (n=376) vs. anxiety (n=327), no depression (n=405) vs. depression (n=298), no anxiety and depression (n=450) vs. anxiety and depression (n=253).

As the data did not meet the assumptions for parametric testing, the group comparisons in the study were conducted using the non-parametric Mann–Whitney U test. However, since G*power does not directly support power analysis for this test, a two-tailed Independent Samples t-test was used as a reasonable approximation, which is an accepted practice in the literature for large samples. The analysis was conducted assuming a medium effect size (Cohen's d=0.50) and a significance level of α=0.05. The calculated post-hoc statistical power for all group comparisons was approximately 99% (0.99), indicating a very high likelihood of detecting clinically meaningful differences between the groups.

RESULTS

Table 1 presents the demographic and clinical characteristics of the study participants (n=703). The mean age was 59.46±12.39 years, and two-thirds of the sample consisted of females (66%). Most participants had completed primary (52.6%) or high school education (32.3%), while a smaller proportion were illiterate (9.1%) or university graduates (6.0%). The majority were married (78.4%) and lived with their spouse and children (68.6%), while 11.8% were widowed, 7.1% were single, and 2.7% were divorced. A large proportion were unemployed (84.9%) and non-smokers (77.4%). Clinically, breast (42.2%) and gastrointestinal cancers (30.6%) were the most common diagnoses, followed by prostate (12.1%), gynecological (8.1%), and lung cancers (7.0%). Nearly half of the participants (47.4%) had metastatic disease, and 39% reported at least one comorbidity.

Table 1. Demographic and clinical characteristics of participants (n=703)

Variable	Category	Frequency (n)	Percent (%)/ mean±SD
Demographic characteristics			
Age (years)			59.46±12.39
Gender	Female	464	66
	Male	239	34
Education level	Illiterate	64	9.1
	Primary school	370	52.6
	High school	227	32.3
	University	42	6.0
Marital status	Single	50	7.1
	Married	551	78.4
	Widowed	83	11.8
	Divorced	19	2.7
Living arrangement	Parents	39	5.5
	Spouse	93	13.2
	Spouse and children	482	68.6
	Other	89	12.7
Employment status	Unemployed	597	84.9
	Employed	106	15.1
Smoking status			
	Nonsmoker	544	77.4
	Smoker	159	22.6
Clinical characteristics			
Cancer diagnosis	Lung	49	7.0
	Gynecological	57	8.1
	Gastrointestinal	215	30.6
	Breast	297	42.2
	Prostate	85	12.1
Metastasis status		333	47.4
Comorbidities		274	39

SD: Standard deviation

Table 2 summarizes the distribution of anxiety, depression, and quality-of-life (QoL) scores among participants. The median BAI score was 14 [6-24], with 46.5% meeting the criteria for anxiety. The median BDI score was 13 [5-24], and 42.4% of participants met the threshold for depression; 36% had both anxiety and depression. Regarding QoL (EORTC QLQ-C30), role function showed the highest median score (100 [66.6-100]), followed by cognitive (83.3 [66.6-100]) and social function (83.3 [66.6–100]). Emotional function (83.3 [58.3-91.6]) and physical function (73.3 [53.3-80.0]) were comparatively lower, and the median Global Health/QoL score was 66.6 [50.0-83.3]. Overall, the emotional and physical domains appeared to be most affected, indicating reduced well-being despite preserved functional performance.

Table 2. Beck Anxiety and Depression Inventory Scores and QLQ-C30 quality of life subscales

		Participants (n=703)
Beck Anxiety Inventory (BAI) scoring		14 (6-24)[a]
Anxiety level	No anxiety	376 (53.5%)
	Anxiety	327 (46.5%)
Beck Depression Inventory (BDI) scoring		13 (5-24)[a]
Depression level	No depression	405 (57.6%)
	Depression	298 (42.4%)
Anxiety+depression		253 (36%)
QLQ-C30 subscales		
	Physical function	73.3 (53.3-80.0)[a]
	Emotional function	83.3 (58.3-91.6)[a]
	Role function	100 (66.6-100)[a]
	Cognitive function	83.3 (66.6-100)[a]
	Social function	83.3 (66.6-100)[a]
	General health/QoL	66.6 (50.0-83.3)[a]

QLQ-C30: Cancer Quality of Life Questionnaire, QoL: Quality of life, a: Median (interquartile range)

Table 3 summarizes the correlations between BAI and BDI scores and quality-of-life domains measured by the EORTC QLQ-C30. There was a statistically significant negative correlation between higher BAI scores and emotional, cognitive, and social functioning (p<0.001, p=0.001, p=0.004). There was a negative correlation between BAI scores and physical functioning, Global Health/QoL, and overall functioning; however, these associations did not reach statistical significance (p>0.05) (Table 3). A significant negative correlation was found between BDI scores and emotional functioning (p<0.001). No significant correlations were found between BDI scores and the physical, role, cognitive, social, or Global QoL subscales (p>0.05). These findings emphasize that emotional well-being is the QoL domain most consistently affected by psychological distress in this population (Table 3).

Table 4 presents statistically significant differences in demographic and clinical characteristics among participants based on anxiety, depression, and comorbid anxiety-depression status (n=703). Individuals with anxiety were significantly more likely to be female, to live in "other" living arrangements, and to have a gynecological cancer diagnosis compared to those without anxiety (p=0.002, p=0.034, and p=0.028, respectively). In contrast, no statistically significant

Table 3. Correlations between Beck Anxiety/Depression scores and quality of life measures (QLQ-C30)

	Beck Anxiety Inventory (BAI) scoring		Beck Depression Inventory (BDI) scoring	
	r	p [a]	r	p [a]
QLQ-C30 subscales				
Physical function	-0.074	0.050	-0.005	0.904
Emotional function	-0.150	<0.001*	-0.131	<0.001*
Role function	-0.030	0.435	0.015	0.701
Cognitive function	-0.128	0.001*	-0.068	0.071
Social function	-0.107	0.004*	-0.040	0.289
General health/QoL	-0.072	0.056	-0.034	0.364

r: Spearman's rank correlation coefficient, a: Spearman's Correlation. *: Statistical significance (p<0.05)

demographic or clinical differences were observed between participants with and without depression (p>0.05). When examining comorbid anxiety and depression, those with both conditions were also more likely to be female, widowed, and to live in "other" living arrangements compared to those without either condition (p=0.031, p=0.048, and p=0.041, respectively). These findings suggest that female gender, limited or nontraditional living situations, and widowhood may be associated with a higher likelihood of experiencing anxiety or comorbid anxiety and depression among cancer patients. In contrast, depression alone did not show significant demographic or clinical associations.

Table 4. Statistically significant demographic and clinical differences by anxiety, depression, and comorbid anxiety-depression status (n=703)

Variable	Category	No anxiety (n=376)	Anxiety (n=327)	p
Gender				0.002 [a,*]
	Female	229 (60.9%)	235 (71.9%)	
	Male	147 (39.1%)	92 (28.1%)	
Living arrangement				0.034 [a,*]
	Other	38 (10.1%)	51 (15.6%)	
Cancer diagnosis				0.028 [a,*]
	Gynecological	20 (5.3%)	37 (11.3%)	

According to the depression status (BDI), no statistically significant differences in demographic or clinical characteristics were found between groups (p>0.05).

Variable	Category	No anxiety and depression (n=450)	Anxiety and depression (n=253)	p
Gender				0.031[a,*]
	Female	284 (63.1%)	180 (71.1%)	
	Male	166 (36.9%)	73 (28.9%)	
Marital status				
	Married	363 (80.7%)	188 (74.3%)	0.049[a,*]
	Widowed	45 (10.0%)	38 (15.0%)	0.048[a,*]
Living arrangement				0.041[a,*]
	Other	45 (10.0%)	44 (17.4%)	

a: Chi-square test. *: Statistical significance (p<0.05)

Table 5 compares depressive symptom severity (BDI) and quality-of-life (QLQ-C30) domains between participants with and without anxiety. Participants with anxiety had

significantly higher BDI scores and lower emotional and cognitive function scores than those without anxiety (p<0.001, p<0.001, p=0.003). Differences in physical, role, social, and Global QoL were not statistically significant (all p>0.05). These results highlight the close interrelationship between anxiety and emotional-cognitive dimensions of well-being.

Table 5. Comparison of depression severity and quality of life according to anxiety status among participants (n=703)

Variable	No anxiety (n=376)	Anxiety (n=327)	p
Beck Depression Inventory (BDI) scoring	6 (3-11) [a]	24 (17-31)[a]	<0.001[b,*]
QLQ-C30 subscales			
Physical function	73.3 (53.3-80.0)[a]	66.6 (46.6-80.0)[a]	0.087[b]
Emotional function	83.3 (66.6-100)[a]	75 (50.0-91.6)[a]	<0.001[b,*]
Role function	100 (66.6-100)[a]	100 (66.6-100)[a]	0.337[b]
Cognitive function	83.3 (66.6-100)[a,ł]	83.3 (66.6-100)[a]	0.003[b,*]
Social function	83.3 (66.6-100)[a]	83.3 (50.0-100)[a]	0.054[b]
General health/QoL	66.6 (50.0-83.3)[a]	58.3 (41.6-83.3)[a]	0.081[b]

QLQ-C30: Cancer Quality of Life Questionnaire, QoL: Quality of life, a: Median (interquartile range), b: Mann-Whitney U test. ł: Indicates the significant difference. *: Statistical significance (p<0.05).

Table 6 compares anxiety symptom severity (BAI) and quality-of-life (QLQ-C30) domains between participants with and without depression. Participants with depression had significantly higher BAI scores and lower emotional function scores than those without depression (p<0.001, p=0.026). Differences in physical, role, cognitive, social, and Global QoL were not statistically significant (all p>0.05).

Table 6. Comparison of anxiety severity and quality of life according to depression status among participants (n=703)

Variable	No depression (n=405)	Depression (n=298)	p
Beck Anxiety Inventory (BAI) scoring	8 (4-13)[a]	25 (19-31)[a]	<0.001[b,*]
QLQ-C30 subscales			
Physical function	73.3 (46.6-80.0)[a]	70 (53.3-86.6)[a]	0.533[b]
Emotional function	83.3 (66.6-91.6)[a]	75 (50.0-91.6)[a]	0.026[b,*]
Role function	100 (66.6-100)[a]	100 (66.6-100)[a]	0.435[b]
Cognitive function	83.3 (66.6-100)[a]	83.3 (66.6-100)[a]	0.265[b]
Social function	83.3 (66.6-100)[a]	83.3 (66.6-100)[a]	0.886[b]
General health/QoL	66.6 (50.0-83.3)[a]	58.3 (41.6-83.3)[a]	0.488[b]

QLQ-C30: Cancer Quality of Life Questionnaire, QoL: Quality of life, a: Median (interquartile range), b: Mann-Whitney U test. *: Statistical significance (p<0.05).

Table 7 summarizes psychometric and quality-of-life outcomes, comparing participants with comorbid anxiety and depression to those without either condition. The comorbid group had significantly higher BAI and BDI scores (p<0.001 for both), indicating substantial overlap between anxiety and depressive symptoms. Consistent with earlier findings, only the emotional function subscale of the QLQ-C30 showed a significant difference between groups, with lower median scores in the comorbid group compared to the non-comorbid group (p=0.027). Physical, role, cognitive, social, and Global QoL domains showed no significant group differences (all p>0.05).

Table 7. Comparison of psychometric scores and quality of life according to comorbid anxiety and depression status among participants (n=703)

Variable	No anxiety and depression (n=450)	Anxiety and depression (n=253)	p
Beck Anxiety Inventory (BAI) scoring	9 (4-14)[a]	27 (22-33.50)[a]	<0.001[b,*]
Beck Depression Inventory (BDI) scoring	7 (3-13)[a]	27 (22-32)[a]	<0.001[b,*]
QLQ-C30 subscales			
Physical function	73.3 (51.6-80.0)[a]	66.6 (53.3-83.3)[a]	0.863[b]
Emotional function	83.3 (66.6-91.6)[a]	75 (50.0-91.6)[a]	0.027[b,*]
Role function	100 (66.6-100)[a]	100 (66.6-100)[a]	0.574[b]
Cognitive function	83.3 (66.6-100)[a]	83.3 (66.6-100)[a]	0.113[b]
Social function	83.3 (66.6-100)[a]	83.3 (66.6-100)[a]	0.873[b]
General health/QoL	66.6 (50.0-83.3)[a]	58.3 (41.6-83.3)[a]	0.322[b]

QLQ-C30: Cancer Quality of Life Questionnaire, QoL: Quality of life, a: Median (interquartile range), b: Mann-Whitney U test. *: Statistical significance (p<0.05).

DISCUSSION

In this large cohort of cancer patients, we found high prevalence rates of anxiety (46.5%) and depression (42.4%), both showing significant associations with sociodemographic factors and QoL. These results align with prior meta-analyses demonstrating that psychiatric disorders are highly prevalent in oncology and frequently undertreated.[15] Our prevalence estimates are consistent with previous meta-analyses reporting that 30-40% of cancer patients experience depression or anxiety, depending on the assessment method.[1] Importantly, these conditions are not only common but also prognostically relevant, as both anxiety and depression have been linked to increased recurrence, mortality, and reduced survival.[16]

Female sex was significantly associated with anxiety, as reported in earlier studies.[16] Widowed patients and those living without stable family support also experienced higher distress levels, supporting the protective effect of social connectedness and marital stability.[17] Financial strain and unemployment—frequent in our cohort—further contributed to psychological distress, consistent with previous research on financial toxicity.[18]

Comorbidity between anxiety and depression was common, with patients exhibiting elevated scores in both domains. This overlap magnifies psychological burden and complicates management.[19] Anxiety was associated with poorer QoL across emotional, cognitive, and social domains, whereas depression primarily affected emotional well-being. Prior studies similarly demonstrated that anxiety predicts multidimensional QoL impairment, while depression mainly influences emotional health.[20] Although many participants reported relatively preserved role and cognitive functioning, emotional and global QoL scores were significantly lower among those with psychological distress. Emotional functioning emerged as the most consistently affected domain across anxiety, depression, and comorbid states, in agreement with earlier longitudinal data.[21] Fear of recurrence, particularly among breast cancer patients, remains a significant source of distress.[22] Conversely,

optimism and resilience appear to mitigate the impact of psychological symptoms on QoL.[23]

The clinical consequences of unrecognized or untreated distress are substantial. Depression and anxiety reduce QoL, impair adherence, increase the risk of treatment discontinuation, and may worsen overall survival.[24] Continued smoking has been linked to higher complication rates and poorer prognosis, whereas cessation improves fatigue and QoL.[25] These findings emphasize the importance of comprehensive supportive care. In accordance with current ASCO and NCCN guidelines, routine screening for distress and integration of psychosocial support into standard cancer care are strongly recommended.[26] Our findings reinforce these recommendations, highlighting that psychological morbidity is widespread and not limited to easily identifiable high-risk subgroups.

Limitations

The strengths of this study include its large sample size, systematic evaluation of both anxiety and depression using validated instruments, and domain-specific QoL analysis. Unlike previous studies that evaluated psychological distress or QoL separately, this research provides an integrated assessment of anxiety, depression, and multiple QoL domains in a large oncology cohort. Furthermore, it offers real-world data from a public hospital setting, reflecting the psychosocial burden of cancer patients in routine clinical practice. These findings help clinicians identify high-risk patients earlier and implement targeted psychosocial interventions to improve treatment adherence and overall well-being. Limitations include the cross-sectional design, which prevents causal inference, and the absence of direct measures of coping style, optimism, or resilience—factors shown to shape psychological outcomes in cancer. Future longitudinal studies incorporating these variables could refine predictive models and inform the development of tailored interventions.

CONCLUSION

Anxiety and depression are highly prevalent in cancer patients and strongly associated with impaired QoL, particularly emotional functioning. Female sex, widowhood, and reduced social support emerged as key risk factors, whereas clinical variables such as cancer type, metastasis, and comorbidities showed limited associations. Anxiety exerts a broader impact across multiple QoL domains, while depression is more selectively tied to emotional well-being. Patients with comorbid anxiety and depression represent a particularly vulnerable subgroup. These findings reinforce the need for universal distress screening and integrated psychosocial interventions as essential components of comprehensive cancer care.

ETHICAL DECLARATIONS

Ethics Committee Approval

Ethical approval for this research was obtained from the Scientific Researches Ethics Committee of Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital (Date: 17.04.2024, Decision No: 2024/127).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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