Quality of life, distress, anxiety and depression of ambulatory cancer patients receiving chemotherapy

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Abstract

Objective and aim. Cancer and its treatment have substantial physical and psychological consequences that severely affect the patients' quality of life (QoL) and emotional status. This study aimed to investigate the relationship between distress, anxiety, depression, and QoL of ambulatory cancer patients undergoing chemotherapy.

Methods. A descriptive, cross-sectional study of 150 cancer patients who were receiving chemotherapy in the outpatient unit of a central anticancer hospital in Athens. The data were collected through convenience sampling between November 2017 and January 2018, using a demographic and clinical characteristics questionnaire, the Distress Thermometer (DT) and Problem List (PL), the Hospital Anxiety and Depression Scale (HADS) and the European Organization for Research and Treatment for Cancer QoL assessment Questionnaire (EORTC QLQ-C30).

Results. Variability characterized the sample's demographic and clinical characteristics. The majority of patients were women (64%), married (66%), high school graduates (43%), had breast cancer (35%), with a mean age of 60.07 ± 11.42. 83% reported anxiety, 75% reported fear, 51% nervousness and sadness, 34% depression and 84.7% fatigue. The DT was positively correlated with HADS (p<0.001) and with almost all EORTC QLQ-C30 functional subscales and symptoms (p<0.001). The HADS-Anxiety was significantly correlated with overall QoL and with almost all the EORTC QLQ-C30 functional scales and symptoms (p<0.001). HADS-Depression was significantly correlated with overall QoL and all the EORTC QLQ-C30 functional scales and symptoms (p<0.001). Women tended to have higher level of distress (p=0.003). There was a statistically significant relationship between educational level, the cognitive functioning scale (p=0.017) and financial difficulties (p=0.026).

Conclusions. Ambulatory cancer patients undergoing chemotherapy are at risk of facing distress in all aspects of daily living, along with anxiety and depression, which decreases their QoL. Oncology nurses as members of multidisciplinary teams should assess the affected aspects of patients' QoL and appropriate interventions should be implemented at community level.

Keywords: anxiety, cancer patient, chemotherapy, depression, quality of life

Introduction

Cancer is a major public health problem worldwide [1], with the number of survivors continuing to increase due to advances in early diagnosis and treatment, and due to aging and population growth [2]. Cancer is a disease that includes different therapeutic approaches such as surgery, radiotherapy and chemotherapy, which in combination with the disease burden can contribute to the development of mental health problems. The prevalence and severity of mental disorders and distress vary and are influenced by social and demographic factors as well as factors related to the disease and its treatment [3]. Chemotherapy has been one of the most important cancer treatments due to the use of combined treatment regimens, different dosages and methods of administration and due to toxic chemotherapeutic agents, which are often used to improve the results. At the same time, a large number of chemotherapy-induced symptoms decrease the patients' quality of life (QoL), therefore the impact of chemotherapy on the quality of life should be taken into account in the care of such patients [4].

Cancer patients at time of diagnosis and commencement of chemotherapy experience high levels of anxiety and depression [5]. The most common symptoms experienced along the therapy trajectory are fatigue, sleep disorders, nausea, vomiting, diarrhea, weakness, cognitive deficits, withdrawal from the usual daily activities and roles and worsening QoL [6,7]. Given the negative consequences that these problems can induce, it is important to asses any signs of psychological distress in cancer patients at time of diagnosis, in order to receive due attention and appropriate treatment [5].

Cancer-related distress is "an unpleasant experience of psychological (cognitive, behavioral, emotional), physical, social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms, and its treatment" [8]. The term distress was chosen for its lack of associated psychological implications and ability to be defined and measured and, moreover, it is believed to be more acceptable and understood by oncology patients [9]. Distress in cancer patients is multifactorial, impacts their QoL and can occur anywhere along the cancer care trajectory [10,11]. Cancer-related distress is highly prevalent in women, young patients, hospitalized patients, patients who have low income or level of education, poor performance status or prognosis, or practical, family, emotional, or physical problems [11,12]. In addition, research evidence suggests that distress among cancer patients and their families is associated with unmet psychosocial healthcare needs. Also, research shows the effectiveness of interventions to reduce distress and the positive downstream impact on patients, families, cancer outcomes and the healthcare system when distress is properly addressed [9].

On the other hand, anxiety is defined by the ICD-10 diagnostic criteria as "a period of at least six months with prominent tension, worry, and feelings of apprehension, about every-day events and problems" [13]. The DSM-V diagnostic criteria also defines it as an "Excessive anxiety and worry (apprehensive expectation), occurring for not less than 6 months, about a number of events or activities (such as work or school performance)" [14]. Cancer patients' level of anxiety is related to various factors, such as the timing of the diagnosis of cancer, the history of the disease, the treatments, etc. For example, at diagnosis anxiety increases, it decreases over time with adaptation to the disease, but later as the disease progresses it may increase again. Thus, it is difficult to apply the anxiety definitions in cancer clinical practice [15]. Therefore, regular screening and clinical evaluation of cancer patients is essential [16].

Depression is a mood disorder characterized by persistent feelings of sadness, hopelessness and a loss of interest in previously enjoyable activities. The depressed mood must represent a change from the individual's baseline status, resulting in impaired everyday functioning. For a diagnosis of major depressive disorder, the DSM-V requires the presence of a depressed mood or a loss of interest or pleasure in everyday activities for more than two weeks [14]. Overall, depression and anxiety are prevalent among cancer patients, affecting up to 20% and 10% of cancer patients respectively [17]. Depression and anxiety as assessed by diagnostic criteria and symptom scales are associated with cancer incidence, cancer's specific mortality, and cancer survival [18]. Moreover, poor recognition of both depression and anxiety is associated with reduced quality of life and overall survival [15]. Also, anxiety and depression in cancer patients are underdiagnosed and patients receive little support to address their psychosocial needs [16]. Depression as a clinical entity, also prolongs hospital stay, decreases tolerance to chemotherapy and deteriorates QoL. Though anxiety and depression are different clinical entities, they are generally referred to as psychological distress [19].

It is obvious that the existence of distress, anxiety or depression severely impacts cancer patients' QoL. Health related QoL is related to patients' perceptions regarding their physical, emotional, social and mental functions [20] and expresses patients' perceptions about their life, at any given time in the course of the disease [21]. The QoL of cancer patients undergoing chemotherapy is much worse than the general population's. QoL in patients on chemotherapy is decreased as a result of treatment-induced changes including physical, psychological and cognitive changes [22]. Improving the quality of provided care presupposes that healthcare professionals will seriously take into account the patient's perspective of QoL [23]. Nurses, through their interaction with ambulatory cancer patients undergoing chemotherapy,

are in a unique position to identify patients at risk for psychological distress, to refer them to specialist care and act timely to help them along with other members of the interdisciplinary team. The ability of nurses to help cancer patients understand, deal with and manage the changes that cancer and its treatment bring at every stage of their lives significantly affects their QoL [24,25].

Worldwide, many studies assess psychological distress in general, anxiety, depression and cancer patients' QoL combined or separately. However, it is of major importance to conduct studies in different populations and cultures, in order to assess psychological distress and QoL of cancer patients. Culture encompasses ideas, customs, social behavior, attitudes and characteristics of a particular social group and influences peoples' cancer beliefs. These beliefs are also affected by other economic, social, and health-related determinants, shaping their expression and kinds of needs, problems and symptoms [26]. It is obvious that cancer patients' diverse cultural attributes certainly affect their behavior and reports [27]. In Greece, there are few studies assessing the combination of QoL, distress, anxiety and depression in ambulatory cancer patients undergoing chemotherapy [28-30].

Thus, the aim of this study was to investigate the relationship between distress, anxiety, depression, and QoL experienced by Greek ambulatory cancer patients undergoing chemotherapy and to explore the factors affecting them.

Materials and methods
Research design
We carried out a descriptive, cross-sectional study using a convenience sample, and were guided by the following research questions:

a) What is the perceived level of distress, anxiety, depression and QoL reported by ambulatory cancer patients undergoing chemotherapy?

b) Are there any important correlations between QoL, distress, anxiety and depression?

c) Are there any correlations between QoL, distress, anxiety and depression and patients' demographic and clinical characteristics?

Study sample
The convenient study sample consisted of 150 ambulatory cancer patients undergoing chemotherapy at the chemotherapy day unit of a central anticancer hospital in Athens, as outpatients, during a period of 3 months. Inclusion criteria were as follows: having a diagnosis of cancer, being currently under chemotherapy treatment (after completion of second chemotherapeutic cycle) and having the ability to speak and understand the Greek language. Exclusion criteria were: undergoing targeted therapy or immunotherapy and having brain metastasis which could affect the reliability of patients' answers.

Of the 200 patients who met the inclusion criteria, 150 agreed to participate in the study (response rate 75%). The most common reason for refusal to participate was lack of interest and time.

Data collection
The set of self-administered questionnaires included the patients' demographic and clinical characteristics, the Distress Thermometer (DT) and list of symptoms (Problem list, PL) by the National Comprehensive Cancer Network (NCCN), the Hospital Anxiety and Depression Scale (HADS) and the European Organization for Research and Treatment for Cancer quality of life assessment questionnaire (EORTC QLQ-C30). Estimated time for questionnaire completion was 15-20 min. The data were collected by the principal researcher before patients' chemotherapy sessions, after receiving written consent. Patients completed the self-administered questionnaires themselves, unless help was needed by the main researcher. Clinical data were then compared with the patients' medical records.

NCCN Distress Thermometer and Problem List for Patient Version 2.2013 [31]

The DT is a single-item, self-report measure of psychological distress. The DT has an 11-point range with endpoints labeled "no distress" (0) and "extreme distress" (10). Patients have to choose the number (0 –10) that best describes how distressed they have been in the past week. A score of 5 or greater on the DT should trigger further evaluation and referral to a psychosocial service.

The PL consists of 34 problems commonly experienced by cancer patients. There are five categories (practical problems, family problems, emotional problems, spiritual/religious concerns, and physical problems). Patients have to indicate whether or not, the items listed have been a problem for them in the past week. In the present study the PL's Cronbach's alpha coefficient was 0.876.

Hospital Anxiety and Depression Scale (HADS)

The HADS is a handy and reliable tool for recognizing anxiety and depression [32]. HADS has been translated into the Greek language and validated for a population of patients with advanced cancer and for general hospital patients [33]. It consists of 14 questions (7 for anxiety assessment and 7 for depression assessment) and is rated on a four-point scale, with possible values of 0–3. A score >11 is considered pathological, scores<7 are considered nonpathological, while scores from 8 to 10 are considered moderate. In this study Cronbach›s alpha coefficient for HADS-Anxiety was 0.803, for depression was 0.882 and HADS-total was 0.902.

European Organization for Research and Treatment for Cancer quality assessment questionnaire (EORTC QLQ-C30)

The instrument assesses health related QoL in

cancer patients [34]. It consists of 30 questions, divided into 5 functional scales (physical, social, emotional, cognitive and role functioning), 3 scales of symptoms (fatigue, pain, and nausea/vomiting) and overall health and QoL scale. The questionnaire also presents 6 single-item scales, dyspnea, insomnia, appetite, constipation, diarrhea and financial difficulties. The score is calculated from 0 to 100. For the functional subscales and overall health and QoL, higher scores mean a better level of functionality and quality of life. For the symptom subscales, a higher score means more severe symptoms. The Cronbach's alpha coefficient for this study was 0.968. The validation of the questionnaire in Greek revealed a valid and reliable tool [35].

Statistical analysis

Initially, a descriptive analysis of the demographics of patients was carried out: for qualitative variables the percentage and frequency were measured, while for quantitative variables the mean values (standard deviations [SD]) were calculated.

Mean or median and dispersion indicators (standard deviation [SD] and interquartile range [IQR]) of scales scores were calculated separately. Finally, a calculation was made of median, IQR and range of values by item.

Appropriate parametric methods (t-test and ANOVA) were used to examine the differences in scores in relation to specific characteristics. Non-parametric Mann–Whitney (for two groups) and Kruskal–Wallis (for three groups) tests, and calculation of Spearman's r_s correlation coefficient were used, as the assumptions of parametric tests (normality of distributions and equality of fluctuations) were not met.

Ethical consideration

The research was carried out after permission had been obtained from the hospital's ethics and research committee. Patients *were informed verbally and in writing* and signed their consent to participate in the study. In addition, protection of the participants' personal data was ensured by anonymous completion of questionnaires and code assignment.

Results

Characteristics of participants

Of the 150 cancer patients recruited, 64% were women, 66% were married, 43.3% was high school graduates, and 40% were retired. The mean age of the patients was 60.07±11.42 years (range 25-89) and the median time from cancer diagnosis was 8 months (IQR=13, range=1-72). Regarding their diagnosis, 34.7% had breast cancer, 18% colorectal cancer, while 18.9% of patients had metastatic cancer; 81.1% of patients had been receiving neoadjuvant/adjuvant chemotherapy and 18.9% of them used antidepressants (Table I).

Table I. Descriptive characteristics of the participants.

		n (%)
Gender	Male	54 (36.0)
	Female	96 (64.0)
Age (mean ± SD) (range)	60.07 ± 11.42 (range 25-89)	
Marital Status	Married	99 (66.0)
	Single	11 (7.3)
	Widowed	18 (12.0)
	Divorced	13 (8.7)
Educational level	Middle school graduate	38 (25.3)
	High School graduate	64 (43.3)
	University graduate	36 (24.0)
	MSc degree	11 (7.3)
Occupation	Unemployed	17 (11.3)
	Public sector employee	16 (10.7)
	Private sector employee	24 (16.0)
	Freelance	3 (2.0)
	Housekeeping	21 (14.0)
	Retired	60 (40.0)
	Farmer	7 (4.7)
	Other	2 (1.3)
Monthly income	none	39 (26.0)
	Up to 500 €	23 (15.3)
	501-1000 €	54 (36.0)
	1001-1500 €	32 (21.3)
	Over 1501 €	2 (1.3)
Cancer type	Breast	52 (34.7)
	Brain	4 (2.7)
	Head and neck	6 (4.0)
	Lung	21 (14.0)
	Prostate	9 (6.0)
	Colorectal	27 (18.0)
	Liver	3 (2.0)
	Other solid tumors	28 (18.7)
Type of therapy	Neoadjuvant/Adjuvant	122 (81.1)
	Palliative	28 (18.9)
Metastasis	Yes	28 (18.9)
	No	122 (81.1)
Time since chemotherapy initiation	<1 month	39 (26.0)
	2-4 months	34 (22.7)
	>4 months	49 (32.7)
	other	28 (18.7)
Antidepressants	Yes	28 (18.9)
	No	122 (81.1)

Descriptive data of variables

Descriptive characteristics of the study scales are presented in the table II.

Regarding the PL items, 82.7% reported anxiety, 74.7% reported fear, 51.3% nervousness and sadness, 34.0% depression and 24.7% loss of interest in performing everyday activities. Other problems that emerged as important for the patients were health insurance / financial issues (30%), fatigue (84.7%) and other physical problems (Table III).

Table II. Descriptive characteristics of the study scales.

Scale	Mean	SD	Median	IQR	Range
DT	4.65	3.12	4.00	5.00	0-10
HADS					
HADS-Anxiety	7.93	4.57	7.00	7.00	0-21
HADS-Depression	6.57	5.42	5.00	8.25	0-21
HADS-Total	14.50	9.17	13.00	13.00	1-42
EORTC QLQ-C30					
Global health status / QoL*					
Global health status	60.72	29.08	66.67	35.42	0-100
Functional scales*					
Physical functioning	64.84	24.07	66.67	28.33	0-100
Role functioning	50.33	31.70	50.00	33.33	0-100
Emotional functioning	65.83	26.63	66.67	33.33	0-100
Cognitive functioning	87.44	22.59	100.00	16.67	0-100
Social functioning	58.55	34.74	66.67	66.65	0-100
Symptom scales / items*					
Fatigue	50.00	28.14	44.44	33.33	0-100
Nausea and vomiting	19.44	28.47	0.00	33.33	0-100
Pain	25.44	29.14	16.67	37.50	0-100
Dyspnea	35.11	31.08	33.33	66.67	0-100
Insomnia	26.44	29.48	33.33	33.33	0-100
Appetite loss	33.11	33.78	33.33	66.67	0-100
Constipation	21.33	28.97	0.00	33.33	0-100
Diarrhea	19.33	30.23	0.00	33.33	0-100
Financial difficulties	23.78	36.71	0.00	33.33	0-100

SD: standard deviation, IQR: interquartile range;

* Use of median (IQR) as representative descriptive measures for specific scales-subscales.

Table III. Descriptive characteristics of PL-NCCN.

	n(%)		n(%)
Practical Problems		**Physical Problems**	
Child care	24 (16.0)	Appearance	44 (29.3)
Housing	30 (20.0)	Bathing/dressing	27 (18.0)
Insurance/financial	45 (30.0)	Breathing	48 (32.0)
Transportation	35 (23.3)	Changes in urination	15 (10.0)
Work/school	32 (21.3)	Constipation	59 (39.3)
Treatment decisions	33 (22.0)	Diarrhea	53 (35.3)
Family Problems		Eating	74 (49.3)
Dealing with children	23 (15.3)	Fatigue	127 (84.7)
Dealing with partner	25 (16.7)	Feeling swollen	34 (22.7)
Ability to have children	9 (6.0)	Fevers	15 (10.0)
Family health issues	12 (8.0)	Getting around	32 (21.3)
Emotional Problems		Indigestion	28 (18.7)
Depression	51 (34.0)	Memory/concentration	12 (8.0)
Fear	112 (74.7)	Mouth sores	15 (10.0)
Nervousness	77 (51.3)	Nausea	62 (41.3)
Sadness	77 (51.3)	Nose dry/congested	18 (12.0)
Worry	124 (82.7)	Pain	47 (31.3)
Loss of interest in usual activities	37 (24.7)	Sexual	32 (21.3)
Spiritual/religious concerns	22 (14.7)	Skin dry/itchy	48 (32.0)
		Sleep	56 (37.3)
		Substance use	2 (1.3)
		Tingling in hands/feet	52 (34.7)

Table IV. Correlations between EORTC QLQ-C30 and DT, HADS-A, HADS-D.

EORTC QLQ-C30	DT	HADS-Anxiety	HADS-Depression
	Correlation coef. (p-value)	Correlation coef. (p-value)	Correlation coef. (p-value)
QOL	-0.742 (<0.001)	-0.628 (<0.001)	-0.731 (<0.001)
PF	-0.576 (<0.001)	-0.437 (<0.001)	-0.705 (<0.001)
RF	-0.561 (<0.001)	-0.423 (<0.001)	-0.603 (<0.001)
EF	-0.583 (<0.001)	-0.660 (<0.001)	-0.757 (<0.001)
CF	-0.492 (<0.001)	-0.414 (<0.001)	-0.464 (<0.001)
SF	-0.627 (<0.001)	-0.605 (<0.001)	-0.685 (<0.001)
F	0.674 (<0.001)	0.536 (<0.001)	0.709 (<0.001)
NV	0.518 (<0.001)	0.514 (<0.001)	0.492 (<0.001)
P	0.524 (<0.001)	0.410 (<0.001)	0.572 (<0.001)
Dys	0.330 (<0.001)	0.332 (<0.001)	0.439 (<0.001)
IN	0.334 (<0.001)	0.353 (<0.001)	0.424 (<0.001)
AL	0.539 (<0.001)	0.505 (<0.001)	0.596 (<0.001)
C	0.063 (0.447)	0.195 (0.017)	0.169 (0.039)
Diar	0.250 (0.002)	0.153 (0.062)	0.227 (0.005)
Fin	0.303 (<0.001)	0.304 (<0.001)	0.287 (<0.001)

QOL: Global quality of life, PF: Physical Functioning, RF: Role Functioning, EF: Emotional Functioning, CF: Cognitive Functioning, SF: Social Functioning, F: Fatigue, NV: Nausea and vomiting, P: Pain, Dys: Dyspnea, IN: Insomnia, AL: Appetite loss, C: Constipation, Diar: Diarrhea, Fin: Financial Problems.

Correlations between distress, anxiety, depression, and quality of life

To investigate the correlation between DT and HADS-Anxiety, HADS-Depression and HADS-total, the Spearman correlation coefficient was used. There was a statistically significant positive correlation between DT and HADS-Anxiety (r_s=0.584, p<0.001). There was also a statistically significant positive and high correlation between DT and HADS-Depression (r_s=0.729, p<0.001) as well as between DT and HADS-total score (r_s=0.730, p<0.001) (Table IV).

The associations between DT, the EORTC QLQ-C30 subscales and HADS were also analyzed**.** DT was significantly correlated with overall QoL, all the EORTC QLQ-C30 functional scales and symptoms (p<0.001), except constipation. Moreover, HADS-Anxiety was significantly correlated with overall QoL, all the EORTC QLQ-C30 functional scales and symptoms (p<0.001), except diarrhea. Finally, HADS-Depression was significantly correlated with overall QoL, all the EORTC QLQ-C30 functional scales and symptoms (p<0.001). So, all three scales appeared to be correlated with each other (Table IV).

Effect of patients' characteristics on distress, anxiety, depression, and quality of life

No correlation was observed between age and HADS-A (r_s=0.004, p=0.957), HADS-D (r_s=0.020, p=0.810) and DT (r_s=-0.053, p=0.523), according to the Spearman correlation coefficient. Similarly, there were no correlations between time since the diagnosis of the disease (in months) and HADS-A (r_s=0.018, p=0.827), HADS-D (r_s=0.060, p=0.468) and DT (r_s=-0.131, p=0.109). Only, women tended to have higher distress measured with the DT compared to men (p=0.003).

Regarding the subscales of EORTC QLQ-C30 and their relationship with the demographic and clinical characteristics, there were no correlations between gender, marital status, educational level and monthly income with most of the EORTC QLQ-C30 subscales (p>0.05).

There was a negative statistically significant relationship between the educational level and the Cognitive functioning scale of the EORTC QLQ-C30 (p=0.017) and financial difficulties (p=0.026), based on the Kruskal-Wallis test. Also, based on the Jonckheere Terpstra test, there was a statistically significant tendency to decrease the median cognitive functioning scores with the increase of the educational level (JT=3159.00, z=-2.024, p=0.035). Moreover, there was a statistically significant tendency to increase financial difficulties median scores with the increase of the educational level (JT=4311.50, z=2.688, p=0.007).

Furthermore, based on the Spearman correlation coefficient**,** correlations were observed between age and role functioning (r_s=-0.177, p=0.031), age and constipation (r_s=0.176, p=0.032), time from cancer diagnosis and cognitive functioning (r_s=0.209, p=0.010) and time from cancer diagnosis and financial difficulties (r_s=-0.176, p=0.031).

Discussion

The purpose of this study was to investigate the relationship between distress, anxiety and depression and QoL of 150 ambulatory cancer patients undergoing chemotherapy in a day unit of a central cancer hospital in Athens.

Perceived level of distress, anxiety, depression and QoL of ambulatory cancer patients during chemotherapy

Based on our findings, HADS-A and HADS-D had a mean value of 7,93 (SD=4.57) and 6,57 (SD=5.42) respectively. Cinkir & Elgoba (2020) assessed the psychological distress with HADS in 182 cancer patients undergoing chemotherapy [36]. Their findings showed that 25.3% (mean=7.87, SD=4.35) and 26.4% (mean=7.95, SD=4.40) had possible clinical levels of anxiety and depression respectively. Similarly, to our patients, most of them had breast (the most), lung and gastrointestinal cancers. The prevalence rates of depression and anxiety might be different in patients with different tumor sites [37]. Researchers have suggested that patients with breast and lung cancers have a high risk of depression [37]. Depression was present in 32.8% of breast cancer patients, while anxiety at 18-33% [38]. The diagnosis of breast cancer and the chemotherapy treatment induce fatigue, depression, anxiety, mood disorders, sleep disorders and sexual problems and deteriorate women's QoL [39]. The results of a study in 436 breast cancer patients using both DT and HADS are in line with our results where the DT score was positively associated with HADS-A, HADS-D and HADS-Total [40]. Also, 152 Greek breast cancer outpatients were depressed at 38.2% and anxious at 32.2% [41]. Moreover, 256 Ethiopian cancer patients were assessed using HADS and were compared with 1664 German cancer patients in the study of Wondie et al. [42]. The Ethiopian study population's anxiety mean value was 7.9 (SD=4.60) and the depression mean 9.3 (SD=5) compared to the German population's anxiety mean value which was 6.8 (SD=4) and the depression mean 5.5 (SD=4.1).

Our results indicated a Global Health Status/QoL of the EORTC-QLQ-C30 mean value of 60.72 (SD=29.08). In a Brazilian study [43] the Global Health Status/QoL had a higher mean value of 71.0 (SD=23.7) in a sample of 107 cancer outpatients undergoing chemotherapy (the majority) and radiotherapy who were evaluated using the HADS and the EORTC-QLQ-C30. Fatigue, insomnia, pain, loss of appetite, anxiety (31.8%, mean=5.7, SD=3.9) and depression (21.5% mean=4.7, SD=3.7) were identified. Anxiety and depression showed a negative correlation with QoL and a positive correlation with physical symptoms. Finally, our scores are lower than the EORTC QLQ-C30 reference values for the Europe Region (mean=75, SD=19.6) [44].

The argument whether chemotherapy treatment induces biochemical changes in the brain, which in turn induce anxiety symptoms and behavior [45], should be taken into account when studying psychological distress. If this is the case, depression and anxiety are predictors of worsening QoL among cancer patients undergoing chemotherapy. However, despite many years of research the effect of anxiety and depression on the QoL of cancer patients undergoing chemotherapy remains unclear [46].

Relationship between QoL, distress, anxiety and depression

The main finding of this study was that patients' overall QoL was negatively related to distress, anxiety and depression levels. Women tended to have higher distress, but no other significant correlations were found between the patients' characteristics and the study scales. The present results are in agreement with earlier studies. Özalp et al. [47], found that overall QoL and most subscales of the EORTC QLQ-C 30 were moderately correlated with the DT and the HADS. Also, gender and the DT were associated with women tending to have higher distress levels. Based on these findings, it could be considered that psychosocial discomfort, anxiety and depression have a negative effect on the QoL of cancer patients. Another study [48] with 655 Brazilian cancer patients undergoing chemotherapy, concluded that emotional symptoms, albeit decreasing over time, remained associated with problem-related distress. Patients with increased level of problem-related distress before treatment initiation tended to have higher HADS scores across the three time points (initiation, middle, last day of treatment) compared to patients with lower distress. Carlson et al. [12] assessed distress levels of 4664 cancer patients in North America. 46% of the patients experienced significant distress, with women experiencing more clinically significant distress than men. Cha et al. [7] from South Korea, evaluated 208 cancer patients referred to a specialized psycho-oncology clinic. They concluded that distress and depression were negatively correlated with patients' QoL. Also, 408 Japanese breast cancer patients' needs were significantly associated with both psychological distress and QoL [49]. Similar results and correlations were also found in previous studies using other measurement scales [50,51]. A Greek study has shown that women are more vulnerable to depression than men, but without a statistically significant difference in relation to anxiety [52], while Zahra et al. suggested that patient's gender is not a factor that influences the appearance of depression [51]. In a longitudinal study, breast cancer patients had psychological distress, anxiety and depression during intermittent periods between adjuvant chemotherapy, which were highest in the third cycle. At the same time, QoL was lowest at the third chemotherapy cycle and highest at the first cycle [53]. Also, high levels of

psychological distress (symptoms of depression and anxiety) were associated with a 41% increased risk of cancer death, while this relationship was not observed among these with low levels of distress [54]. Thus, psychological distress is an important factor that affects cancer related outcomes and patient's QoL.

Relationship between QoL, distress, anxiety and depression and patients' demographic and clinical characteristics

A negative relationship was also found between a patient's educational level and the Cognitive functioning scale of the EORTC QLQ-C30. In general, complaints from cancer patients about impaired cognitive function after chemotherapy are quite common, with older patients at greater risk of cognitive impairment [55]. Cancer-related cognitive deficits may have a dramatic effect on patients' QoL, impact treatment decisions and have been identified as a problem by cancer survivors [56]. Age has been used as an explanation for cognitive dysfunction, however, research suggests both younger and older patients experience chemotherapy-related cognitive impairment [56]. The low cognitive capacity of a person (taking into account education, environment and occupation) prior to chemotherapy could explain the risk of post-chemotherapy decline in processing speed [57]. Nevertheless, there could be many other demographic or clinical features that could affect cognitive function but haven't been studied, such as among others, race, ethnicity, socioeconomic status, menopausal status, stage of disease [56]. Li et al. [58] evaluated cognitive functioning in a longitudinal study. There was a serious decline in cognitive function after the chemotherapy initiation and was followed by a slow improvement after completion of chemotherapy. The decline of cognitive function was significantly associated with the score of QoL at each time point after chemotherapy (P< 0.05). Also, seventy-three women diagnosed with gynecological cancer and undergoing active treatment have been studied in a prospective study [59]. Six months after the end of treatment there was a significant reduction in cognitive functioning and in depression symptoms. So, cancer-related cognitive impairment has been recognized and should be given prompt attention and consideration.

Moreover, in the present study a relationship was found between the educational level of patients and the financial difficulties. Similarly, De Souza et al. reported that a lower educational level was associated with more financial strain and worse patient outcomes [60]. They also reported that patients with lower levels of education were expected to be more vulnerable and have fewer mechanisms to deal with financial difficulties. Another study found that, for cancer survivors under 65, important factors in predicting financial difficulties were, among others, health status and years of education. Interpreting this finding by the fact that individuals of above average levels of education may hold jobs that put them at particular risk for medically related financial problems in this age group, perhaps due to underinsurance or other competing financial burdens (e.g., childcare, etc.) [61]. The financial burden or financial toxicity of cancer and its treatment can be significant and related to loss of income, unpaid health insurance contributions, increased insurance costs, transportation costs, childcare costs [62] and out-of-pocket expenses [63]. Financial toxicity is a side effect of cancer that results from the perceived financial distress an individual may experience during the course of the disease [64]. Financial distress and the intensity of financial problems in cancer survivors have been associated with poorer health-related QoL [62] and with increased risk of adverse psychological effects and particularly severe depression, anxiety, mental pain or despair [65]. A recent systematic review indicated that the experience and reporting of financial distress strongly depends on sociodemographic factors such as family status, working status or educational level and especially on financial status prior to the disease influencing the degree of financial resources used to mitigate the financial burden during the disease [64].

Additionally, a low negative correlation was found between the time from the disease diagnosis and the appearance of financial strain. Apparently, with the progress and termination of intensive treatment and the reduction of supportive care medications, laboratory or imaging tests, the financial costs are reduced. As shown by Pauge et al (2021), financial distress is determined by the time since the onset of the disease and the design of healthcare as well as the social benefit system [64]. Many of the identified risk factors are directly associated with the diagnosis of cancer and/or its treatment, cancer itself elevates the risk of financial distress [64]. In particular, the risk for financial distress is mainly occurring at a shorter (<1 year) and longer time (>5 years) [66]. Based on all the above, financial distress shouldn't be ignored and efforts should be made by healthcare professionals to meet cancer patients' health insurance related, financial and practical needs. There is a need for a consulting and support service at an early stage of the disease by using screening tools for financial distress. The psychosocial approach should be part of cancer treatment, including the detection, monitoring, and treatment of the psychosocial discomfort that accompanies the disease [67].

In addition, we found a correlation between patients' age and role functions as well as a correlation between patients' age and constipation. Jansen et al. found that in cancer survivors <70 years of age, chemotherapy is associated with lower physical and role-cognitive function as well as higher levels of pain, loss of appetite, hair loss and taste-related problems [68]. A study also

found that the impact of cancer on specific areas of QoL varies with age [23]. When comparing cancer patients with the general population, younger patients had worse financial problems, social functionality, and functionality provided through the performance of various roles. Also, among cancer patients, increasing age was associated with a deterioration in QoL in terms of physical function and constipation-related parameters, while improving in terms of social function-related parameters, insomnia and financial problems. Moreover, ovarian cancer patients and those who underwent chemotherapy for gynecological cancer had impaired role functioning in the EORTC-QLQ-C30 [59].

In our study 18.9% of the sample used antidepressants, a similar finding with previous studies (15.5%) [69] and (19%) [70].The relatively limited use of antidepressants warns for better and systematic assessment for mental disorders which should be incorporated in the cancer patients' treatment protocol.

Limitations of this study include its cross-sectional nature which precludes the establishment of direction in the relationships explored as well as the fact that it does not provide causative relationships. Moreover, the study sample from a single hospital as well as the convenience method of sampling where variability exists between patients (differences were existing between type, stage and treatment of cancer) do not allow for the generalization of our findings. Despite the heterogeneity of the sample in terms of cancer type, all participants in this study were regarded as a single sample group and this is another limitation for the generalization of our results. Time restrictions were also present during the study which limited sample size and design method. Finally, the questionnaires used to collect the data have the limitations of all subjective assessments. A longitudinal or a qualitative study might be able to reveal how quality of life is affected by chemotherapy over time, as well as the impact of the chemotherapy on patients' psychological status and the relative factors with more accuracy.

Conclusions

To conclude, distress, anxiety and depression had a negative correlation with the overall QoL of outpatients undergoing chemotherapy. Patients are troubled with a variety of important problems that emerge; emotional problems, financial issues and physical symptoms such as fatigue.

The present study, despite its limitations, has shown important results regarding the factors that affect the level of distress, anxiety, depression and QoL of ambulatory cancer patients undergoing chemotherapy. These findings are of major importance since the present study is one of the very few conducted in the Greek population and may increase nurses' awareness of patients' needs for psychological support during the chemotherapy process. Findings could also assist clinicians to identify higher-risk populations that could benefit from targeted screening and additional psychological and social support.

Despite the constant development and research in cancer care and its consequences for cancer patients' physical, mental health and overall QoL, the deeper understanding of their experience and distress is still under much consideration for healthcare professionals. Future studies could perform longitudinal designs and include many cancer centers, applying interventions to improve QoL and well-being of cancer patients in the community. The continuous investigation of the changing needs of this specific group of patients will contribute to their successful meeting. Systematic evaluation of ambulatory cancer patients' emotional status and QoL throughout their disease trajectory should be an important priority of tertiary prevention in the community for the timely identification and care of those at risk.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics. CA Cancer J Clin. 2018;68:7–30.

2. Miller KD, Siegel RL, Lin CC, Mariotto AB, Kramer JL, Rowland JH, et al. Cancer treatment and survivorship statistics. CA Cancer J Clin. 2016;66:271–289.

3. McMullen M, Lau PKH, Taylor S, McTigue J, Cook A, Bamblett M, et al. Factors associated with psychological distress amongst outpatient chemotherapy patients: An analysis of depression, anxiety and stress using the DASS-21. Appl Nurs Res. 2018;40:45–50.

4. Temiz G, Durna Z. Evaluation of Quality of Life and Health Care Needs in Cancer Patients Receiving Chemotherapy. J Cancer Educ. 2020;35:796-807.

5. Cook SA, Salmon P, Hayes G, Byrne A, Fisher PL. Predictors of emotional distress a year or more after diagnosis of cancer: A systematic review of the literature. Psychooncology. 2018;27:791-801.

6. Jim HS, Small B, Faul LA, Franzen J, Apte S, Jacobsen PB. Fatigue, depression, sleep, and activity during chemotherapy: daily and intraday variation and relationships among symptom changes. Ann Behav Med. 2011;42:321–333.

7. Cha KM, Chung YK, Lim KY, Noh JS, Chun M, Hyun SY, et al. Depression and insomnia as mediators of the relationship between distress and quality of life in cancer patients. J Affect Disord. 2017;217:260–265.

8. NCCN. Distress during cancer care. NCCN Guidelines for Patients, National Comprehensive Cancer Network. 2020. Available from https://www.nccn.org/patients/guidelines/content/PDF/distress-patient.pdf .

9. Ehlers SL, Davis K, Bluethmann SM, Quintiliani LM, Kendall J, Ratwani RM, et al. Screening for psychosocial distress among patients with cancer: implications for clinical practice, healthcare policy, and dissemination to enhance cancer survivorship. Trans Behav Med. 2019;9:282-291.

10. Mitchell AJ. Screening for cancer-related distress: when is implementation successful and when is it unsuccessful? Acta Oncol. 2013;52:216-224.

11. Cormio C, Caporale F, Spatuzzi R, Lagattolla F, Lisi A, Graziano G. Psychosocial distress in oncology: using the distress thermometer for assessing risk classes. Support Care Cancer. 2019;27:4115-4121.

12. Carlson LE, Zelinski EL, Toivonen KI, Sundstrom L, Jobin CT, Damaskos P, et al. Prevalence of psychosocial distress in cancer patients across 55 North American cancer centers. J Psychosoc Oncol. 2019;37:5-21.

13. World Health Organization. The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research (Vol. 2). Geneva: WHO; 1993.

14. Diagnostic and statistical manual of mental disorders. 5th edition, 2013. Am Psychiatric Assoc, 2013.

15. Pitman A, Suleman S, Hyde N, Hodgkiss A. Depression and anxiety in patients with cancer. BMJ. 2018;361:k1415.

16. Milligan F, Martinez F, Aal SHMA, Ahmed SA, Joby B, Matalam JS, et al. Assessing anxiety and depression in cancer patients. Br J Nurs. 2018;27:S18–S23.

17. Mitchell AJ, Chan M, Bhatti H, Halton M, Grassi L, Johansen C, et al. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. Lancet Oncol. 2011;12:160–174.

18. Wang YH, Li JQ, Shi JF, Que JY, Liu JJ, Lappin JM, et al. Depression and anxiety in relation to cancer incidence and mortality: a systematic review and meta-analysis of cohort studies. Mol Psychiatry. 2020;25:1487-1499.

19. Diaz-Frutos D, Baca-Garcia E, García-Foncillas J, López-Castroman J. Predictors of psychological distress in advanced cancer patients under palliative treatments. Eur J Cancer Care (Engl). 2016;25:608-615.

20. Husson O, Mols F, van de Poll-Franse LV. The relation between information provision and health-related quality of life, anxiety and depression among cancer survivors: a systematic review. Ann Oncol. 2011;22:761–772.

21. Adamakidou T, Kalokerinou A. Quality of life and cancer patient. Balkan Military Medical Review. 2011;14:289-303.

22. Charalambous A, Kaite CP, Charalambous M, Tistsi T, Kouta C. The effects on anxiety and quality of life of breast cancer patients following completion of the first cycle of chemotherapy. SAGE Open Med. 2017;5:2050312117717507.

23. Quinten C, Coens C, Ghislain I, Zikos E, Sprangers MA, Ringash J, et al. The effects of age on health-related quality of life in cancer populations: A pooled analysis of randomized controlled trials using the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 involving 6024 cancer patients. Eur J Cancer. 2015;51:2808-2819.

24. Tuominen L, Stolt M, Meretoja R, Leino-Kilpi H. Effectiveness of nursing interventions among patients with cancer: an overview of systematic reviews. J Clin Nurs. 2019;28:2401-2419.

25. Hong YU, Zhang M. Personalized Interventions for More Effective Nursing Care. Journal of International Translational Medicine. 2019;7:103-104.

26. Dein S. Explanatory models of and attitudes towards cancer in different cultures. Lancet Oncol. 2004;5:119-124.

27. Guidry JJ, Torrence W, Herbelin S. Closing the divide: diverse populations and cancer survivorship. Cancer. 2005;104(11 Suppl):2577-2583.

28. Iconomou G, Iconomou AV, Argyriou AA, Nikolopoulos A, Ifanti AA, Kalofonos HP. Emotional distress in cancer patients at the beginning of chemotherapy and its relation to quality of life. J BUON. 2008;13: 217-222.

29. Mystakidou K, Tsilika E, Parpa E, Katsouda E, Galanos A, Vlahos L. Assessment of anxiety and depression in advanced cancer patients and their relationship with quality of life. Qual Life Res. 2005;14:1825-1833.

30. Fradelos EC, Papathanasiou IV, Veneti A, Daglas A, Christodoulou E, Zyga S, et al. Psychological Distress and Resilience in Women Diagnosed with Breast Cancer in Greece. Asian Pac J Cancer Prev. 2017;18:2545-2550.

31. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Guidelines for Supportive Care/Distress Management. Version 2.2013. 2013. Jenkintown, PA: NCCN. Available from: www.nccn.org

32. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67:361-370.

33. Michopoulos I, Douzenis A, Kalkavoura C, Christodoulou C, Michalopoulou P, Kalemi G, et al. Hospital Anxiety and Depression Scale (HADS): validation in a Greek general hospital sample. Ann Gen Psychiatry. 2008;7:4.

34. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst. 1993;85:365–376.

35. Kyriaki M, Eleni T, Efi P, Ourania K, Vassilios S, Lambros V. The EORTC core quality of life questionnaire (QLQ-C30, version 3.0) in terminally ill cancer patients under palliative care: validity and reliability in a Hellenic sample. Int J Cancer. 2001;94:135–139.

36. Çinkir HY, Elboğa G. The Illness Perception and its Association with Distress in Cancer Patients Receiving Chemotherapy. Turkish Journal of Oncology. 2020;35:1-7.

37. Massie MJ. Prevalence of depression in patients with cancer. J Natl Cancer Inst Monogr. 2004;32:57−71.

38. Maass SW, Roorda C, Berendsen AJ, Verhaak PF, de Bock GH. The prevalence of long-term symptoms of depression

and anxiety after breast cancer treatment: A systematic review. Maturitas. 2015;82:100-108.

39. Rogers LQ, Courneya KS, Anton PM, Verhulst S, Vicari SK, Robbs RS, et al. Effects of a multicomponent physical activity behavior change intervention on fatigue, anxiety, and depressive symptomatology in breast cancer survivors: randomized trial. Psychooncology. 2017;26:1901–1906.

40. Civilotti C, Acquadro Maran D, Santagata F, Varetto A, Stanizzo MR. The use of the Distress Thermometer and the Hospital Anxiety and Depression Scale for screening of anxiety and depression in Italian women newly diagnosed with breast cancer. Support Care Cancer. 2020;28:4997-5004.

41. Tsaras K, Papathanasiou IV, Mitsi D, Veneti A, Kelesi M, Zyga S, et al. Assessment of Depression and Anxiety in Breast Cancer Patients: Prevalence and Associated Factors. Asian Pac J Cancer Prev. 2018;19:1661–1669.

42. Wondie Y, Mehnert A, Hinz A. The Hospital Anxiety and Depression Scale (HADS) applied to Ethiopian cancer patients. PloS One. 2020;15:e0243357.

43. Salvetti MG, Machado CSP, Donato SCT, Silva AMD. Prevalence of symptoms and quality of life of cancer patients. Rev Bras Enferm. 2020;73:e20180287.

44. Hinz A, Singer S, Brähler E. European reference values for the quality of life questionnaire EORTC QLQ-C30: Results of a German investigation and a summarizing analysis of six European general population normative studies. Acta Oncol. 2014;53:958-965.

45. Kitamura Y, Hattori S, Yoneda S, Watanabe S, Kanemoto E, Sugimoto M, et al. Doxorubicin and cyclophosphamide treatment produces anxiety-like behavior and spatial cognition impairment in rats: Possible involvement of hippocampal neurogenesis via brain-derived neurotrophic factor and cyclin D1 regulation. Behav Brain Res. 2015;292:184–193.

46. Yasin YM, Al-Hamad A. Anxiety and depression as key determinants of cancer related fatigue among patients receiving chemotherapy. European Scientific Journal. 2015;11:39–53.

47. Özalp E, Cankurtaran ES, Soygür H, Geyik PO, Jacobsen PB. Screening for psychological distress in Turkish cancer patients. Psychooncology. 2007;16:304–311.

48. Bergerot CD, Razavi M, Philip EJ, Bergerot PG, Buso MM, Clark KL, et al. Association between hospital anxiety and depression scale and problem-related distress in patients with cancer in a Brazilian private institution. Psychooncology. 2021;30:296-302.

49. Akechi T, Okuyama T, Endo C, Sagawa R, Uchida M, Nakaguchi T, et al. Patient's perceived need and psychological distress and/or quality of life in ambulatory breast cancer patients in Japan. Psychooncology. 2011;20:497-505.

50. Jacobsen PB, Donovan KA, Trask PC, Fleishman SB, Zabora J, Baker F, et al. Screening for psychologic distress in ambulatory cancer patients. Cancer. 2005;103:1494–1502.

51. Shayan Z, Shahkolahi Z, Ahmadlo N, Vafaee L, Shayan L.

52. Karapoulios D, Getsios I, Rizou V, Tsiklitara A, Kostopoulou S, Balodimou C, et al. Anxiety and depression in patients with lung cancer under chemotherapy. Assessment with the Hospital Anxiety and Depression Scale. Rostrum of Asclepius. 2013;12:428-440.

53. Zhang J, Zhou Y, Feng Z, Xu Y, Zeng G. Longitudinal Trends in Anxiety, Depression, and Quality of Life During Different Intermittent Periods of Adjuvant Breast Cancer Chemotherapy, Cancer Nurs. 2018;41:62-68.

54. Russ TC, Stamatakis E, Hamer M, Starr JM, Kivimäki M, Batty GD. Association between psychological distress and mortality: individual participant pooled analysis of 10 prospective cohort studies. BMJ. 2012;345:e4933.

55. Mandelblatt JS, Hurria A, McDonald BC, Saykin AJ, Stern RA, VanMeter JW, et al. Cognitive effects of cancer and its treatments at the intersection of aging: what do we know; what do we need to know? Semin Oncol. 2013;40:709–725.

56. Janelsins MC, Kesler SR, Ahles TA, Morrow GR. Prevalence, mechanisms, and management of cancer-related cognitive impairment. Int Rev Psychiatry. 2014;26:102–113.

57. Ahles TA, Saykin AJ, McDonald BC, Li Y, Furstenberg CT, Hanscom BS, et al. Longitudinal assessment of cognitive changes associated with adjuvant treatment for breast cancer: impact of age and cognitive reserve. J Clin Oncol. 2010;28:4434–4440.

58. Li FF, Hou LM, Li JS, Deng SS, Huang YH, Liu Y, et al. The impact of chemotherapy on cognitive function and life quality of breast cancer patient. TMR Integrative Medicine. 2020;4:e20023. Available from: https://www.tmrjournals.com/public/articlePDF/20201205/038c4057c0a9a28f7b163e1da857c4ba.pdf

59. De Rosa N, Della Corte L, Giannattasio A, Giampaolino P, Di Carlo C, Bifulco G. Cancer-related cognitive impairment (CRCI), depression and quality of life in gynecological cancer patients: a prospective study. Arch Gynecol Obstet. 2021;303:1581–1588.

60. de Souza JA, Yap BJ, Hlubocky FJ, Wroblewski K, Ratain MJ, Cella D, et al. The development of a financial toxicity patient-reported outcome in cancer: The COST measure. Cancer. 2014;120:3245-3253.

61. Whitney RL, Bell JF, Reed SC, Lash R, Bold RJ, Kim KK, et al. Predictors of financial difficulties and work modifications among cancer survivors in the United States. J Cancer Surviv. 2016;10:241–250.

62. Kent EE, Forsythe LP, Yabroff KR, Weaver KE, de Moor JS, Rodriguez JL, et al. Are survivors who report cancer-related financial problems more likely to forgo or delay medical care? Cancer. 2013;119: 3710-3717.

63. Zafar SY, McNeil RB, Thomas CM, Lathan CS, Ayanian JZ, Provenzale D. Population-based assessment of cancer survivors' financial burden and quality of life: a prospective cohort study. J Oncol Pract. 2015;11:145–150.

64. Pauge S, Surmann B, Mehlis K, Zueger A, Richter L,

Menold N, et al. Patient-Reported Financial Distress in Cancer: A Systematic Review of Risk Factors in Universal Healthcare Systems. Cancers (Basel). 2021;13:5015.

65. Sharp L, Carsin AE, Timmons A. Associations between cancer-related financial stress and strain and psychological well-being among individuals living with cancer. Psychooncology. 2013;22:745–755.

66. Arndt V, Koch-Gallenkamp L, Bertram H, Eberle A, Holleczek B, Pritzkuleit R, et al. Return to work after cancer. A multi-regional population-based study from Germany. Acta Oncol. 2019;58:811-818.

67. Book K, Marten-Mittag B, Henrich G, Dinkel A, Scheddel P, Sehlen S, et al. Distress screening in oncology-evaluation of the Questionnaire on Distress in Cancer Patients-short form (QSC-R10) in a German sample. Psychooncology. 2011;20:287–293.

68. Jansen L, Hoffmeister M, Chang-Claude J, Koch M, Brenner H, Arndt V. Age-specific administration of chemotherapy and long-term quality of life in stage II and III colorectal cancer patients: a population-based prospective cohort. Oncologist. 2011;16:1741–1751.

69. Naser AY, Hameed AN, Mustafa N, Alwafi H, Dahmash EZ, Alyami HS, et al. Depression and Anxiety in Patients With Cancer: A Cross-Sectional Study. Front Psychol. 2021;12,585534.

70. Fisch MJ, Zhao F, Manola J, Miller AH, Pirl WF, Wagner LI. Patterns and predictors of antidepressant use in ambulatory cancer patients with common solid tumors. Psychooncology. 2015;24:523-532.