Predictors of Anxiety, Depression, and Somatization: A Prospective Study of 1807 Cancer Patients

Short title

Keywords: Anxiety, cancer, depression, coping, somatization, spirituality

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Cancer causes distress, resulting in anxiety, depression or somatization. The aim was to investigate sociodemographic, clinical, and psychological factors associated with psychological distress in cancer patients. This prospective and multicenter study, conducted by the Spanish Society of Medical Oncology (SEOM), included two cohorts of patients with cancer (localized resected or advanced unresectable). They completed surveys to evaluate psychological distress (BSI-18), coping (MINI-MAC), and spirituality (FACT-Sp). A multivariable logistic regression analysis was conducted. Between 2019-2022, 1807 patients were evaluated, mostly women (54%), average age 64 years. The most frequent primary cancers were colorectal (30%), breast (25%) and lung (18%). Older individuals (OR0.98, CI95% 0.97-0.99), and males (OR0.66, CI95% 0.51-0.84 and OR0.75, CI95% 0.58-0.97) had less anxiety and depression. Colorectal cancer patients had less depression (OR0.67, CI95% 0.47-0.95) and somatization (OR0.71, CI95% 0.52-0.97). Patients with localized cancer and with spiritual beliefs had lower levels of psychological distress, while those with anxious preoccupation had higher levels. After treatment, patients with pre-existing distress and anxious preoccupation experienced an increase in psychological distress while those with localized cancer showed reduced levels of anxiety and somatization. This study suggests that age, sex, extension and location of cancer, coping and spirituality influence psychological distress in cancer patients.

Introduction
Cancer is a growing concern worldwide, with the International Agency for Research on Cancer (IARC) estimating 18.1 million cases in 2020, rising to 28 million in 2040. According to the Spanish Society of Medical Oncology (SEOM), there will be an estimated 279260 cases in 2023, potentially reaching 341000 in 2040. Its impact on physical and mental health is significant, and its prognosis is often poor. As such, despite advances in diagnosis and treatment, it remains one of the leading causes of death, with 9.89 million fatalities in 2020, and an estimated 113000 in Spain. This number is expected to grow to 16 million worldwide and 159000 in Spain by 2040.

It is widely known that cancer patients are more likely to experience psychological distress, such as anxiety, depressive disorders, and somatization, due to the severity of the disease and its unfavorable prognosis. Recent research, including Wang Y-H et al.’s 2020 meta-analysis, has further emphasized the connection between psychological distress and increased mortality risk and poorer survival outcomes. Anxiety is the most widely reported psychological disorder found in up to 38% of cancer patients. Age, gender, and cancer location are believed to be mediators, with higher anxiety levels generally seen in younger patients. An Iranian meta-analysis in 2022 and another meta-analysis conducted in Iran revealed a higher prevalence of both anxiety and depression, as well as depression alone in breast cancer patients, respectively. Moreover, depression is a common issue among cancer patients, affecting up to 16%. Its prevalence is likely to vary throughout the course of the disease, as various elements, such as the patient's response to their diagnosis, fear of the appearance of symptoms related to the disease, and the adverse effects of treatments, can contribute to it. Additionally, living with the uncertainty of a recurrence or progression of the cancer, as well as the fear of death, can have a significant impact. Relative to somatic symptoms, it has been observed that cancer patients may experience a plethora of symptoms, both from their cancer treatments and the tumor disease. Common examples include pain, fatigue, anorexia, tiredness, lack of energy, trembling and lethargy. A meta-analysis published in 2020 found an association between female gender and a higher level of fatigue in cancer patients. It is important to note that it can be difficult to distinguish between physical symptoms caused by cancer and those caused by psychological issues, which might lead to misdiagnosis and a delay in providing psychological interventions.

Coping is an essential psychological factor for cancer patients, as it can provide a sense of protection and adjustment from the negative effects associated with diagnosis, treatment adverse events, the risk of recurrence, and potential socio-economic and familial repercussions. Adaptive coping strategies, such as displaying a fighting spirit or maintaining a positive attitude, have been shown to facilitate positive psychosocial adaptation to the cancer experience. In contrast, those using a non-adaptive coping style, such as fatalism or anxious preoccupation-based approaches, are more likely to experience anxiety, depression, social isolation, and reduced quality of life. In addition, research has demonstrated that those with a greater sense of psychospiritual well-being are better able to handle the terminal illness process.

Spirituality is commonly understood as an individual’s search for significance and purpose in life, as well as a connection with intangible aspects of existence and transcendence. Patients may draw from their spiritual beliefs to find strength, hope and meaning in the face of a cancer diagnosis and its associated phases. Factors such as prognostic knowledge, family and social support, autonomy, hope and meaning in life have been identified to contribute to psychospiritual well-being, while emotional distress, anxiety, helplessness, hopelessness, and fear of death are known to detract from it process. Patients facing a chronic, incurable, or terminal illness may begin to question the meaning of life. Studies have suggested a positive relationship between religion/spirituality and mental health in cancer patients. Furthermore, meaning-focused interventions may be beneficial for improving quality of life in those with advanced cancer. In addition, spiritual interventions have been found to reduce anxiety, depression, and hopelessness in cancer patients, leading to physical and psychological benefit. As such, it is important for the medical team to consider the patient's spirituality, and to provide interventions if necessary or requested.

With all the above in mind, the aim of this study was to evaluate the sociodemographic, clinical, and psychological factors that are predictive of anxiety, depression, and somatization in cancer patients. Furthermore, the correlation between psychological distress and coping, spirituality and age was also explored.

Materials And Methods
Patients and study design
This study, sponsored by the Spanish Society of Medical Oncology (SEOM) Bioethics Section, was prospective, observational, and consecutive in nature. It was approved by the Ethics Committee of each institution, as well as the Spanish Agency of Medicines and Health Products, and all participants signed an informed consent form prior to inclusion.

The participants were those who had a histologically confirmed cancer and were candidates for systemic therapy. Individuals under the age of 18 and those with any serious mental illness that would impede their understanding of the study, as well as any underlying personal, family, sociological, geographic, and/or medical condition that might impede their participation, were excluded. Moreover, individuals who had already received any systemic cancer treatment or patients with resected metastatic cancer were also excluded.

The study was based on a series of questionnaires that the medical oncologist provided to the patient during the same visit in which they discussed the potential benefits of adjuvant (for resected localized cancer) or palliative (for unresectable advanced cancer) systemic cancer treatment. These forms were completed by the patient at home prior to the start of treatment and then handed in to the study assistants at the next visit. Each form contained clear instructions and specified that its completion was voluntary and anonymous. Patients with resected localized cancer completed the psychological distress questionnaire at the end of their adjuvant treatment, which was 6 months after starting treatment. Subjects with unresectable advanced cancer completed the questionnaire after their first radiological response evaluation study, which was 2-3 months after their antineoplastic treatment began. This was closer to baseline, as this population has a poorer prognosis and increased risk of premature death.

Measures and variables

The information was collected and updated by medical oncologists specially trained to meet the requirements of the study. Demographic and clinical data (age, sex, marital status, educational level, employment status, cancer location, and stage, and treatment received) were obtained directly from the patients and their medical records. Cancer location was classified into breast, bronchopulmonary, colon, non-colorectal digestive (encompassing esophagus, stomach, pancreas, biliary tract, liver, and anal canal) and all other cases were categorized as ‘other’. Stage I-III cancers that had been resected were categorized as resected localized whereas stage III-IV cancers that were deemed unresectable were classified as unresectable advanced.

The participants filled the questionnaires BSI-18 (psychological distress), MINI-MAC (coping), and FACIT-sp (spirituality). The Brief Symptom Inventory (BSI-18) was employed, consisting of 18 items which measure the respondent's overall emotional adjustment or psychological distress over the preceding 7 days, each rated on a five-point Likert scale, from zero (not at all) to four (extremely). Cronbach's alpha for the scale has been reported to range from 0.81 to 0.90, and its validity has been established among Spanish-speaking populations. In the current study, it was evaluated both at the start and conclusion of adjuvant treatment (in those with resected localized cancer) or following the first response assessment imaging study (in those with unresectable advanced disease).

The Mini-Mental Adjustment to Cancer (Mini-MAC) is a 29-item scale that evaluates the cancer-specific coping strategies of individuals as either adaptive (cognitive avoidance, fighting spirit) or maladaptive (helplessness, anxious preoccupation, and fatalism). When examining the psychometric properties of the scale in Spanish, we identified a four-factor structure, which was utilized in this study and includes the three original subscales of helplessness, anxious preoccupation, and cognitive avoidance, as well as a new subscale, positive attitude, that incorporates fighting spirit and fatalism. Each item is rated on a four-point Likert scale from one (definitely does not apply to me) to four (definitely applies to me). The Cronbach's alpha coefficients for each domain range from 0.62 to 0.88.

The Functional Assessment of Chronic Illness-Spiritual Well-Being Scale (FACIT-Sp) is an 12-item questionnaire which uses a five-point Likert-type scale, with responses ranging from not at all (0) to very much (4). The scale is divided into three subdomains which assess spiritual well-being (meaning, peace and faith). The Spanish version of the scale was divided into two factors, meaning/peace and faith, and were both analyzed in this study. Internal consistency reliability coefficients for the scale were found to range from 0.81 to 0.88.

Statistical analysis

Descriptive statistics were employed to analyze demographic data and questionnaire responses. Categorical variables were expressed as percentages and compared using Chi-square tests, while quantitative variables were reported in terms of mean and standard deviation (SD). Pearson's correlation was used to determine the level of association between psychological variables and age. Analysis of covariance (ANCOVA) was carried out to identify risk factor for anxiety, depression and somatization pre and post-treatment. The number of sociodemographic, clinical, and psychological predictors was chosen based on the sample size. These potential predictive factors were selected by the study coordinators after thorough literature review. Sociodemographic variables (sex, and age), clinical variables (performance status measured with the Eastern Cooperative Oncology Group scale (ECOG), cancer location and stage), and psychological variables (coping and spiritual well-being) were included in a multivariate logistic regression analysis (ANCOVA) to examine their influence on psychological distress pre- and post-treatment (anxiety, depression, and somatization) which was assessed with the BSI-18 scale. Cancer localization were re-categorized into k-1 dummy variables, where bronchopulmonary was the reference groups. For all analyses, a significance level of α<0.05 was adopted.

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, N.Y., USA).

Results

Sociodemographic and clinical features

Between 2019 and 2022, 1977 patients were recruited, of which 1807 were eligible and 170 were excluded. Of those excluded, 40 did not meet any inclusion criteria, 42 met any exclusion criteria, and 88 had incomplete data at the time of analysis. Table 1 provides the baseline socio-demographic and clinical
characteristics. A roughly equal proportion of men (46%) and women (54%) were included, with an average age of 64 years and 57% of participants being ≤65 years. Many participants were married or living with a partner (72%), had basic education levels (51%), and were either unemployed or retired (59%). The most common primary cancers were colorectal (30%), breast (25%), bronchopulmonary (18%), and non-colorectal digestive neoplasms (15%). Of the 944 participants with resected localized cancer, 19% were stage I, 36% were stage II, and 45% were stage III. Of the 863 participants with unresectable advanced cancer, 20% were stage III and 80% were stage IV.

Table 1 summarizes the adjuvant treatments administered to patients with resected cancer, and the first-line treatments given to those with unresectable advanced cancer. Chemotherapy was the systemic treatment given to patients with resected cancer (100%), and radiotherapy was also included in 33% of cases. For those with unresectable advanced cancer, the most common therapy was chemotherapy (55%), and 34% received immunotherapy or 11% were treated with targeted therapy either alone or in combination with chemotherapy. Prior to the completion of adjuvant treatment (6 months) in patients with resected cancer, and prior to the first response evaluation study (2-3 months) in those with advanced cancer, 5% (n=86) had passed away, with a greater proportion of deaths seen in patients with advanced cancer (17.8%) than those with localized cancer (3.3%).

Based on the BSI score, it was observed that 57% had scores indicating anxiety, 44% indicating depression and 48% indicating somatization. As illustrated in Table 1, women were found to have higher levels of anxiety (p=0.001) and depression (p=0.003) than men, and those ≤65 years had higher levels of anxiety (p=0.002) and somatization (p=0.044) than the elderly. Additionally, patients without a partner displayed more depression than those with a partner (p=0.006), and those in employment showed higher levels of anxiety, depression, and somatization than non-working patients (p=0.002, p=0.001, and p=0.001, respectively). Patients with colorectal cancer were found to have the lowest levels of anxiety, depression and somatization compared to all other neoplasms (all p=0.001). Furthermore, patients with advanced unresectable cancer had higher levels of anxiety, depression, and somatization than those with resected stage III cancer (all p=0.001). Lastly, patients who only received chemotherapy (n=1087) had significantly lower levels of anxiety, depression and somatization when compared to other groups (p=0.001, p=0.005, p=0.001, respectively).

Correlations across psychological variables and age

Table 2 presents the means, standard deviations, and Pearson correlation analyses of the psychological variables and age. The mean scores of anxiety, depression, and somatization were 63.2, 61.7, and 62.9, respectively. The two most employed coping strategies were positive attitude and cognitive avoidance, with respective mean scores of 77.3 and 59.3, whilst anxious preoccupation and hopelessness were the least utilized (33.4 and 33.8, respectively). Furthermore, the mean score of the FACIT-Sp spirituality scale was 34.7. The results demonstrated that there were significant correlations between all psychological variables apart from helplessness and positive attitude. It was found that positive attitude-based coping was associated with lower levels of anxiety (r=−0.142, p<0.001), depression (r=−0.231, p<0.001), somatization (r=−0.087, p<0.001) and anxious preoccupation (r=−0.182, p<0.001). Similarly, spirituality was linked to decreased anxiety (r=−0.240, p<0.001), depression (r=−0.342, p<0.001), somatization (r=−0.148, p<0.001) and anxious worry (r=−0.295, p<0.001). Additionally, older age was associated with lower levels of anxiety (r=−0.074, p<0.001) and anxious preoccupation (r=−0.103, p<0.001), as well as higher levels of positive attitude (r=0.046, p<0.001), cognitive avoidance (r=0.107, p<0.001), and spirituality (r=0.263, p<0.001).

Sociodemographic and clinical risk factors for anxiety, depression, and somatization

Multivariable logistic regression assessing the association between pre-treatment psychological distress and sociodemographic, clinical, and psychological variables is shown in Table 3. Higher levels of anxiety and depression were identified in individuals who reported using helplessness (OR 1.01, 95% CI 1.01-1.02 and OR 1.02, 95% CI 1.01-1.02, respectively) and anxious preoccupation-based coping (OR 1.03, 95% CI 1.03-1.04 and OR 1.04, 95% CI 1.03-1.05, respectively). Additionally, cognitive avoidance was associated with greater anxiety (OR 1.07, 95% CI 1.02-1.01). In contrast, lower levels of anxiety and depression were observed in older patients (OR 0.98, 95% CI 0.97-0.99 for both), men (OR 0.66, 95% CI 0.51-0.84 and OR 0.75, 95% CI 0.58-0.97, respectively), those with a localized cancer (OR 0.39, 95% CI 0.27-0.56 and OR 0.26, 95% CI 0.17-0.38, respectively), and those with spiritual well-being (OR 0.97, 95% CI 0.95-0.98) and or 0.92, 95% CI 0.90-0.94, respectively). In addition, those with a positive attitude demonstrated lower level of anxiety (OR 0.99, 95% CI 0.98-0.99) and those with colorectal cancer a lower level of depression (OR 0.67, 95% CI 0.47-0.95). Furthermore, somatization was observed to be higher in those with anxious preoccupation (OR 1.01, 95% CI 1.01-1.02), while older age (OR 0.99, 95% CI 0.98-0.99), colorectal cancer (OR 0.72, 95% CI 0.53-0.98), and localized cancer (OR 0.37, 95% CI 0.27-0.52) had lower levels, as did those with spiritual well-being (OR 0.96, 95% CI 0.95-0.98).

Multivariable logistic regression assessing the association between post-treatment psychological distress and sociodemographic, clinical and psychological variables is shown in Table 4. Anxious preoccupation was associated with increased risk of post-treatment anxiety (OR 1.02, 95% CI 1.01-1.03), depression (OR 1.01, 95% CI 1.01-1.03) and somatization (OR 1.01, 95% CI 1.00-1.02). In addition, higher levels of baseline anxiety (OR 2.18, 95% CI, 1.60-2.96), depression (OR 3.20, 95% CI, 2.30-4.46) and somatization (OR 2.78, 95% CI, 2.07-3.72) were found to be associated with higher post-treatment psychological distress. Moreover, patients with a localized cancer were observed to have lower levels of anxiety (OR 0.41 CI 95%, 0.25-0.67) and somatization (OR 0.58 CI, 95%, 0.37-0.95). Helplessness was also linked to a greater risk of somatization (OR 0.98, CI 95%, 0.98-0.99).

Discussion

This study found a correlation between psychological distress (including anxiety, depression, and somatization), younger age, and anxious preoccupation-based coping in a large sample of cancer patients (n=1807). Conversely, localized resected cancer and spirituality were found to be protective factors. Male patients and those with a positive attitude were less likely to present with anxiety and depression and those with colorectal cancer were less prone to depression and somatization. After systemic cancer treatment, it was observed that patients with pre-existing anxiety, depression and somatization, as well as those with anxious preoccupation, experienced an increased risk in psychological distress. On the other hand, those with localized cancer showed reduced levels of anxiety and somatization.
We have yet to uncover prospective studies assessing the impact of sociodemographic, clinical, coping and spirituality variables on psychological distress in cancer patients, though studies analyzing the influence of several of these variables have been identified. Concerning sociodemographic factors, the available data suggests that gender and age influence psychological distress in cancer patients. A Chinese study conducted in patients with thyroid cancer, for example, reported that gender could be a predictor of psychological distress. Additionally, a Turkish study showed that female gender was associated with a higher level of anxiety and depression in outpatients with cancer, while a Spanish study that focused on patients with resected localized cancer noted that females were more likely to suffer from depression. In terms of age, several publications have demonstrated that younger age can be a predictor of psychological distress. For instance, a study of patients with localized prostate cancer reported that younger age was associated with poorer psychological functioning, while a study of breast cancer patients showed that younger age predicted greater psychological distress. Similarly, an American study looking at the role of younger age in psychological distress found that younger age also predicted greater psychological distress. This greater psychological distress found in younger patients may be associated with having cancer at a time of personal, family, and professional development when the disease can interfere with and compromise responsibilities.

To the best of our knowledge, no studies have examined tumor location as a predictor of psychological distress. However, some studies have evaluated psychological distress in patients with different tumor sites. Our group previously investigated the biopsychosocial and clinical characteristics of patients with resected localized colon and breast cancer and observed that patients with breast cancer had higher levels of anxiety, depression, and somatization before the start of adjuvant treatment. These findings may be attributed to the psychological distress caused by the body image impact of surgical treatment. Interestingly, the differences are lost after adjuvant treatment is completed, possibly due to the adverse effects of systemic cancer treatment toxicity. In the present study, we found that colon cancer is associated with lower baseline depression and somatization. However, this effect is again lost in the analyses performed at the end of treatment, probably due to the toxicity accumulated by cancer treatments, which is associated with an increase in psychological distress and affects all patients equally, regardless of tumor location. A study analyzing the spectrum of psychological disorders in cancer patients found that the greatest anxiety was suffered by patients receiving chemotherapy, a higher level of somatization was for those receiving both chemotherapy and associated radiotherapy, and depression affected more patients receiving only radiotherapy. Our study also observed that patients receiving chemotherapy were the group with the lowest level of psychological distress compared to patients receiving other systemic cancer treatments (immunotherapy or targeted therapy).

The relationship between different coping strategies and psychological distress has been studied in several contexts. A study of patients with esophageal cancer found that anxious preoccupation and fighting spirit were strongly associated with psychological distress before surgical treatment, while after treatment, helplessness was the most linked coping strategy. In a European study of patients with nasopharyngeal cancer, those with higher levels of anxiety and depression were more likely to use dysfunctional coping strategies such as helplessness and anxious preoccupation. Similarly, cancer patients with an optimistic outlook had the fewest symptoms of anxiety and depression in other study. It should be noted that most of these studies analyze the impact of coping strategies on psychological distress using a linear regression model, unlike our study which uses a multivariate model controlling for confounding factors. We found that anxious preoccupation was associated with anxiety, depression and somatization, helplessness with anxiety and depression, and cognitive avoidance with anxiety, while a positive attitude had a protective effect against anxiety and depression. Spirituality has been found to predict psychological distress in cancer patients during the Covid-19 pandemic, with higher spirituality associated with lower distress. Age and gender were also associated with psychological distress. Previous research has corroborated the finding in our series that spiritual well-being is associated with mental well-being and less anxiety, depression, and somatization.

The current study has several limitations that should be noted. Firstly, although the effect of different coping strategies was statistically significant, it was minimal in a large sample size with sufficient power. Secondly, the definition of psychological distress, anxiety, depression, and somatization was based on the BSI-18 scale rather than a clinical diagnosis. Thirdly, post-treatment analyses were conducted at different times for patients with localized or advanced cancer, at 6 months and 2-3 months, respectively. This was due to the prolonged treatment of patients with advanced disease until progression or start of adjuvant treatment. These findings may be attributed to the psychological distress caused by the body image impact of surgical treatment. Interestingly, the differences are lost after adjuvant treatment is completed, possibly due to the adverse effects of systemic cancer treatment toxicity. In the present study, we found that colon cancer is associated with lower baseline depression and somatization. However, this effect is again lost in the analyses performed at the end of treatment, probably due to the toxicity accumulated by cancer treatments, which is associated with an increase in psychological distress and affects all patients equally, regardless of tumor location. A study analyzing the spectrum of psychological disorders in cancer patients found that the greatest anxiety was suffered by patients receiving chemotherapy, a higher level of somatization was for those receiving both chemotherapy and associated radiotherapy, and depression affected more patients receiving only radiotherapy. Our study also observed that patients receiving chemotherapy were the group with the lowest level of psychological distress compared to patients receiving other systemic cancer treatments (immunotherapy or targeted therapy).

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In conclusion, this study has identified several sociodemographic, clinical, and psychological variables that may predict psychological distress in cancer patients. These include young age and female sex, the presence of advanced unresectable cancer, and cancer location outside the colon, as well as anxious preoccupation and lack of spirituality. Further research is needed to confirm these findings and inform effective interventions to address psychological distress in cancer patients.

Declarations

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Authors’ contributions V.V., C.C. and P.J.F developed the project, analyzed the data, and drafted the manuscript. The other authors recruited patients and provided clinical information, data curation, comments, and improvements to the manuscript. All authors participated in the conceptualization, interpretation and discussion of data, supervision, visualization, and the critical review and edition of the manuscript.

Compliance with ethical standards

Competing interests The authors declare that they have no conflict of interest related to the scope of this work.

Ethics approval This study was approved by the Research Ethics Committee of the Principality of Asturias (May 17, 2019) and by the AEMPS (May 8, 2019). The studies have been performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments.

This study is a prospective, observational, non-interventionist trial.

Consent to participate Signed informed consent was obtained from all patients.

Consent for publication Informed consent and approval by the national competent authorities includes permission for publication and diffusion of the data.

Data availability Statistical analyses were performed with Statistical Package for Social Sciences (SPSS) software, 25.0 version (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp). The code is available upon request to the authors.

Code availability Patients are identified by an encrypted code known only to the local researcher. The code of the analyses is available upon request to the authors.

References


**Tables**

**Table 1.** Demographic and clinical characteristics of patients (n=1807).
<table>
<thead>
<tr>
<th>Demographic and clinical characteristics</th>
<th>N (%)</th>
<th>Anxiety (mean ± SD)</th>
<th>Depression (mean ± SD)</th>
<th>Somatization (mean ± SD)</th>
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</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>843 (46)</td>
<td>63.3 (7.9)</td>
<td>61.3 (6.5)</td>
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<td>Women</td>
<td>964 (54)</td>
<td>63.9 (7.8)</td>
<td>62.1 (6.4)</td>
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<td>0.001</td>
<td>0.003</td>
<td>0.107</td>
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<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>≤ 65</td>
<td>1035 (57)</td>
<td>63.7 (7.9)</td>
<td>62.0 (6.4)</td>
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<td>&gt; 65</td>
<td>772 (43)</td>
<td>62.5 (7.9)</td>
<td>61.5 (6.6)</td>
<td>62.5 (7.6)</td>
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<tr>
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<td>0.002</td>
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<td>0.044</td>
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<tr>
<td><strong>Marital Status</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Married/partnered</td>
<td>1301 (72)</td>
<td>63.1 (7.9)</td>
<td>61.5 (6.3)</td>
<td>62.7 (7.6)</td>
</tr>
<tr>
<td>No partnered</td>
<td>506 (28)</td>
<td>63.3 (7.9)</td>
<td>62.4 (6.8)</td>
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<td>0.697</td>
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<td><strong>Educational level</strong></td>
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<tr>
<td>Basic</td>
<td>919 (51)</td>
<td>63.3 (7.9)</td>
<td>61.7 (6.5)</td>
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<td>Intermediate</td>
<td>888 (49)</td>
<td>63.1 (7.8)</td>
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<td>0.612</td>
<td>0.786</td>
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<td>Employed</td>
<td>849 (47)</td>
<td>63.8 (7.9)</td>
<td>62.1 (6.5)</td>
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<td>Retired or unemployed</td>
<td>958 (59)</td>
<td>62.6 (7.9)</td>
<td>61.4 (6.4)</td>
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<td>0.002</td>
<td>0.001</td>
<td>0.001</td>
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<tr>
<td>Colorectal</td>
<td>534 (30)</td>
<td>61.6 (7.8)</td>
<td>60.1 (6.1)</td>
<td>60.7 (7.1)</td>
</tr>
<tr>
<td>Breast</td>
<td>458 (25)</td>
<td>63.8 (8.0)</td>
<td>62.1 (6.3)</td>
<td>62.8 (7.3)</td>
</tr>
<tr>
<td>Bronchopulmonary</td>
<td>320 (18)</td>
<td>63.8 (8.0)</td>
<td>62.3 (6.8)</td>
<td>64.5 (8.1)</td>
</tr>
<tr>
<td>Digestive no colorectal</td>
<td>268 (15)</td>
<td>64.3 (7.9)</td>
<td>63.2 (6.2)</td>
<td>64.7 (7.3)</td>
</tr>
<tr>
<td>Others</td>
<td>227 (13)</td>
<td>63.2 (7.9)</td>
<td>62.6 (6.6)</td>
<td>64.1 (6.6)</td>
</tr>
<tr>
<td>p value</td>
<td>0.001</td>
<td>0.001</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td><strong>Stage</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Localized resected</td>
<td>944 (52)</td>
<td>62.1 (7.7)</td>
<td>60.6 (5.9)</td>
<td>61.1 (7.0)</td>
</tr>
<tr>
<td>Advanced unresectable</td>
<td>863 (48)</td>
<td>64.4 (7.9)</td>
<td>62.9 (6.9)</td>
<td>64.9 (7.8)</td>
</tr>
<tr>
<td>p value</td>
<td>0.001</td>
<td>0.001</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td><strong>Systemic treatment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemotherapy (CT)</td>
<td>1087 (60)</td>
<td>62.6 (7.9)</td>
<td>61.4 (6.5)</td>
<td>62.3 (7.7)</td>
</tr>
<tr>
<td>CT and radiotherapy</td>
<td>312 (17)</td>
<td>63.0 (7.7)</td>
<td>61.6 (5.8)</td>
<td>62.1 (7.0)</td>
</tr>
<tr>
<td>Immunotherapy + CT</td>
<td>62 (34)</td>
<td>65.7 (8.1)</td>
<td>63.2 (7.6)</td>
<td>65.3 (8.9)</td>
</tr>
<tr>
<td>Targeted therapy + CT</td>
<td>46 (3)</td>
<td>62.7 (7.4)</td>
<td>61.8 (6.4)</td>
<td>65.0 (7.0)</td>
</tr>
<tr>
<td>Others</td>
<td>300 (17)</td>
<td>64.9 (7.8)</td>
<td>62.8 (6.8)</td>
<td>64.9 (7.6)</td>
</tr>
<tr>
<td>p value</td>
<td>0.001</td>
<td>0.005</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td><strong>Death</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1721 (95)</td>
<td>63.2 (7.9)</td>
<td>61.7 (6.5)</td>
<td>62.8 (7.6)</td>
</tr>
<tr>
<td>Yes</td>
<td>86 (5)</td>
<td>63.4 (7.6)</td>
<td>62.0 (6.9)</td>
<td>63.8 (8.6)</td>
</tr>
<tr>
<td>p value</td>
<td>0.822</td>
<td>0.712</td>
<td>0.272</td>
<td></td>
</tr>
</tbody>
</table>
Table 2. Pearson's correlations across psychological variables and age.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean ± SD</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSI. Anxiety</td>
<td>63.2 ± 7.9</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BSI. Depression</td>
<td>61.7 ± 6.5</td>
<td>0.763**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BSI. Somatization</td>
<td>62.9 ± 7.6</td>
<td>0.514**</td>
<td>0.550**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAC: Helplessness</td>
<td>33.8 ± 25.3</td>
<td>0.385**</td>
<td>0.426**</td>
<td>0.300**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAC: Anxious preoccupation</td>
<td>33.4 ±24.3</td>
<td>0.439**</td>
<td>0.441**</td>
<td>0.177**</td>
<td>0.238**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAC: Positive attitude</td>
<td>77.3 ± 16.7</td>
<td>-0.142**</td>
<td>-0.231**</td>
<td>-0.087**</td>
<td>0.040</td>
<td>-0.182**</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAC: Cognitive avoidance</td>
<td>59.3 ± 26.3</td>
<td>0.190**</td>
<td>0.138**</td>
<td>0.100**</td>
<td>0.395**</td>
<td>0.168**</td>
<td>0.426**</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>FACIT: Spiritual well-being</td>
<td>34.7 ± 7.6</td>
<td>-0.240**</td>
<td>-0.342**</td>
<td>-0.148**</td>
<td>0.039**</td>
<td>-0.295**</td>
<td>0.487**</td>
<td>0.178**</td>
<td>1</td>
</tr>
<tr>
<td>Age</td>
<td>62.1 ± 11.9</td>
<td>-0.074**</td>
<td>-0.035</td>
<td>-0.006</td>
<td>0.212**</td>
<td>-0.103**</td>
<td>0.046**</td>
<td>0.107**</td>
<td>0.263**</td>
</tr>
</tbody>
</table>

Abbreviations: n, number; SD, standard deviation.

Table 3. Multivariate logistic regression of sociodemographic and clinic variables correlated with psychological distress (anxiety, depression, and somatization) pre-treatment.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Anxiety</th>
<th>Depression</th>
<th>Somatization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>b</td>
<td>Odds ratio</td>
<td>Lower</td>
</tr>
<tr>
<td>Age</td>
<td>-0.013</td>
<td>6.290</td>
<td>0.987 ±</td>
</tr>
<tr>
<td>Sex: Male</td>
<td>-0.417</td>
<td>11.294</td>
<td>0.659 ±</td>
</tr>
<tr>
<td>ECOG: 0-1</td>
<td>0.071</td>
<td>0.063</td>
<td>1.074 ±</td>
</tr>
<tr>
<td>Site: Bronchopulmonary</td>
<td>-0.318</td>
<td>2.411</td>
<td>0.727 ±</td>
</tr>
<tr>
<td>Site: Colorectal</td>
<td>-0.458</td>
<td>5.664</td>
<td>0.632 ±</td>
</tr>
<tr>
<td>Site: Digestive no colorectal</td>
<td>-0.363</td>
<td>2.956</td>
<td>0.696 ±</td>
</tr>
<tr>
<td>Site: Breast</td>
<td>-0.185</td>
<td>0.792</td>
<td>0.831 ±</td>
</tr>
<tr>
<td>Stage: Localized</td>
<td>-0.949</td>
<td>27.759</td>
<td>0.387 ±</td>
</tr>
<tr>
<td>MAC: Helplessness</td>
<td>0.015</td>
<td>21.309</td>
<td>1.015 ±</td>
</tr>
<tr>
<td>MAC: Anxious preoccupation</td>
<td>0.035</td>
<td>116.643</td>
<td>1.035 ±</td>
</tr>
<tr>
<td>MAC: Positive attitude</td>
<td>-0.008</td>
<td>3.310</td>
<td>0.992 ±</td>
</tr>
<tr>
<td>MAC: Cognitive avoidance</td>
<td>0.007</td>
<td>6.945</td>
<td>1.007 ±</td>
</tr>
<tr>
<td>FACIT: Spiritual well-being</td>
<td>-0.033</td>
<td>14.705</td>
<td>0.967 ±</td>
</tr>
<tr>
<td>Intercept</td>
<td>1.775</td>
<td>9.722</td>
<td>5.897 ±</td>
</tr>
</tbody>
</table>

Abbreviations: ECOG, Eastern Cooperative Oncology Group scale; BSI, Brief Symptom Inventory; MAC, Mental Adjustment Cancer; FACIT, Functional Assessment of Chronic Illness Therapy-Spiritual Well-Being. * Adjusted for demographic and clinical variables (sex, age, tumor site, tumor stage, and ECOG performance status).

Bold values indicate the significant at 5% level.
Table 4. Multivariate logistic regression of sociodemographic and clinic variables correlated with psychological distress (anxiety, depression, and somatization) post-treatment.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Anxiety</th>
<th>Depression</th>
<th>Somatization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>b</td>
<td>Wald test (z-ratio)</td>
<td>Odds ratio</td>
</tr>
<tr>
<td>Age</td>
<td>-0.003</td>
<td>0.186</td>
<td>0.997</td>
</tr>
<tr>
<td>Sex: Male</td>
<td>-0.218</td>
<td>1.779</td>
<td>0.804</td>
</tr>
<tr>
<td>ECOG: 0-1</td>
<td>-0.363</td>
<td>0.942</td>
<td>0.696</td>
</tr>
<tr>
<td>Site: Bronchopulmonary</td>
<td>-0.231</td>
<td>0.642</td>
<td>0.794</td>
</tr>
<tr>
<td>Site: Colorectal</td>
<td>-0.358</td>
<td>2.025</td>
<td>0.699</td>
</tr>
<tr>
<td>Site: Digestive no colorectal</td>
<td>-0.274</td>
<td>0.903</td>
<td>0.760</td>
</tr>
<tr>
<td>Site: Breast</td>
<td>-0.167</td>
<td>0.389</td>
<td>0.846</td>
</tr>
<tr>
<td>Stage: Localized</td>
<td>-0.815</td>
<td>11.357</td>
<td>0.443</td>
</tr>
<tr>
<td>MAC: Helplessness</td>
<td>-0.007</td>
<td>3.095</td>
<td>0.993</td>
</tr>
<tr>
<td>MAC: Anxious Preoccupation</td>
<td>0.022</td>
<td>30.936</td>
<td>1.022</td>
</tr>
<tr>
<td>MAC: Positive Attitude</td>
<td>0.000</td>
<td>0.000</td>
<td>1.000</td>
</tr>
<tr>
<td>MAC: Cognitive Avoidance</td>
<td>0.001</td>
<td>0.170</td>
<td>1.001</td>
</tr>
<tr>
<td>FACIT: Spiritual well-being</td>
<td>-0.018</td>
<td>2.672</td>
<td>0.982</td>
</tr>
<tr>
<td>Score pretreatment</td>
<td>0.779</td>
<td>24.282</td>
<td>2.159</td>
</tr>
<tr>
<td>Intercept</td>
<td>0.766</td>
<td>1.050</td>
<td>2.150</td>
</tr>
</tbody>
</table>

**Abbreviations:** ECOG, Eastern Cooperative Oncology Group scale; BSI, Brief Symptom Inventory; MAC, Mental Adjustment Cancer; FACIT, Functional Assessment of Chronic Illness Therapy-Spiritual Well-Being. * Adjusted for demographic and clinical variables (sex, age, tumor site, tumor stage, and ECOG performance status)

Bold values indicate the significant at 5% level.