RESEARCH ARTICLE

Screening patients with metastatic breast cancer for psychiatric disease: a cross sectional study [version 1; peer review: awaiting peer review]

Raquel Basto ¹, Cecília Caramujo¹, Inês Ferreira Gomes¹, Teresa Fraga¹, Joana Correia Magalhães¹, Maria João Sousa¹, Sabrina de Jesus², Ana Raquel Monteiro^{1,3}, Adriana Pestana-Santos⁴, Teresa Carvalho¹, Emília Albuquerque⁴, Gabriela Sousa¹

¹Medical Oncology, Instituto Português de Oncologia de Coimbra, Coimbra, Portugal

²Psychiatry, Centro Hospitalar do Baixo Vouga, Aveiro, Portugal

³Medical Oncology, Centro Hospitalar de Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal

⁴Psychiatry, Instituto Português de Oncologia de Coimbra, Coimbra, Portugal

V1 First published: 21 Jan 2022, 11:73
<https://doi.org/10.12688/f1000research.79400.1>

Latest published: 21 Jan 2022, 11:73
<https://doi.org/10.12688/f1000research.79400.1>

Open Peer Review

Approval Status Awaiting Peer Review

Any reports and responses or comments on the article can be found at the end of the article.

Abstract

Background: Cancer patients are at risk of developing some level of psychological dysregulation, depending on a series of variables related to the tumor, the environment, and the patient. In this context, it becomes important to define the difference between psychological and psychiatric disorder and to study its prevalence. The primary endpoint of this study is to evaluate the prevalence of psychiatric disorders in a sample of Portuguese patients with metastatic breast cancer and assess the relationship between these disorders and the characteristics of the oncological disease.

Methods: Cross-sectional, single-center study with female patients diagnosed with metastatic breast carcinoma and under palliative treatment between November 2020 and May 2021. Psychiatric disorders were screened by applying and filling-out the MMSE, HADS, BSI, and WHOQoL-Bref instruments at the outpatient daycare unit when patients were present for treatment.

Results: A total of 91 female patients were included, median age 59.79 years. None of the patients had cognitive impairment (MMSE). HADS scale: 18.7% of the patients scored for anxiety and 17.6% for depression. The anxiety subscale score of > 8 (HADS) was related to ovarian function suppression ($p < 0.001$), neoadjuvant therapy ($p < 0.001$), and type of second-line of palliative treatment ($p = 0.024$). The depression subscale score > 8 (HADS) was related to the type of surgery performed ($p = 0.022$), molecular subtype of the tumor ($p = 0.020$), and occurrence of grade 3-4 toxicities in the first ($p = 0.018$), and third-line treatments ($p = 0.031$).

Conclusion: The screening of psychiatric disorders through the application of these scales by the medical oncology team may be able to aid in diagnosis and potentially lead to psychiatric referral and intervention at an earlier stage.

Keywords

oncology, psychiatric, disorder

This article is included in the **Oncology** gateway.

Corresponding author: Raquel Basto (raquelcbasto@gmail.com)

Author roles: **Basto R:** Conceptualization, Data Curation, Formal Analysis, Funding Acquisition, Investigation, Methodology, Project Administration, Resources, Software, Supervision, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing; **Caramujo C:** Data Curation; **Ferreira Gomes I:** Data Curation; **Fraga T:** Data Curation; **Correia Magalhães J:** Data Curation; **Sousa MJ:** Data Curation; **de Jesus S:** Writing – Review & Editing; **Monteiro AR:** Project Administration, Supervision, Validation, Writing – Review & Editing; **Pestana-Santos A:** Conceptualization, Investigation, Methodology, Project Administration, Supervision, Validation, Writing – Review & Editing; **Carvalho T:** Project Administration, Supervision, Validation, Writing – Review & Editing; **Albuquerque E:** Conceptualization, Investigation, Resources; **Sousa G:** Supervision, Validation, Visualization, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

Copyright: © 2022 Basto R *et al.* This is an open access article distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Basto R, Caramujo C, Ferreira Gomes I *et al.* **Screening patients with metastatic breast cancer for psychiatric disease: a cross sectional study [version 1; peer review: awaiting peer review]** F1000Research 2022, 11:73 <https://doi.org/10.12688/f1000research.79400.1>

First published: 21 Jan 2022, 11:73 <https://doi.org/10.12688/f1000research.79400.1>

Introduction

Cancer is the second leading cause of death worldwide, after cardiovascular disease.¹ In the 21st century, we have been witnessing a great evolution in oncology, both regarding our knowledge of cancer biology and physiopathology, as well as regarding its diagnosis and treatment. Still, cancer is regarded as an accelerated enhancer of suffering, uncontrolled pain, and death. This preconceived idea is directly related to some types of psychological disorders, regardless of the type of tumor and the stage at diagnosis.^{2,3} Therefore, cancer patients are at risk of developing some level of psychological dysregulation, depending on a series of variables related to the tumor, the environment, and the patient.⁴⁻⁶ In this context, it becomes important to define the difference between psychological and psychiatric disorder,⁷ since several studies have shown that there is a large percentage of cancer patients with psychological disorders⁷⁻⁹ but only a few meet the criteria for the diagnosis of psychiatric disorder.^{10,11} A few studies which surveyed the prevalence of psychiatric diagnoses in cancer patients have been conducted and demonstrated that the most frequent disorders were depression and anxiety.^{7,10} The correct and timely diagnosis of these disorders or diseases is of the utmost importance in order to help patients, since the absence of diagnosis, monitoring, and treatment of these pathologies can culminate in lack of treatment adherence and tolerance,¹² lower survival rates,¹³ and decreased quality of life.^{14,15}

There are several screening tools for psychological or psychiatric disorders validated for cancer patients. It is known that psychiatric morbidity affects women with breast cancer both in the initial and advanced stages,¹⁶ but few studies corroborate this. Furthermore, to the best of our knowledge, there are no data regarding the prevalence of psychiatric disorders in Portuguese patients with advanced breast cancer. Hence, our study aims to evaluate the prevalence of psychiatric disorders in a sample of Portuguese patients with metastatic breast cancer, as well as to assess the relationship between these disorders and the characteristics of the oncological disease.

Methods

Study design and procedure

We conducted a cross-sectional, single-center study. The convenience sample was designed with inclusion criteria consisting of female patients 18 years of age or older, diagnosed with metastatic breast carcinoma under palliative treatment with chemotherapy, hormone therapy, cyclin inhibitors, or targeted anti-HER2 therapy, between November 2020 and May 2021, at the Medical Oncology Department of the Instituto Português de Oncologia de Coimbra Francisco Gentil, E.P.E. Exclusion criteria for the study were known brain metastasis, baseline cognitive impairment, refusal to participate in the study, and incomplete clinical records. The final sample size after included 91 of the initial 128 participants evaluated.

Patients were recruited at the outpatient daycare unit when they were present for treatment. The application and filling-out of the various scales (Mini Mental State Examination (MMSE), HADS, BSI, and WHOQoL-Bref instruments) was conducted by the first author before treatment in order to minimize bias that could be developed in the post-treatment period. MMSE was the first instrument to be used, since a score compatible with cognitive impairment would represent and exclusion criteria. Afterwards, HADS, BSI and WHOQoL-Bref scales were applied through direct questioning of the patients and presentation of various possibilities of response, with repetition of each if solicited. The referral for the Psychiatry appointment was made whenever the HADS scale exceeded the cut-off score of 8 in each part of the instrument¹⁷ or when the BSI exceeded the cut-off of 1.7.^{18,19} The referred patients were posteriorly evaluated by an element of the psychiatric team consisting of two specialists, ideally within a month after the application of scales and at times within a week if the screening determined an elevated psychopathological risk. Determinants of elevated risk or severity included suicidal ideation and depressive symptoms with significant impact on daily functioning. The results, including possible diagnoses and eventual necessity of psychiatric medication from this evaluation were determined at this observation. The codification of psychiatric diagnoses was carried out using the International Classification of Diseases, Tenth Revision (ICD-10).

The following complementary data were collected either by direct questioning of the patient or consultation of the electronic files: gender; age; Eastern Cooperative Oncology Group – Performance Status (ECOG-PS); gynecological history; obstetric history; psychiatric; social history and characteristics of oncological disease.

The primary endpoints were assessing prevalence and type of psychiatric disorder and determining its relationship with characteristics of the oncological disease and treatment. Regarding secondary endpoints, quality of life (QoL) was evaluated.

Instruments

Various scales were applied including MMSE which is the most widespread cognitive impairment/dementia screening tool.²⁰ It is a brief 30-item measure that assesses six cognitive domains: visuospatial construction, language function,

attention and concentration, working memory, memory recall, and orientation to time and place.²¹ Each item on the test is scored as 0 or 1 with the total score varying between 0 and 30. The MMSE utilized in this study was adapted to the Portuguese population.²² In this study, the cut-off points were based on the educational level of the Portuguese population, where cognitive impairment was present if ≤ 1 points if illiterate, ≤ 22 if 1-11 years of formal education and ≤ 27 if more than 11 years of school.

The Hospital Anxiety and Depression Scale (HADS) helps the diagnosis of anxiety and depression in patients without previous psychiatric history. This instrument excludes symptoms of severe psychiatric disease and physical disease and it is divided into two parts, anxiety and depression, with each sub-section consisting of seven questions. These two parts are classified separately and cover several domains with control of possible confounding factors.²³ A total subscale score of eight or more points out of 21 denotes considerable symptoms of anxiety or depression. The scale applied in this study was validated for the Portuguese population.²⁴

The Brief Symptom Index (BSI) instrument consists of 53 items which the subject must rate how much a certain problem has affected them within the last week. It is a smaller version of the instrument Symptom Checklist-90-Revised (SCL-90-R) and the classification is based on a Likert-type scale (a psychometric scale). An approach to nine symptom dimensions is made (somatization, obsession-compulsion, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism) and three global indices of distress (Global Severity Index, Positive Symptom Distress Index, and Positive Symptom Total). The cutoff point for considering the existence of positive symptoms/pathology is above 1.7.¹⁹ An adapted and validated scale aimed at the Portuguese population was utilized.²⁵

To assess QoL and due to the need for an instrument that would be easily applicable in clinical trials or large-scale epidemiological studies, the World Health Organization (WHO) created the WHO-QoL Bref, which encompasses four domains related to quality of life (physical, psychological, social, and environmental). The score can be calculated in all or each domain, and QoL is better the higher the score.²⁶ An adapted and translated scale was applied to the sample.^{27,28}

Statistical analysis

Data were analyzed using SPSS statistics (IBM SPSS Data Editor Version 25.0 IBM Corp, Armonk, NY) software. Descriptive statistics (median and range for continuous variables, frequency and percentages for categorical variables) and univariate analysis (Mann-Whitney U Test, linear regression, one-way ANOVA and independent sample T-test for continuous data, chi-square and Fisher exact test for categorical data) were utilized, presenting data on the odds ratio (OR) and 95% confidence interval (CI), $p \leq 0.05$ was considered significant.

Ethics approval

The study was reviewed and approved by the Ethics Committee of the Instituto Português de Oncologia de Coimbra Francisco Gentil, E.P.E (02/2020), and performed following the ethical standards of the 1964 Declaration of Helsinki,²⁹ as well as its subsequent amendments. Upon inclusion, the study was carefully explained to all patients and an informed consent form was presented and signed by the patients who agreed to participate.

Results

Demographic sample characterization

A total of 128 patients were evaluated and 91 included (37 patients refused to participate because they did not consider this evaluation necessary). All patients were female, median age was 59.79 years at study inclusion, 49.90 years at breast cancer diagnosis and ECOG-PS was 0 in 62.6% of patients.

Regarding gynecological and obstetric history, menarche was between 10 and 12 years old in 58.3%; 69.2% of patients had used oral contraceptives at some point in their lives; 96.7% of patients had children and 64.8% had their first child before age 30; 75.8% of patients were postmenopausal or under ovarian function suppression at the time of data collection.

A history of psychiatric disorder was present in 16.5%: anxiety was the most frequent disease (7.7%), 16.5% were using psychiatric medication and 6.6% were already followed in a Psychiatry consultation. Regarding habits, 73.6% were non-smokers and 65.9% did not have alcoholic habits.

The most frequent molecular subtype was Luminal B HER2 negative (47.3%). At diagnosis 60.4% of patients had non-metastatic tumors, 19.8% underwent neoadjuvant chemotherapy, 51.6% underwent surgery with curative intent – more frequently mastectomy with axillary dissection (25.3%), and 34.1% underwent adjuvant chemotherapy. At the time of data collection 26.3% of patients were under first-line of palliative treatment, 51.8% under second-line, and 21.9% under

third-line. Treatment consisted in hormonal therapy in 69.19% of patients, chemotherapy in 36.2%, chemotherapy with anti-HER2 therapy in 31.8%, hormonal therapy with cyclin inhibitors 4/6 in 20.8%, hormonal with anti-HER2 therapy in 9.89% and anti-HER2 therapy in 5.49%. Grade 3–4 toxicity had occurred in 32.9% of patients. Patient characteristics can be consulted in [Table 1](#).

Prevalence of psychiatric disorder

MMSE scale application showed that none of the patients had cognitive impairment. HADS scale results showed that 18.7% of the patients scored positively for anxiety and 17.6% for depression. BSI scale application showed that 2.2% of patients surpassed the cut-off of 1.7, presenting positive symptoms. A total of 17 (18.6%) patients fulfilled HADS (n=17) or BSI criteria (n=2) for Psychiatric referral, of these, only 52.9% were consulted by a psychiatrist since the remaining patients refused observation.

There was a statistically significant relationship between an anxiety subscale score of >8 (HADS) and ovarian function suppression (median 12.40, $p<0.001$), use of neoadjuvant therapy regardless of the type of treatment (median 7.47, $p<0.001$), and use of hormonal and anti-HER2 therapy in tsecond-line of palliative treatment (median 7.44, $p=0.024$).

The anxiety subscale general score was higher in postmenopausal patients (median 6.53, $p=0.002$), particularly in patients with ovarian function suppression (median 12.40, $p<0.001$). It was also higher in patients with stage IV disease at diagnosis (median 6.86, $p=0.045$), treated with hormonal therapy as first-line (median 6.64, $p=0.041$), treated with anti-HER2 therapy and chemotherapy as second-line (median 11, $p=0.044$), and treated with chemotherapy as third-line (median 7.82, $p=0.020$).

Regarding the depression subscale score >8 of HADS, there was a statistically significant relationship with previous mastectomy with axillary dissection (median 7.96, $p=0.022$), HER2-negative Luminal B tumors (median 6.52, $p=0.020$), and grade 3–4 toxicities in the first (median 6.44, $p=0.018$) and third-line treatments regardless of the type of treatment (median 9.43, $p=0.031$). The depression subscale general score of HADS was also higher in older patients (median 6.43, $p=0.006$), postmenopausal patients (median 6.37, $p=0.007$), and in those treated with chemotherapy as third-line (median 10, $p<0.001$).

Regarding BSI score >1.7, there was a statistically significant relationship with moderate alcohol habits ($p=0.013$). Details concerning the HADS and BSI scores can be consulted in [Table 2](#).

Psychiatric diagnosis

Of the 17 patients with referral criteria for a Psychiatry appointment (17 scored positively on the HADS scale and 2 on the BSI scale), only 9 patients accepted the referral and of these all were diagnosed with some type of psychiatric disorder.

Of the nine patients who accepted referral for psychiatric consultation, 55.55% were diagnosed with dysthymic disorder (F34.1), 33.33% with depression (F33), and 11.11% with adjustment disorder (F43.2). All patients were considered to have indication from treatment with an antidepressant, 44.44% required an association with an anxiolytic, and 22.22% with an antipsychotic.

Quality of life assessment

The median total score on the WHOQoL-Bref was 92.33 points, the environment domain was the highest with a median score of 80.53, followed by the social relationships domain with 77.89, psychological domain with 77.05, and physical domain with 69.79.

The better the ECOG-PS the higher the WHOQoL-Bref score, particularly in the physical and social relationships domains ($p<0.001$). Menopause also seemed to influence physical, psychological and social relationships domains, particularly the physical domain, in which premenopausal women had a higher median scored postmenopausal women (median 79.14 versus 66.81, $p<0.001$). On the other hand, women who underwent ovarian function suppression scored lower in the psychological domain (median 57.83 versus 74.80 for natural menopause vs 80.94 for surgical menopause, $p=0.002$). The absence of previous psychiatric history/medication seemed to influence the environmental domain (median 81.58, $p=0.002$), which was also related to alcoholic habits with abstinent patients scoring higher (median 80.13, $p=0.018$). Patients with initial stage IV tumors scored lower in all domains, except social relationships (median 78.31, $p=0.007$). Patients under hormone therapy and cyclin inhibitors 4/6 as second-line treatment scored higher in all domains, particularly the environment domain (median 89.29, $p<0.001$). Occurrence of grade 3–4 toxicities also seemed to affect scores, particularly the physical domain in patients under first-line treatment (median 61.75, $p=0.016$), social

Table 1. Demographics.

	All patients (n=91) (%)
Age group	
20-29	1 (1,1%)
30-39	4 (4,4%)
40-49	22 (24,2%)
50-59	20 (22%)
60-69	18 (19,8%)
70-79	16 (17,6%)
80-89	10 (11%)
Previous psychiatric disease (n)	
Anxiety	7 (7,7%)
Depression	4 (4,4%)
Insomnia	3 (3,3%)
Anxiety, Depression	1 (1,1%)
Previous psychiatric medication (n)	
Anxiolytics	7 (7,7%)
Antidepressants	4 (4,4%)
Sleep inducers	3 (3,3%)
Anxiolytics, Antipsychotics	1 (1,1%)
Previous follow-up in a Psychiatric consultation	
Follow-up	6 (6,6%)
No-follow-up	84 (92,3%)
Molecular subtype	
Luminal A like	12 (13,2%)
Luminal B like HER2 negative	43 (47,3%)
Luminal B like HER2 positive	15 (16,5%)
HER2 positive (negative hormonal receptors)	12 (13,2%)
Triple negative	9 (9,9%)
Stage at diagnosis	
< IV	55 (60,4%)
≥ IV	36 (39,6%)
Neoadjuvant therapy	
Use	18 (19,8%)
No use	36 (39,6%)
Surgery previous to stage IV	
Yes	47 (51,6%)
No	8 (8,8%)
Type of surgery	
Mastectomy	2 (2,2%)
Mastectomy with SGB	13 (14,3%)
Mastectomy with axillary emptying	23 (25,3%)
Tumorectomy with SGB	9 (9,9%)

Table 2. HADS and BSI score.

	Anxiety Subscale Score (HADS) > 8	Anxiety subscale general score (HADS)	Depression Subscale Score (HADS) > 8	Depression subscale general score (HADS)	BSI Score > 1.7
	p value	p value	p value	p value	p value
Age	0.317	0.475; R=0.076; B=0.023	0.488	0.006; R=0.286; B=0.074	<0.001
ECOG-PS	0.999	0.295	0.231	0.065	0.582
Menarche	0.730	0.956; R=0.006; B=0.015	0.268	0.690; R=0.042; B=-0.093	0.869
Menopause	0.547	0.002	0.752	0.007	0.056
Type of menopause	<0.001	<0.001	0.107	0.653	No statistics are computed because BSI (cut off) is a constant.
Previous follow-up in a psychiatric consultation	0.327	0.996	0.288	0.190	0.999
Psychiatric Background	0.726	0.032	0.999	0.507	0.999
Use of previous psychiatric medication	0.726	0.032	0.999	0.507	0.999
Smoking Habits	0.348	0.727	0.348	0.153	0.999
Alcoholic Habits	0.999	0.484	0.247	0.228	0.013
Initial Stage	0.785	0.045	0.347	0.974	0.154
Neoadjuvant chemotherapy	0.005	0.329	0.999	0.890	No statistics are computed because BSI (cut off) is a constant.
Surgery	0.665	0.830	0.587	0.446	No statistics are computed because BSI (cut off) is a constant.
Type of Surgery	0.356	0.256	0.022	0.001	No statistics are computed because BSI (cut off) is a constant.
Adjuvant chemotherapy	0.247	0.724	0.999	0.474	No statistics are computed because BSI (cut off) is a constant.
Tumor's Molecular Subtype	0.326	0.776	0.020	0.847	0.067
The first line of palliative treatment	0.944	0.041	0.064	0.052	0.341
The second line of palliative treatment	0.024	0.044	0.594	0.722	0.212
The third line of palliative treatment	0.237	0.020	0.308	<0.001	No statistics are computed because BSI (cut off) is a constant.

Table 2. *Continued*

	Anxiety Subscale Score (HADS) > 8	Anxiety subscale general score (HADS)	Depression Subscale Score (HADS) > 8	Depression subscale general score (HADS)	BSI Score > 1.7
	p value	p value	p value	p value	p value
Treatment interruption (First line)	0.579	0.235	0.582	0.180	0.999
Treatment interruption (Second line)	0.565	0.154	0.999	0.463	0.999
Treatment interruption (Third line)	0.999	0.531	0.999	0.515	No statistics are computed because BSI (cut off) is a constant.
Grade 3-4 Toxicity (First Line)	0.054	0.884	0.018	0.056	0.999
Grade 3-4 Toxicity (Second Line)	0.565	0.154	0.999	0.463	0.999
Grade 3-4 Toxicity (Third Line)	0.999	0.858	0.031	0.088	No statistics are computed because BSI (cut off) is a constant.
Lack of treatment adherence (First Line)	0.009	0.225	0.213	0.400	0.999
Lack of treatment adherence (Second Line)	0.228	0.339	0.674	0.042	0.999
Lack of treatment adherence (Third Line)	0.999	0.394	0.999	0.879	No statistics are computed because BSI (cut off) is a constant.

relationships domain in second-line (median 88.60, $p < 0.001$) and third-line ($p = 0.009$), and environment domain in third-line (median 83.71, $p = 0.013$). Details concerning the scores of WHO-QOL Bref are shown in [Table 3](#).

Discussion

In this study, 5.49% of our patients were diagnosed with a dysthymic disorder and 3.28% with depression, with the diagnosis of anxiety playing a secondary role in this sample of patients. The prevalence of psychiatric disorder in cancer patients, not specifically breast cancer patients, has been assessed before and it varies between studies, ranging from 13 to 56%.^{7,10} Our study showed a prevalence closer to the lower percentages reported. On the other hand, the prevalence of adjustment disorders has been assessed as high as 68%, and in our study these disorders played a secondary role (1.09%).⁷

The BSI scale positively screened only two of the nine patients (22.2%) referred for Psychiatry appointment, and we postulate that this may be due to the scale's extension, with 53 items, and the patient's exhaustion while responding to it.^{21,22} Indeed, the fact that BSI scale requires a considered amount of time and concentration might be one of its main drawbacks. Hence, in our study, HADS seemed to be the scale with the best efficacy at screening patients, by identifying 17 patients (18.6%) that could benefit from psychiatric appointment. The fact that this tool has proven to be the most effective in identifying patients is possibly related, among other factors, to its quick applicability.²³ All patients who were positively screened by the scales and who were evaluated by a psychiatrist were eventually diagnosed with psychiatric pathology, suggesting a high specificity of this scale, which is in accordance with other studies - For distress (any mental ill health) the HADS-T, HADS-D and HADS-A had a pooled sensitivity and specificity of 72.8%, 80.6%; 75.7%, 66.3% and 65.7%, 71.3%, respectively.³⁰

QoL assessment also proved to be a lengthy process, since it was the researchers' perception that this scale took the longest time both in the response phase by participants and in the interpretation phase by the researchers. Since QoL is such an

Table 3. WHO-QoL Bref Score.

	WHO-QoL Bref - Domain Score	WHO-QoL Bref - Domain 2Score	WHO-QoL Bref - Domain 3 Score	WHO-QoL Bref - Domain 4 Score
	p value	p value	p value	p value
Age	0.055; R=0.202; B=-0.247	0.076; R=0.187; B=-0.195	<0.001; R=0.382; B=-0.367	0.004; R=0.296; B= -0.181
ECOG-PS	<0.001	0.009	<0.001	0.008
Menarche	0.782; R=0.029; B=0.309	0.816; R=0.025; B=0.220	0.820; R= 0.024; B=0.199	0.319; R=0.106; B=0.551
Menopause	<0.001	0.013	0.001	0.125
Type of menopause	0.056	0.002	0.112	0.056
Previous follow-up in a psychiatric consultation	0.259	0.083	0.784	0.027
Psychiatric Background	0.260	0.731	0.213	0.002
Use of previous psychiatric medication	0.260	0.731	0.213	0.002
Smoking Habits	0.581	0.108	0.326	0.482
Alcoholic Habits	0.018	0.421	0.918	0.429
Initial Stage	0.007	0.046	0.812	0.044
Neoadjuvant chemotherapy	0.685	0.982	0.643	0.613
Surgery	0.526	0.491	0.747	0.075
Type of Surgery	0.601	0.307	0.776	0.910
Adjuvant chemotherapy	0.007	0.887	0.067	0.241
Tumor's Molecular Subtype	0.314	0.337	0.445	0.048
First line of palliative treatment	0.403	0.929	0.038	0.222
Second line of palliative treatment	0.001	0.042	0.022	<0.001
Third line of palliative treatment	0.062	0.026	0.260	0.299
Treatment interruption (First line)	0.421	0.453	0.011	0.506
Treatment interruption (Second line)	0.883	0.937	<0.001	0.819
Treatment interruption (Third line)	0.822	0.994	0.429	0.674
Grade 3-4 Toxicity (First Line)	0.016	0.999	0.762	0.927
Grade 3-4 Toxicity (Second Line)	0.883	0.937	<0.001	0.819
Grade 3-4 Toxicity (Third Line)	0.577	0.849	0.009	0.013
Lack of treatment adherence (First Line)	0.902	0.344	0.988	0.507
Lack of treatment adherence (Second Line)	0.015	0.012	0.667	0.028
Lack of treatment adherence (Third Line)	0.929	0.759	0.777	0.017

important measure in oncology, particularly in a palliative setting, this drawback of the WHOQoL-Bref score highlights the importance of developing quicker and simpler scales for use in an outpatient setting. According to our experience, the WHOQoL-Bref may not serve as an effective pillar as a screening tool for psychiatric illness.

We were also able to demonstrate that the presence of psychiatric pathology was possibly related to several variables related to the characteristics of the tumor and the patient similar to what was described in previous studies.⁴⁻⁶ Thus, after applying the scales, we could determine a few relationships - moderate alcohol habit seems to influence the existence of positive psychiatric symptoms, similarly to what is described in Arias F. et al³¹; patients who underwent ovarian suppression therapy scored higher on the anxiety subscale, which is contrary to what is shown by Yi HW et al, in which no differences in anxiety score were demonstrated in this subgroup of patients, compared to patients without ovarian suppression therapy³² and patients who underwent mastectomy with axillary dissection demonstrated to score more on the depression subscale, and this is in agreement with other studies, in which it is demonstrated that patients who undergo this type of surgical procedure have a higher prevalence of depression compared to those who do not.³³

The QoL score on the quality-of-life assessment questionnaire, either in totality or in any of the domains, it was more influenced by factors related to advanced disease, which is in agreement with another study - the quality of life decreases substantially in advanced breast cancer.³⁴

We find it important to note that 28.9% of patients refused to participate in the study and 47% of patients who were offered a psychiatric consultation refused. There are several reasons for this and our study was not designed to explore that, but we postulate that a certain level of prejudice regarding psychiatric disorder may be one of them.

To our knowledge, this is the first study to evaluate the prevalence of psychiatric disease in patients with metastatic breast cancer from Portugal, and it highlights the importance of educating both health care professionals and patients regarding the spectrum of psychiatric and psychologic disorders, as well as the importance of developing and using effective tools at screening these patients.

Study limitations

Our study has some limitations: the fact that it is a single-center study limits the generalization of our findings, and our sample of patients is heterogeneous, since we included patients under different treatments and at different stages of advanced disease. We were also subjected to selection bias by selecting our patients at the outpatient daycare unit where most patients are present for treatment with subcutaneous or intravenous treatments such as ovarian suppression medications and chemotherapy, which translates into a younger sample of patients than expected for patients with breast cancer.

Clinical implications

Screening for psychological and psychiatric disorders requires a specific time allocated to the oncology consultation or more time available for patient observation, which may not be possible in all cancer centers and departments. This highlights the importance of screening tools that are simple and quick to apply, such as the HADS scale. On the other hand, the existence of a Psychiatry department with a quick response capacity and patient orientation is necessary in order to guarantee timely and adequate evaluation as well as detection and intervention of relevant psychopathology which may influence patient orientation and response.

Conclusion/Generalisability

Screening patients with metastatic breast cancer for psychiatric disorders is of the utmost importance. Not all patients can and need to be observed in a psychiatric appointment; hence, providing medical and radiation oncology teams with simple and quick to implement tools to screen their patients can lead to referral for consultation and subsequent diagnosis and treatment of psychiatric disease at an earlier stage. In our study, HADS proved to be particularly helpful at this task, since it was quick to apply and showed a good specificity for psychiatric disease.

Data availability

Underlying data

Figshare: Database.xlsx, <https://doi.org/10.6084/m9.figshare.18364970.v1>.

Data are available under the terms of the [Creative Commons Attribution 4.0 International license](#) (CC-BY 4.0).

Acknowledgements

An earlier version of this article can be found on Research Square (DOI: [10.21203/rs.3.rs-946803/v1](https://doi.org/10.21203/rs.3.rs-946803/v1))

References

1. Lopez AD, Murray CC: **The global burden of disease, 1990–2020.** *Nat. Med.* 1998; **4**(11): 1241–1243.
[PubMed Abstract](#) | [Publisher Full Text](#)
2. Anuk D, Özkan M, Kizir A, et al.: **The characteristics and risk factors for common psychiatric disorders in patients with cancer seeking help for mental health.** *BMC Psychiatry.* 2019; **19**(1): 1–11.
[Publisher Full Text](#)
3. McGuire S: *World cancer report 2014.* Geneva, Switzerland: World Health Organization, international agency for research on cancer, WHO Press; 2016; **7**(2): 418–419. 2015. Advances in nutrition.
4. Zabora J, BrintzenhofeSzoc K, Curbow B, et al.: **The prevalence of psychological distress by cancer site. Psycho-Oncology: Journal of the Psychological, Social and Behavioral Dimensions of.** *Cancer.* 2001; **10**(1): 19–28.
[Publisher Full Text](#)
5. Bultz BD, Holland JC: **Emotional distress in patients with cancer: the sixth vital sign.** *Commun. Oncol.* 2006; **3**(3): 311–314.
[Publisher Full Text](#)
6. Holland JC, Andersen B, Breitbart WS, et al.: **Distress management.** *J. Natl. Compr. Cancer Netw.* 2010; **8**(4): 448–485.
[Publisher Full Text](#)
7. Derogatis LR, Morrow GR, Fetting J, et al.: **The prevalence of psychiatric disorders among cancer patients.** *JAMA.* 1983; **249**(6): 751–757.
[Publisher Full Text](#)
8. Chahl P, Bond A: **T'm sorry but you've got cancer: the role of psycho-oncology.** *British Journal of Hospital Medicine* (2005). 2009; **70**(9): 514–517.
[PubMed Abstract](#) | [Publisher Full Text](#)
9. Breitbart W: **Identifying patients at risk for, and treatment of major psychiatric complications of cancer.** *Support. Care Cancer.* 1995; **3**(1): 45–60.
[PubMed Abstract](#) | [Publisher Full Text](#)
10. Levine PM, Silberfarb PM, Lipowski ZJ: **Mental disorders in cancer patients. A study of 100 psychiatric referrals.** *Cancer.* 1978; **42**(3): 1385–1391.
[PubMed Abstract](#) | [Publisher Full Text](#)
11. Tada Y, Matsubara M, Kawada S, et al.: **Psychiatric disorders in cancer patients at a university hospital in Japan: descriptive analysis of 765 psychiatric referrals.** *Jpn. J. Clin. Oncol.* 2012; **42**(3): 183–188.
[PubMed Abstract](#) | [Publisher Full Text](#)
12. Massie J: **Overview of normal reactions and prevalence of psychiatric disorders.** *Handbook of psycho-oncology.* 1989.
13. Loberiza FR Jr, Rizzo JD, Bredeson CN, et al.: **Association of depressive syndrome and early deaths among patients after stem-cell transplantation for malignant diseases.** *J. Clin. Oncol.* 2002; **20**(8): 2118–2126.
[PubMed Abstract](#) | [Publisher Full Text](#)
14. Valdimarsdottir U, Helgason ÁR, Fürst CJ, et al.: **The unrecognized cost of cancer patients' unrelieved symptoms: a nationwide follow-up of their surviving partners.** *Br. J. Cancer.* 2002; **86**(10): 1540–1545.
[PubMed Abstract](#) | [Publisher Full Text](#)
15. Kurtz ME, Kurtz JC, Given CW, et al.: **Relationship of caregiver reactions and depression to cancer patients' symptoms, functional states and depression—a longitudinal view.** *Soc. Sci. Med.* 1995; **40**(6): 837–846.
[PubMed Abstract](#) | [Publisher Full Text](#)
16. Kissane DW, Grabsch B, Love A, et al.: **Psychiatric disorder in women with early-stage and advanced breast cancer: a comparative analysis.** *Aust. N. Z. J. Psychiatry.* 2004; **38**(5): 320–326.
[PubMed Abstract](#) | [Publisher Full Text](#)
17. Rishi P, Rishi E, Maitray A, et al.: **Hospital anxiety and depression scale assessment of 100 patients before and after using low vision care: A prospective study in a tertiary eye-care setting.** *Indian J. Ophthalmol.* 2017; **65**(11): 1203–1208.
[PubMed Abstract](#) | [Publisher Full Text](#)
18. Canavarro MCCDSP: **Relações Afectivas ao Longo do Ciclo de Vida e Saúde Mental (Doctoral dissertation).** 1997.
19. Derogatis LR, Melisaratos N: **The brief symptom inventory: an introductory report.** *Psychol. Med.* 1983; **13**(3): 595–605.
[PubMed Abstract](#) | [Publisher Full Text](#)
20. Santana I, Duro D, Lemos R, et al.: **Mini-Mental State Examination: Screening and diagnosis of cognitive decline, using new normative data.** *Acta Medica Port.* 2016; **29**(4): 240–248.
[PubMed Abstract](#) | [Publisher Full Text](#)
21. Folstein MF, Folstein SE, McHugh PR: **"Mini-mental state": a practical method for grading the cognitive state of patients for the clinician.** *J. Psychiatr. Res.* 1975; **12**(3): 189–198.
[Publisher Full Text](#)
22. Guerreiro M, Silva AP, Botelho M, et al.: **Adaptação a população portuguesa da tradução do Mini Mental State Examination (MMSE).** *Revista Portuguesa de Neurologia.* 1994; **1**: 9.
23. Bjelland I, Dahl AA, Haug TT, et al.: **The validity of the Hospital Anxiety and Depression Scale: an updated literature review.** *J. Psychosom. Res.* 2002; **52**(2): 69–77.
[Publisher Full Text](#)
24. Pais-Ribeiro J, Silva I, Ferreira T, et al.: **Validation study of a Portuguese version of the Hospital Anxiety and Depression Scale.** *Psychol. Health Med.* 2007; **12**: 225–237.
[PubMed Abstract](#) | [Publisher Full Text](#)
25. Canavarro MC: **Inventário de Sintomas Psicopatológicos: BSI.** Simões MR, Gonçalves M, Almeida LS, editors. *Testes e provas psicológicas em Portugal.* Braga: SHO/APPORT; 1999; (vol. II, pp. 87–109).
26. Skevington SM, Lotfy M, O'Connell KA: **The World Health Organization's WHOQOL-BREF quality of life assessment: psychometric properties and results of the international field trial. A report from the WHOQOL group.** *Qual. Life Res.* 2004; **13**(2): 299–310.
[PubMed Abstract](#) | [Publisher Full Text](#)
27. Canavarro MC, Simões MR, Vaz Serra A, et al.: **Instrumento de avaliação da qualidade de vida da Organização Mundial de Saúde: WHOQOL-Bref.** Simões M, Machado C, Gonçalves M, et al., editors. *Avaliação psicológica: Instrumentos validados para a população portuguesa.* Coimbra: Quarteto Editora; 2007; (Vol. III, pp. 77–100).
28. Canavarro MC, Vaz Serra A, Pereira M, et al.: **WHOQOL disponível para Portugal: Desenvolvimento dos instrumentos de avaliação da qualidade de vida da Organização Mundial de Saúde (WHOQOL-100 e WHOQOL-BREF).** Canavarro MC, Vaz Serra A, editors. *Qualidade de vida e saúde: Uma abordagem na perspectiva da Organização Mundial de Saúde.* Lisboa: Fundação Calouste Gulbenkian; 2010; (pp. 171–190).
29. Rickham PP: **Human Experimentatio. Code of ethics of the world medical association of Helsinki.** *Br. Med. J.* 1964; **2**(5402): 177.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
30. Mitchell AJ, Meader N, Symonds P: **Diagnostic validity of the Hospital Anxiety and Depression Scale (HADS) in cancer and palliative settings: a meta-analysis.** *J. Affect. Disord.* 2010; **126**(3): 335–348.
[PubMed Abstract](#) | [Publisher Full Text](#)
31. Arias F, Szerman N, Vega P, et al.: **Alcohol abuse or dependence and other psychiatric disorders. Madrid study on the prevalence of dual pathology.** *Ment. Health Subst. Use.* 2013; **6**(4): 339–350.
[Publisher Full Text](#)
32. Yi HW, Nam SJ, Kim SW, et al.: **Abstract P1-11-01: Depression and anxiety after adjuvant ovarian function suppression in premenopausal breast cancer patients.** 2016.
33. Kim MS, Kim SY, Kim JH, et al.: **Depression in breast cancer patients who have undergone mastectomy: a national cohort study.** *PLoS One.* 2017; **12**(4): e0175395.
[PubMed Abstract](#) | [Publisher Full Text](#)
34. Grabsch B, Clarke DM, Love A, et al.: **Psychological morbidity and quality of life in women with advanced breast cancer: a cross-sectional survey.** *Palliat. Support. Care.* 2006; **4**(1): 47–56.
[PubMed Abstract](#) | [Publisher Full Text](#)

The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias
- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

For pre-submission enquiries, contact research@f1000.com

F1000Research