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RETROSPECTIVE ANALYSES OF PSYCHOLOGICAL DISTRESS AND DEFENSE STYLE AMONG CANCER PATIENTS

Ciro Conversano, Mariagrazia Di Giuseppe, Mario Miccoli, Rebecca Ciacchini, Annarita Di Silvestre, Rosa Lo Sterzo, Angelo Gemignani, Graziella Orrù

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Abstract

Objective: Psychological distress is common in cancer patients during the diagnostic phase. Research demonstrated that anxiety, depression and defense mechanisms may influence physical and psychological well-being in patients with malignant tumors. The present retrospective study investigated the associations between clinical and psychological characteristics of cancer patients waiting for the diagnosis, focusing on metastatic cancer (MC) and breast cancer (BC).

Methods: Patients with a new diagnosis of cancer referring to a Clinical Oncology Unit in Central Italy were interviewed during the 2017 for psychological assessment. Double-blind information about anxiety, depression, sleep disorders, defense style, and cancer diagnosis were available for the 567 patients included in this study. T-test, chi-squared and regression analyses were performed to detect associations between psychological variables and the presence of metastasis (MC) in the whole sample and in the subgroup of breast cancer (BC) patients.

Results: Female gender and younger age were associated with anxiety, depression, and maladaptive defense style. A significant positive relationship was found between presence of metastasis and symptoms of anxiety. Depression resulted significantly more frequent in BC, while there was a trend close to statistical significance in MC. Immature defense style was widely used by BC women, with a score close to statistical significance.

Conclusions: This retrospective study provided empirical evidence of the relationship between psychological functioning and clinical characteristics of cancer. In line with previous research, our findings confirmed the peculiar psychological functioning of BC patients. Further investigations are needed to understand how the diagnosis of cancer may influence the individual psychological functioning and vice versa.

Key words: anxiety, depression, defense style, breast cancer, metastasis, somatization, adaptiveness

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Introduction

As an increasingly widespread illness, the etiology of cancer is being studied while considering multiple pathways associated with its onset and progression (Usset et al., 2016; Lugo et al., 2018). Besides the well-known influence of biological, genetic and environmental factors, recent studies highlighted the impact of psychological aspects (Lemogne et al., 2013; Nakaya, 2014; Schoormans, Husson, Denollet & Mols, 2017; Settineri, Frisone, & Merlo, 2018; Di Giuseppe, Miniati et al., 2020; Martino, Catalano et al., 2020; Martino,

Bellone et al., 2019). Cancer disease has been classified as a chronic disease, although some of its characteristics may be acute at certain stages (Phillips & Currow, 2010). As a chronic illness, cancer is expected to share the same psychopathogenic characteristics present in chronic and stress-related conditions, the most common being anxious depressive manifestations, neuropsychological impairments, post-traumatic stress, and mood disorders, with all the expected consequences (Conversano et al., 2019; 2020; Dell'Osso et al., 2014; Marazziti et al., 2008; Marazziti et al., 2015; Marchi et al., 2019).

Both depression and anxiety seem to play an

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important role in cancer initiation (Shen et al., 2013; Jia et al., 2017), while increasing sleep disturbance and daytime sleepiness, and are associated with maladaptive defense mechanisms and coping strategies (Colovic, Lecic Tosevski, Perunic Mladenovic, 2016; Gould et al., 2018; Di Giuseppe, Ciacchini, Piarulli, Napa & Conversano, 2019; Martino, Caputo, Bellone, Quattropiani, & Vicario, 2020b). Research on defense mechanisms in cancer progression reported that maladaptive defenses are associated with psychological distress, worst treatment outcome, and lower survival probability (Beresford, Alfors, Mangum, Clapp & Martin, 2006; Di Giuseppe et al., 2018; Lin et al., 2018), whereas other studies reported controversial findings (Sawada et al., 2016). Despite the considerable progress made on cancer prevention and treatment, there is still scarce understanding of how psychological functioning might influence its development and progression (Giuse-Davis, 2008; Satin, Linden & Philips, 2009; Catalano et al., 2019; Conversano, 2019; Merlo, 2019). In this study we analyzed the associations between these aspects of psychological functioning and several demographic and clinical characteristics of cancer patients (CP), as age, gender, and the presence of metastasis (MC), with particular attention to psychological responses of breast cancer (BC) patients.

Anxiety, depression, and defense style in cancer patients

A large body of literature tried to analyze the influence of psychological distress in cancer progression (Reiche, Morimoto & Nunes, 2005). Recent studies observed associations between cancer progression and both low quality of life and global health state (Wagner et al., 2018), whereas optimistic thinking predicted lower level of anxiety (Fisher, Cripe & Rand, 2018). In their study, Bronner and colleagues found that the level of anxiety in diagnostic phase is associated with the patient's coping style (Bronner, Nguyen, Smets, van der Ven & van Weert, 2018). Furthermore, the relationship between depression and poorer prognosis in cancer patients has been widely demonstrated (Sotelo, Musselman & Nemeroff, 2014). A recent review highlighted how depression and psychosocial stressors in cancer promote inflammation and oxidative/nitrosative stress, a decreased immunosurveillance, and a dysfunctional activation of the autonomic nervous system and of the hypothalamic-pituitary-adrenal axis (Bartolatto et al., 2017). Again, psychotherapeutic interventions resulted effective in reducing symptoms of psychological distress (Lingiardi et al., 2010 that, in turn, might affect disease progression and mortality of cancer patients (Barrera & Spiegel, 2014). Results of recent studies showed that different types of psychotherapies promoted similar improvements in depression (Blanco et al., 2019), while modest improvement in outcome occurred after 8-weeks of Mindful Yoga intervention (Porter et al., 2019).

Researches on defense mechanisms and coping strategies demonstrated that the way cancer patients deal with internal conflicts and external stressors may influence illness progression and the treatment outcome (Ollonen & Eskelinen, 2007; Di Giuseppe et al., 2018; Settineri et al., 2018b; Lenzo, Sardella, Martino, & Quattropiani, 2020). Patients with cancer show lower overall defensive functioning than cancer survivors and controls (Di Giuseppe, Miniati et al., 2020; Perry, Metzfer & Sigal, 2015), and the use of repression is associated with a lower quality of life (Paika et al., 2010), and worse illness progression (Hyphantis, Paika, Almyroudi,

Kampletsas & Pavlidis, 2011). Moreover, Baitar and colleagues found that coping strategies influence well-being of patients with cancer, but the impact is higher in middle-aged patients, and palliative reacting resulted the only predictor of well-being in older cancer patients (Baitar et al., 2018).

Psychological characteristic of breast cancer women

Research explored psychological characteristics of BC women, supporting the hypothesis of a relationship between BC and personality characteristics (Cardenal, Ortiz-Tallo, Martín Frías & Martínez Lozano, 2008). Recent studies demonstrated that anxiety contributes to the feeling of distress in BC women more than depression (Ng et al., 2017). Patients with low-level anxiety tend to use problem-solving strategies, while women with medium to high-level anxiety tend to use emotion-focused coping (Silva, Zandonade & Amorim, 2017). Furthermore, a recent pilot study analyzing the defensive profile of BC women in comparison with other primary site cancer patients found higher use of reaction formation, omnipotence and rationalization, as compared with other cancer patients, while repression and displacement were equally used in all patients (Di Giuseppe, Di Silvestre et al., 2019).

Research objectives

The present study aimed at identifying relationships between psychiatric symptoms, defensive style and the clinical characteristics of cancer. We intended to verify the following hypotheses: 1) psychological distress and defense style maturity in cancer patients are related to age and gender characteristics; 2) metastatic cancer is associated to higher psychological distress and immature defense style; and finally 3) BC differentiates from other primary site cancer for psychological distress and defensive maturity.

Method

Participants

The sample consisted in retrospective data of 669 new cancer patients referring to a Clinical Oncology in Central Italy during the year 2017. For each patient we extracted socio-demographic information (age, gender, marital status, and number of descendants), psychological functioning (anxiety, depression, sleep disturbance, and defense style) and clinical diagnosis (cancer primary site and presence/absence of metastasis). Complete data were available for 567 patients that constituted the final sample for the study. Participants were mainly women ($N=313$; 55%) and the mean age \pm SD was 64.3 ± 13.21 years, while 85.4% of the sample ($N=484$) was older than 50 years. About 2 of 3 of participants were married or cohabitant ($N=371$; 65.4%), followed by 17.1% widowed ($N=97$), 10.8% single or ecclesiastic ($N=61$), and 6.7% divorced ($N=38$). The 86.2% of the sample ($N=489$) had living descendants and about one third of them ($N=127$) had more than three children.

Psychological assessment

A clinical interview and a clinical data form were used for the psychological assessment of each patient. This routine, non-standardized assessment procedure

was performed during the diagnostic process. The main aim of the psychological assessment procedure was to evaluate the patient psychological functioning and eventually provide psychological assistance to either the patient, his/her caregivers, or both.

The clinical interview included questions about socio-demographic characteristics, family composition, history of cancer in relatives, history of psychiatric illness, presence/absence of psychological symptoms, and maturity of defensive strategies. Psychological symptoms of depression, anxiety and sleep disturbance were assessed on the basis of participants responses to direct question about their presence/absence. The defensive maturity was evaluated using a non-standardized 3-point Likert scale basing on the clinical observation of the patient's defensive responses during the clinical interview, scoring 1 for immature defense style, 2 for neurotic, and 3 for mature defense style.

Procedure

After signing an informed consent, patients were individually interviewed by a psycho-oncologists for the pre-treatment psychological assessment. At the end of each interview, the clinician filled a clinical form about the patient's socio-demographic, professional and psychological information. At the time of the interview, neither the patient nor the interviewer known information regarding cancer severity and further treatment indications. Data were entered in a database including clinical information obtained from the patient's histologic exam. Patients identity was kept anonymous and substituted by a number code.

We did not seek ethical committee approval for this study, because: 1) all data analyzed were collected as part of routine diagnosis and treatment; 2) patients were diagnosed and treated according to national guidelines and agreements; 3) the paper does not report on the use of experimental or new protocols; 4) the program was not set up as a study or research project, but as a treatment program; 5) our analysis looked retrospectively at outcomes for a large cohort of patients treated. This was done internally as part of an evaluation, so as to improve our quality of care. The decision to change the threshold was based on our clinical impression that psychological distress might be associated with specific clinical conditions. We felt that this information should be shared with the wider clinical community.

Data Analyses

The Mann-Whitney test was used to compare defense

style score between the two groups. Chi-squared test was performed to analyze the association between categorical variables. Logistic regression was carried out to study the influence of age on anxiety, depression and defense style. The significance level was set to 5%, the statistical analysis was conducted using the statistical software R 3.5.0.

Results

Clinical characteristics of the sample

One third of the total sample was represented by BC (95/567; 16.7%) and colon-rectal cancer (95/567; 16.7%) patients. The third more frequent diagnosis was lung cancer (56/567; 9.9%), followed by gastro-intestinal (44/567; 7.8%), cervical-uterine (40/567; 7.1%), head-neck (39/567; 6.9%), melanoma (36/567; 6.3%), brain (23/567; 4.0%), ovary (21/567; 3.7%), prostate (21/567; 3.7%), pancreas (19/567; 3.3%), bladder (15/567; 2.6%), and renal (14/567; 2.5%). About 6% of the sample was affected other primary-site cancers as sarcoma (9/567; 1.6%), liver (9/567; 1.4%), testicular (7/567; 1.2%), thyroid (6/567; 1.1%), marrow (3/567; 0.5%), and lymph node (1/567; 0.2%), while only 2.6% received a diagnosis of unknown primary-site cancer (15/567). Less than 20% of the sample showed metastasis at the time of first diagnosis (109/567; 19.2%).

Psychological conditions in our sample indicated high level of distress: More than three in four patients (444/567; 78.3%) reported psychiatric symptoms, in particular symptoms of anxiety (312/567; 55.0%), depression (241/567; 42.6%) and sleep disturbance (225/567; 39.7%). Defense style was generally assessed as immature (272/567; 48.0%), demonstrating that severe traumatic experiences of a cancer diagnosis might affects the individual defensive responses to stress.

Age and gender interactions in psychological functioning of cancer patients

Psychological functioning in cancer patients resulted associated with both age and gender. **Table 1** displays results from logistic regression analyses showing that younger age was significantly related to the presence of anxiety ($p < 0.0001$) and depression ($p = 0.0009$), and to a less adaptive defense style ($p < 0.0001$). Similarly, gender differences showed significant association with anxiety (186/313 vs 125/254; 59.4% vs 49.2%; $p = .015$), depression (157/313 vs 84/254; 50% vs 33.1%; $p < 0.0001$), and defense style (median of the groups: 2 vs 1; $p = 0.005$). As displayed in **table 2**, women

Table 1. Associations between age and psychological functioning (logistic regression)

	Mean	SD	Odds ratio	P-value
Anxiety			1.03	<00001
presence	62.18	13.40		
absence	66.89	12.52		
Depression			1.02	.0009
presence	62.14	13.39		
absence	65.90	12.86		
Sleep disturbance			1	.995
presence	64.30	12.62		
absence	64.31	13.60		
Defense style			1.04	<00001
mature	63.83	11.87		
neurotic	69.82	12.98		
immature	60.14	12.18		

reported psychological distress more frequently than men. No significant associations were found between demographic characteristics and the occurrence of sleep disturbance.

line with gender differences, depression was significant more frequent in BC patients, as compared with the rest of the sample (50/241 vs 45/325; 20.7% vs 13.8%; $p = .04$). Metastatic cancer resulted significant less frequent

Table 2. Associations between gender and psychological functioning

	Male		Female		P-value
	N	%	N	%	
Anxiety					.015
presence	125	22.1	186	32.9	
absence	129	22.8	127	22.2	
Depression					<.0001
presence	84	14.8	157	27.8	
absence	170	30	156	27.5	
Sleep disturbance					.697
presence	98	17.3	125	22.1	
absence	156	27.5	186	32.9	
Defense style					.005
mature	33	5.8	50	8.8	
neurotic	123	21.7	89	15.7	
immature	98	17.3	174	30.7	

Note: for the defense style Mann-Whitney test was performed to compare the scores

Psychological characteristics of MC patients

Relationships between the presence of metastasis and psychological variables are displayed in **table 3**. We investigated if anxiety, depression, sleep disturbance and defense style were associated with MC. A significant and positive association was found with anxiety (72/109 vs 240/458; 66.1% vs 52.4%; $p = .01$). Association coefficients showed that people with anxiety symptoms have almost double probability of developing MC (odds ratio = 1.768). Statistical significance was not reached for the other variables, although the association between depression and MC resulted close to the set value of .05 (54/108 vs 187/458; 50% vs 40.8%; $p = .1$, odds ratio = 1.45).

Psychological characteristics of BC patients

Associations between psychological studied variables and the presence metastasis in BC patients were analyzed and results are displayed in **table 4**. In

in BC women (8/95 vs 100/471; 8.4% vs 21.2%; $p = .004$), whereas no significant associations were found with anxiety and sleep disturbance. Moreover, the association between breast cancer and defense style was close to statistical significance (medians of defense style: 2 vs 1; $p = .072$).

Discussions

It has been suggested that psychological distress might play a potential role in cancer progression (Giese-Davis, 2008; Satin et al., 2009; Perry et al., 2015). The present retrospective study supported this assumption and demonstrated that psychological distress and defense style assessed during the diagnostic phase are associated with specific clinical characteristics of cancer diagnosis (Jia et al., 2017; Lemogne et al., 2013).

In line with previous study (Di Giuseppe, Perry et al., 2020), we found that demographic characteristics were associated to both psychological distress and defense style (Baitar et al., 2018; Marchini et al., 2018).

Table 3. Differences in psychological functioning between metastatic and non-metastatic cancers

	Metastatic Cancer		Non-metastatic Cancer		P-value
	N	%	N	%	
Anxiety					.011
presence	72	66.1	240	52.4	
absence	37	33.9	218	47.6	
Depression					.083
presence	54	49.5	188	41.0	
absence	55	50.5	270	59.0	
Sleep disturbance					.225
presence	50	45.9	175	38.2	
absence	59	54.1	283	61.8	
Defense style					.28
mature	15	13.8	68	14.8	
neurotic	36	33.0	176	38.4	
immature	58	53.2	214	46.7	

Table 4. Differences in psychological functioning between breast cancer and other site cancers

	Breast Cancer		Other Cancers		P-value
	N	%	N	%	
Anxiety					.828
presence	52	9.2	259	45.7	
absence	43	7.6	212	37.4	
Depression					.031
presence	50	8.8	191	33.7	
absence	45	7.9	279	49.3	
Sleep disturbance					.696
presence	36	6.3	189	33.4	
absence	59	10.4	283	50	
Defense style					.072
mature	15	2.6	68	12	
neurotic	24	4.2	188	33.2	
immature	56	9.9	216	38.1	

Results confirmed our first hypothesis of age and gender difference in psychological functioning. Younger people, in particular women, show more anxiety, depression and immature defense style as compare to older cancer patients (Marazziti, Pozza, Di Giuseppe, & Conversano, 2020). This finding might be interpreted as the result of higher fear of death and preoccupation about family and professional responsibilities of middle-age people, whereas older retired people tend to be disengaged from everyday stressors and might feel luckier for being healthy so long. Further studies with age-stratified cancer and community samples are needed to add evidence to such an interpretation of our results.

Our second hypothesis of a relationship between the diagnosis of metastatic cancer and both higher psychological distress and defensive immaturity was partially confirmed. We noted that only anxiety was associated with metastasis, while the association with depression resulted close to the point of statistical significance. Consistent with previous studies reporting anxiety disorders associated with a higher rate of comorbid somatization disorder than that observed in the absence of anxiety disorders (Nisenson, Pepper, Schwenk & Coyne, 1998), our findings revealed that the presence of anxiety in cancer patients is associated with the more severe diagnosis of MC. From the psychosomatic perspective, anxiety might be interpreted as the psychological condition enhancing somatization, defined as the phenomenon in which patients experience and express their feelings or emotions through physical complaints and distress (Baughman, 1994). However, no causal association can be supported by this study.

Frequent depression and higher defensive maturity characterized the subgroup of BC patients, in comparison with the rest of our sample, confirming our last hypothesis of differences in psychological functioning between BC women and other primary site cancer patients. Previously we reported that BC patients show a peculiar use of defense mechanisms, in particular manic defenses of omnipotence and rationalization (Di Giuseppe, Di Silvestre et al., 2019). By definition, manic defenses are immature, and their function is to distort, deny and obscure the awareness of depressive feelings with the result of an apparent psychological well-being (Rudan, Jakovljevic & Marcinko, 2016). According with previous findings, this finding confirmed that BC patients manage their feeling of depression using immature defense mechanisms, although available information did not specify which defense mechanisms was particularly involved in the BC immature defense style. Finally, these findings arise

a research question that further research should try to address and highlight how it seems important to choose appropriate measure for the assessment of defense mechanisms (Conversano, Di Giuseppe et al., 2020).

The large sample size and the double-blind design are the major strengths of this work that, however, shows important limitations. First, the proportion of how each primary site cancer is represented in the sample was influenced by the availability of complete retrospective data and might not represent the exact prevalence in the population of cancer patients. Moreover, this proportion might be influenced by the exclusion of about a hundred of cases for the lack of complete data. Second, the retrospective research design prevented to control the studied variables and limited the analyses only to available information. Third, the correct use of observer-rated procedure for the assessment of defense mechanisms was not supported by a valid and reliable measure, which might have biased results on the patients' defense style. Another important limitation of the study is the lack of standardized measures for the assessment of psychological studied variables. Although data collection was provided by expert psycho-oncologists, the assessment of patients' psychological functioning was based only clinical interviews. Furthermore, the assessment of psychological symptoms and defense style was reported as categorical or ordinal variables, impeding sophisticated data analyses and consequently reducing findings interpretations. Further studies should be designed considering the representativeness of cancer population, the inclusion of other relevant psychological aspects, and the use of valid and reliable empirical methodologies.

Despite its limitations, promising findings emerged from the present study. The evidence of the relationships between psychological distress, defense style and clinical characteristics of cancer diagnosis highlights the impact of a cancer diagnosis on psychological functioning. The availability of psychological information about a large clinical sample, double-blind about the severity of cancer diagnosis from the patient and the interviewer perspective, allowed the comparison between subgroups of MC and BC with the whole sample of cancer patients. Findings demonstrated that both cancer severity and cancer site are associated with a specific impairment of psychological functioning, confirming previous findings on MC (Hyphantis et al., 2011) and BC (Di Giuseppe, Di Silvestre et al., 2020). Further research is needed to implement the understanding of cancer progression with a multidisciplinary approach taking into consideration biological, psycho-social, and environmental variables (Halbach et al., 2019; Midding

et al., 2019). From the psychological perspective, our findings suggest the need of further investigations about the possible role of anxiety symptoms and defensive functioning in promoting a trend towards somatization that might represent one of converging factors in eventually promoting cancer onset.

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