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Depression and Anxiety - Risk Factors in the Evolution of Breast Cancer in Women

Ramona Adriana SCHENKER[1],
Marius Eugen CIUREA[2],
Puiu Olivian STOVICEK[3],
Anamaria CIUBARA[4],
Michael SCHENKER[5],
Ileana MARINESCU[6]

[1] PhD student, University of Medicine and Pharmacy of Craiova, Romania, ramona_schenker@yahoo.com
[2] Professor, Department of Plastic Surgery, University of Medicine and Pharmacy of Craiova, Romania, meciurea@gmail.com
[3] Lecturer, Department of Pharmacology, Faculty of Nursing, Târgu Jiu Subsidiary, "Titu Maiorescu" University, Bucharest, Romania, puiuolivian@yahoo.com
[4] Professor, Clinical Medical Department, Faculty of Medicine and Pharmacy, "Dunărea de Jos" University, Galați, Romania, anamburlea@yahoo.com
[5] Associate Professor, Department of Oncology, University of Medicine and Pharmacy of Craiova, Romania, mike_schenker@yahoo.com
[6] Associate Professor, Discipline of Psychiatry, 5th Department, Faculty of Medicine, University of Medicine and Pharmacy of Craiova, Romania, marinescu_psy@yahoo.com

Abstract: *Psychological evaluation of women with suspected or diagnosed breast cancer can provide psychooncological elements for predicting the evolution of the disease and imperative customization of specific oncological therapies. In this study, we assessed the psychological status in terms of depression, anxiety and dysfunctional attitudes in both the group of patients with a confirmed diagnosis of breast cancer and that of patients with suspected breast cancer who are in the stage of histopathological evaluation of the diagnosis. The results of the psychometric evaluations allowed the development of a common neurobiological model for the two categories of patients. Given the staging model of breast cancer, the clinical and psychometric data obtained through our study allowed us to develop an integrative neurobiological model based on the evolutionary staging of anxiety and depressive disorders (Zhao et al., 2013). Based on these hypotheses, we argue that the staging of psychological disorders, the customization of specific psychotherapeutic prophylaxis strategies and the prudent pharmacological approach to these psychological changes can significantly improve the evolution and prognosis of cancer and the quality of life of patients. The state of relative psychoemotional balance (objectified by psychometric scales), without its validation by normalizing multisystemic biological indicators of depression (C-reactive protein, proinflammatory cytokines, blood-brain barrier disruption and cerebral blood flow decrease), suggests the risk of progression of the neoplastic process. We argue that when communicating the diagnosis and the therapeutic plan, a special methodology (specific protocol) must be applied to reduce distress, correct emotional balance and improve cognitive dysfunction by supporting the motivation to survive, as well as increasing patients' self-esteem.*

Keywords: *breast cancer, depression, anxiety, dysfunctional attitudes, body dysmorphic disorder.*

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Introduction

Breast cancer in women is a real public health problem due to the high incidence, late diagnosis in advanced stages of the disease that leads to a negative evolution and prognosis. This condition causes multiple physical disabilities, but especially psychological, which change the social status of women with breast cancer, disrupting the integration of macrosocial and microsocial. Psychooncological evaluations have shown that depressive and anxiety disorders are major risk factors for the unfavorable evolution of oncological disease.

In breast cancer, depression has been linked to a high risk of recurrence and mortality and anxiety to recurrence. The combination of the two types of pathology causes a negative prognosis, especially in women under 60 years of age (Wang et al., 2020). From this perspective, anxiety and depressive symptoms should be identified early, prior to suspicion or diagnosis of cancer, but should also be monitored over time to reduce psychosocial distress (Burgess et al., 2005). Depression and anxiety are the most common mental health changes in breast cancer patients, with an incidence of 68.6% and 73.3%, respectively. The severity of this symptomatology depends on the stage of the disease, mutilating surgery, social and family status. Anxiety is especially correlated with uncertainty in the diagnosis, treatment and prognosis of breast cancer (Alagizy et al., 2020).

In the case of women with breast cancer, this clinical picture is dominated by existential specific features, caused especially by the existence in the personal history of psychotraumas, caused especially by different types of abuse. Although the epidemiological data are variable, the main forms of abuse have the following prevalence data: physical abuse approximately 22%, sexual abuse 12% and emotional abuse with 36% of cases (Christ et al., 2019).

It has been estimated that approximately 70% of adult patients who have suffered a psychotrauma have experienced childhood abuse. These antecedents affected the psychological status, determining the impairment of cognitive patterns, behavioral and emotional changes, depression and anxiety, having as substrate the impairment of several brain areas such as the frontal, parietal or cingulate cortex (Huang et al., 2021). The strongest link with depressive disorder is the presence of poor emotional treatment in childhood, about 44% of patients developing this type of disease. Childhood sexual abuse causes depressive disorder in over 50% of adult cases, suicidal

ideation in approximately 23-40% of cases, and suicide attempts in up to 19% of patients (Radell et al., 2021; Xu et al., 2013).

The uncertainty of the diagnosis of breast cancer was correlated with the presence of anxiety when deciding to perform a breast biopsy, at the time of the biopsy or communication of the diagnosis. In patients diagnosed with benign tumor, anxiety was present, but at a lower level than in those with breast cancer (Liao et al., 2008). The main fears of breast cancer patients are related to the uncertainties regarding the evolution of the disease, the treatment options and the risk of side effects, the erroneous or limited information as well as those regarding the coping capacity to overcome the trauma induced by the oncological pathology (Shaha et al., 2008).

During the period of diagnostic uncertainty, a major role in the psychological picture is played by anticipatory anxiety, which disturbs the neurobiological balance between the cortical and subcortical systems. A serious threat disrupts the ability to avoid or ameliorate negative consequences and increases the level of anxiety due to uncertainties related to sensory area, general condition, new rules in the pathological context, as well as evolution and therapeutic results (Grupe & Nitschke, 2013). Thus, cognitive dysfunctions are triggered, which significantly decrease the resilience of breast cancer patients, delaying both the early diagnosis and the therapeutic approach.

The period of diagnostic uncertainty or the stage between the suspicion of the diagnosis and the certainty of the breast cancer diagnosis, based on histopathological examination, is the most important period for possible prophylaxis of psychological disorders. Prophylactic interventions can limit neurobiological changes whose progression can generate pathogenic support that causes the onset of psychiatric nosographic entities of the depressive and anxious type.

In breast cancer in women, a major problem is the onset of body dysmorphic disorder (BDD), which amplifies depressive-anxiety pathology and increases the risk of suicidal behavior (Shaw et al., 2016). It is estimated that approximately 80% of patients with BDD had suicidal ideation and up to 28% attempted suicide (Phillips, 2007). In breast cancer, excessive worries about a certain change in one's body image are mainly related to alopecia, partial or total excision of a breast or skin changes (rashes). Often this disorder is underdiagnosed because patients are reluctant to seek psychiatric medical advice, preferring to resolve the defect through cosmetic or dermatological surgery.

If in the general population the incidence of BDD is about 2%, in the case of patients who went to a plastic surgery service, the incidence rises to about 15% (Metcalfe et al., 2014). The association of BDD with depression increases the risk of metastases and recurrences due to immune dysfunction induced by depression or prolonged distress caused by cancer, as well as by the decrease or total lack of compliance with specific oncological treatment (Bender et al., 2014; Smith, 2015).

Psychological evaluation of women with suspected or diagnosed breast cancer can provide psychooncological elements for predicting the evolution of the disease and imperative personalization of specific oncological therapies. In this regard, we assessed the psychological status in terms of depression, anxiety and dysfunctional attitudes in both the group of patients with a confirmed breast cancer diagnosis and that of patients with suspected breast cancer who are in the stage of histopathological evaluation of the diagnosis. The results of psychometric evaluations could allow the development of a common neurobiological model for the two categories of patients. Based on these arguments, we want to emphasize the importance of the psychooncological approach of patients with depressive-anxiety disorders or dysfunctional attitudes even at the time of biopsy, before receiving the histopathological result. At the same time, the personalization of psychotherapeutic strategies must be considered in the conditions of a positive diagnosis for breast cancer, which leads to the prospect of a mutilating surgery or a specific oncological treatment with a high risk of side effects.

Material and method

This study aimed to assess the level of anxiety, depression and dysfunctional attitudes in patients diagnosed with breast cancer, but before surgery or other specific oncological treatments. The study enrolled 58 patients with histopathologically confirmed breast cancer (group A). Also included in the study, as a comparative group, were 61 patients with breast lumps in the post-biopsy period, until they received the histopathological result (group B). All patients signed an informed consent to participate in the study, within the Oncology Center „Sfântul Nectarie", Craiova. The inclusion criteria were: female gender, age over 18 years, lack of personal medical oncological or psychiatric history.

The following psychometric evaluation scales were applied for evaluation: Hamilton Depression Rating Scale (Hamilton, 1960), Hamilton Anxiety Rating Scale (Hamilton, 1959) and Dysfunctional Attitude Scale

Form A (DAS-A) (de Graaf et al., 2009). All patients answered the questionnaires after the psychooncologist answered all questions, with no time limit. The results were statistically processed following the differences between the two groups based on the proportionality tests and the p value for statistical significance. The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of University of Medicine and Pharmacy of Craiova, Romania (No. 70/01.04.2019).

Results

The statistical analysis showed that depression and anxiety had different degrees of severity, both in patients diagnosed with breast cancer (group A) and in women with breast lumps in observation (group B), regardless of staging of the disease. Depending on the scores obtained, the depression was classified as mild (score 7-17), moderate (score 18-24) and severe (score ≥ 25). Anxiety was considered significant at a score above 20. In group A, significant anxiety (74.14%) and moderate depression (44.83%) predominated, while in group B, significant anxiety (62.30%) and mild depression (54.10%) predominated (Figure 1). Although the only statistically significant difference was observed in mild depression, patients diagnosed with cancer were more likely to experience severe depression and significant anxiety than those in group B.

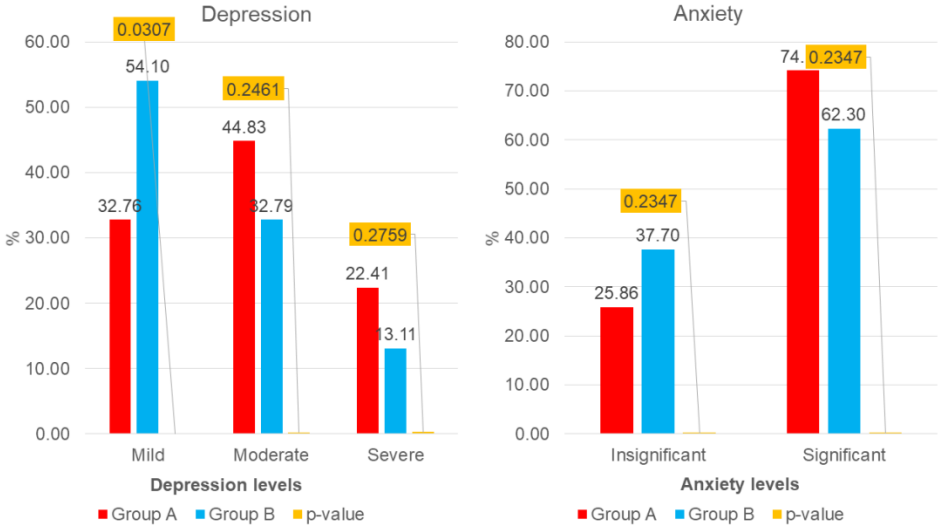

Figure 1. Depression and anxiety levels in the two groups of patients

Source: Authors' own conception

The analysis of dysfunctional attitudes according to the degree of depression showed that there are statistically significant differences between the 2 groups (Figure 2). In the stage of mild depression, undiagnosed patients had low but also high dysfunctional attitudes, statistically significant ($p<0.05$) compared to patients with breast cancer. In cases of moderate depression, high dysfunctional attitudes are more common in group A and low ones in group B. Significant differences for severe depression were found for moderate dysfunctional attitudes, which predominate in group A, and for very high ones that are more common in group B.

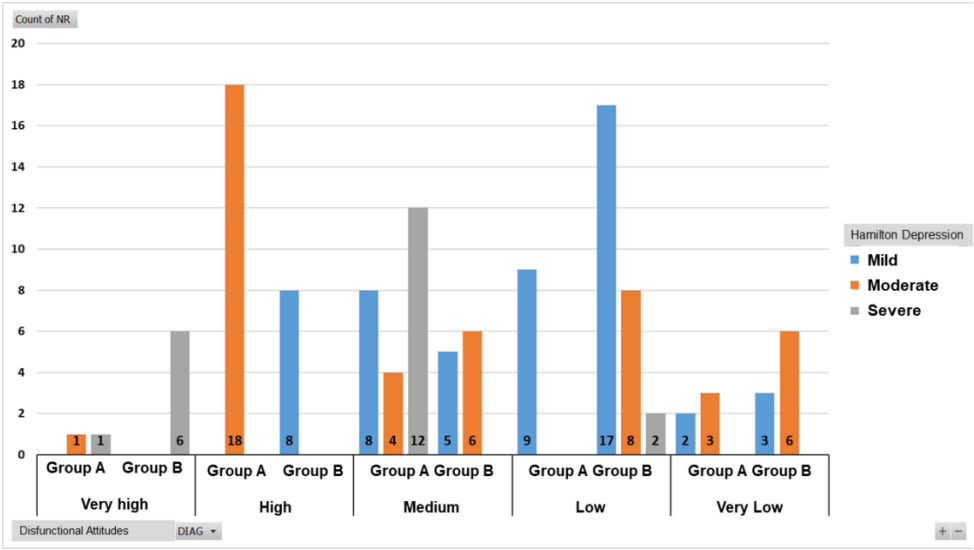

Figure 2. Dysfunctional attitudes depending on the level of depression in the two groups of patients
Source: Authors' own conception

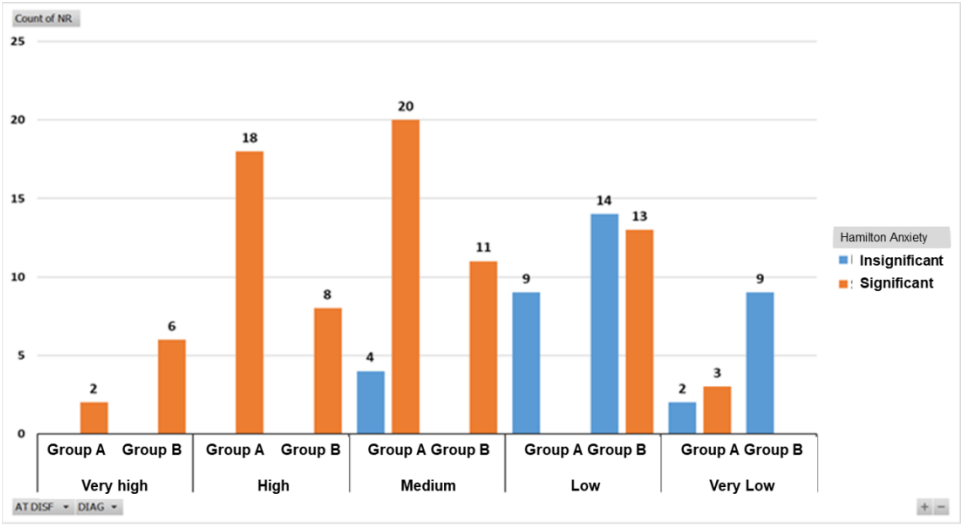

Figure 3. Dysfunctional attitudes depending on the level of anxiety in the two groups of patients
Source: Authors' own conception

The analysis of the correlations between dysfunctional attitudes and anxiety showed statistically significant differences between the 2 groups (Figure 3). In cases with insignificant levels of anxiety, undiagnosed patients more frequently had very low dysfunctional attitudes, significantly static ($p<0.05$) compared to patients with breast cancer. For the level of significant anxiety, group A had more frequently high, medium and very low dysfunctional attitudes, and less frequently low dysfunctional attitudes towards group B ($p<0.05$).

The correlation of dysfunctional attitudes with depression and anxiety showed differences between the two groups of patients. Insignificant anxiety was most commonly associated with mild depression and dysfunctional attitudes for both groups. Patients with breast cancer and significant anxiety most commonly associated moderate depression with high dysfunctional attitudes and severe depression with low dysfunctional attitudes. Patients in group B with significant anxiety had a wider distribution depending on the state of depression and dysfunctional attitudes. Most cases associated mild depression with high or low dysfunctional attitudes, moderate depression with moderate dysfunctional attitudes, and severe depression with high dysfunctional attitudes.

Discussions

Given the staging model of breast cancer, the clinical and psychometric data obtained through our study allowed us to develop an integrative neurobiological model based on the evolutionary staging of anxiety and depressive disorders. Based on these hypotheses, we argue that the staging of psychological disorders, the customization of specific psychotherapeutic prophylaxis strategies and the prudent pharmacological approach to these psychological changes can significantly improve the evolution and prognosis of cancer and the quality of life for patients.

Anticipatory anxiety is considered a psychological condition that does not meet the criteria of a psychiatric nosographic entity according to Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-5) and International Classification of Diseases 10 (ICD-10). However, in the conditions of oncological pathology and especially in the case of breast cancer in women, anticipatory anxiety causes a strong state of distress that can change the physiological parameters and the influence of the biological diagnostic marker (Dhama et al., 2019; Labbe-Coldsmith et al., 2017). In this context, the recognition of this particular psychological status is of major importance because it can influence the pace of evolution of neoplastic pathology and lead to misbehavior dominated by the abandonment of specific therapies. Anticipatory anxiety can occur in a psychological field previously vulnerable to multiple negative life events or the existence of a cancerous pathology in people of great emotional importance to the patient (Jacobsen et al., 1993).

Patients who have been cared for by people diagnosed with cancer have a high potential for developing this form of anxiety. Anticipatory anxiety is generated by the cognitive processing of potentially dangerous factors regarding the existence of the subject or of possible existential changes determined by the disturbance of the physical or mental status, with an imminent impact on the perception or identification of one's own person. Thus, a real gap is established between "what I feel" and "what I am" in my own perception and "what I will be if ...". Undoubtedly, this unclear perspective in the first phase is orchestrated by psychotraumatic events and previous negative emotional experiences related to oncological pathology.

The intensification of anxiety symptoms is determined by the long duration of the diagnostic uncertainties regarding breast cancer, but also by the prospect of an unfavorable evolution that would require radical surgeries such as mastectomy with or without ovarectomy, as well as chemotherapy and radiotherapy (Maheu et al., 2021). The general psychological evaluation

performed before the first suspicions of neoplastic breast disease may give the clinician and psychooncologist data on the presence or absence of anxious personality traits (Stark & House, 2000). A particular aspect of anxious personality traits may be the presence of compulsivity (compulsive anxiety) and repetitive cognitive changes, suggesting obsessive and compulsive tendencies (Helbig-Lang et al., 2012).

In this context, at the beginning of oncological disease, breast cancer patients may have a psychological profile in which the anxious-compulsive and obsessive component is predominant, and another profile in which it is of small amplitude. Patients with a positive anxiety profile have a low resilience to the development of an anxious, depressive-anxious pathology or BDD, while patients with insignificant anxiety traits have a good resilience for psychiatric pathology in the context of breast cancer. The increase in anxiety was correlated with the way in which the bad news related to the oncologic diagnosis and treatment as well as the lack of specialized psychooncological support were communicated (Liénard et al., 2006).

The first category suggests evolutionary risks and an unfavorable prognosis, with the rapid progression of neoplastic disease or in the case of BDD following mastectomy with the appearance of suicidal behavior. BDD can occur in patients with anticipatory anxiety from the moment of certainty of the diagnosis of breast cancer, and can be amplified by side effects of chemotherapy that change the status of one's body image (excessive weight loss, hair loss, sarcopenia, skin dermatological changes, especially on the face). Anticipatory anxiety greatly increases patients' fear of surgery, chemotherapy (DiLorenzo et al., 1995) or radiotherapy, being an important factor in delaying the start of treatment, but also in poor adherence and adherence to treatment caused by psychogenic intolerance to possible side effects (Singer et al., 2015).

Radiotherapy, as well as specific oncological pharmacological medication, can cause changes in the cognitive areas of the brain by stopping the process of neurogenesis and significantly decreasing neuroprotective factors. Hippocampal atrophy and frontal cortex may be associated with marked cognitive dysfunction, which may disrupt patients' daily activities and thus contribute to decreased self-esteem and feelings of worthlessness that support the amplification of depressive symptoms (Pazzaglia et al., 2020; Pereira Dias et al., 2014).

The neurobiological support of anticipatory anxiety is complex and from our point of view, we can discuss their staging, in accordance with the evolution of psychopathological changes. Initially in the stage of diagnostic uncertainty, the disconnections between the anterior cingulate cortex and the

medial and orbito-frontal areas of the prefrontal cortex are mainly involved, which causes a loss of the balance of cognitive information processing (Rolls, et al., 2019). At the level of these cerebral areas there is a hyperactivity caused by an excessive increase in cerebral blood flow (CBF) in contrast to its decrease in important subcortical areas such as the amygdala and thalamus.

Normally, the cortical and subcortical areas need to process sensory information in a synergistic cognitive manner (Grupe & Nitschke, 2013). In the presence of anticipatory anxiety, this processing is dysinergic, dominated by cognitive-emotional processing with multiple error factors. Moreover, in the repetitive conditions of informational, sensory or cognitive stimuli with anxiogenic potential, there is a marked increase in CBF in the left area of the brain island, while in the right area it decreases (Hasler et al., 2007). This cerebral insular interhemispheric imbalance calls into question the dysfunctional involvement of the mirror neuron system (Rajmohan & Mohandas, 2007). This interhemispheric dysfunction can lead to aberrant cognitive processing by swinging informational signals between the two hemispheres. Each stage of information crossing from the dominant hemisphere to the non-dominant hemisphere generates an amplification of the signal and implicitly an increase in the level of anticipatory anxiety. The increase in intensity of this neuronal signal overstimulates the right temporal cortex and the right anterior cingulate cortex in the non-dominated hemisphere, with a significant increase in CBF (Wang et al., 2005). This is the moment of transition from anticipatory anxiety to the anxiety pathology itself, dominated by the general anxiety disorder, with or without panic attacks, as well as obsessive-compulsive disorder. Favoring elements of hippocampal atrophy and overuse exhaustion of the amygdala and cingulate cortex as well as the prefrontal cortex are the neurobiological elements that suggest the transition to mixed anxiety-depressive pathology (Cha et al., 2016).

Thus, in the evolution of anxiety and depressive disorders from breast cancer in women, we can support their classification into three clinical-biological stages that evolve against the background of personality traits of depressive or anxious type. These three stages, each with a particular neurobiological substrate, are: anticipatory anxiety (Figure 4); generalized anxiety disorder with or without panic attacks (Figure 5); mixed anxiety-depressive disorder (Figure 6). At any of these stages of anxiety-depressive pathology, present in women with breast cancer, BDD may occur, this risk being amplified by mastectomy, chemotherapy or radiation therapy.

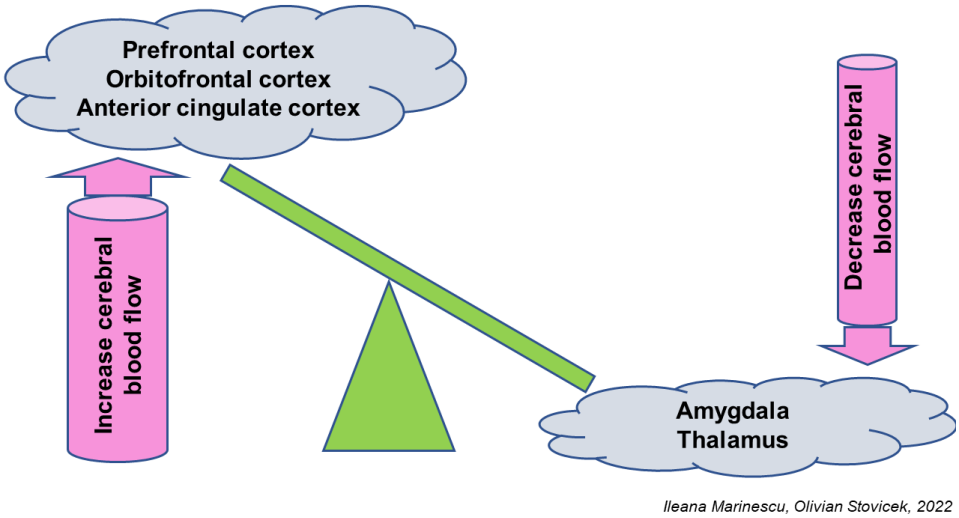

Figure 4. Neurobiological model of anticipatory anxiety in women's breast cancer
Source: Marinescu & Stovicek, 2022

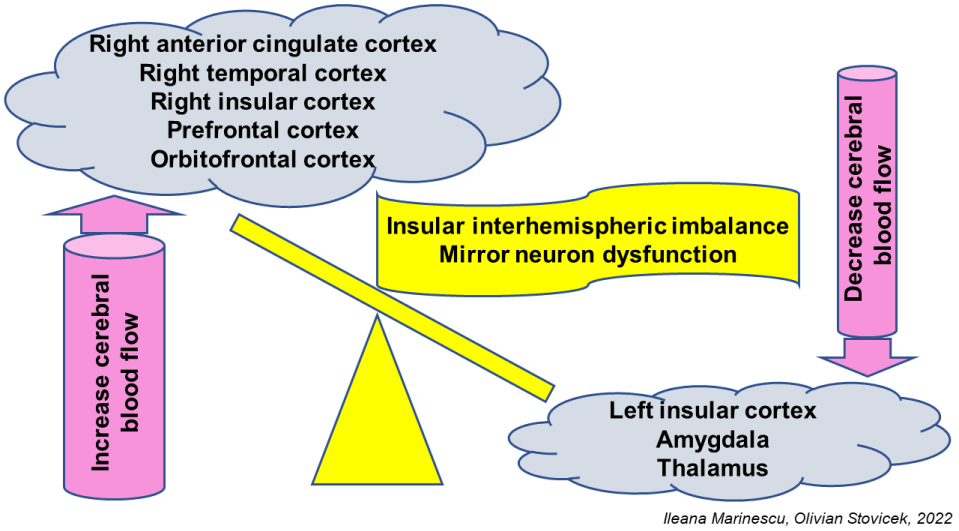

Figure 5. Neurobiological model of generalized anxiety disorder, with or without panic attacks, in women's breast cancer
Source: Marinescu & Stovicek, 2022

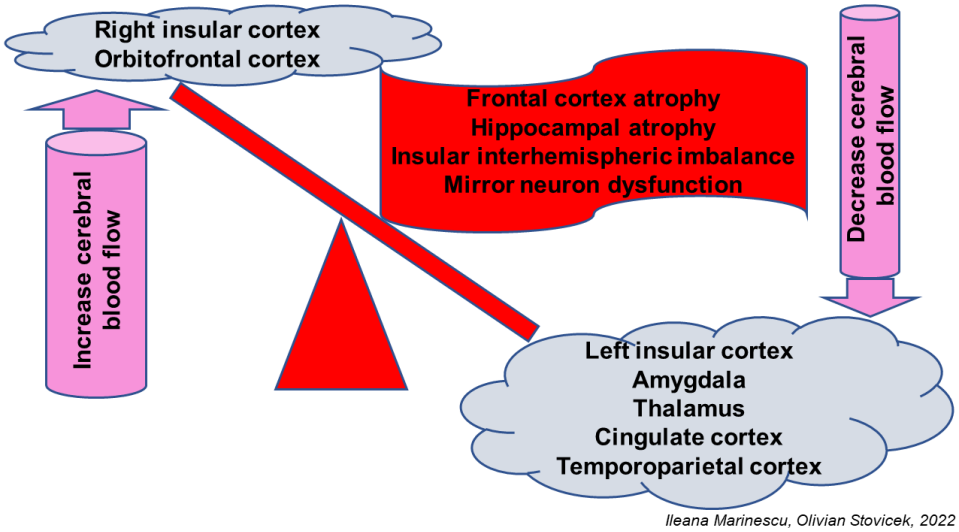

Figure 6. Neurobiological model of mixed anxiety-depressive disorder in women's breast cancer
Source: Marinescu & Stovicek, 2022

Clinical data and psychometric assessments suggest the presence of depressive manifestations, independently or simultaneously with the anxiety-type changes, which do not fall within the nosographic criteria for depressive disorder in DSM-V and ICD 10. We can initially discuss depressive personality traits related to women with the presence of verbal, psychological, physical, or sexual abuse during childhood or adolescence. Childhood abuse and psychological trauma are associated with depressive pathology accompanied by hippocampal atrophy partially explained by overactivation of the hypothalamic–pituitary–adrenal axis (HPA) over a long period of time and high levels of endogenous cortisol (Vythilingam et al., 2002).

This pattern of depression suggests early cognitive dysfunction, especially by disrupting cognitive patterns with a significant decrease in resilience and adaptability to new events with potential psychostress. Breast cancer is a major distress event that acts over a long period of time, and impaired cognitive function can be exacerbated both psychologically and by the action of specific oncological pharmacological medication or radiotherapy (Ng et al., 2017). This form of depression is most often associated with BDD pathology and high risk of suicide.

The decrease in cognitive status is amplified by the presence of dysfunctional attitudes highlighted by the assessment with the dysfunctional

attitude scale form A (DAS-A). In these patients, the evolution may be cognitive impairment (Fatahi et al., 2021), especially if it is associated with: age over 55 years, postmenopausal condition, history of traumatic brain or epileptic symptoms. (Kim & Jung, 2015). From a neurobiological point of view, the presence of dysfunctional attitudes correlates early with blood-brain barrier (BBB) disruption (Nation et al., 2019). Early recognition of BBB permeability plays a major role in anticipating the adverse side effects of specific pharmacological antineoplastic medication (Fan et al., 2018). On the other hand, BBB damage is associated with functional impairment of the cerebral neurovascular unit, and alteration of arterial capillaries promotes neurodegenerative invasion with beta-amyloid (Aβ) and tau proteins (Marinescu et al., 2017).

Dysfunction of small cerebral vessels also unbalances the functional relationship between neuron and astroglia, with the appearance of high levels of glutamate which accentuates the potential of neural apoptotic mechanisms but also chronic global cerebral vascular hypoperfusion, with the appearance of cerebral small vessel disease (CSVD) and white matter hyperintensities identifiable on neuroimaging examination (Huang et al., 2021).

Dysfunctional attitudes are also associated with decreased vascular perfusion in the hippocampus and parahippocampal gyrus, favoring, in terms of depressive anxiety symptoms and increased HPA axis activity with high levels of endogenous cortisol, severe hippocampal atrophy and severe cognitive impairment (Conway et al., 2015; Ju et al., 2020).

The main mechanism is based on the neural disconnectivity between the basal structure of complex cognitive processes, represented by the hippocampus and the parahippocampal cortex that ensures interconnectedness with the amygdala controlling emotional cognition, and the entorinal and peririnal cortex that ensures the integration of sensory or cognitive information in memory, by connecting with the temporo-parietal cortical area, thus supporting the function of contextual associative memory (Aminoff et al., 2013; Burwell, 2000).

Changes associated with dysfunctional attitudes involve both the hippocampal-parahippocampal disconnect that controls declarative memory and the disconnectivity between the parahippocampal cortex and the striatum that controls non-declarative memory, directly (Lin et al., 2021). Indirectly, the interaxonal disconnections at the level of the striato-frontal circuits contribute significantly to the alteration of the cognitive function of the prefrontal and frontal area, causing the alteration of the working memory (Li & Mody, 2016).

The separate investigation of the mnemonic function including working memory, declarative and non-declarative, but also contextual associative memory, whose low efficiency announces the aggravation of dysfunctional attitudes with the installation of dementia-type cognitive impairment. The importance of early detection of impaired functional segments of memory can be precipitated by the use of chemotherapy and radiotherapy, imposing personalized therapeutic attitudes based on increased neuroprotection and avoidance of chemotherapeutic agents with neurotoxic action and aggressive radiotherapy (Figure 7).

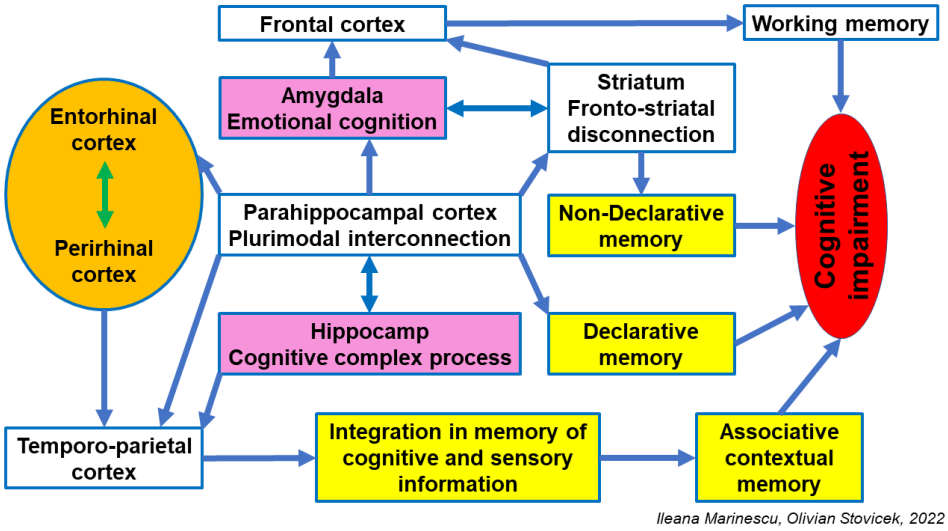

Figure 7. Neurobiological mechanisms of cognitive impairment in women's breast cancer, with mixed anxiety-depressive disorder
Source: Marinescu & Stovicek, 2022

Dysfunctional cognitive attitudes in women with breast cancer associated with BBB permeability and hippocampal atrophy may anticipate an increased risk of developing dementia. Under these circumstances, the use of potentially neurotoxic drugs of major antineoplastic potential or radiotherapy sessions may precipitate the rapid progression of minor cognitive dysfunction to dementia. BBB dysfunction has an important peripheral marker represented by increased serum level of S100 calcium-binding protein B (S100B) (Choi et al., 2016). In patients with cognitive impairments, we consider that, prior to any oncological therapeutic strategy, it is necessary to evaluate the S100B protein (Marchi et al., 2004), as well as

monitoring its level during treatment (Karmur et al., 2020). BBB integrity, lack of hippocampal atrophy, and normal S100B protein levels may be important markers for initiating cognitive-behavioral psychotherapy sessions for anxiety-depressive disorder in women with breast cancer.

On the other hand, cognitive status can be disrupted by epigenetic factors, especially in the elderly, such as mild traumatic brain injury (mTBI) (Stovicek et al., 2020), alcohol or opioids consumption (Bruijnen et al., 2019), chronic respiratory illness, (Andrianopoulos et al., 2017) or cardiac dysfunction (Hilal et al., 2015). Cardiac dysfunction with decreased ejection fraction, accentuates vascular hypoperfusion, thus amplifying neuronal damage in the frontal and cingulate cortex, and disruption of connectivity between the striatum and the frontal cortex (Dehelean et al., 2019).

Depressive disorder associated with anticipatory anxiety has a particular clinical feature, represented by the dominance of anxiety disorders compared to depressive symptoms, often ignored. The therapeutic attitude based exclusively on anxiolytic or thymostabilizing drugs, as well as on psychotherapy aimed at the symptoms and anxious behaviors, maintains the neurobiological potential for the evolution of depressive disorders. This prolongs the period in which an activation of the microglial systems occurs with the increase of proinflammatory cytokines and endothelial dysfunction. (Brites & Fernandes, 2015; Jo et al., 2015).

In this context, we can consider depression as a depression with a biological facade, because the proinflammatory processes and endothelial dysfunction favor the rapid progression of neoplastic disease. At the time of the patient's impact with the certainty of a positive diagnosis for breast cancer, anxiety disorders are associated with depression (Cardoso et al., 2016). This depression is initially dominated by anxiety symptoms, being considered comorbid to anxiety, so that in a later phase of evolution to shape the mixed anxiety-depressive disorder as an independent nosographic entity.

Anxious depression is neurobiochemically caused mainly by serotonin deficiency, and is associated with hostility and explosive addictive or impulsive behaviors. In such situations, it is recommended to use therapies with selective serotonin reuptake inhibitors (SSRIs) (Garakani et al., 2020). However, the excessive presence of elevated serotonin levels after treatment favors vascular endothelial growth factor (VEGF) activity which amplifies vascularization and tumor progression with a higher risk of metastases (Udo et al., 2014). An alternative pharmacological solution may be tianeptine, especially in elderly patients, as it does not interfere with cytochrome P450 and has a very good tolerance (Emsley et al., 2018).

Anxious depression is a psychiatric condition often associated with the developmental stages of the tumor and may be exacerbated by side effects of specific oncological treatments or psychotraumatic surgery.

In the previous stage of clinical or biological suspicion of breast cancer, patients with a history of anxiety depression have a significant risk factor for neoplastic disease, especially when associated with depressive and anxiety disorders, increased proinflammatory indicators C-reactive protein, tumor necrosis factor alpha (TNF-α) and proinflammatory cytokines. as well as high levels of endogenous cortisol (Berthold-Losleben & Himmerich, 2008; Felger & Lotrich, 2013). The presence of these indicators and social distress increase the risk of accelerating proneoplastic mechanisms.

Patient stress is amplified by the clinical and paraclinical investigations imposed by the diagnostic confirmation protocols for breast cancer, but especially by the time of the biopsy. This diagnostic intervention becomes an important traumatic factor that destabilizes the emotional balance, promotes depression, amplifies distress and anxiety and potentiates both patients with uncertain histopathological status and those with a confirmed breast cancer diagnosis. In these circumstances, the patient must be evaluated by a complex therapeutic team led by a psychooncologist, who must apply personalized psychotherapy techniques, but also effectively manage communication with the patient. If mastectomy is required, depending on the type of histopathology and stage of the breast cancer, psychotherapy and communication techniques should ensure that patients will be able to rehabilitate the body defect through treatment of plastic and reparative surgery, which will provide the certainty of regaining the previous body aesthetic level, sometimes even better. This discussion will be led by the coordinator of the team of plastic surgeons in close collaboration with the psychooncologist.

The pharmacological treatment of depression and anxiety in breast cancer patients requires the avoidance of any psychotropic or non-psychotropic drugs that may induce an increase in prolactin but also antidepressants that may increase the growth of VEGF, which are indicators of metastatic risk (Liu et al., 2011; Wang et al., 2016). Dysfunction and cognitive impairment are important factors in the pathogenesis of anxiety depression and BDD, which is why specific identification and approach through specific psychooncological strategies can be achieved early and can be supported by the use of neuroprotective medication, especially in specific cancer therapy. We believe that the data provided by this study have an important potential to improve the evolution of breast cancer in women and significantly increase the quality of life for patients with this condition.

Conclusions

Depression, anxiety, decreased cognitive abilities, and dysfunctional cognitive patterns amplify the deteriorating quality of life of breast cancer patients. At the same time, through multisystemic molecular and cellular mechanisms, there is a significant deterioration of the evolution of the oncological condition and the risk of metastatic dissemination. Thus, in our opinion, psychooncology acquires a major importance in the therapeutic strategies of breast cancer. The complex neurobiological model of mixed anxiety-depressive disorder offers the oncologist, as well as the psychooncologist, arguments for the effectiveness of personalized therapies, but also for the importance of objective monitoring supported by oncological markers and biological markers of depressive disorder. The state of relative psycho-emotional balance (objectified by psychometric scales), without its validation by normalizing multisystemic biological indicators of depression (C-reactive protein, proinflammatory cytokines, BBB disruption and CBF decrease), suggests the risk of progression of the neoplastic process. We argue that, when communicating the diagnosis and the therapeutic plan, a special methodology (specific protocol) must be applied to reduce distress, correct emotional balance and improve cognitive dysfunction by supporting the motivation to survive, and increase self-esteem. Patients.

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