CORRELATIONS BETWEEN STATE ANXIETY AND QUALITY OF LIFE IN METASTATIC BREAST CANCER PATIENTS

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CORRELATIONS BETWEEN STATE ANXIETY AND QUALITY OF LIFE IN METASTATIC BREAST CANCER PATIENTS (Abstract) **Aim:** to evaluate the correlations between perceived state anxiety during chemotherapy and quality of life in metastatic breast cancer patients. **Material and methods:** 62 metastatic breast cancer patients were evaluated during chemotherapy concerning age, living environment, marital status, social support and preexisting financial difficulties, the histological type of cancer, the site of the metastasis, the time from diagnosis, the type of surgical intervention, dexamethasone use, somatic comorbidities and the radiotherapy. The STAI-X1, BDI-IIA and the QLQ 30 (Quality of Life Questionnaire 30) plus BR 23 (Breast 23) questionnaires were applied. For the statistical analysis we used the SPSS 13 package. **Results:** 24 subjects were experiencing low state anxiety (≤39), whilst 38 had significant state anxiety (>39). Statistically significant differences were encountered between the two compared subgroups concerning the living environment, the type of surgical intervention, the marital status, the social support and the mean BDI scores, adjusted means were calculated for the items considered to potentially influence quality of life. Social, emotional and role functioning had lower scores in the low state anxiety group. Fatigue, future perspective, chemotherapy induced side effects, breast symptoms, upset by hair loss and sexual functioning were more disturbing in the high state anxiety group. The general health/quality of life mean score was lower in the low state anxiety group. **Conclusions:** Higher state anxiety correlates with certain quality of life items, suggesting that psychological counselling and appropriate therapy induced side effects management should be a priority in the palliative care for metastatic breast cancer patients. **Keywords:** CANCER, BREAST, ANXIETY, QUALITY OF LIFE, PAIN.

Breast cancer is the most frequently encountered form of malignancy in women and it represents around 28% of the reported cancers in Europe (1). The National Cancer Institute estimates that 12.7% of women born today will be diagnosed with breast cancer during their lifetime (2). In Romania over 6000 new cases, usually in an advanced stage, are diagnosed every year, with an incidence of 56.84/100000 and a reported mortality of 39.28/100000. A recent study of the International Agency for Cancer, published in 2010 in the British Medical Journal, describes an increase with 17% of the mortality generated by breast cancer in Romania in the last few years, most probable due to the dysfunctional strategies of early detection and treatment.
Correlations between state anxiety and quality of life in metastatic breast cancer patients

Cancer signifies a serious threat on someone’s existence and there are studies that evaluate over 77% of the subjects having this diagnosis as experiencing anxiety symptoms generated by the disorder itself or by its therapy (4). In 2005, Burgess et al. described a decreasing annual prevalence of depression and anxiety of 50% in the first year, 25% in the second, third and fourth year and 15% in the fifth year after being diagnosed with breast cancer (5).

Anxiety in cancer is a sensitive issue, generating relational problems with both medical staff and caregivers. Its prevalence at a psychopathological level is reported to be 10-30% (6). Moreover, its relation with quality of life is complex and bivariate. Although anxiety disorders are correlated with deficits in the quality of life, there are studies that postulate that their impact is not a significant one (7). Nevertheless, state anxiety was considered to be a risk factor for chemotherapy induced nausea and vomiting (8). In 2004, Schreier et al. found a negative correlation between state and trait anxiety scores and quality of life in a sample of 48 women receiving chemotherapy for breast cancer (9). It is of great interest to determine the causing factors and the specificity of anxiety in oncology, and its correlation with quality of life items, in order to have a better management of complex situations, leading to best palliative care.

MATERIAL AND METHODS

We conducted a clinical study at the Oncological Institute “Ioan Chiricuță” Cluj-Napoca, starting from January 2011 until November 2012, on a group of 62 women, aged over 18, suffering from metastatic breast cancer, evaluated in the day care hospital. All of the subjects were undergoing chemotherapy at the moment of the evaluation. The exclusion criteria were brain metastasis, psychiatric history, psychotropic medication administration (current or within the last 6 months), alcohol or illicit substances abuse/addiction, confusion, unable or unwilling to sign the written consent, patients taking psychoactive medications, others than chemotherapy and premedication for chemotherapy. The STAI-X1, BDI-IIA and the EORTC QLQ 30 (Quality of Life Questionnaire 30) plus BR 23 (Breast 23) questionnaires were applied. The evaluated items were the age, the living environment, the marital status, the social support and pre-existing financial difficulties, the histological type of cancer, the site of the metastasis, the time from the announcement of the diagnosis, the type of surgical intervention, the use of dexamethasone as premedication, the somatic co-morbidities and the radiotherapy. A cut off value of 39 was established for STAI-X1 scores, splitting the group into clinically significant state anxiety (>39) and low state anxiety (≤39). The two resulting groups were compared regarding the quality of life items. For the statistical analysis we used the SPSS 13 package, including the T Student test. The distribution of the variables was tested with Skewnes and Kurtosis, and the general data were analyzed with the Chi Square test.

The study was approved by the medical ethics commission of the University of Medicine and Pharmacy “Iuliu Hațieganu” Cluj-Napoca.

RESULTS

The age mean in the group was 54.37 years old, with a minimum of 30 and a maximum of 81. The majority lived in the urban area (79%), were married (77.4%) and bene-
fited from a strong social support (91.9%). Approximately half of the group reported important financial difficulties (51.6%).

According to the TNM staging system, all patients were in the IVth stage evolution of the disease. Most of the subject had bone metastasis (51.61%). From the histological perspective, as expected, the majority (85.5%) were infiltrating ductal carcinomas, followed by the infiltrating lobular carcinomas (7.14%), the intraductal (3.2%) and the undifferentiated types (3.2%) and in a smaller percent we discovered lobular pleomorphic (1.6%) and medullar carcinomas (1.6%). A number of 34 patients had a history of unilateral breast mastectomy, 19 of them breast-conserving surgery, whilst 9 were considered to be inoperable. 48.4% underwent radiotherapy (tab. I).

Most of the participants were not suffering from other somatic illnesses (40 cases), part of them having however co morbidities (hypertension, diabetes mellitus, gastritis, goitre, anaemia, leyomioma, spondylitis, deep vein thrombosis).

According to the STAI X1 scores, 24 subjects (38.70%) were experiencing low state anxiety (≤39), whilst 38 of them (61.29%) had significant state anxiety (>39) (tab. II).

### TABLE I

**Previous therapies**

<table>
<thead>
<tr>
<th></th>
<th>Yes (number)</th>
<th>No (number)</th>
<th>Yes (percent)</th>
<th>No (percent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>radiotherapy</td>
<td>30</td>
<td>32</td>
<td>48.4%</td>
<td>51.6%</td>
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</table>

### TABLE II

**BDI IIA scores**

<table>
<thead>
<tr>
<th>STAI X1</th>
<th>N</th>
<th>Mean</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDI &lt;= 39</td>
<td>24</td>
<td>11.0417</td>
<td>7.77666</td>
</tr>
<tr>
<td>BDI &gt; 39</td>
<td>38</td>
<td>19.2895</td>
<td>8.47224</td>
</tr>
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</table>

Statistically significant differences were encountered between the two compared subgroups (the low state anxiety and the high state anxiety one) concerning the living environment (p<0.0001), the type of surgical intervention (p=0.010), the marital status (p=0.0001), the social support (p<0.0001) and mean BDI scores.

Previously published research report showed that living environment (10), marital status (11) and depressive symptoms (12) have an influence on the quality of life. Moreover, the type of surgical treatment (breast-conserving versus mastectomy) (13), and the subject’s perceived social support (14) also were proved to impact on the quality of life. In consequence, we used the general linear model in order to adjust the means of quality of life questionnaire for those items. After these corrections significant variations were observed for certain quality of life items between the two subgroups (tab. III).

The functional scales mean scores were significantly higher in subjects with low state anxiety.

Concerning the QLQ 30 symptom scales, the only item having a higher ad-
Correlations between state anxiety and quality of life in metastatic breast cancer patients

justed mean score in the higher state anxiety group was fatigue. The adjusted mean score for diarrhoea did not register a normal distribution.

Evaluating specific breast cancer items by QLQ 30 BR 23, significant variations were documented for future perspective; chemotherapy induced side effects, breast symptoms, upset by hair loss and sexual functioning, with higher mean scores for subjects with state anxiety over the cut off score of 39 points in STAI X1. The adjusted mean score for sexual functioning did not register a normal distribution (tab. IV).

TABLE III
Functional scales

<table>
<thead>
<tr>
<th>Prediction value for role functioning</th>
<th>STAI X1</th>
<th>N</th>
<th>MEAN</th>
<th>Standard deviation</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>≤ 39</td>
<td>24</td>
<td>38</td>
<td>48.3890</td>
<td>19.43992</td>
<td>0.0290</td>
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<tr>
<td>≥40</td>
<td></td>
<td></td>
<td>35.6617</td>
<td>23.08044</td>
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<tr>
<td>Prediction value for emotional functioning</td>
<td>≤ 39</td>
<td>24</td>
<td>74.9347</td>
<td>69.5731</td>
<td>0.0160</td>
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<tr>
<td></td>
<td>≥40</td>
<td>38</td>
<td>56.4796</td>
<td>56.9373</td>
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<tr>
<td>Prediction value for social functioning</td>
<td>≤ 39</td>
<td>24</td>
<td>69.4036</td>
<td>21.47722</td>
<td>0.0360</td>
</tr>
<tr>
<td></td>
<td>≥40</td>
<td>38</td>
<td>59.0151</td>
<td>21.47474</td>
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TABLE IV
Specific subscales

<table>
<thead>
<tr>
<th>Prediction value for future perspective</th>
<th>STAI X1</th>
<th>N</th>
<th>Mean</th>
<th>p</th>
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</thead>
<tbody>
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<td>≤ 39</td>
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<td>46.5890</td>
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<td>≥40</td>
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<td>Prediction value for side effects</td>
<td>≤39</td>
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<td>32.2360</td>
<td>0.016</td>
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<tr>
<td></td>
<td>≥40</td>
<td>38</td>
<td>42.1011</td>
<td></td>
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<tr>
<td>Prediction value for breast symptoms</td>
<td>≤39</td>
<td>24</td>
<td>16.2071</td>
<td>0.016</td>
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<tr>
<td></td>
<td>≥40</td>
<td>38</td>
<td>25.5781</td>
<td></td>
</tr>
<tr>
<td>Prediction value for upset by hair loss</td>
<td>≤39</td>
<td>16</td>
<td>32.9202</td>
<td>0.015</td>
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<tr>
<td></td>
<td>≥40</td>
<td>26</td>
<td>54.0972</td>
<td></td>
</tr>
<tr>
<td>Prediction value for sexual functioning</td>
<td>≤39</td>
<td>24</td>
<td>11.2968</td>
<td>0.004</td>
</tr>
<tr>
<td></td>
<td>≥40</td>
<td></td>
<td>4.3518</td>
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DISCUSSION

The STAI Y inventory is one of the most frequently administered anxiety self-report scales, especially in somatic comorbidities (16). The decision to only use the STAI X1 questionnaire was driven by the aim of the study, specifically the evaluation of state anxiety experienced in the context of both cancer diagnosis and outpatient chemotherapy. The statistical analysis of our data resulted in interesting results concerning the quality of life subscales, evaluated by the EORTC QLQ 30 and BR 23 questionnaire (17).

Regarding the functional scales, those refer to the last week in subject’s life. Pa
tients with dysfunctional role and social status were encountered in the higher state anxiety group, which is suggestive for a lower frustration tolerance and certain dysfunctional copying mechanisms involved in their adjustment to the somatic disorder. The differences in the emotional functioning mean scores are not surprising, considering the fact that they go along with STAI X1 evaluating the same issue.

Cancer treatment–related fatigue is categorized as chronic fatigue because it is present over a long period of time, interferes with functioning, and is not completely relieved by sleep and rest (15) and it is an important symptom to target in the treatment of cancer survivors (16). It is well recognized to generate depression and anxiety, and in our study it correlated with higher levels of state anxiety. Higher scores for chemotherapy side effects, breast symptoms and upset by hair loss were found in the high state anxiety group, suggesting that cancer therapies are perceived as aggressive and stressful.

The last months of sexual life was evaluated by BR 23 questionnaire. The results of our study suggest that dysfunctional sex life generated higher state anxiety during chemotherapy. Still, the relationship could be bivariate, as anxiety is known to be detrimental to sexual life (17). A pessimistic future perspective also generates a higher state anxiety during chemotherapy.

The limits of the study consist in the relatively small sample of evaluated subjects and in disregarding the trait anxiety of the subjects.

CONCLUSIONS
Higher state anxiety correlates with certain quality of life items, suggesting that psychological counselling and management of side effects induced by appropriate therapy should be a priority in the palliative care for metastatic breast cancer patients.

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No conflict of interests.

REFERENCES
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**NEWS**

**PARKIN PROTEIN - THE LINK BETWEEN TUBERCULOSIS AND PARKINSON'S DISEASE**

Tuberculosis (TB) is a major public health problem worldwide through incidence and mortality. Parkinson's disease is a common neurodegenerative disorder that affects million people. The pathogenesis of TB is the result of interaction between foreign bacteria and the immune response of the host organism. In macrophages, mycobacteria are surrounded by a chain of ubiquitin protein that promotes bacterial destruction (xenophagy). The mitochondrial dysfunction has a causal role in Parkinson's disease pathogenesis. The malfunction mitochondria are disposed by autophagy. According to Cox and colleagues, the Parkin protein is a ubiquitin ligase that has an important role in ubiquitin-mediated xenophagy of mycobacteria and also in autophagy. They showed that Parkin gene polymorphisms that induce a Parkin protein deficit, increase susceptibility to bacterial infection with intracellular pathogens (*Mycobacterium tuberculosis*, *M. leprae* and *Salmonella enterica* serovar Typhi). Also, mutations in the Parkin gene increased susceptibility to Parkinson’s disease. The malfunction of this protein is associated with a loss of nerve cells. The finding suggests that Parkin protein could be a target for new drugs from fight with tuberculosis infection. (Manzanillo PS, Ayres JS, Watson RO, Collins AC, Souza G, Rae CS et al. The ubiquitin ligase parkin mediates resistance to intracellular pathogens. *Nature*, 2013; DOI: 10.1038/nature12566).

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