

Depression, anxiety and quality of life of women with breast cancer.

running title: breast cancer patients' depression and anxiety

ABSTRACT

Purpose: The primary aim of this research was to detect and to assess anxiety, depression in women with breast cancer undergoing radiotherapy. The study was conducted in the Department of Radiotherapy at the University Hospital of Heraklion, Crete during October 2015 and April 2016.

Methods: A total number of 120 women diagnosed with non-metastatic breast cancer were recruited for this cross-sectional survey. Following informed consent, patients were asked to complete a demographics and clinical data questionnaire comprising with, the DASS-21 scale, the Hospital Anxiety and Depression Scale- HADS. Data was analyzed using IBM SPSS software system.

Results: The incidence of depression and anxiety for breast cancer patients is high. Results highlight similar prevalence of depression with HADS (37.5% mild and moderate depression and 62.5% serious depression) DASS-21 (39.2% mild and moderate 60.8% serious depression) but not similar for anxiety.

Conclusion: the psychological complications in breast cancer patients is remarkable. Efforts to detect and treat depression and anxiety should be a priority, since they contribute to better tolerance and effectiveness in anti-neoplastic therapies.

KEY WORDS: Breast cancer, Depression, Anxiety, HADS, DASS-21

1. Introduction

Breast cancer is the most common cancer in women and the second cause of death after lung cancer. One in eight women will become ill during their lifetime. Deaths from

breast cancer made up around 7.2 % of all deaths from cancer while among women, breast cancer accounted for 16.2 % of all deaths from cancer.^[1] In Greece it has been estimated that approximately 4.500 new cases occur per year and 1.500 deaths per annum are reported.^[2] Statistical data show that Greece has a lower incidence of breast cancer compared to other member countries of the European Union. Studies have shown very different breast cancer outcomes based on patient age with younger women typically to have more aggressive tumors and older women more commonly to have less aggressive disease^[3].

The incidence of breast cancer is strongly correlated with age, with the highest rates occurring at an older age (> 55 years). The incidence of the disease is lower for women around 40, and higher for ages between 55 – 69.^[4] Breast cancer treatment may involve surgery and radiotherapy, as well as systemic therapy including chemotherapy, hormone therapy and immunotherapy.^[5] The choice of the most appropriate treatment method depends on the stage of the disease and on a number of prognostic factors such as the histological characteristics of the primary tumor (degree of differentiation, histological type of neoplasm), the infiltration of axillary lymph nodes, the expression of hormone receptors, over-expression of HER2 inhibitors, the patient's age as well as the general condition of the patient^[6]. Radiotherapy is a complementary treatment that is applied locally to the breast and axillary lymph nodes, always administered postoperatively in cases of breast retention. Radiotherapy after mastectomy is applied in the case of lymph node filtration, in tumors larger than 5 cm, T3 or T4 disease, or in proximal or infected surgical incisions. The side effects of radiotherapy are either immediate or distant. The time interval that separates the immediate from the later complications is, on average 90 days from the start of the radiotherapy. Direct complications may occur during or after the completion of radiotherapy, and last up to a few weeks. The acute side effects of radiation therapy include skin eruption and irritation throughout the radiated area (in 100 % of the cases), fatigue (in 50 % of the cases), radial pneumonitis in 1 % of the patients, especially those that undergo lymph node radiation, and bladder lymphedema in less than 7 % of all breast cancer cases^{[7], [8]}.

Women with breast cancer regardless of age, ethnicity or disease stage, have the same problems in adaptation to the diagnosis of cancer. Their treatment options are influenced by personality and the particular concerns and life-stage of the patient. Psychological processes such as focusing on the problem and solving it, searching for information, designing a new course of life, interpreting and confronting the disease, seeking social support, expressing

64 emotions, linking to religion, searching for meaning and hope and, ultimately, accepting the
65 disease, take place in a difficult period for patients as they try to reconcile both the
66 occurrence of the disease as well as the painful therapeutic processes.^[9] Problems arising
67 during this period can be mitigated or exacerbated by particular psychosocial interventions.
68 Approximately one in two cancer patients have psychiatric morbidity due to their disease,
69 with reactive depression and reactive anxiety occurring in 70 % of cases. On the other hand,
70 in 10 – 15 % of cases, major depression and organic psycho-syndromes are experienced.
71 Depression cannot be declared a predisposing factor in breast cancer.^{[10], [11]} However, other
72 studies have shown a negative impact of depression to the course of the disease and to its
73 progression^[12]. This can be attributed to the negative effect of depression on the patient's
74 behavior resulting in her noncompliance with treatment and preventative control^[13]. Women
75 with breast cancer have to adapt and withstand physical malformations, side effects of
76 chemotherapy, emotional insecurity, and changes in family, work and social roles^[14]. The
77 incidence of psychological morbidity in cancer patients is high. Inability to recognize the co-
78 morbidity of psychiatric conditions can have an aggravating effect on patient compliance in
79 therapeutic interventions, resulting in often long treatment delays and an impact on overall
80 survival^[15].

81 Every person understands and appreciates differently the level of quality of their life
82 based on their personal expectations and values. The assessment therefore of their quality of
83 life, gives us important information about patient's perception about personal health and
84 wellness^[16]. Studies in breast cancer patients have shown that assessing the quality of life
85 and its dimensions, such as psychosocial wellbeing, organic wellness, and emotional
86 functioning, are predictive indicators of patient survival^[17]. The study of the quality of life in
87 clinical studies assessing the effectiveness of anti-neoplastic therapies, allows the systematic
88 collection of data on adverse reactions and symptoms as well as the significance of therapy to
89 patients^[18]. This information combined with data on total survival, free disease time interval,
90 and drug toxicity contribute to the formation of more effective and better tolerated therapeutic
91 regimens. In addition, the assessment of the quality of life allows for a better assessment of
92 the outcome of treatment in relation to patients' needs^[19].

93 **2. Aim**

94 This cross-sectional study aimed to explore the relationship between breast cancer and
95 depression subjected to external radiotherapy.

96 **3. Material and methods**

97 The study was conducted from October 2015 to March 2016 at the Department of
98 Radiotherapy of the University General Hospital of Heraklion. It involved patients suffering
99 from non-metastatic breast cancer visiting the Radiotherapy department daily. The
100 department features a 6 MV and an 18 MV linear accelerators. Every day, 120 patients were
101 subjected to external palliative auxiliary or radical radiotherapy.

102 **Patient inclusion criteria in the study:** Patients should be in good mental state with an
103 ability to read and complete the questionnaire. The age range of patients participating in
104 this study was patients up to 65 years of age. The study includes patients with Stage I / II
105 / III breast cancer. Staging was based on the TNM system ^[20].

106 **Patient exclusion criteria from the study:** In this study patients with metastatic breast
107 cancer, second-line primary cancer as well as patients with a history of depressive illness
108 or the use of antidepressants prior to the diagnosis of Ca, were excluded.

109 **Tools**

110 Tools that were used in the study were the HADS, DASS 21 and EORTCQLQ-C30.

111 Hospital Anxiety and Depression Scale was developed by Zigmond and Snaith for diagnosing
112 anxiety and depression among patients hospitalized in non-psychiatric clinics ^[21]. HADS has
113 been widely used in the general population and in cancer care units. It has been translated
114 into the Greek language and culturally adapted to Greek environment ^[22]. It contains 14
115 questions, 7 of which refer to the assessment of anxiety disorders while the rest refer to the
116 assessment of depressive symptoms. Each question corresponds to a multiple choice answer
117 of 4 selections rated from 0 - 3, giving a total score in the range of 0 – 21 for each disorder.
118 When the total score exceeds 11 then it is assumed as a pathological condition.

119 The DASS 21 scale is a questionnaire consisting of 21 questions and is designed to measure
120 the intensity range of anxiety and depression symptoms. Patients are asked to respond to the
121 presence of specific symptoms during the previous week from the day of completion. Each
122 question is rated from 0 – 3 ^[23].

123 Cronbach-a of HADS questionnaire has, in both categories (depression - anxiety), high
124 internal reliability (Table 6). The DASS 21 questionnaire, on the other hand, while having
125 high internal credibility for "depression", however, it does not show such a consequence for
126 "anxiety". However, Cronbach-a is within the tolerable range (> 0.70).

EORTCQLQ-C30 was created by the European Agency for Research and Cancer Treatment as a tool for studying the quality of life of patients who have been diagnosed and suffer from a neoplastic disease ^[24]. Unlike other questionnaires, the EORTCQLQ-30 questionnaire adopts a parallel approach taking into account linguistic and cultural differences at all stages of its creation. It can therefore be safely used in patients with different cultural backgrounds. It consists of 30 questions related to physical and cognitive functioning as well as emotional and social functioning. The questionnaire is translated into Greek and is fully weighted with regard to its psychometric features ^[22]. Since values for the Cronbach coefficient for each variable in the quality of life questionnaire are more than 0.7 (Table), internal consistency and reliability can be assumed.

4. Results

In tables 1 and 2 we can see that 55.8 % of the participants are aged 40 - 55, 49.2 % are married, 66.7 % are primary education graduates, 45.0 % are at disease stage II while 51.7 % had undergone partial mastectomy. At the same time, 55.8 % have done additional chemotherapy, and 40.8 % say they have not noticed side effects from the treatment. Regarding the frequency of drug use, 50 % declare they use painkillers very often, 39.2 % use no tranquillizers followed by 34.2 % who say they take tranquilizers very often while 41.7 % say they do not take any antidepressants.

Using both DASS 21 and HADS, we observe that approximately 40 % of the sample appear to have mild depression, while the remaining 60% appear to have significant, intense or very significant depressive symptoms (Table 3, 4). DASS 21 scale (depression) correlates positively with the disease stage ($r = .203$, $p = 0.026$), with the type of chemotherapy ($r = .193$, $p = 0.035$) with the side effects of the treatment ($r = .225$, $p = .013$) and the frequency of use of painkillers ($r = .292$, $p = 0.001$). The correlation of DASS21 (depression) is moderately positive with the type of surgery ($r = .385$, $p = .000$) and the number of medications received by the patient ($r = .315$, $p = .000$). The correlation of the DASS21 scale (depression) is strong with the frequency of use of antidepressants ($r = .706$, $p = .000$). (Table 5)

The DASS21 (anxiety) scale correlates positively with the disease stage ($r = .181$, $p = .048$), as with the frequency of use of tranquilizers ($r = .339$, $p = .000$). The correlation of this variable with the medications received by the patient ($r = .353$, $p = .000$) is moderately

positive.

On the other hand, the HADS (depression) scale correlates positively with the disease stage ($r = .169$, $p = 0.064$), with the frequency of use of tranquillizers ($r = .229$, $p = .012$), with the side - effects of treatment ($r = .183$, $p = .046$) and the frequency of use of painkillers ($r = .281$, $p = .002$). It is moderately correlated with the type of treatment ($r = .393$, $p = .000$) and a number of drugs taken by the patient ($r = .374$, $p = .000$). It, also, exhibits a strong correlation with the frequency of use of antidepressants ($r = .628$, $p = .000$).

The HADS (anxiety) scale correlates positively with the educational level ($r = .203$, $p = .026$) and the frequency of use of painkillers ($r = .209$, $p = .022$), moderately positively with the disease stage ($r = .332$, $p = .000$), strongly with the number of drugs received by the patient ($r = .614$, $p = .000$) and particularly strongly with the frequency of use of tranquilizers ($r = .935$, $p = .000$).

In reference to the EORTC QLQ-C30 v3.0 questionnaire we can see that patients with a higher degree of depression (HADS (especially strong negative correlation: $R = -.810$, $p = .000$), DASS 21 (strong negative correlation: $r = -.682$, $p = .000$)) but not anxiety (HADS ($r = -.076$, $p = .411$), DASS 21 ($r = -.158$, $p = .084$)), report a lower quality of life. Physical and emotional functionalities are negatively correlated with the presence of depression (HADS (PF: particularly strong negative correlation: $r = -.755$, $p = .000$, EF: strong negative correlation: $r = -.690$, $p = .000$), DASS21 (PF: strong negative correlation: $r = -.552$, $p = .000$, EF: strong negative correlation: $r = -.533$, $p = .000$) as well as the presence of anxiety (DASS 21 (PF: weakly negative correlation: $r = -.234$, $p = .010$, EF: moderate negative correlation: $r = -.263$, $p = .004$)). Role functioning is negatively correlated with the presence of depression (HADS (moderate negative correlation: $r = -.371$, $p = .000$), DASS21 (moderate negative correlation: $r = -.391$, $p = .000$)) as well as the presence of anxiety (HADS (moderate negative correlation: $r = -.321$, $p = .000$)). Social and cognitive functions are negatively correlated to depression (HADS (SF: strongly negative correlation: $r = -.470$, $p = .000$, CF: strongly negative correlation: $r = -.528$, $p = .000$), DASS21 (SF: strongly negative correlation: $r = -.428$, $p = .000$, CF: strongly negative correlation: $r = -.441$, $p = .000$)) and anxiety (HADS: $r = .384$, $p = .000$, CF: moderate negative correlation: $r = -.354$, $p = .000$), DASS21 (SF: weakly negative correlation: $r = -.209$, $p = .022$, CF: moderately negative correlation $r = -.336$, $p = .000$)).

Diarrhea, constipation and anorexia are not associated with depression or anxiety (HADS, DASS21). Insomnia correlates positively with anxiety (HADS (strong positive correlation: $r = .435$, $p = .000$)), as are dyspnea, pain and nausea - vomiting (HADS: DY: weak positive

193 correlation: .227, $p = .013$, PA: weak positive correlation: $r = .206$, $p = .024$, NV: moderate
194 positive correlation: $r = .262$, $p = .004$), DASS21 (DY: strong positive correlation: $r = .560$, p
195 $= .000$, PA: moderate positive correlation: $r = .273$, $p = .003$, NV: moderate positive
196 correlation: $r = .304$, $p = .001$)). The latter also correlate positively with depression (HADS
197 (DY: weak positive correlation: $r = .207$, $p = .023$, PA: moderate positive correlation: $r =$
198 $.340$, $p = .000$, NV: weak positive correlation: $r = .210$, $p = .021$)) as is fatigue with
199 depression (HADS (strong positive correlation: $r = .503$, $p = .000$), DASS21 (strong positive
200 correlation: $r = .445$, $p = .000$)) and anxiety (HADS (moderate positive correlation: $r = .265$,
201 $p = .004$)).

202 According to the data on **Error! Reference source not found.**, we find that all functional
203 scales are positively correlated with the quality of life (PF: particularly strong positive
204 correlation: $r = .778$, $p = .000$, EF: particularly strong positive correlation: $r = .817$, $P = .000$,
205 CF: strong positive correlation: $r = .540$, $p = .000$, SF: strong positive correlation: $r = .471$, p
206 $= .000$, RF: moderate positive correlation: $= .000$). This means that the higher the score on a
207 functional scale (e.g. physical functionality), the higher the score in the quality of life. Of the
208 symptom scales, only fatigue (strongly negative correlation: $r = -.414$, $p = .000$), nausea -
209 vomiting (weakly negative correlation: $r = -.204$, $p = .000$) and pain (moderate negative
210 correlation: $r = -.329$, $p = .000$) correlate with quality of life. This means that the higher the
211 score in pain, fatigue or nausea - vomiting, the lower the score on the quality of life.
212 Symptoms' scales nausea and vomiting (FA = strong positive correlation: $r = .430$, $p = .000$,
213 PA: particularly strong positive correlation: $r = .769$, $p = .000$), fatigue (PA: moderate positive
214 correlation: $= .331$, $p = .000$) and pain correlate positively with each other. This means that
215 the higher the pain score, the higher the score in nausea - vomiting or fatigue and vice versa.
216 Economic difficulties positively correlate with insomnia (moderate positive correlation: $r =$
217 $.338$, $p = .000$) and fatigue (weakly positive correlation: $r = .223$, $p = .014$). Symptoms scales
218 and functional scales are negatively correlated with each other, meaning that the higher the
219 score in the functional scales (e.g. emotional functionality), the less the score in the symptom
220 scales (e.g. pain). More specifically, physical, emotional and cognitive functioning correlates
221 negatively with dyspnea (PF: moderate negative correlation: $r = -.267$, $p = .003$, EF: weakly
222 negative correlation: $r = -.212$, $p = .020$, CF: weak negative correlation: $r = -.194$, $p = .034$),
223 pain (PF: moderate negative correlation: $r = -.376$, $p = .000$, EF: moderate negative
224 correlation: $r = -.372$, $p = .000$, CF: moderate negative correlation: $r = -.347$, $p = .000$),
225 nausea - vomiting (PF: weak negative correlation: $r = -.157$, $p = .087$, EF: $R = -.203$, $p = .026$,
226 CF: moderate negative correlation: $r = -.360$, $p = .000$) and fatigue (PF: Correlation: $r = -.462$,

p = .000, EF: strongly negative correlation: $r = -.428$, $p = .000$, CF: strong negative correlation: $r = -.705$, $p = .000$). Social functionality is negatively correlated with fatigue (intense negative correlation: $r = -.745$, $p = .000$), with nausea - vomiting (moderate negative correlation: $r = -.351$, $p = .000$), pain (moderate negative correlation: $r = -.326$, $p = .000$) and insomnia (weakly negative correlation: $r = -.188$, $p = .040$). Role functionality is negatively correlated with fatigue (particularly strong negative correlation: $r = -.806$, $p = .000$), nausea - vomiting (moderate negative correlation: $r = -.323$, $p = .000$) and pain (weakly negative correlation: $r = -.187$, $p = .041$). Functional scales are positively correlated with each other. Physical functionality is positively correlated with emotional (particularly strong positive correlation: $r = .915$, $p = .000$), cognitive (strong positive correlation: $r = .509$, $p = .000$), social (strong positive correlation: $r = .467$, $p = .000$) and role functionalities (moderate positive correlation: $r = .281$, $p = .002$). Emotional functionality is positively correlated with cognitive (strong positive correlation: $r = .521$, $p = .000$), social (strong positive correlation: $r = .464$, $p = .000$) and role functionalities (moderate positive correlation: $r = .292$, $p = .001$). Cognitive functionality is also correlated with social (particularly strong positive correlation: $r = .887$, $p = .000$) and role functionalities (strong positive correlation: $r = .744$, $p = .000$). Social functionality is also correlated with role functionality (particularly strong positive correlation: $r = .842$, $p = .000$).

The type of surgery correlates negatively with the physical (moderate negative correlation: $r = -.296$, $p = .001$) and emotional functionalities (weak negative correlation: $r = -.291$, $p = .001$) and the quality of life (moderate negative correlation: $r = -.282$, $p = .002$). The frequency of use of antidepressants has a negative correlation with all functional ranges (PF: strong negative correlation: $r = -.472$, $p = .000$, EF: strong negative correlation: $r = -.462$, $p = .000$, CF: moderate negative correlation: $r = -.346$, $p = .000$, SF: moderate negative correlation: $r = -.349$, $p = .000$, RF: moderate negative correlation: $r = -.365$, $p = .000$) as well as quality of life (strong negative correlation: $r = -.553$, $p = .000$). On the other hand, it is positively correlated to fatigue (moderate positive correlation: $r = .302$, $p = .001$). The side effects of treatment are positively correlated to insomnia (weak positive correlation: $r = .209$, $p = .022$) and negatively with cognitive (moderate negative correlation: $r = -.289$, $p = .001$) and social functionalities (moderate negative correlation: $r = -.268$, $p = .003$) as well as role functionality (moderate negative correlation: $r = -.267$, $p = .003$). Finally, the number of drugs received by the patient correlates negatively with all the functional scales (PF: moderate negative correlation: $r = -.330$, $p = .000$, EF: moderate negative correlation: $r = -.370$, $p = .000$, CF: moderate negative correlation: $r = -.372$, $p = .000$, SF: moderate negative

correlation: $r = -.388$, $p = .000$, RF: moderate negative correlation: $r = -.362$, $p = .000$) and quality of life (moderate negative correlation: $r = -.304$, $p = .001$) while on the other hand it is positively correlated to all symptom scales (FA: moderate positive correlation: $r = .373$, $p = .000$, NV: weak positive correlation: $r = .248$, $p = .006$, PA: moderate positive correlation: $r = .250$, $p = .006$, DY: weak positive correlation: $r = .219$, $p = .016$, SL: moderate positive correlation: $r = .284$, $p = .002$) except for constipation, diarrhea and anorexia.

5. Discussion

According to the results obtained the occurrence of mental disorders is common in patients suffering from non-metastatic breast cancer corresponding to findings of similar studies conducted in the past in patients with neoplastic disease^[25]. Especially for breast cancer among Western patients, studies have reported rates of depression ranging from very low to very high and a medium level of anxiety. Previous studies have shown that low levels of anxiety and depression correlated with a better quality of life for^{[26], [27]}. Results from depression assessment scales show an increased risk of developing psychiatric symptoms in the first year of diagnosis and gradual decrease over time. The personality of the patient and his adaptive capacity determine the respond to the diagnosis of a life-threatening illness²⁸. However, the incidence of anxiety and depression shows significant differences between studies something which is often due to the differences in its assessment methods²⁷. Recent studies have shown that there is a tendency to overestimate the symptoms of depression by between 10 % and 25 %^[29]. While others argue that patients undergoing screening after completing adjuvant therapy, have a tendency to neglect the anxiety and symptoms of depression they experience^[30].

The present study showed a higher rate of anxiety in Stage II and III patients compared to those with lower stages, while patients with in-situ breast cancer show high levels of anxiety when compared to Stage I patients (HADS). Also the stage of the disease is positively correlated with the treatment of economic problems and negatively with the emotional functioning of patients. Increased anxiety and depression is also seen in patients undergoing preoperative or adjuvant chemotherapy as well as in heavier surgical procedures such as partial or total mastectomy^[31]. The type of surgery performed by the patients appeared to be negatively related to their physical and emotional functionality as well as their quality of life. However, a recent study reported that chemotherapy patients reported more stress than non-chemotherapy but not statistically significant^[32].

Regarding the educational level of the participants in the study it was found that primary education patients are less stressed than those with higher education. This finding is not consistent with research findings, which found that 31 % of patients with depressive symptoms have completed only primary education ^[33]. However, in a previous study, 15 % of depressive symptoms were reported among primary education patients compared to upper-secondary education patients ^[34].

6. Conclusion

A large part of the literature regarding the investigation of breast cancer is related to the researchers' involvement in the quality of life of these patients. The psychological complications in breast cancer patients are remarkable. The psychological burden of patients with breast cancer, mostly associated with depression, anxiety and low emotional functioning in nearly all studies, has been associated with poor quality of life. Breast cancer affects the dimensions of quality of life ^[35]. The diagnosis of the illness and the accompanying fears such as fear of death, fear of relapse, impairment of body image, alteration of femininity, sexuality and attractiveness are factors that can cause unexpected psychological discomfort even for years after diagnosis of the disease ^[36]. Research done at this level has provided a significant benefit to patient care, but it is difficult to determine accurately. Patient quality of life studies should take into account the clinical morbidity that originates from the disease being studied and how the symptoms of side effects from treatment affect daily activity and impact patient satisfaction. However, the data provide important evidence for therapeutic decisions when considering the psychological state of patients and the quality of life they enjoy ^[37]. The psychological complications in breast cancer patients are remarkable. Efforts to detect and treat depression and anxiety should be a priority, since they contribute to better tolerance and effectiveness in anti-neoplastic therapies.

References

1. Eurostat, 2017. Available http://ec.europa.eu/eurostat/statistics-explained/index.php/Cancer_statistics_-_specific_cancers#Breast_cancer Accessed on 18th August 2017
2. Sasieni PD, Shelton J, Ormiston-Smith N. What is the lifetime risk of developing cancer? The effect of adjusting for multiple primaries. Br J Cancer 2011; 105(3):460-465.

3. Beadle BM, Woodward WA, Buchholz TA. The Impact of Age on Outcome in Early-Stage Breast Cancer. *Seminars in radiation oncology*. 2011;21(1):26-34. doi:10.1016/j.semradonc.2010.09.001.
4. American Cancer Society. *Breast Cancer Facts & Figures 2015-2016*. Atlanta: American Cancer Society, Inc. 2015
5. Palumbo MO, Kavan P, Miller WH, et al. Systemic cancer therapy: achievements and challenges that lie ahead. *Frontiers in Pharmacology*. 2013;4:57. doi:10.3389/fphar.2013.00057.
6. Jones HA, Antonini N, Hart G. Significance of margins of excision on breast cancer recurrence. *Eur J Cancer*, 2004; 2: 316.
7. American Cancer Society. Available <https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/radiation/coping.html> Accessed on 18th August 2017
8. Leibel ST, Phillips TH. *Textbook of Radiation Oncology*. 3rd ed. Philadelphia: Saunders, 2010.
9. Solving Problems – Cancer Survival Toolbox Available <https://www.canceradvocacy.org/resources/cancer-survival-toolbox/basic-skills/solving-problems/> Accessed on 18th August 2017
10. Yeh M-L, Lee T-Y. A Prospective Study of the Relationship between Psychological Factors and Breast Cancer. *Asia-Pacific Journal of Oncology Nursing* 2016;3(2):170-175. doi:10.4103/2347-5625.170223.
11. Sun HL, Dong XX, Cong YJ, Gan Y, Deng J, Cao SY, Lu ZX. Depression and the risk of breast cancer: a meta-analysis of cohort studies. *Asian Pac J Cancer Prev* 2015; 16(8):3233-9.
12. Giese-Davis J, Spiegel D. Depression and cancer mechanisms and disease progression. *Biol Psychiatry* 2003; 54(3): 269-82.
13. Chen S-J, Chang C-H, Chen K-C, Liu C-Y. Association between depressive disorders and risk of breast cancer recurrence after curative surgery. *Gulinello. M, ed. Medicine*. 2016;95(33):e4547. doi:10.1097/MD.0000000000004547.
14. Hoffman R, Smith S. Women with breast cancer have to adapt and withstand physical malformations, side effects of chemotherapy, emotional insecurity, and changes in family, work and social roles. American Childhood Cancer Organization® (ACCO), 2014. <http://www.icpcn.org/wp-content/uploads/2013/06/Enhancing-Quality-of-Life.pdf>

15. Potossek J, Curry M, Buss M, Chittenden E. Integration of Palliative Care in End-Stage Liver Disease and Liver Transplantation. *Journal of Palliative Medicine* 2014;17(11):1271-1277. doi:10.1089/jpm.2013.0167.
16. Dancey J, Zee B, Osoba D, Whitehead M, Lu F, Kaizer, L. Quality of life scores: an independent prognostic variable in a general population of cancer patients receiving chemotherapy. *Quality of Life Research* 1997; 6:151-8.
17. Filiberti A, Flechtner H, Fleishman S, De Haes, J, Kaasa S, Klee M, Osoba Fraser SCA, Ramirez AJ, Ebbs SR, Fallowfield LJ, Dobbs HJ, Richards MA. A daily diary for quality of life measurement in advanced breast cancer trials. *British Journal of Cancer* 1993; 67: 341-346.
18. Cheung WY, Neville BA, Cameron, DB. Comparisons of patient and physician expectations for cancer survivorship care. *J ClinOncol* 2009;27:2489.
19. Patient Experience in Adult NHS Services: Improving the Experience of Care for People Using Adult NHS Services: Patient Experience in Generic Terms. NICE Clinical Guidelines, No. 138. National Clinical Guideline Centre (UK). London: Royal College of Physicians 2012.
20. Sobin LH, Gospodarowicz MK Wittekind Ch., eds. *TNM classification of malignant tumours* (7th ed.). Chichester, West Sussex, UK: Wiley-Blackwell, 2010. [ISBN 978-1-4443-3241-4](#).
21. Zigmond AS, Snaith, RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatrica Scand* 1983; 67:361-70.
22. Taylor R, Lonibond PF, Nicholas MK, Cayley C, Wilson PH. The utility of somatic items in the assessment of depression in chronic pain patients: A comparison of the Zung Self-rating Depression Scale (SDS) and the Depression Anxiety Stress Scale (DASS) in chronic pain and clinical and community samples. *Clinical Journal of Pain* 2005; 21:91-100.
23. Lovibond SH, Lovibond PF. *Manual for the Depression Anxiety & Stress Scales*. (2nd Ed.) Sydney: Psychology Foundation, 1995.
24. Aaronson N, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez, N. The European Organization for Research and treatment of cancer QLQ-C30: A Quality-of-Life Instrument for Use in International Clinical Trials in Oncology. *J Natl Cancer Inst*, 1993;85(5): 365-376.
25. Linden D. The challenges and promise of neuroimaging in Psychiatry. *Neuron* 2012;73:8-22

26. Ng CG, Mohamed S, Mee Hoong S, Faizah H, Maznah D, Ahmad Hatim S, Nor Zuraida Z, Nur Aishah T. Anxiety, depression, perceived social support and quality of life in Malaysian breast cancer patients: a 1-year prospective study. *Health and Quality of Life Outcomes* 2015;13:205 <https://doi.org/10.1186/s12955-015-0401-7>
27. Maass SW, Roorda C, Berendsen AJ, Verhaak, PF, deBock GH. The prevalence of long term symptoms of depression and anxiety after breast cancer treatment: A systemic review. *Maturitas* 2015; 82(1):100-108.
28. Alfnsson S, Olsson E, Hursti T, Lundh, MH, Johansson B. Socio-demographic and clinical variables associated with psychological distress 1 and 3 years after breast cancer diagnosis. *Support CareCancer*, 2016
29. Cheung YT, Ong YY, Ng T, Tan YP, Fan G, Chan CW, Molassiotis A, Chan A. Assessment of mental health literacy in patients with breast cancer. *J Oncol Pharm Pract* 2015;22(3):437-47
30. Qiu J, Yang M, Chen W. Prevalence and correlates of major depressive disorder in breast cancer survivors in Shanghai. *China Psychooncology* 2012; 21:1331-1337.
31. Park K, Hwang S. Unmet needs of breast cancer patients relative to survival duration. *Yonsei Med J* 2012; 53:118-25.
32. Vahdaninia M, Omidvari S, Montazeri A. What do predict anxiety and depression in breast cancer patients' A follow-up study 2010;45(3):355-61.
33. Fayers PM, Aaronson NK, Bjordal K, Groenvold M, Curran D, Bottomley A, on behalf of the EORTC Quality of Life Group. The EORTC QLQ-C30 Scoring Manual (3rd Edition). Published by: European Organization for Research and Treatment of Cancer, Brussels 2001.
34. Alcalar N, Ozkan S, Kucucuk S, Aslay I, Ozkan M. Association of coping style, cognitive errors and cancer-related variables with depression in women treated for breast cancer. *Jpn J ClinOncol* 2012; 42(10):940-947.
35. Gavric Z, Vukovic-Kostic Z. Assessment of Quality of Life of Women with Breast Cancer. *Glob J Health Sc.*, 2012; 8(9):52792.
36. Morrill EF, Brewer NT, O'Neill SC. The interaction of post-traumatic growth and post-traumatic stress symptoms in predicting depressive symptoms and quality of life. *Psychooncology* 2008; 17:948-53.

425 37. Montazeri A. Health-related quality of life in breast cancer patients: A bibliographic
 426 review of the literature from 1974 to 2007. Journal of Experimental & Clinical Cancer
 427 Research 2008;27:32.
 428

Table 1 - demographic data (age; marital status; education)

Age		
	N	%
<40	14	11,7
40-54	67	55,8
55-65	39	32,5
Total	120	100
Marital Status		
	N	%
Single	38	31,7
Married	59	49,2
Divorced	13	10,8
Widowed	10	8,3
Total	120	100
Education		
	N	%
University	40	33,3
High School	80	66,7
Total	120	100
Disease Stage		
	N	%
in situ	12	10
I	41	34,2
II	54	45
III	13	10,8
Total	120	100

Type of surgical procedure

	N	%
Lymphectomy	47	39,2
Partial Mastectomy	62	51,7
Total Mastectomy	11	9,2
Total	120	100

429

430 Table 2 - Disease Stage; Type of surgical procedure; Chemotherapy; Side – Effects;

431 Frequency of painkiller use; Frequency of tranquilizer use; Frequency of antidepressant use

Chemotherapy

	N	%
No Chemotherapy	24	20
Pre-surgical Chemotherapy	29	24,2
Complimentary Chemotherapy	67	55,8
Total	120	100

Side - Effects

	N	%
No Side - Effects	49	40,8
Skin problems	36	30
Hypoesthesia of same – side arm	24	20

Lymphedema	11	9,2
Total	120	100
Frequency of painkiller use		
	N	%
No paikillers used	29	24,2
Rarely	14	11,7
Often	10	8,3
Very often	60	50
Daily	7	5,8
Total	120	100
Frequency of tranquilizer use		
	N	%
No tranquilizers used	47	39,2
Rarely	25	20,8
Often	7	5,8
Very often	41	34,2
Daily	0	0
Total	120	100
Frequency of anti-depressant use		
	N	%
No anti-depressants used	50	41,7
Rarely	24	20
Often	12	10
Very often	21	17,5
Daily	13	10,8
Total	120	100

433 Table 3 - DASS 21 level distribution

	DASS 21 (anxiety)		DASS 21 (depression)	
	N	%	N	%
Normal	19	15,8	23	19,2
Mild	13	10,8	24	20,0
Moderate	66	55,0	35	29,2
Severe	5	4,2	23	19,2
Extremely Severe	17	14,2	15	12,5
Total	120	100	120	100

434

435 Table 4 - HADS level distribution

	HADS (anxiety)		HADS (depression)	
	N	%	N	%
Normal	72	60,0	27	21,7
Borderline abnormal	4	3,3	18	15,8
Abnormal	44	36,7	75	62,5
Total	120	100	120	100

436

Table 5 - DASS21 and HADS scales with Demographics

	Disease Stage	Age groups	Marital Status	Education	Type of surgical procedure	Chemotherapy	Frequency of tranquilizer use	Frequency of anti-depressant use	Side-effects	Frequency of painkiller use	Number of drugs used
DASS21 (depression)	,203 [*]	,079	,075	,140	,385 ^{**}	,193 [*]	,047	,706 ^{**}	,225 [*]	,292 ^{**}	,315 ^{**}
DASS21 (anxiety)	,181 [*]	,036	-,106	-,044	,052	,132	,339 ^{**}	,101	,009	,057	,353 ^{**}
HADS (depression)	,169	,049	,088	,026	,393 ^{**}	,140	,229 [*]	,628 ^{**}	,183 [*]	,281 [*]	,374 ^{**}
HADS (anxiety)	,332 ^{**}	,075	,068	-,203 [*]	,142	,071	,935 ^{**}	,124	,175	,209 [*]	,614 ^{**}

Note: * $p < .05$, ** $p < .01$

Table 6 - a-Cronbach for DASS21 and HADS

	Mean	Std. Deviation	95% Conf. Interval	α
HADS (depression)	11,29	4,69	10,44 – 12,14	0,796
HADS (anxiety)	7,88	6,01	6,63 – 9,13	0,950
DASS21 (depression)	16,02	9,05	14,38 – 17,65	0,921
DASS21 (anxiety)	12,48	6,52	11,31 – 13,66	0,703

Table 7 - DASS21 and HADS with Quality of Life

	FI	DI	CO	AP	SL	DY	PA	NV	FA	RF	SF	CF	QoL	EF	PF
DASS21 (depression)	,315**	,089	,014	,030	,055	,054	,156	,120	,445**	-,391**	-,428**	-,441**	-,682**	-,533**	-,552**
DASS21 (anxiety)	,353**	,059	,053	,125	,015	,560**	,273**	,304**	,161	-,062	-,209*	-,336**	-,158	-,263*	-,234*
HADS (depression)	,374**	-,038	,017	-,042	,099	,207*	,340**	,210*	,503**	-,371**	-,470**	-,528**	-,810**	-,690**	-,755**
HADS (anxiety)	,614**	,084	,147	,104	,435**	,227*	,206*	,262*	,265*	-,321**	-,384**	-,354**	-,076	-,159	-,121
439 Note:	*			p<		.05,			**		p<			.01	

Table 8 - α -Cronbach and quality of life

	Mean	Std. Deviation	95% Conf. Interval	α
Financial difficulties (FI)	34,44	29,60	29,09 - 39,79	1,000
Diarrhoea (DI)	40,27	30,22	34,82 – 45,74	1,000
Constipation (CO)	35,83	29,04	30,58 – 41,08	1,000
Appetite loss (AP)	42,78	29,68	37,41 – 48,14	1,000
Insomnia (SL)	31,11	29,86	25,71 – 36,51	1,000
Dyspnoea (DY)	30,00	25,71	25,35 – 34,65	1,000
Pain (PA)	42,50	31,30	36,84 – 48,16	0,744
Nausea and vomiting (NV)	21,53	21,76	17,60 – 25,46	0,753
Fatigue (FA)	46,20	28,04	41,13 – 51,27	0,831
Role functioning(RF)	53,19	29,41	47,88 – 58,51	0,714
Social functioning (SF)	55,69	30,06	50,26 – 61,13	0,827
Cognitive functioning (CF)	53,47	27,49	48,50 – 58,44	0,792
Global health status/QoL (QoL)	41,81	19,83	38,22 – 45,39	0,882
Emotional functioning (EF)	40,14	20,27	36,48 – 43,80	0,734
Physical functioning (PF)	49,61	18,43	46,28 – 52,94	0,702

	FI	DI	CO	AP	SL	DY	PA	NV	FA	RF	SF	CF	QoL	EF	PF
FI	1,000	,019	,170	,106	,338**	,116	,142	,163	,223*	-,263*	-,273*	-,241*	-,157	-,216*	-,158
DI	,019	1,000	,073	,043	,022	,027	,173	,106	-,081	,002	-,083	-,076	-,007	-,015	-,037
CO	,170	,073	1,000	,125	,122	-,028	,103	,147	-,028	-,072	-,078	-,031	-,080	-,125	-,083
AP	,106	,043	,125	1,000	-,029	-,076	-,036	-,010	,039	-,040	-,112	-,042	,085	,009	,040
SL	,338**	,022	,122	-,029	1,000	-,062	,012	,071	,079	-,162	-,188*	-,160	-,014	-,077	-,057
DY	,116	,027	-,028	-,076	-,062	1,000	,103	-,026	,103	-,033	-,122	-,194*	-,169	-,212*	-,267*
PA	,142	,173	,103	-,036	,012	,103	1,000	,769**	,331**	-,187**	-,326**	-,347**	-,329**	-,372**	-,376**
NV	,163	,106	,147	-,010	,071	-,026	,769**	1,000	,430**	-,323**	-,351**	-,360**	-,204*	-,203*	-,157
FA	,223*	-,081	-,028	,039	,079	,103	,331**	,430**	1,000	-,806**	-,745**	-,705**	-,414**	-,428**	-,462**
RF	-,263*	,002	-,072	-,040	-,162	-,033	-,187**	-,323**	-,806**	1,000	,842**	,744**	,319**	,292*	,281*
SF	-,273*	-,083	-,078	-,112	-,188*	-,122	-,326**	-,351**	-,745**	,842**	1,000	,887**	,471**	,464**	,467**
CF	-,241*	-,076	-,031	-,042	-,160	-,194*	-,347**	-,360**	-,705**	,744**	,887**	1,000	,540**	,521**	,509**
QoL	-,157	-,007	-,080	,085	-,014	-,169	-,329**	-,204*	-,414**	,319**	,471**	,540**	1,000	,817**	,778**
EF	-,216*	-,015	-,125	,009	-,077	-,212*	-,372**	-,203**	-,428**	,292**	,464**	,521**	,817**	1,000	,915**
PF	-,158	-,037	-,083	,040	-,057	-,267*	-,376**	-,157*	-,462**	,281**	,467**	,509**	,778**	,915**	1,000

441 Note: * $p < .05$, ** $p < .01$

442

Table 9 - Intra-correlation among quality of life scales

	Disease Stage	Age Groups	Marital Status	Type of surgical procedure	Frequency of anti-depressant use	Side-effects	Number of drugs used
FI	,298*	-.011	-,016	,306**	,254*	,115	,858**
DI	,092	.117	,008	-,148	-,080	,036	-,068
CO	-,006	.028	,125	,099	-,004	-,015	,135
AP	,109	.076	,060	-,018	,061	-,050	,080
SL	,143	.102	,074	,086	,018	,209*	,284*
DY	,081	-.012	-,088	-,005	,086	,039	,219*
PA	,100	.046	,082	-,018	,124	-,006	,250**
NV	,160	-.023	,129	-,003	,065	-,047	,248**
FA	,099	.039	,072	,163	,302*	,135	,373**
RF	-,119	-.158	-,059	-,171	-,365**	-,267**	-,362**
SF	-,179*	-.178	-,054	-,092	-,349**	-,268**	-,388**
CF	-,173	-.146	-,052	-,100	-,346**	-,289**	-,372**
QoL	-,051	-.101	-,103	-,282*	-,553**	-,136	-,304**
EF	-,017	-.036	-,051	-,291**	-,462**	-,015	-,370**
PF	-,033	-.032	-,009	-,296**	-,472**	-,033	-,330**

Note: * $p < .05$, ** $p < .01$