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# **Symptoms, Cluster Symptoms and Quality of Life Among Breast Cancer Survivors Compared to Healthy Women**

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**Background:** Over 80% of women diagnosed with breast cancer will survive the disease and yet studies demonstrate that many will continue to experience multiple symptoms such as fatigue, pain, depression and sleep disturbance for years after diagnosis. Clustering of symptoms is a method used to categorize two or more symptoms occurring simultaneously and associations exist between cluster symptoms and quality of life (QOL). Our study assessed prevalence and severity of cluster symptoms and the associated impact on QOL amongst Israeli breast cancer survivors.

**Methods:** 59 breast cancer survivors who were one year post-completion of adjuvant treatment and a control group of 43 healthy women were included. Participants completed questionnaires using established and validated tools assessing distress, severity, and frequency of symptoms, fatigue, sleep disturbances, depression, and pain intensity. Functional QOL and general QOL were measured for the survivor group. Cluster analysis was conducted to identify clusters symptoms.

**Results:** Among survivors, symptoms of fatigue, pain, depression and sleep disturbance were significantly higher compared to the control group (p-value <0.001 for each of the symptoms). Three clusters of symptoms were identified among survivors and categorized from low to high intensity of all symptoms. 39% of the survivors belonged to the 'low cluster', 37.3% to the 'Moderate cluster', and 23.7% to the 'High cluster'. In the control group, only 2 cluster symptom subgroups were identified: a low (56%) and moderate (44%) cluster. Significant differences in functional QOL were found between survivors and the controls. Of the 32 symptoms assessed, eight symptoms occurred more frequently among survivors (sleep difficulties, anxiety, lack of energy, pain, stress, nervousness, bloating and sadness). There were a strong negative correlation between the average distress caused by these symptoms and general QOL and functional QOL ( $r = -0.51$ ,  $p < 0.01$ ,  $r = -0.47$ ,  $p < 0.001$  respectively). Thus, higher levels of distress caused by the symptoms were associated with lower QOL, and vice versa.

**Conclusions:** Our study demonstrates that many breast cancer survivors will suffer from a significantly higher level of cluster symptoms and lower QOL than healthy women. Our findings highlight the importance of assessing symptoms and QOL amongst breast cancer survivors and the need for further research into the etiology of these symptoms and effective interventions.

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# **Depression Associated with Goserelin in Premenopausal Breast Cancer Patients – Preliminary Study**

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**Background:** LHRH agonists (Goserelin) have been shown to be effective adjuvant therapies for hormone receptor-positive early breast cancer patients with good tolerance except for menopausal-like adverse events. The purpose of this study was to investigate the prevalence of depression and to evaluate its influence on quality of life in breast cancer patients undergoing goserelin treatment.

**Materials and Methods:** All premenopausal and hormone receptor-positive breast cancer women who underwent surgery in Samsung Medical Center between September 1, 2007 and August 31, 2009 and who received goserelin as adjuvant treatment were included. After the completion of goserelin treatment, a survey composed of five questionnaires, including the Hospital Anxiety and Depression Scale (HADS), the Insomnia Severity Index (ISI), the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30), the Breast Cancer-specific Quality of Life Questionnaire (EORTC QLQ-BR23), and the Menopause Rating Scale (MRS) was conducted.

**Results:** Among 73 women who agreed to participate, a total of 37 patients completed and returned the questionnaires to the investigator (return rate = 50.7%). Clinically significant levels of anxiety and depressive symptoms were found in 32.4% and 29.7% of patients, respectively. The prevalence of insomnia was 37.8%. Compared to the normative reference, study participants reported clinically meaningful lower global health status/QoL, emotional, cognitive and social functioning, body image and future perspective as well as higher levels of fatigue, insomnia, financial difficulties, and breast cancer-specific symptoms. Patients with depressive symptoms represented higher MRS scores.

**Conclusion:** Breast cancer patients who were treated with goserelin experienced considerable depression, anxiety and insomnia and poorer health-related quality of life. When clinicians treat breast cancer patients

with goserelin, they should be concerned about patients' psychological health and quality of life.

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# **Breast-cancer Related Lymphoedema After Nerve-sparing Axillary Lymph Node Dissection**

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**Background:** Axillary lymph node dissection (ALND) is classically associated with a high rate of morbidity – lymphoedema (6–43%), intercostobrachial nerve syndrome (58–81%), arm mobility restriction (17–33%), stiffness/weakness of upper extremity (17–33%) [Arnaud S, 2004; Ivens D, 1992].

**Material and Methods:** We conducted a prospective study to evaluate the frequency, character and distribution of lymphoedema of upper extremity (primary end-point) in two consecutive groups (2 arms) of women who underwent level-2 ALND for operable breast cancer at National Center of Oncology in the period of 2005–2010 years.

In group I (nerve-preserved or experimental group – 110 patients) besides of motor nerves (long thoracic and thoracodorsal nerves) the intercostobrachial nerve (ICBN) was preserved (nerve-sparing or functional ALND). In group II (control, standard or nerve-sacrificed group – 110 patients) the ICBN was transected (conventional ALND).

The ICBN was preserved in the absence of grossly involved nodes.

Lymphoedema of upper extremity was assessed after 6 months from the surgery by two methods. The circumferential measurements were made at 4 points along both arms: 10 cm above the olecranon, 10 cm below the olecranon, at the wrist and at the palmar crease. The criterion for the diagnosis of lymphoedema was 2 cm or more difference in upper extremity circumference when compared with the nonaffected limb. In volumetric analysis (water-displacement technique described by Kissin et al) lymphoedema was defined as being present when the volume of the ipsilateral arm was 200cm<sup>3</sup>/10% or greater than that of the contralateral arm.

The mean age of the patients was 47.8±12. Patients' demographic characteristics were alike. The two groups (preserved and sacrificed) were well balanced for TNM, type of surgery, number of nodes dissected and positive, postoperative adjuvant treatment.

Statistical differences between the groups were calculated using Pearson chi-square test ( $\chi^2$ ). A P value of <0.05 was considered statistically significant.

**Results:** The analyses of results showed, that prevalence rate of lymphoedema of upper extremity was 27.3% (30/110) in the experimental group and 30.9% (34/110) in the control group ( $\chi^2 = 0.89$ ,  $p = 0.766$ ). In both groups the first (respectively 20 and 22) and the second (respectively 10 and 12) degrees of lymphoedema according to classification of Stilwell were revealed. But it is noteworthy, that the frequency of lymphoedema in the arm (brachial) region (which corresponds to the innervation zone of ICBN) in experimental group was significantly different from that of the control group (2/30 versus 28/34,  $\chi^2 = 12.971$ ,  $p < 0.001$ ).

**Conclusion:** Our study demonstrates, nerve-sparing ALND produces minimal postoperative lymphoedema in the brachial (humeral) region of operated patients.

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# **Use of Complementary and Alternative Medicine by Breast Cancer Patients**

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**Background:** Breast cancer patients are known to be frequent users of Complementary and Alternative Medicine (CAM) in the USA and Great Britain. However, using CAM could be potentially dangerous since several studies have shown interactions between natural CAM and conventional cancer treatment. The aim of this study was to determine the prevalence and predictors of use of CAM by breast cancer patients in the Netherlands, and to explore the association between CAM therapy use, quality of life (QOL), trust in conventional therapies, and feelings of self-control over health and illness.

**Material and Methods:** A questionnaire assessing the use of CAM, focusing on natural products, was sent prospectively to a cohort of 275 breast cancer patients within 2 weeks after diagnosis in the period from July 2010 to September 2011. Clinical variables were obtained from medical records.

Descriptive statistics, t-tests and logistic regression analyses were conducted.

**Results:** The response rate was 47.4%. Of the 130 respondents 43.8% used CAM. Vitamins and minerals were the most common (50.9%) used CAM product. Patients usually started with CAM on their own initiative and the most common reason to use CAM was to stimulate the immune system (56.1%). 66.7% did not report CAM use to the physician, usually because patients thought it was unimportant (48.6%). Most CAM users (89.1%) thought CAM was effective.

There was no significant difference in age ( $p=0.496$ ), educational level ( $p=0.175$ ), relationship status ( $p=0.681$ ), having children ( $p=0.175$ ), or smoking ( $p=0.154$ ) between CAM-users and non-users. More CAM-users (71.9%) drank more than 1 alcohol consumption per week than non-users (46.6%) with an odds ratio of 2.93 ( $p=0.004$ ). The average Body Mass Index of CAM-users (20.6) was lower than of non-users (22.5,  $p=0.009$ ).

No statistical significant difference existed in faith in conventional treatment ( $p=0.547$ ) or QOL ( $p=0.371$ ). The Multidimensional Health Locus of Control (MHLC), for determining the locus of control over a patient's health or illness showed no significant difference between the two groups.

**Conclusions:** CAM use appeared common among recently diagnosed breast cancer patients in the Netherlands. Most CAM-users did not discuss this with their physician. Since clinically significant drug interactions have been described for CAM, physicians and other health care providers should discuss this topic with their patients.

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### Sexual Dysfunction in Married Breast Cancer Patients: a Follow-up Study

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**Background:** Sexual function affects quality of life in patients with breast cancer especially younger patients. This study aimed to assess sexual function among Iranian breast cancer patients.

**Material and Methods:** This was a follow-up study of sexual function in breast cancer patients attending the Cancer Institute of Iran. Sexual function was assessed using the Female Sexual Function Index (FSFI) at two points in time: baseline (pre-treatment) and after completion of treatment at follow-up visits (post-treatment). Pre- and post-treatment data were compared. In addition logistic regression was performed to find out factors contributing to post-treatment sexual dysfunction.

**Results:** In all 277 breast cancer patients were approached. Of these, 231 patients (83%) were sexually active and data for 216 patients (93.5% of sexually active patients) were available at pre-and post-treatment. Overall pre-and post-treatment sexual dysfunction was found to be 52% and 84%, respectively; indicating a significant deterioration in sexual function among breast cancer patients. Logistic regression analysis indicated that younger age ( $OR=0.94$ ), receiving endocrine therapy ( $OR=3.29$ ) and poor sexual function at pre-treatment ( $OR=12.4$ ) were the most significant contributing factors to post-treatment sexual disorders.

**Conclusions:** Breast cancer patients might show deterioration in sexual function over time. The findings from this study indicated that younger age, receiving endocrine therapy, and poor sexual function at diagnosis were the most significant predicting factors for sexual disorders in breast cancer patients after treatment.

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### The Effect of Chemotherapy on Objective Cognitive Functioning in Breast Cancer Patients

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**Background:** Recent studies suggest that chemotherapy may induce cognitive decline in women treated for breast cancer. However, evidence for this chemotherapy-induced cognitive decline is inconclusive. Therefore, the purposes of this multicenter, prospective longitudinal study was to examine the effect of chemotherapy on objective cognitive functioning in breast cancer patients three months after chemotherapy administration.

**Materials and Methods:** Post-operatively and before chemotherapy, breast cancer patients were asked to participate in this study. The control group consisted of women who were diagnosed with a benign breast problem. Before the chemotherapy started and three months after completion of chemotherapy (and at comparable moments for the benign breast problem group), a neuropsychological test battery was administered

covering the following domains: verbal memory, visual memory, information processing speed, executive functioning, verbal fluency, motor speed and reaction speed.

**Results:** At the moment of analysis 52 breast cancer patients (mean age 51, range: 28–69) and 50 patients with a benign breast problem (mean age 47, range 21–71) had completed both neuropsychological assessments. With age and verbal intelligent quotient as covariates we found no interaction effects ( $p \geq 0.145$ ) and no significant effects for time on the neuropsychological domains ( $p \geq 0.270$ ), indicating that objective cognitive functioning remained stable over time. In addition, no significant differences between the breast cancer patients and the patients with a benign breast problem were found on any of the neuropsychological domains ( $p \geq 0.232$ ).

**Conclusion:** Three months after ending chemotherapy no effect was found on objective cognitive functioning in breast cancer patients.

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### Association of Triple-negative Breast Cancer with Extracapsular Extension of Axillary Lymph Node Metastasis

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**Background:** Triple-negative breast cancers (TNBC) are defined by a lack of expression of estrogen, progesterone, and ERBB2 receptors. We compare the clinical features and prognosis of association of triple-negative breast cancer with extracapsular extension of axillary lymph node metastasis.

**Materials and Methods:** From January 2000 to December 2009, 591 breast cancer patients operated in General hospital 'Sveti Vracevi' in Bijeljina. We selected 301 (50.9%) patients with breast cancer who had metastases to axillary lymph nodes.

**Results:** Extracapsular extension (ECM) was found in 122 (40.5%). Eighty-three patients (14%) were classified as TNBC. The patients were identified and divided into two groups: 22 patients with triple-negative breast cancer with extracapsular extension of axillary lymph node metastasis (TNBCECM) and 14 patients with triple-negative breast cancer without extracapsular extension of axillary lymph node metastasis (TNBCICM). 49 patients (40.1%) were identified with three or less lymph nodes involved, 30 patients (24.5%) patients four to six, 24 patients (19.6%) seven to nine, and 19 patients (15.5%) ten or more nodes, respectively. Total number of lymph nodes showing ECM were also significantly more in the TNBCECM (48 of 81, 59.25%) vs. (13 of 60, 21.66%) in the TNBCICM group ( $P < 0.001$ ).

**Conclusion:** New strategies in the search for effective treatment options for patients with TNBC have focused on both new chemotherapy regimens and targeted therapies. In patients TNBCECM prognosis was significantly worse compared with those who were TNBCICM. These findings have led to the conclusion that TNBC is associated with a more aggressive subtype of cancer.

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### Lifestyle and Change in Bone Mineral Density in Japanese Postmenopausal Women with Hormone Receptor-positive Breast Cancer Before and After 1 Year of Aromatase Inhibitor Treatment

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**Background:** Unlike tamoxifen, aromatase inhibitors (AIs) reduce bone mass and significantly increase the risk of fractures. [1,2] Therefore, clinicians and patients need to be aware of this risk during long-term treatment with AIs. Genetic factors and lifestyle habits such as diet and exercise are involved in the maintenance of bone mineral density (BMD). However, since lifestyle habits differ between Western and Japanese individuals, it is important to confirm whether the same risk can be applied to Japanese patients. Therefore, we assessed the lifestyle and bone status of Japanese postmenopausal women with hormone receptor-positive early-stage breast cancer before and after 1 year of initial treatment with AI treatment.