ΕΘΝΙΚΟ ΚΑΙ ΚΑΠΟΔΙΣΤΡΙΑΚΟ ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ-

ΙΑΤΡΙΚΗ ΣΧΟΛΗ

ΠΡΟΓΡΑΜΜΑ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ

«Η ΕΠΙΣΤΗΜΗ ΤΟΥ ΣΤΡΕΣ ΚΑΙ Η ΠΡΟΑΓΩΓΗ ΤΗΣ ΥΓΕΙΑΣ»

ΠΤΥΧΙΑΚΗ ΕΡΓΑΣΙΑ:

“Παρεμβατικό πρόγραμμα διαχείρισης του στρες και προαγωγής της υγείας σε γυναίκες με καρκίνο του μαστού ”

Η διερεύνηση των επιδράσεων ενός ολιστικού προγράμματος διαχείρισης στρες και προαγωγής της υγείας, διάρκειας 8 εβδομάδων σε γυναίκες με καρκίνο του μαστού που ακολουθούν διάφορα είδη ενεργούς θεραπείας σε σύγκριση με ομάδα ελέγχου παρόμοιων ασθενών που έλαβαν μία ενημερωτική συνεδρία.

Συγγραφέας-ερευνήτρια

ΧΑΡΑΛΑΜΠΟΠΟΥΛΟΥ ΜΑΡΙΑ

Τριμελής Επιτροπή

ΧΡΟΥΣΟΣ ΓΕΩΡΓΙΟΣ

ΔΑΡΒΙΡΗ ΧΡΙΣΤΙΝΑ

ΣΥΡΙΓΟΣ ΚΩΝ/ΝΟΣ

ΑΘΗΝΑ

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Περίληψη

Εισαγωγή-Οι ασθενείς με καρκίνο του μαστού υποβάλλονται σε μακρόχρονες θεραπείες που επιδρούν αρνητικά τόσο στη φυσική τους όσο και στην ψυχολογική τους κατάσταση. Για το λόγο αυτό χρειάζονται ολιστικές παρεμβάσεις για την στήριξή των γυναικών αυτών κατά τη διάρκεια της αντικαρκινικής αγωγής.

Μέθοδος και Υλικό-Αυτή η πιλοτική τυχαιοποιημένη κλινική δοκιμή παρέχει την πρώτη αξιολόγηση μίας καινοτόμου γνωσιακής παρέμβασης για γυναίκες με καρκίνο του μαστού κατά τη διάρκεια της αντικαρκινικής αγωγής με στόχο τη βελτίωση της ποιότητας ζωής, τη μείωση του αντιλαμβανόμενου στρες, του άγχους και των καταθλιπτικών συμπτωμάτων. Σαράντα πέντε γυναίκες διαγνωσμένες με καρκίνο του μαστού που βρίσκονταν σε ενεργή αντικαρκινική αγωγή τυχαιοποιήθηκαν και κατανεμήθηκαν στην ομάδα της Πυθαγορείου Αυτογνωσίας(N=25) και στην ομάδα ελέγχου που έλαβε μία ενημερωτική συνεδρία(N=20). Για την αξιολόγηση των επιδράσεων του προγράμματος χρησιμοποιήθηκαν σταθμισμένα στην Ελληνική γλώσσα ερωτηματολόγια πριν την έναρξη του προγράμματος και 8 εβδομάδες μετά. Τα ερωτηματολόγια που χρησιμοποιήθηκαν αξιολόγησαν την ποιότητα ζωής, το στρες, το άγχος και τα καταθλιπτικά συμπτώματα (πρωτογενείς στόχοι), καθώς και την ποιότητα ύπνου, την υιοθέτηση υγιεινού τρόπου ζωής (δευτερογενείς στόχοι) των ασθενών. Επιπλέον, για την αντικειμενική μέτρηση του στρες και συγκεκριμένα την συγκέντρωση κορτιζόλης, ελήφθησαν δείγματα τρίχας κεφαλής, πριν την έναρξη του προγράμματος και ένα μήνα μετά την ολοκλήρωση του προγράμματος.

Αποτελέσματα-Οι ομάδα της Πυθαγορείου Αυτογνωσίας ανέφερε στατιστικά σημαντική βελτίωση στη συνολική Ποιότητα Ζωής (P=0.004) και στις επιμέρους παραμέτρους της Ποιότητας Ζωής οι οποίες περιλαμβάνουν :την Φυσική Ευεξία(*P*=0.025), την Κοινωνική Ευεξία (*P*=0.001), τη Συναισθηματική Ευεξία (P=0.002), τη Λειτουργική Ευεξία (P=0.001), τις Ανησυχίες που σχετίζονται με τον καρκίνο του μαστού(P=0.001), καθώς επίσης σημειώθηκε στατιστικά σημαντική μείωση του αντιλαμβανόμενου στρες(*P*=0.000), των καταθλιπτικών συμπτωμάτων (P=0.017), του άγχους (P=0.007) και του στρες (P=0.003) ως πρωτογενείς στόχοι. Όσον αφορά τους δευτερογενείς στόχους σημειώθηκαν στατιστικά σημαντικές βελτιώσεις στην ποιότητα του ύπνου, στην ενδυνάμωση υιοθέτησης ενός υγιεινού τρόπου ζωής καθώς και στην συνολική συγκέντρωση κορτιζόλης τρίχας (P<0.05 για όλα).

Συμπεράσματα-Η Πυθαγόρειος Αυτογνωσία μπορεί να εφαρμοστεί με πιθανά οφέλη σε γυναίκες με καρκίνο του μαστού κατά τη διάρκεια ενεργής αντικαρκινικής αγωγής.

Ωστόσο, για την επιβεβαίωση των επιδράσεων του προγράμματος, είναι απαραίτητη η εφαρμογή σε μεγαλύτερο τυχαιοποιημένο δείγμα με μεγαλύτερη διάρκεια παρακολούθησης.

Λέξεις κλειδιά: γνωσιακή τεχνική, καρκίνος μαστού, αντικαρκινική αγωγή, ποιότητα ζωής, στρες, κορτιζόλη τρίχας

Stress management and health promotion intervention onbreast cancer patients

Abstract

Background-Breast cancer patients undergo extended treatments that affect their physical and psychological state, leading to deterioration in quality of life. Holistic interventions are needed to support these patients.

Method-This a pilot randomized trial that provided the first assessment of a novel, cognitive-based intervention for breast cancer patients undergoing adjuvant therapy targeting to improve health-related quality of life, reduce perceived stress, anxiety, depression. Forty five breast cancer patients undergoing adjuvant therapy were randomly assigned to the Pythagorean Self-Awareness Intervention (PSAI) group (n = 25) or an informative session control group (n = 20). Standardized questionnaires were administered before and 8-weeks after intervention to evaluate quality of life, stress, depression and anxiety (primary outcomes), as well as sleep quality, adopting of a healthy lifestyle (secondary outcomes). In addition, hair samples were collected to assess cortisol concentration, at baseline and 12-weeks after the end of the program.

Results-Women in the PSAI group reported significantly improvement in total Quality of Life at week 8 (P=0.004),specific aspects of Quality of Life; Physical well-being(P=0.025),Social well-being(P=0.001), Emotional well-being (P=0.002), Functional well-being(P=0.001), Breast cancer concerns(P=0.001) as well as Perceived stress (P=0.000), depression (P=0.017), anxiety(P=0.007), stress (P=0.003) as primary outcomes. Improvements in secondary outcomes included increase in quality of sleep, empowerment of a healthy lifestyle and reduction in hair cortisol concentrations (P<0.05 for all).

Conclusions-The Pythagorean Self-Awareness Intervention can be considered as feasible and potentially beneficial for women undergoing breast cancer adjuvant therapy. However, it is necessary to be tested through a larger randomized controlled trial with longer follow-up to ascertain its effects.

Keywords: cognitive-based, breast cancer, adjuvant therapy, quality of life, stress, hair cortisol

Στάθμιση του ερωτηματολογίου "Κλίμακα Στρες σε Πρόσφατα Διαγνωσμένες με Καρκίνο του Μαστού".

Περίληψη

Στόχος-Ο στόχος αυτής της μελέτης ήταν να εξεταστεί η εγκυρότητα και η αξιοπιστία ενός νέου εργαλείου, την Κλίμακα Στρες σε Πρόσφατα Διαγνωσμένες με Καρκίνο του Μαστού στον Ελληνικό πληθυσμό, εργαλείο το οποίο δημιουργήθηκε για να αξιολογεί το στρες γυναικών πρόσφατα διαγνωσμένων με καρκίνο του μαστού.

Μέθοδος-Εφαρμόσαμε ΑνάλυσηΚύριων Συνιστωσών (ΑΚΣ) στα 17 αντικείμενα της κλίμακας.

Αποτελέσματα-Από την ΑΚΣ προέκυψαν 4 παράγοντες: 1. Προσωπική ζωή, 2. Διαδικαστικά θέματα, 3. Αντιμετώπιση προκλήσεων, 4. Ψυχολογικό φορτίο. Όλες οι υποκλίμακες φάνηκε να έχουν ικανοποιητική εσωτερική συνοχή και διακύμανση, σχετικά με τη διακύμανση των θεωρητικών σκορ. Επιπλέον, το συνολικό σκορ των υποκλιμάκων καθώς και τα επιμέρους σκορ της κάθε υποκλίμακας συσχετίστηκαν σημαντικά με την Κλίμακα Αντιλαμβανόμενου Στρες και την Κλίμακα Νοσοκομειακού Άγχους και Κατάθλιψης, υποδεικνύοντας καλή εγκυρότητα κριτηρίου. Τέλος, βρέθηκαν σημαντικές συσχετίσεις με τα κοινωνικά-δημογραφικά χαρακτηριστικά καθώς και με τις πληροφορίες σχετιζόμενες με την πάθηση του δείγματος.

Συμπέρασμα- Η εξεταζόμενη κλίμακα βρέθηκε να έχει αποδεκτή αξιοπιστία και καλή εγκυρότητα στη μέτρηση του στρες σε πρόσφατα διαγνωσμένες γυναίκες με καρκίνο του μαστού.

Reliability and validity of the instrument Newly Diagnosed Breast Cancer Stress Scale in Greek population

Abstract

Aim: The aim of this study was to examine the validity and the reliability of a novel measurement tool, the Newly Diagnosed Breast Cancer Stress Scale (NDBCSS) in Greek population, which aimed to assess distress in patients recently diagnosed with breast cancer.

Methods: We performed principal component analysis (PCA) of the 17 items of the scale.

Results: The PCA resulted in 4 factors: 1.Personal life, 2. Procedural issues, 3.Facing challenges and 4. Psychological load. All subscales showed satisfactory internal consistency and variance, relative to theoretical score ranges. Subscale scores and total score were significantly correlated with perceived stress and hospital anxiety and depression scale, implying good criterion validity. Associations with Sociodemographic and disease related information was also found.

Conclusion: The NDBCSS resulted in acceptable reliability and good validity in measuring distress in patients newly diagnosed with breast cancer.

Key words: Validation, Newly Diagnosed Breast Cancer Stress Scale (NDBCSS), breast cancer, distress

Contents

Stress Management and health promotion intervention in Breast Cancer Patients.

1. Introduction

Health related quality of life is a major explored variable in oncology clinical trials nowadays, not only as a parameter of quality care[1,2]but alsoas a prognostic health factor.[3]Among cancer types, breast cancer represents a unique condition for several reasons. Firstly, it is enlisted as the first most diagnosed type of female malignancy, with 2,088,849 new cases in 2018.[4]Secondly; steadily arising percentages of long-term survival rates after diagnosisare transforming breast cancer, from a life-threatening illness into a chronic disease.[5] Thirdly, loss of breast can affect the female identity, contributing negatively to her already stressful with multiple roles life, in today's society.
What is more, breast cancer patients undergo prolonged treatments that inevitably raise psychological and physical issues.[6]Such issues include symptoms of stress, anxiety and depression as well as disturbed sleep quality that come along with negative effects on Health related Quality of Life-HrQoL.[7,8] HrQoL refers to physical and psychological functioning and it is also dependent on health, professional, family life, living conditions as well as the surrounding environment.[9]Among,the various medical, sociodemographic, and psychological elements, stress remains a distinctelement in deteriorating the HrQoL in cancer patients, which further hinders their disease prognosis.[10]
While acute stress serves as a protective mechanism, chronic stress accompanied by behavioral changes in response to chronic stress(increase in alcohol consumption, a loss of sleep, a sedentary life or a degradation of the diet) has devastating effects in human body.[11] Chronic stimulation of the Stress system and dysregulation of Hypothalamic Pituitary Adrenal axis by means of stress hormonesareconsidered etiologic factors for several disorders of neuro-endocrine, gastrointestinal and immune system.[12]
Regarding breast cancer, it has been found that both stress and life style are implicated in breast cancer metastasis as well as in cancer survival.[13,14,15,16]

In more details, Sephton et al.[16]examined the association between diurnal variation of salivarycortisol in 104 patients with metastatic breast cancer and subsequent survival and concluded that dysregulation of diurnal cortisol rhythm was associated with earlier mortality**.** Furthermore, the recent study of Obradović et al.[17]examined the role of

glucocorticoids in breast cancer metastasis based on animal models. Researchers found that increased levels of stress hormones activate glucocorticoid receptors, leading to increased colonization and heterogeneity of cancer cells that finally lead to decreased survivorship. Glucocorticoid receptors also mediate in the effects of synthetic products of cortisol, such as dexamethasone that is widely prescribed for side effects of chemotherapy.

Several psychosocial interventions in oncology care such as cognitive behavioral therapy, mindfulness, and relaxation therapy have shown to successfully improve psychological issues, QoL[18,19,20,21,22]as well as cortisol reduction in blood serum[23,24]or saliva.[25,26,27] Such interventions not only assist patients during their cancer treatment but also mediate to the transition phase from disease to survivorship. [28,39]

Preparing breast cancer patients to survivorship is another important issue.According to the recommendations of Lifestyle Medicine, health awareness and the adopting of a healthy lifestyle (healthy weight, healthy eating, active living, improvement of sleep quality and lymphedema awareness),must be implemented[30,31,32,33] shortly after diagnosis.[34]

Based on the aforementioned needs, we hypothesize that a holistic program of stress management along with lifestyle modifications, will improve QoL in breast cancer patients during adjuvant therapy. In this way, we formulated an 8-week cognitive based-stress management and health promotion program for newly diagnosed breast cancer patients undergoing adjuvant therapy(chemotherapy, radiation therapy, hormonal therapy), using a non-conventional technique, the “Pythagorean Self-Awareness Intervention” and we tested it in a pilot randomized controlled trialon psychological well-being (stress, anxiety, depression), HrQoL with cancer treatment (primary outcomes), sleep quality ,adopting of a healthy lifestyle and hair cortisol concentration(secondary outcomes).

2. Method

2.1 Study design

This is a pilot, non-blinded, randomized, two-armed group with a follow up of 8 weeks with a distribution of 27 patients in the intervention group and 23 in the control group. No changes were made to the study protocol after initiation.

2.2 Participants and procedure

The study was conducted at the outpatient breast department of Agios Savvas Regional Cancer Hospital in Athens,Greece from February to December 2018. The study protocol was approved by the hospital's Scientific and Ethics Committee and was consistent with the Declaration of Helsinki. Participants were informed in person by the researcher CM, about the purposes and processes of the study and were enrolled only after submitting written informed consent. Conforming to the inclusion criteria, individuals' age had to be above 20 years, had been operated forprimary malignancy of breast while receiving adjuvant therapy for breast cancer. Exclusion criteria included co-morbidity with any psychiatric disease (e.g. major depression, psychosisor drug abuse), any metastasis or autoimmune disease, oral intake of synthetic cortisol, previous participation in any study related to stress management and inability to read or write in Greek language.

2.3 Baseline and final measurements

A battery of self-report questionnaires was administered to participants before initiation and after the end of the intervention.

2.3.1 Socio-demographic, health and disease related information

Participants' socio-demographics included age, personal status, educational level, professional status and maternity. Participants were also asked about their weight, height and smoking habit. Disease related information such as type of surgery (mastectomy or lumpectomy), stage of cancer based on American Joint Committee on Cancer TNM system (0-III), adjuvant therapy (chemotherapy, radiation therapy, hormonal therapy) and hormonal status were retrieved from patients' medical records.

2.3.2 Perceived Stress Scale (PSS-14)

The PSS consists of 14 items that evaluate the degree of stress levels perceived by an individual in the exposure of several life conditions over the previous month. Each item is rated on a 5-degreeLikert scale (scoring from 0=never to 4= very often). There are seven positive and seven negative items and the total score results by reversing the seven positive items and then summing all 14 items (maximum total score=56, minimum total score=0). Higher PSS scores indicate higher levels of perceived stress for the last month.[35]

This scale has proved satisfactory psychometric properties in the Greek population.[36] Reliability and internal consistency for this scale of the fourteen points was very good in both baseline and final measurements (Cronbach's alpha: 0.91 and 0.96, respectively).

2.3.3 Depression, Anxiety, Stress Scale 21 (DASS-21)

DASS-21 is a questionnaire that consists of 3 axes that measure symptoms of depression, anxiety and stress in the past week. The individual replies in a 5-degree Likert scale from 0= "not true for me at all", to 3= "applied to me very much or most of the times".[37]At the end, 3 scores come up, one for each axis.Specific cut-off scores for each axis describe the degree of severity (Normal, Mild, Moderate, Severe, Extremely severe). The scale has shown good psychometric properties in the Greek population.[38]The reliability an internal consistency in each axis was satisfactory (Cronbach's alpha initially DassDepression 0.93, DassAnxiety 0.92, DassStress 0.90, finally DassDepression 0.95, DassAnxiety 0.93, DassStress 0.92)

2.3.4 Health related quality of life with breast cancer

Version 4 of the Functional Assessment of Cancer Therapy-Breast module(FACT-B)[39] was used to measure quality of life in the past week. The instrument contains 35 items that are distributed in five subscales: Physical well-being (PWB, 7 items), Social well-being (SWB, 7 items), Emotional well-being (EWB, 5 items), Functional well-being (FWB, 7 items), and the Breast Cancer Concerns subscale (BCC, 9 items). The BCC contains items specific to the concerns of patients with breast malignancy that are not included to the other subscales (e.g. bothered by hair loss, worry about the risk of cancer in family member, swelling or sensitivity of the arm, bothered about changes in body weight). All questionsarerated on a 5-point scale ranging from 0=not at all to 4=very much.Scores range were 0-28 for the PWB, 0-28 for SWB, 0-24 for EWB, 0-28 for FWB , 0-40 for the BCC and 0-148 for FACT- total score. The authors kindly provided us permission for the use of the Greek version of FACT-B, as well as information about the specific methodology of the final scoring. Higher final score indicates better quality of life of the person. The reliability an internal consistency in each category was satisfactory (Cronbach's alpha initially PWB 0.91, SWB 0.81, EWB 0.72, FWB 0.92 BCS 0.83, FACT-B 0.90and finally PWB 0.92, SWB 0.85, EWB 0.75, FWB 0.95, BCC 0.86, FACT- B 0.97).

2.3.5 Quality of Sleep Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index-PSQI[40] is a self-report questionnaire that assesses subjective sleep quality over a 1-month time interval. The index consists of 19

self-reference questions, grouped in 7 components (subjective sense of quality of sleep, awaking time, latency, duration, usual productivity of sleep, use of medication for sleep and dysfunction during the day). Scoring ranges from 0 to 3, that results in a global scorethat ranges from 0=high quality of sleep to 21=low quality of sleep. A total score of 5 or greater is indicative of poor sleep quality. In this study we used the Greek version of the scale that has shown good psychometric properties in the Greek cancer patients receiving chemotherapy.[41]The reliability an internal consistency in each category was satisfactory (Cronbach's alpha PSQIpre 0.85 and PSQIpost 0.88, respectively)

2.3.6 Health related daily activities

Participants were asked about their health related daily activities with the use of the Healthy Lifestyle and Personal Control questionnaire-HLPCQ.[42] The HLPCQ was designed to assess the degree of someone's control over his/her daily activities in terms of dietary habits, daily program, physical exercise, socialization and negative thoughts. The questionnaire consists of 26 items in a 4-point Likert scale ranging from 1=Never/rarely to 4=Always. Total score results from summation of all items. Higher score indicates increased health empowerment**.** The reliability and internal consistency in each category was satisfactory (Cronbach's alpha for HLPCQpre 0.88 and HLPCQpost 0.91, respectively).

2.3.7 Hair cortisol concentration measurement

In order to objectively assess long-term stress and cortisol mobility, hair tufts were collected from both groups. According to previously described methodology[43,44], hair was collected from posterior vertex of the scalp and were cut off as close to the scalp as possible. The hair was taped to a piece of paper and was stored at room temperature until analysis. Proximal 3cm hair segment from each sample was weighted (samples approximately between 20 and 40 mg) and placed in grinding tubes (Precellys Lysing Kits, Bertin Technologies) followed by their lysis at 5,000 rpm using homogenizer by Minilys, Bertin Technologies. Then, the powder-form hair was extracted in 1ml methanol at room temperature with shaking for 16h. The tubes were centrifuged using Biofuge 13 (Heraeus Instruments) centrifuge, the extract was transferred to a glass tube and the methanol was left at room temperature for evaporation until the samples were completely dried. Samples were then reconstituted in 100 uL phosphate-buffered saline (Ph 8.0, 1x PBS) and were vortexed for 1,5 min. Before analysis, samples were vortexed again.

Finally, samples were analyzed using automated Electro chemilumin escense immunoassay “Cortisol II” on the automated analyzer Cobas e411-ROCHE DIAGNOSTICS (GmbH, Mannheim). The limit of detection as reported by manufacturer’s directions was 0.054ug/Dl. Hair has a fairly predictable growth rate of approximately 1 cm/month. Therefore the most proximal 1 cm segment to the scalp approximates the last month's cortisol production; the second most proximal 1 cm segment approximates the production during the month before that and so on.[45] Analyses were performed at Choremeion Research Center, Department of Endocrinology, Agia Sophia Hospital.

2.4 Randomization and blindness

Patients who met the inclusion criteria were randomized in two groups based on random numbers generated by an online random number generator (www.random.org). Randomization was not blinded, as well as the initial and final measurements.

2.5 Pythagorean Self-Awareness Intervention and related measurements

Monitoring of the participants in both groups lasted for 8 weeks. During the first individualized session participants completed the questionnaires and both groups gained the same knowledge about stress and its effect on health. They were also encouraged to adopt a healthy lifestyle (dietary habits, retain or lower Body Mass Index, get active and adopt a sleep routine), received information about lymphedema and specific exercises as well as training in diaphragmatic breathing. The PSAI group (PG) was given pedometers as an incentive for physical activity.In the second session, PG was introduced to the PSAI technique. PSAI group sessions took place once a week and lasted for 180’ with 10 min interval. Participants were instructed topractice the technique twice a day (morning and bedtime) in a quiet place at home.

At bedtime each individual started with breathing diaphragmatically for 5 minutes and proceeded with three cognitive processes. At first, patients were instructed to recall every event of the day in the exact sequence that it happened and visualize themselves as they were observing another person. To enhance recall, events were categorized as follows: diet, physical activity, sleep and interpersonal contacts. In the next step, each selected experience was critically appraised using three questions: “Is what I have done wrong? Is what I have done right? What have I omitted that I ought to have done?” The individual was advised to remain emotionally detached and examine the performed actions. Regarding diet, exercise and sleep, guidance had been already given during first

session. Events or choices relevant to personal relationships were assessed freely by the individual, since the primary goal was to enhance self-awareness and not criticize them. In the morning, each participant was instructed to quickly summarize the results of the previous night practice and set goals for the upcoming day.

The next 5 sessions included lectures abouthealth-awareness, lifestyle modifications, circadian rhythms, memory,cognitive reconstruction and appraisal of interpersonal relationships according to the Pythagorean philosophy in relation to today's scientific research. During the final meeting, final assessments were made. Each session included feedback from participants' experiences.Compliance to the technique was assessed by weekly diaries that participants had to keep and submitted to the researchers in each session. Sessions were instructed by CM (MSc physiotherapist, specialized in lymphedema and expert in stress management) and DC (professor of health promotion and expert in stress management).

Patients in the control group were contacted once per week via telephone. In each telephone call, patients were briefly asked about their physical and mental status with no further discussion or in-depth counseling.

2.6 Statistical methods

Between-group comparisons for baseline data were performed by the use of Pearson's exact chi-square and Mann-Whitney *U* tests for categorical and interval characteristics, respectively. Absolute differences (Δ = final measurement minus baseline measurement) were used as dependent variables in the Mann-Whitney *U* tests for the between-group comparisons. The effect sizes of the intervention were calculated by the following formula: rho=$Z/N^{0.5}$, where rho is the effect size (<0.3 small, 0.3-0.5 moderate and >0.5 large effect size), *Z* is the score of each Mann-Whitney *U* test, and *N* is the study sample. The level of significance was set 0.05 for all analyses. Statistical calculations were performed using the SPSS for Windows (version 25.0) statistical software (SPSS Inc., Chicago, IL, USA).

3. Results

3.1 Baseline characteristics

Baseline characteristics of the sample are presented in Table 1. The sample consisted of 50 female patients, 27 in the intervention group and 23 in the control group.

No drop-outs were noted during the follow up in either group. However, 5 patients were not analyzed, even though they completed the program, because they had to receive oral intake of synthetic cortisol. Figure 1 illustrates the Flow diagram of the study. Patients in the intervention group showed full compliance to PSAI that was assessed by the weekly diaries and full participation in all sessions. No harm or any side-effect was reported by any participant. There were no significant differences between study groups at baseline. The majority of the study's participants was middle aged (52.7 ± 8.5), non-smokers(46.7%), divorced(37.8%), with children(56.6%), had completed higher education(57.8%) and was employed(68.9%). As for their health and disease related characteristics most of the subjects were overweight according to their body mass index(27.8 ± 5.6), had undergone single mastectomy(51.1%), were diagnosed with cancer stage I(35.6%) ,they were in premenopausal status(51.1%) as well as, at the time of the assessment, participants were being treated with radiation therapy(62.2%). Concerning psychological status, participantsshowed mild to moderate depression and distress and moderate degree of anxiety (DASS 21). Regarding quality of life with breast cancer treatment, patients had moderate quality of life (FACT-B). As for their sleep both groups showed very poor quality (GR-PSQI). Finally, participants showed low empowerment in healthy lifestyle and personal control measurement (HLPCQ).

3.2 Primary endpoint analyses

Forty five participants were analyzed(Intervention group N=25/ Control group N=20). In Table 2 the adjusted mean differences, standard deviations, *p* values and effect sizes for the PG versus CG are presented for each primary outcome. Statistically significant improvements in favor of PG were noted for BMI (p=0.037), perceived stress (p=0.000), depression (p=0.017), anxiety (p=0.007) and distress (p=0.003). Moreover, statistical improvements were noted in all axes that comprise health related quality of life with cancer therapy. In more details, Physical Well Being (p=0.025), Social well-being (p=0.001), Emotional well-being (p=0.002), Functional well-being (p=0.001), Breast cancer specific concerns (p=0.001)and total health related quality of life with cancer treatment (p=0.004). Further statistically significant improvements were noticed in sleep quality (p=0.002), healthy lifestyle and personal control (p=0.004) and total hair cortisol concentration (p=0.000). According to the effect size, PSAI had a large impact on Perceived stress,Total health related quality of life, Social well-being, Emotional well-being, Functional well-being, Sleep quality, Healthy lifestyle empowerment and Total hair

cortisol concentration. Moderate effect size was found in depression, anxiety, stress (DASS) and physical well-being.Finally, small effect was found in Body Mass Index.

4. Discussion

While, breast cancer remains the first common diagnosis in female population, progress in Oncology has contributed to raising survival rates. However, breast cancer patients undergo extended treatments that affect their physical and psychological state, leading to deterioration in quality of life.

The present study shows for the first time the benefits of a nonconventional stress management technique (PSAI) in combination with lifestyle modifications for newly breast cancer patients treated with adjuvant therapy. Our hypothesis that a holistic program of stress management along with lifestyle modifications, will improve QoL in breast cancer patients during adjuvant therapy was confirmed.

Quality of life is an important outcome in breast cancer studies. Our findings that PSAI improved all aspects of quality of life, sleep quality and psychological issues in breast cancer patients are consistent with Carlson et al[27,46] who evaluated 49 breast cancer patients and 10 prostate cancer patients and found significant improvements in overall quality of life and symptoms ofstress and sleep quality.

Sleep quality improvement in this study is another important finding as there is evidence that insufficient sleep might be associated with decreased QoL and increased breast cancer mortality.[47]PSAI has already been used in a pilot study for 30 outpatients diagnosed with chronic insomnia and showed statistical improvements in sleep quality.[48]

In terms of hair cortisol findings, PSAI group demonstrated to have a decreasing effect. However, our findings cannot be compared toother studies due to the fact that previous research has focused on measuring plasma or saliva cortisol. However, both saliva and serum samples provide a measurement of the cortisol concentration at a single point in time. They can therefore be used to test acute changes, but are subject to major physiological daily fluctuations, making the assessment of overall long-term systemic cortisol exposure difficult. In healthy individuals, plasma cortisol levels reach the peak in the early morning, and gradually decrease thereafter. Hence, a single measurement cannot reflect the integral of systemic exposure.[49,50] Furthermore, we quote some qualitative comments which have been recorded during intervention period: a) on stress and anxiety, “Whatever I do, I do it without stress and with absolute calmness”, “I feel relieved. This was beneficial for me and my family”, “My mood has changed and I feel

more optimistic", b) sleep, "I wake up early and feel rejuvenated", "I stopped taking sleeping pills", c)cognitive reconstruction, "I realized that before PSAI, I was taking care of everything and everyone but myself", "I can face reality and I am able to find solutions on my own", d)interpersonal relationships "I realized that ,even though I was doing many things during the day, I was never pleased with myself. Now I do less and get more pleasure from family moments and myself", "I stopped arguing with my kids as I realized that it was all about setting boundaries" ,e) other "Chemotherapy changed my body but PSAI taught me that I have the means and the weapons to fight back"

We suggest that the theory behind PSAI in based on neurobiological pathways that indirectly support that PSAI leads to a metacognitive process,[51] that activate circuits of introspection("internal cognition") and in specific the Default Mode Network. Through this system the individual makes use of higher cognitive functions and at the same time behaviors based on impulses, instincts and emotions are inhibited.[52] Finally, decisions and choices are made in an objective, rationaland more explicit manner.

The advantage of PSAI in breast cancer patients compared to other cognitive behavioral practices for stress management is based on the fact that as a holistic program teaches the patient to practically concentrate on a dysfunctional situation or idea and through the moral framework settled by the Pythagorean philosophy, "judges" him/herself in an objective way in order to find a solution by his/her own resources and attempts. At the same time PSAI offers the opportunity to the breast cancer patient to actively self-regulate, redefine needs and achieve personal changes such as adopting a healthier (body and mind) lifestyle in everyday life, after a short period of appropriate training.

Nonetheless, it remains ambiguous whether the changes mentioned can be maintained, leading to a protective effect and healthier outcomes.

This study had a number of limitations such assmall sample, semi-active control group, and lack of long-term follow-up. As such, generalization and validity of the results cannot be safely verified.Future researchers should focus on large randomized controlled studies greater sample size, and longer follow-up.

Besides these limitations, we showed that PSAI is a feasible, promising, self-administered intervention that is worth investigated in larger studies.

5. Conclusion

In conclusion, we state that the present program is a feasible one for stress management; improvement of health related quality of life and health promotion in

women undergoing different kinds of adjuvant therapy and could lead to several beneficial outcomes. However, as it is not clear whether this program, targeting at the patient's health promotion, may decrease future morbidity and hospitalization. For these reasons, a larger clinical trial is essential.

Conflict of interest

All authors declare that they have no conflicts of interest.

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Protocol n.12350/16-11-2017

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Literature

1. Cella D, & Stone AA. (2015) Health-related quality of life measurement in oncology: Advances and opportunities. *American Psychologist70*(2), 175-185. http://dx.doi.org/10.1037/a0037821

2. Padmaja G, Vanlalhruaii C, Rana S, Tiamongla, Kopparty S.(2017) Quality of life of patients with cancer: A determinant of the quality of life of Their Family Caregivers. J CancEduc32: 655. https://doi.org/10.1007/s13187-016-1000-y

3. Steel JL, Geller DA, Robinson TL, Savkova AY, Brower DS, Marsh JW, Tsung (2014) Health related quality of life as a prognostic factor in patients with advanced cancer.Cancer;1;120(23):3717-21. https://dx.doi.org/10.1002/cncr.28902

4. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A.(2018) Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin68:394–424 https://dx.doi.org/10.3322/caac.21492

5. PhilipsJL, Currow DC.(2010) Cancer as a chronic disease.Collegian.17(2):47-50

6. Perry S, Kowalski TL, Chang CH. (2007) Quality of life assessment in women with breast cancer: benefits, acceptability and utilization. Health Qual life Outcomes5(1):24. https://dx.doi.org/10.1186/1477-7525-5-24

7. Kreitler S, Peleg D, Ehrenfeld M. (2007) Stress, self-efficacy and quality of life in cancer patients. Psychooncology16:329–41https://dx.doi.org:10.1002/pon.1063

8. Kang DH, Park NJ, McArdle T. (2012) Cancer-specific stress and mood disturbance: Implications for symptom perception, quality of life, and immune response in women shortly after diagnosis of breast cancer. ISRN Nurs:608039https://dx.doi.org/10.5402/2012/608039

9. Bowling BA. (1995) What things are important in people's lives?A survey of the public's judgments to inform scales of health related quality of life. SocSci Med41 (10),1447-1462.https://dx.doi.org/10.1016/0277-9536(95)00113-L

10. Rottmann N, Dalton SO, Christensen J et al. (2010) Self-efficacy, adjustment style and well-being in breast cancer patients: a longitudinal study Qual Life Res 19: 827. https://dx.doi.org/10.1007/s11136-010-9653-1

11. Chrousos GP. (2009) Stress and disorders of the stress system. Nat Rev Endocrinol5,374–381https://dx.doi.org/ 10.1038/nrendo.2009.106

12. Nader N, Chrousos GP, Kino T. (2010) Interactions of the circadian clock system and the HPA axis. Trends in Endocrinology & Metabolism.21:5,277-286,https://dx.doi.org/10.1016/j.tem.2009.12.011.

13. Lin Y, Wang C, Zhong Y, Huang X, Peng L, Shan G. (2013) Striking life events associated with primary breast cancer susceptibility in women: a meta-analysis study. J ExpClin Cancer Res CR.;32:53.https://dx.doi.org/10.1186/1756-9966-32-53

14. Ellsworth RL, Valente AL, Shriver CD, Bittman B, Ellsworth DL.(2012) Impact of lifestyle factors on prognosis among breast cancer survivors in the USA, Expert Review of Pharmacoeconomics& Outcomes Research. 12:4. 451-464,https://dx.doi.org/10.1586/erp.12.37

15. Pant S, Ramaswamy B. (2009) Association of major stressors with elevated risk of breast cancer incidence or relapse. Drugs Today Barc Spain:1998.45(2):115–26. https://dx.doi.org/10.1358/dot.2009.45.2.1322480

16. Sephton SE, Sapolsky RM, Kraemer HC, Spiegel D. (2000) Diurnal Cortisol Rhythm as a Predictor of Breast Cancer Survival. JNCI J Natl Cancer Inst.21;92(12):994–1000.https://dx.doi.org/10.1093/jnci/92.12.994

17. Obradović MMS, Hamelin B , Manevski N, Couto JP, Sethi A, Coissieux MM, Münst S, Okamoto S, Kohler H , Schmidt A, Bentires-Alj M. (2019) Glucocorticoids promote breast cancer metastasis. Nature.567;540–544 https://dx.doi.org/10.1038/s41586-019-1019-4

18. DuijtsSF,Faber MM, Oldenburg HS, Van BeurdenM,Aaronson NK. (2011) Effectiveness of behavioral techniques and physical exercise on psychological functioning and health related quality of life in breast cancer patients and survivors-A metanalysis. Psycho-Oncology.20:115-26. https://dx.doi.org/10.1002/pon.1728

19. Faller H, Schuler M, Richard M, Heckl U, Weis J, Küffner R, et al. (2013) Effects of psycho-oncologic interventions on emotional distress and quality of life in adult patients with cancer: Systematic review and meta-analysis. J ClinOncol.31:782–93.https://dx.doi.org/10.1200/JCO.2011.40.8922

20. Zhang Q, Zhao H, Zheng Y. (2019) Effectiveness of mindfulness-based stress reduction (MBSR) on symptom variables and health-related quality of life in breast cancer patients—a systematic review and meta-analysis Support Care Cancer;27:771. https://dx.doi.org/10.1007/s00520-018-4570-x

21. Ye M, Du K, Zhou J, et al. (2018) A meta- analysis of the efficacy of cognitive behavior therapy on quality of life and psychological health of breast cancer survivors and patients. Psycho-Oncology27:1695–1703. https://dx.doi.org/10.1002/pon.4687

22. Vargas et al. (2014) Sleep Quality and Fatigue After A Stress Management Intervention For Women With Early-Stage Breast Cancer in Southern Florida. Int J Behav Med.21(6): 971–981. https://dx.doi.org/10.1007/s12529-013-9374-2.

23. Witek-Janusek L, Albuquerque K, Chroniak KR, Chroniak C, Durazo-Arvizu R, Mathews HL. (2008) Effect of mindfulness based stress reduction on immune function, quality of life and coping in women newly diagnosed with early stage breast cancer. Brain BehavImmun. 22:969-981 https://dx.doi.org/10.1016/j.bbi.2008.01.012

24. Phillips KM, Antoni MH, Lechner SC.(2008) Stress Management intervention reduces serum cortisol and increases relaxation during treatment for non metastatic breast cancer. Psychosom Med. 70:1044-1049. https://dx.doi.org/10.1097/PSY.0b013e318186fb27

25. Carlson LE, Speca M, Faris P, Patel KD. (2007) One year pre–post intervention follow-up of psychological, immune, endocrine and blood pressure outcomes of mindfulness-based stress reduction (MBSR) in breast and prostate cancer outpatients. Brain BehavImmun.21:1038-1049 https://dx.doi.org/10.1016/j.bbi.2007.04.002

26. Raghavendra RM, Vadiraja HS, Nagarathna R. (2009)Effects of a yoga program on cortisol rhythm and mood states in early breast cancer patients undergoing adjuvant radiotherapy: a randomized controlled trial. Integr Cancer Ther.8:37-46https://dx.doi.org/10.1177/1534735409331456

27. Carlson LE, Speca M, Patel KD, Goodey E. (2003) Mindfulness-based stress reduction in relation to quality of life, mood, symptoms of stress and levels of cortisol, dehydroepiandrosterone sulfate (DHEAS) and melatonin in breast and prostate cancer outpatients.Psychoneuroendocrinology. 29:448-474
https://dx.doi.org/10.1097/01.PSY.0000074003.35911.41

28. Stanton AL, Ganz PA, Kwan L, et al. (2005) Outcomes from the Moving Beyond Cancer psychoeducational, randomized, controlled trial with breast cancer patients.JClinOncol.23(25):6009-18.https://dx.doi.org/0.1200/JCO.2005.09.101

29. Park JH, Bae SH, Jung YS, Kim KS. (2012) Quality of life and symptom experience in breast cancer survivors after participating in a psychoeducational support program: a pilot study.CancerNurs35(1):E34-41
https://dx.doi.org/10.1097/NCC.0b013e318218266a.

30. Bodai BI, Tuso P. (2015) Breast Cancer Survivorship: A Comprehensive Review of Long-Term Medical Issues and Lifestyle Recommendations. Perm J. 19(2):48-79.https://dx.doi.org/10.7812/TPP/14-241

31. Hamer J., Warner E. (2017) Lifestyle modifications for patients with breast cancer to improve prognosis and optimize overall health. CMAJ.189(7):E268–E274. https://dx.doi.org/10.1503/cmaj.160464

32. Rack B, Andergassen U, Neugebauer J, SalmenJ,et al. (2010) The German SUCCESS C Study — the first European lifestyle study on breast cancer. Breast Care (Basel).5:395–400. https://dx.doi.org/10.1159/000322677

33. Bluethmann SM, Vernon SW, Gabriel KP, et al. (2015) Taking the next step: a systematic review and meta-analysis of physical activity and behavior change interventions in recent post-treatment breast cancer survivors. Breast Cancer Res Treat.149:331–42https://dx.doi.org/10.1007/s10549-014-3255-5

34. Vos PJ, Visser AP, Garssen B, Duivenvoorden HJ, de Haes HCJM.(2005)Effects of delayed psychosocial interventions versus early psychosocial interventions for women with early stage breast cancer. Patient Education and Counseling.60:212–219 https://dx.doi.org/10.1016/j.pec.2005.01.006

35. Cohen S, Kamarck T, Mermelstein(1983) R.A Global Measure of Perceived Stress.J Health SocBehav.24(4):385–96. https://dx.doi.org/10.2307/2136404

36. Andreou E, Alexopoulos EC, Lionis C, Varvogli L, Gnardellis C,Chrousos, GP, Darviri C. (2011) Perceived stress scale :Reliability and validity study in Greece.International Journal of Environmental Research in Public Health. 8:3287-3298 https://dx.doi.org/10.3390/ijerph8083287

37. Lovibond SH&Lovibond, PF. Manual for the Depression Anxiety Stress Scales (2nd.Ed.) Sydney: Psychology Foundation (1995)

38. Lyrakos GN, Arvaniti C, Smyrnioti M, Kostopanagiotou G. (2011)Translation and validation study of the depression anxiety stress scale in the Greek general population and in a psychiatric patient's sample. Eur.Psychiatry. 26,1731 https://dx.doi.org/10.1016/S0924-9338(11)73435-6

39. Brady MJ, Cella DF, Mo F, Bonomi AE, Tulsky DS, Lloyd SR, Deasy S, Cobleigh M, Shiomoto G. (1997) Reliability and validity of the Functional Assessment of CancerTherapy-Breastquality –of-life instrument. Journal of Clinical Oncology.15:3,974-986. https://dx.doi.org/10.1200/JCO.1997.15.3.974

40. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. (1989) The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research.PsychiatryResearch.28(2):193–213https://dx.doi.org/10.1016/0165-781(89)90047-4

41. Kotronoulas GC, Papadopoulou CN, Papapetrou A, Patiraki E.(2011)Psychometric evaluation and feasibility of the Greek Pittsburgh Sleep Quality Index (GR-PSQI) in patients with cancer receiving chemotherapy. Support Care Cancer.19(11):1831-40 https://dx.doi.org/10.1007/s00520-010-1025-4

42. Darviri C, Alexopoulos EC, Artemiadis A, Tigani X, Kraniotou C, Darvyri P, Chrousos GP. (2014) The Healthy Lifestyle and Personal Control Questionnaire (HLPCQ): a novel tool for assessing self-empowerment through a constellation of daily activitiesBMC Public Health.14:995.https://dx.doi.org/10.1186/1471-2458-14-995

43. Wester VL, Van Rossum EF. (2015) Clinical applications of cortisol measurements in hair Eur J Endocrinol.173(4):M1-10. https://dx.doi.org/10.1530/EJE-15-0313.

44. Sauve B, Koren G, Walsh G, Tokmakejian S, Van Uum SH.(2007)Measurement of cortisol in human hair as a biomarker of systemic exposure. Clin Invest Med.30(5):E183-91. https://dx.doi.org/10.1073/pnas.1209888110

45. WennigR. (2000) Potential problems with the interpretation of hair analysis results Forensic SciInt.107 :5-12.https://dx.doi.org/10.1016/S0379-0738(99)00146-2

47. Carlson LE, Garland SN.(2005) Impact of mindfulness-based stress reduction (MBSR) on sleep, mood, stress and fatigue symptoms in cancer outpatients.Int J BehavMed.12(4):278–285. https://dx.doi.org/10.1207/s15327558ijbm1204_9

48. Lehrer S, Green S, Ramanathan L, Rosenzweig KE.(2013) Insufficient sleep associated with increased breast cancer mortality. Sleep Med.;14:469https://dx.doi.org/10.1016/j.sleep.2012.10.012

49. Tsoli S, Vasdekis S, Tigani X, Artemiadis A, Chrousos GP, Darviri C. (2018)A novel cognitive behavioral treatment for patients with chronic insomnia: A pilot experimental study. Complement Ther Med.37: 61-63 https://dx.doi.org/10.1016/j.ctim.2018.01.015

50. Russell E, Koren G, Rieder M, Van Uum S.(2012) Hair cortisol as a biological marker of chronic stress: Current status, future directions and unanswered questions Psychoneuroendocrinology. 37(5):58901.
https://dx.doi.org/10.1016/j.psyneuen.2011.09.009

51. Schraw G. Promoting general metacognitive awareness". InstructionalScience:Kluwer Academic Publishers;1998

52. Shapira-Lichter I, Oren N, Jacob Y, Gruberger M, Hendler T. (2013) Portraying the unique contribution of the default mode network to internally driven mnemonic processes. ProcNatlAcadSci USA. 110(13):4950-5.https://dx.doi.org/10.1073/pnas.1209888110

Figures and tables

Figure 1. Flow diagram of the study

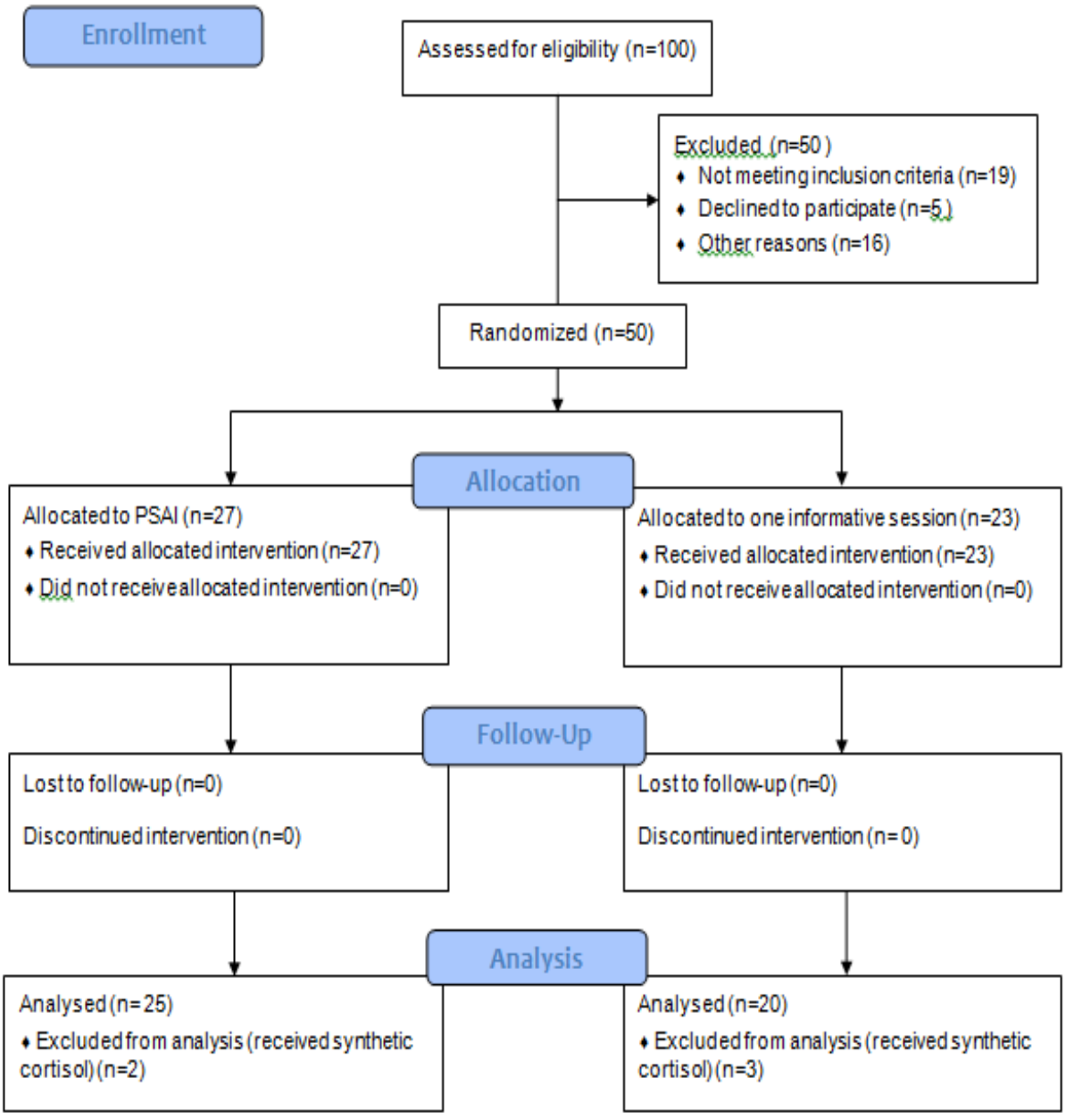

Table1. Baseline socio-demographic and disease-related characteristics of the study's participants.

Referential measurements	PSAI group (N= 25)	Control group (N=20)	*P* value
Age (mean ± SD)	52.8 ± 7.88	51.8 ± 8.63	0.73
Personalstatus			
single	3(12%)	7(35%)	0.35
married	10(40%)	5(25%)	
divorced	11 (44%)	6(30%)	
widowed	1(4%)	2(10%)	
Maternity			
yes	16 (64%)	9(45%)	0.21
no	9(36%)	11(55%)	
Educational level			
primaryschool (6 years)	0%	1(5%)	0.07
secondary (9 years)	0%	3(15%)	
highschool (12 years)	9(36%)	6(30%)	
Higher education (=14 years)	16 (64%)	10(50%)	
Working status			
retired	4(16%)	4(20%)	0.40
unemployed	2(8%)	4(20%)	
employed	19(76%)	12 (60%)	
BMI	28.3 ± 5.12	26.5 ± 6.18	0.34
Smoking habit			
yes	5(20%)	4(20%)	0.78
no	11(44%)	10(50%)	
ex-smoker	9(36%)	6(30%)	
Type of surgery			
lumpectomy	12(48%)	7(35%)	0.21
Single mastectomy	13 (52%)	10(45%)	
Double mastectomy		3(15%)	
Cancer Stage			
In situ	5(20%)	4(20%)	0.88
I	10 (40%)	6(30%)	
IIA	3(12%)	4(20%)	
IIB	3(12%)	4(20%)	
IIIA	4(16%)	2(10%)	
AdjuvantTherapy			
hormonetherapy	6(24%)	4(20%)	0.52
chemotherapy	3(12%)	4(20%)	
radiotherapy	16 (66%)	12(60%)	

*Level of significance $p < 0.05$

Table 2. Psychometric and other measurements

Referential measurements	PSAI group (N= 25)	Control group (N=20)	*P* value
*PSS*score (mean ± SD)	29.55 ± 8.82	31.06 ± 9.09	0.62
*DassDepression*score (mean ± SD)	6.05 ± 6.34	8.8 ± 6.41	0.21
DassAnxietyscore (mean± SD)	6 ± 5.8	6.4 ± 6.66	0.85
DassStressscore (mean± SD)	8.5 ± 5.91	10.2 ± 5.77	0.40
FACT-B score (mean ± SD)	75.6 ± 18.45	80.3 ± 17.58	0.45
PWBscore (mean ± SD)	18.35 ± 5.61	21 ± 2.64	0.10
SWBscore (mean ± SD)	13.85 ± 4.92	12.6 ± 6.33	0.51
EWBscore (mean ± SD)	13.25 ± 4.76	12.46 ± 5.5	0.65
FWBscore (mean ± SD)	9.75 ± 4.58	10.73 ± 5.36	0.56
BCC score (mean ± SD)	20.40 ± 4.88	23.53 ± 6.22	0.10
GR-PSQI score (mean ± SD)	9 ± 5.09	9.4 ± 3.79	0.80
HLPCQ score(mean ± SD)	35.65 ± 13.37	35.26 ± 12.33	0.93
*HCC*mean (min-max)	20.72 (7.01-37)	17,62(6.21-32.53)	0.25

Abbreviations

BCC: Breast Cancer Concerns, BMI: Body Mass Index, EWB: Emotional Well-Being, FACT-B: Functional Assessment in Cancer Treatment-Breast, FWB: Functional Well-Being, HCC: Hair Cortisol Concentration, HLPCQ: Healthy Lifestyle and Personal Control Questionnaire, PSS: Perceived Stress Scale, PSQI: Pittsburgh Sleep Quality Index, PWB: Physical Well-Being, SD: Standard Deviation, SWB: Social Well-Being. [1] Frequencies were analyzed by Pearson's chi-square (categorical by categorical comparisons) and non-parametric Mann-Whitney U-test (categorical by quantitative comparisons),

*Level of significance $p < 0.05$

Table 3. Comparisons of outcomes' differences across study's groups[1]

Measurements	PSAI group (*N* =25)	Control group (*N* =20)	95% CI	*P* value	Effect size
ΔBMI score (mean ± SD)	- 0.77 ± 0.86	0.35 ± 1.73	-1.93,-0.16	0.037*	0.3
ΔPSS score (mean ± SD)	-15.6 ± 10.09	2.6 ± 8.44	-23.86, -10.83	0.000*	0.8
ΔDepression score (mean ± SD)	-3.7 ± 5.22	-0.2 ± 2.27	-6.35, -0.67	0.017*	0.4
Δanxiety score (mean ± SD)	-3.95 ± 5.99	0.53 ± 1.12	-7,54, -1.35	0.007*	0.5
Δstress score (mean ± SD)	-4.5 ± 5.52	-0.26 ± 0.72	-7.20, -1.04	0.003*	0.5
ΔFACT-B score (mean ± SD)†	44.05 ± 17.04	-11.2 ± 17.99	40.16, 65.31	0.004*	0.6
ΔPWB score (mean ± SD)†	7.1 ± 4.49	-3.86 ± 6.99	6.17, 14.27	0.025*	0.4
ΔSWB score (mean ± SD)†	5.25 ± 4.43	-0.13 ± 2.41	2.94, 7.93	0.001*	0.6
ΔEWB score (mean ± SD)†	8.7 ± 4.54	-2.06 ± 5.4	6.83, 13.89	0.002*	0.6
ΔFWB score (mean ± SD)†	10 ± 4	-2.06 ± 3.71	8.80, 14.32	0.001*	0.7
ΔBCC score (mean ± SD)†	13 ± 4.24	-3.06 ± 3.91	12.11, 18.38	0.001*	0.6
ΔGR-PSQI score (mean ± SD)	-4.21 ± 6.45	2.35 ± 3.75	-10.66, -2.47	0.002*	0.6
ΔHLPCQ score (mean ± SD)†	17.4 ± 12.65	-3.86 ± 6.23	12.86, 27.43	0.004*	0.6
ΔHCC (mean ± SD)	-8.14 ± 5.83	1.17 ± 3.46	-12.67, -5.95	0.000*	0.7

Abbreviations

BCC: Breast Cancer Concerns, BMI: Body Mass Index, EWB: Emotional Well-Being, FACT-B: Functional Assessment in Cancer Treatment-Breast, FWB: Functional Well-Being, HCC: Hair Cortisol Concentration, HLPCQ: Healthy Lifestyle and Personal Control Questionnaire, PSS: Perceived Stress Scale, PSQI: Pittsburgh Sleep Quality Index, PWB: Physical Well-Being, SD: Standard Deviation, SWB: Social Well-Being.

[1]Non parametric Mann-Whitney U tests for categorical by numerical comparisons;

†Positive difference on these scales indicate improvement

*Level of significance $p < 0.05$

Effect size is calculated as $rho=Z/N^{0.5}$

Reliability and validity of the instrument Newly Diagnosed Breast Cancer Stress Scale in Greek population

1. Background

Regardless of the improvements in Medicine, breast cancer remains the first most frequent diagnosis in women, with estimated new cases in Europe up to 523,000for 2018[1]. Breast cancer patients face an accumulation of stressors initiating from the diagnosis itself, the surgical procedure, the following anti-cancer treatments plus the hostile side effects of treatments[2].High levels of distress are prominent right after diagnosis. In the study of Henselmans et al. 48% of newly diagnosed breast cancer patients expressed high levels of distress that declined as a few months passed. However, in the same study 15% of those highly stressed ones, continued to report high levels of stress during the first year of the diagnosis[3].[3] In such cases, the long-lasting cancer-related discomfort can lead to poor psychosocial and quality of life outcomes[4,5] as well as debility of adherence to their treatment programs[6]. Several studies pointed out the under-detection of distress in clinical practice[7,8,9,10].For this reason, National Comprehensive Cancer Network released guidelines for managing psychological distress. What is more, surveys in American oncologists showed that only one third (32,3%) were aware of these guidelines[11,12].Health-workers and oncology specialists ought to detect such issues, as part of their medical routine[13].

For the detection of distress in breast cancer patients, proper tools should be implemented in daily practice. Such instruments should be tested for validation and reliability in the specific population. Such instruments are Perceived Stress Scale and Hospital Anxiety and Depression Scale that have shown high psychometric properties in general population. However, these instruments cover general distress perceptions and their items do not specialize in breast cancer patients.

Newly Diagnosed Breast Cancer Stress Scale (NDBCSS) is a novel tool developed by Lee Tso-Ying et al., based on qualitative interviews of women newly diagnosed with breast cancer. Aim of the authors is to aid patients and clinical health-workers recognize in an early stage, the psychosocial, behavioral and cognitive dimensions of a breast cancer patient, as well as, to assist in the development of a “custom-made”and holistic health plan for the patients[14].

The purpose of this study is the validation of NDBCSS in the Greek population.

Finally, in order to test for validity of NDBCSS, we will also correlate this instrument with questionnaire: Perceived Stress Scale (PSS-14) and Hospital Anxiety and Depression Scale (HADS). All these questionnaires will be used as a criterion-related validity testing as in the original paper.

2.Method

The study took place in a general Oncology public hospital in Athens, between February to July 2018.Before the beginning of the study protocol and the recruitment of the participants, ethical approval was obtained from the Scientific and Ethics committee of the hospital (protocol n.12590/23-11-2017). Before completion of the questionnaires, patients were fully informed about the purposes of the study; the researchers assured about the anonymity, the volunteer participation, the processing of personal data and received signed informed consent. Inclusion criteria were the ability to read and write in Greek, females over the age of 20, recently diagnosed with primary malignancy of the breast and scheduled for breast cancer surgery. We administered the questionnaires at the time of their entrance at the hospital for their scheduled surgery (±2 days prior to surgery). The number of the participants was calculated by the number of items of the examining questionnaire times five[15]. Finally, 100 participants completed the questionnaires.

2.1 The Newly Diagnosed Breast Cancer Stress Scale (NDBCSS)

NDBCSS was created to capture stress perceptions related to a recent diagnosis of breast cancer. The original scale is sub-divided in four components (Heavy Psychological Load, Uncontrollable Perceptions, Unpredictable, Facing Challenges) and consists of 17 phrases that are scored in a Likert scale where 0=disagree, 1=more or less agree, 2=mostly agree, 3 totally agree[14].To our knowledge the NDBCSS has not been validated to any other language. Permission was obtained by the authors

2.2 Other measurements

Sociodemographic variables included

Age, domestic status (city/ province), marital status (married / single / widowed / divorced) , presence of children(yes/no), education (primary school / secondary school / high school / higher education) , employment (employed / retired / household / unemployed) , satisfaction from family income (not at all / poor / moderate / well / very

well), faith in God (yes/no), self-awareness of health(not at all / poor / moderate / well / very well), smoking (yes / no), days before operation, family history of breast cancer (yes/no/unknown) . Information regarding the stage of cancer and the type of surgery was retrieved from patients' medical records.

Perceived Stress Scale (PSS 14)

The PSS consists of 14 items that measure to what extend several life conditions are considered stressful by an individual over the previous month. Each item is rated on a 5-degreeLikertscale, where 0=never, 1= almost never, 2=sometimes, 3=fairly often, 4=very often.[15] There are seven positive and seven negative items and the total score results from reversing the scores of positive items and then summing all scores (min .total score=0, max .total score=56). As high scores, as higher the perceived stress[16]. This scale has been used in Greek population reporting good psychometric properties. In this study, the Greek translation was used after permission given by the authors[17].

Hospital Anxiety and Depression Scale (HADS)

The 14 questions of HADS evaluate psychological distress over the past week. The questionnaire is divided in two subscales with seven questions assessing anxiety (HADS-A) and seven questions, assessing depressive symptoms (HADS-D)[18]. Scoring of the instrument ranges from 0 to 3. For calculation of the total score, two questions are reversed and then summation of the scores. This questionnaire has been used in Greek population and reported good psychometric properties. In this study, we administered the Greek version, after permission by the authors[19].

Translation: Translation of NDBCSS was carried out using forward/backward translation method by two experienced bilingual translators. The Greek version was pre-tested on a small sample (five individuals who were survivors of breast cancer) in order to detect any obscurity in the content of the scale and to determine the final translation.

3. Statistical Analyses

Descriptive analyses were used to calculate the means, standard deviations (SD), minimums, maximums and absolute and relative frequencies (%). Principal component analysis (PCA) was used to identify the factors from NDBCSS. Bartlett's test was used to determine whether the correlation between items was adequate; however, a determinant value was calculated to assess unwanted over-correlation of items (determinant should be close to zero). The Kaiser-Meyer-Olkin (KMO) statistic was used to determine sample adequacy. For identifying appropriate number of derived factors we used the scree-plot

(look for inflexion points) and Kaiser's criterion of eigenvalues greater than 1. Loadings of each item on derived factors were maximized by orthogonal varimax rotation. Items with loadings over 0,3 were examined as candidate components of corresponding factor. Cronbach's *α* values were calculated and assessed for meaningful associations with other measurements of the study. For group comparison, we used Student's t-test, and for scale variables, we used Pearson's rho correlation coefficient. The level of significance p was 0,05. Statistical analyses were performed using the SPSS for WINDOWS (version 25.0.0) statistical software (SPSS Inc., Chicago, IL).

4. Results

Table 1 presents the main characteristics of our sample. The analysis was performed in 100 participants with Mean Age X=58.3 (SD=12.3) with 67% being residents of Athens while 33% lived in the provinces of Greece. As for their family status 54% were married, 24% were divorced, 20% were widowed and 2% were single. As to their profession 33% were employed, 27% retired, 27% housekeepers and 12% unemployed. In the question regarding satisfaction over family monthly income, 38% answered moderate satisfaction, 36% not at all, 22% little, 3% very satisfied and 1% very much satisfied.As for the presences of children84% had children while 16% had no children. Regarding belief in God, 97 % believed in God, 3% did not believe in God and 2 did not reply. As to smoking habit 51% were non-smokers, 21% ex-smokers and 28% were smokers.

As for the medical history, 63% had no family history of breast cancer, 30% had family history of breast cancer and 7% were not aware of their family history. As to the degree of self-awareness of health, 39% were very self-aware, 34% had moderate self-awareness, 20% were very much self-aware, 5% had little self-awareness and 2% had no self-awareness. As for the staging of cancer, 37% were diagnosed with stage I, 24% were stage 0, 13% were stage IIA, 12% were stage IIB, 10% were stage IIIA and 4% were stage IIIB. As for the type of surgery 71% had mastectomy and 29% had lumpectomy.

In addition, ***Figure 1.*** presents the Scree-plot of factors' Eigenvalue concerning the NDBCSS. **Table 2** demonstrates the results of Principal Component Analysis (PCA) of the 17 items of NDBCSS as well as Cronbach's *α* if item deleted, according to which there is no need for item deletion, as the index does not increase in any such case.

In order to examine the validity of the scale, a principal component analysis was conducted. In accordance with the statistical analysis of NDBCS scale, based on the

correlation matrix, correlations range from 0.75 to 2.01. The KMO index (0.773>0.5) and the Bartlett's test of sphericity (0.00<0.05) revealed that our sample was sufficient so as to proceed with factor analysis. The results of the factor analysis proposed that the questionnaire's content could be divided into four main factors which explain 61.22 % of the variance of phenomenon. Factor 1 comprises of the phrases2, 3, 5, 6, 12 which is labeled as "Personal life". Factor 2 consists of the phrases7, 8, 11, 13 and can be labeled as "Procedural issues". Factor 3 consists of the phrases 14, 15, 16, 17and is named "Facing challenges". Factor 4 consists of the phrases1, 4, 9,10 which is labeled as "Psychological load". Furthermore, **Table 3** presents the subscales' basic descriptive measures (question 14, 15, 16, 17 have been reversed).

So as to examine the criterion-related validity of the questionnaire, we correlated NDBCSS with two other scales: PSS-14 and HADS. We expect a positive correlation with PSS-14 and sub-scales of HADS 14(HADS-A, HADS-D). Based on the results on **Table 4**, it appears that NDBCSS is positively correlated to PSS-14($r = +0.400$, $p < 0, 01$). There is also positive correlation with HADS-A ($r = 0.612$, $p< 0,01$) and HADS-D($r = 0.468$, $p < 0,01$).

In order to examine the convergent validity of NDBCSS, we tested the intercorrelation of the NDBCSS subscales and the NDBCSS total score. In **Table 5** it is shown that all subscales have positive correlation among them as well as with the NDBCSS total score. ($r=0. 274–0.896$, $p< 0.05$)

Reliability of NDBCSS was examined by the Cronbach's Alpha (α) index. This analysis revealed acceptable reliability of the instrument ($a=0.777$). Cronbach's $\alpha$for subscales of NDBCSS are explained: "Personallife" was 0.659, "Procedural issues" was 0.654, "Facing challenges" was 0.714 and "Psychological load" was 0.713 (shown on **Table 2**).

Tables 6 and **7** present meaningful associations between the NDBCSS subscales and the total scores and the study variables. Significant associations are explained:

1. Younger women (less than 36 years old) seem to worry most about "Personal life" than older ones.
2. Working patients are more concerned about "Personal life" than the rest of the employment groups.
3. Patients that had claimed having no health self-awareness, worry most about "Procedural issues" while scored higher in total score of NDBCSS.
4. Smokers bother most over the "Psychological load".
5. Patients who have undergone lumpectomy agitate most for "Personal life".
6. Patients diagnosed with stage IIIA worry most about "Procedural issues".

7. A higher PSS score was significantly correlated with higher scores in all subscales and the total score of NDBCSS.
8. A higher HADS-A and HADS-D score was significantly correlated with higher scores in all subscales and the total score of NDBCSS.
As for domestic status, marital status, presence of children, educational level, satisfaction from family income, belief in God, days before the operation and family history did not show any level of significances with any of the subscales of NDBCSS (not demonstrated). What is more , no level of significance was found between total score of NDBCSS and age groups, domestic status, smoking habit , marital status educational level, employment, satisfaction from family income, belief in God, family history of breast cancer, stage of cancer, type of surgery, days before operation.

5. Discussion

The present study presents preliminary support for the reliability and validity of the Greek version of NDBCSS. The scale seems to have adequate psychometric properties for the assessment of psychological distress in patients newly diagnosed with breast cancer in the Greek population.
Our adaptation was based on data collected from 100 patients newly diagnosed with breast cancer with the use of PCA. The factors' structure was determined by their Eigenvalues (higher than 1) and by the Scree-plot display. PCA analysis resulted in four factors that were named as follows: 1. Personal life: representing recent worries arising from the diagnosis with breast cancer including work and family, 2. Procedural issues: representing concerns about practical matters including therapy and cancer information, 3. Facing challenges: representing psychological resources to deal with cancer and 4.Psychological load: representing psycho-behavioral patterns towards breast cancer. The labels of our subscales were based upon the meaning of items reflecting psychological distress in response to personal life, procedural issues, facing challenges and the psychological load regarding breast cancer diagnosis. Four factors have been previously supported by the original validation study of Lee T.Y. et al. as well, but with different labels.[14]All factors showed satisfactory internal consistency and the scores demonstrated adequate variances in relation to the theoretical ranges. All subscales were significantly positive correlated to each other, which shows that altogether represent the stress perceptions of patients newly diagnosed with breast cancer.

Validation was based on PSS-14 and subscales of HADS that were significantly correlated with all the already mentioned subscales and the total score of the instrument.
Regarding socio-demographic and health-related information, our results indicate that patients who claimed having no health self-awareness scored higher in total score of NDBCSS.As for scoring of subscales on NDBCSS study shows that young women (under the age of 38), diagnosed with stage IIIA that had undergone lumpectomy, have higher scores in “Personal life”.
Also, those with no health self-awareness scored higher in “Procedural issues”, while smokers scored higher in the “Psychological load”.
Screening of breast cancer patients’ distress is hampered by the lack of an instrument at this specific stage of the disease. Studies have shown that anxiety is more severe prior to the operation for breast cancer removal and that patients at this period of time are more anxious about the impact of this diagnosis to their personal life and work[20]. In order to better serve the newly diagnosed breast cancer patients, health care providers should identify the level and nature (problems and concerns) of the distress. Studies showed that health-care professionals were either unaware of 80% of patients worries or reported other set of concerns than those expressed by the patients[21,22]. The patients’ responses in this study show that stress of women at this stage focuses relates to worries about their family and work as well as with the procedural issues of the disease. The multiple roles of women place stress burdens on women even before the diagnosis of a disease. As for our results regarding health self-awareness and stress, to our point of view, as less information a patient has, as stress increases. This comes in agreement with the published guidelines for cancer patients of the National Comprehensive Cancer Network (NCCN) that encourages patients to seek for information about their disease in order to manage stress by taking control of their health and disease[13]. Meanwhile, our results show the necessity for detailed explanation, starting from the pre-operative stage.

6. Conclusion

In this study with focused on the Greek NDBCSS and its 4 subscales: “Personal life”, “Procedural issues”, “Facing challenges” and “Psychological load”. Our sample consists of 100 women newly diagnosed with breast cancer that were recruited exactly at the admission to the hospital for their scheduled breast operation. Based on our study the scale seems to have construct and criterion validity. As a result health-care workers and oncologists have the tool to measure psychological distress in early stage even since the

diagnosis of the disease. There are several limitations in our study: small sample and due to lack of validation of this scale in other languages the comparisons were restricted only to the original paper. However, future studies could better be based on a larger sample. Moreover, future studies might try to use test-rest analysis for further reliability. However, the time from the initial diagnosis until the operation is so short, making this test almost unattainable. One of our strengths of the present study is that our sample was recruited from one of the biggest central oncology hospital of the country that patients gather from all around Greece. This is the first validation of NDBCSS in a foreign language that could be considered as the basis for future validations.

Conflict of interest

All authors declare that they have no conflicts of interest.

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Literature

1. Ferlay J, Colombet, M, Soerjomataram I, Dyba T, Randi G, Bettio M, Bray, F. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries and 25 major cancers in 2018. European Journal of Cancer.http://dx.doi:10.1016/j.ejca.2018.07.005

2. Brocken P, Prins JB, Dekhuijzen PN R, Heijden HFM. (2012) The faster the better?—A systematic review on distress in the diagnostic phase of suspected cancer, and the influence of rapid diagnostic pathways Psycho-Oncology. 21: 1–10. http://dx.doi: 10.1002/pon.1929

3. Henselmans I, Helgeson VS, Seltman H, de Vries J, Sanderman R, Ranchor AV. (2010) Identification and prediction of distress trajectories in the first year after a breast cancer diagnosis. *Health Psychol*.29(2):160–168.http://dx.doi: 10.1037/a0017806

4. Hulbert-Williams N, Neal R, Morrison V , Hood K, Wilkinson C. (2012) Anxiety, depression and quality of life after cancer diagnosis: what psychosocial variables best predict how patients adjust? Psycho-Oncology.21: 857–867 http://dx.doi: 10.1002/pon.1980

5. Lam WWT, Shing YT, Bonnano GA, Mancini AP, Fielding R. (2012) Distress trajectories at the first year diagnosis of breast cancer in relation to 6 year survivorship. *Psychooncology*.21:90–99 http://dx.doi: 10.1002/pon.1876

6. Barrera I, Spiegel D. (2014) Review of psychotherapeutic interventions on depression in cancer patients and their impact on disease progression. International Review of Psychiatry,26(1), 31–43. http://dx.doi:10.3109/09540261.2013.864259

7. Adler NE, Page AEK, editors. Cancer Care for the Whole Patient: Meeting Psychosocial Health Needs. Washington, DC: The National Academies Press; 2008

8. Passik SD, Dugan W, McDonald MV, Rosenfeld B, Theobald DE, Edgerton S. (1998) Oncologists' recognition of depression in their patients with cancer. J ClinOncol;16:1594–1600 https://doi.org/10.1200/JCO.1998.16.4.1594

9. Newell S, Sanson-Fisher RW, Girgis A, Bonaventura A. (1998) How well do medical oncologists' perceptions reflect their patients' reported physical and psychosocial problems? Data from a survey of five oncologists. Cancer.83:1640–1651. https://doi.org/10.1002/(SICI)1097-0142(19981015)83:8%3C1640::AID-CNCR21%3E3.0.CO;2-%23

10. Söllner W, DeVries A, Steixner E, et al. (2001) How successful are oncologists in identifying patient distress, perceived social support, and need for psychosocial counseling? Br J Cancer.84:179–185.http://dx.doi: 10.1054/ bjoc.2000.1545

11. NCCN practice guidelines for the management of psychosocial distress. Oncology (Williston Park) 1999;13:113–147.

12. Pirl, WF, Muriel A, Hwang V, Kornblith A, Greer J, Donelan K, Schapira, L. (2007) Screening for psychosocial distress: A national survey of oncologists. Journal of Supportive Oncology.;5(10), 499–504. Available online at ResearchGate.com

13. National Comprehensive Cancer Network (nccn) NCCN Clinical Practice Guidelines in Oncology: Distress Management. Fort Washington, PA: NCCN; 2010. Version 1.2011. [Available online at: http://www.nccn.org/professionals/physician_gls/pdf/distress.pdf

14. Lee TY, Chen HH, Yeh ML, Li HL, Chou KR. (2013)Measuring reliability and validity of a newly developed stress instrument: Newly Diagnosed Breast Cancer Stress Scale. J ClinNurs.1:22(17–18):2417–25. https://dx.doi.org/10.1111/jocn.12107

15. Field Andy. Discovering Statistics Using SPSS.3rd edition. London: Sage;2009,p.677-679

16. Cohen S, KamarckT, MermelsteinR..A (1983) Global Measure of Perceived Stress. Journal of Health and Social Behavior,;24:385-396http://dx.doi.org/10.2307/2136404).

17. Andreou E, Alexopoulos EC, Lionis C, Varvogli L, Gnardellis C, Chrousos GP, Darviri C. (2011) Perceived Stress Scale: Reliability and Validity Study in Greece. International Journal of Enviromental Research and Public Health.8:3287-3298. http://dx.doi.org/10.3390/ijerph8083287

18. Zigmond AS, &Snaith RP.(1983)The Hospital Anxiety and Depression Scale, Actapsychiatr.Scand;67: 361-370. https://dx.doi.org/10.1111/j.1600-0447.1983.tb09716.x

19. Michopoulos I, Douzenis A, Kalkavoura C, Christodoulou C, Michalopoulou P, Kalemi G, Lykouras L. (1983) Hospital Anxiety and Depression Scale (HADS): Validation in Greek general hospital sample, Annals of General Psychiatry. 5: 1-5.https://dx.doi.org/10.1186/1744-859X-7-4

20. Cheng SY et al. (2011) Changes in quality of life among newly diagnosed breast cancer patients in Taiwan, Journal of Clinical Nursing.21, 70-79.https://dx.doi.org/10.1111/j.1365-2702.2011.03735

21. Farrell C, Heaven C, Beaver K, Maguire P. (2005) Identifying the concerns of women undergoing chemotherapy.Patient Education and Counseling.56,72-77. https://dx.doi.org/10.1016/j.pec.2003.12.008

22. Lampic C, Sjoden PO. (2007) Patient and staff perceptions of cancer patients' psychological concerns and needs. ActaOncologica.39, 225-232.https://dx.doi.org/10.1080/028418600430923

Tables and Figures

Table.1 Sociodemographic characteristics of the study's sample(N=100)

Mean Age in years (SD)	58.3 (12.3)	**Nonsmokers N**	51
Residency in Athens (SD)	67 (0.4)	**No family history of Ca breast N**	63
Married (SD)	54 (0.8)	**Stage I N**	37
Having children (SD)	84 (0.4)	**Mastectomy N**	71
High school (SD)	35 (1.2)	**Mean PSS score (SD)**	29.83 (4.11)
Employed(SD)	33 (1.6)	**Mean HADS-A (SD)**	7.6 (4.50)
Dissatisfied with family income (SD)	36 (1)	**Mean HADS-D (SD)**	9.3 (2.61)
BelieveinGod(SD)	95 (0.2)		
Very Self-aware of health(SD)	39 (0.9)		
Mean Days before operation(SD)	2.3 (1.3)		

SD: Standard Deviation, Ca: Cancer, PSS: Perceived Stress Scale, HADS-A:Hospital Anxiety Depression

Figure 1.*Scree-plot of factors' Eigenvalue concerning the NDBCSS*

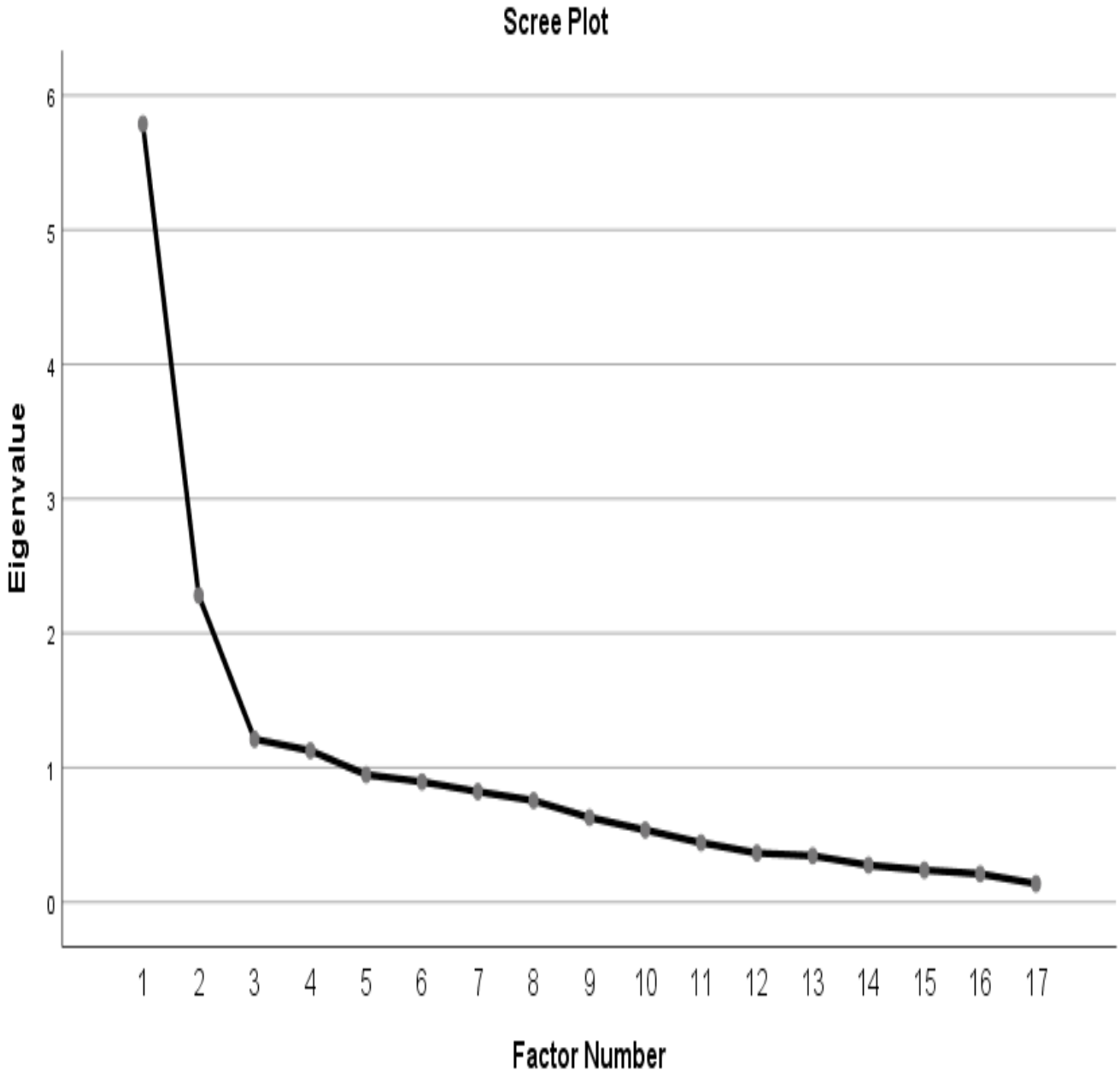

Table 2. Rotated factor loadings of the principal component analysis (PCA) for the 17-items of NDBCSS (N=100)

Item	Factor 1	Factor 2	Factor 3	Factor 4	Cronbach's Alpha if Item Deleted
1. I often cry	0.088	0.400	0.111	**0.514**	0.860
2. Illness makes me worry about my family	**0.475**	0.266	0.119	0.364	0.856
3. Loss of my breast will affect my life	**0.605**	0.269	0.049	0.214	0.857
4. I have fear, anxiety and depression	0.329	0.297	0.379	**0.431**	0.853
5. Illness makes me worry about my work	**0.759**	0.113	-0.109	0.197	0.860
6. I am worried that my arm cannot lift heavy weight and it will affect my life and work	**0.553**	0.155	-0.022	0.499	0.855
7. I am worried that my economic conditions cannot deal with the required expenses	-0,093	**0.709**	-0.081	-0.201	0.872
8. I cannot make decisions for my breast cancer treatment	**0.669**	0.337	0.289	0.035	0.852
9. I think that the road of anti-cancer is lonely, hard and there is lack of support	0.022	0.483	0.306	**0.565**	0.851
10. I am worried about the uncertainty of the progression of the illness	0.541	0.293	0.046	**0.663**	0.849
11. I am worried about the side effects caused by chemotherapy : such as physical discomfort, change of appearance, or future birth plans, etc	0.267	**0.691**	0.151	0.290	0.854
12. Loss of my breast will affect my attractiveness to my partner	**0.817**	-0.011	0.131	0.059	0.860
13. Insufficient breast cancer information scares me	0.241	**0.624**	0.031	0.372	0.855
14. I can accept the diagnosis of breast cancer	-0.061	0.040	**0.843**	-0.078	0.867
15. I am able to make proper arrangements and deal with things affected by illness	0.020	-0.022	**0.827**	0.239	0.863
16. I can accept the staging of breast cancer	0.205	-0.086	**0.714**	0.261	0.862
17. I use some adaptation methods to face cancer	-0.146	0.008	**0.730**	0.210	0.869
Eigenvalues	5.788	2.282	1.212	1.126	
% of Variance	34.045	13.421	7.128	6.626	
Cronbach's *α*	0.659	0.654	0.714	0.713	

Analysis information: Determinant = 0.00, Bartlett's test = χ^2 ($p < 0.001$), Kaiser-Myer-Olkin = 0.773

Table 3 Subscales' basic descriptive measures (question 14, 15, 16, 17 have been reversed).

Factor	Number of items	Mean	SD	Min.	Max.
Personal life	5	9,23	4,48	1	18
Procedural issues	4	4,57	3,47	0	12
Facing challenges	4	5,14	3,49	0	13
Psychological load	4	3,86	1,86	0	6

SD: Standard Deviation

Table 4.NDBCSS correlation to PSS-14, HAD-A and HADS-D

		NDBCSS total	PSS-14 score	HADS-A	HADS-D
NDBCSS total	Pearson Correlation	1	.400**	.612**	.468**
	Sig. (2-tailed)		0.000	0.000	0,000
	N	100	100	100	100

**. Correlation is significant at the 0.01 level (2-tailed).

Table 5. Convergent validity of the NDBCSS

	NDBCSS total	Personal life	Procedural issues	Facing challenges	Psychological load
NDBCSS total	1				
Personal life	0.896**	1			
Procedural issues	0.768**	0.627**	1		
Facing challenges	0.691**	0.447**	0.274**	1	
Psychological load	0.618**	0.502**	0.343**	0.434**	1

**Correlation is significant at the 0.01 level (2-tailed)

Table 6. Associations between NDBCSS subscales and other study variables

Characteristics	Categories	Mean "Personal life" (SD)	Mean "Procedural issues"(SD)	Mean "Facing challenges" (SD)	Mean "Psychological load" (SD)
Age groups	≤ 38	7.66(2.88)	11.66(2.88)	6.33(4.93)	5(1.73)
	39-48	6.25(3.33)	9.65(4.23)	5.05(3.26)	4.20(1.54)
	49-58	5.18(3.87)	8.62(4.20)	4.77(2.63)	3.74(1.95)
	≥ 59	3.38(2.90)	9.24(4.82)	5.30(3.96)	3.72(1.94)
	Statistics	t=5.153	F=0.508	t=0.246	t=0.720
	p value	0.002*	0.678	0.864	0.542
Employment	Household	3.59(2.50)	9.85(3.54)	5.62(3.40)	4.03(1.76)
	Retired	3.14(2.95)	8.46(5.30)	4.67(3.95)	3.39(2.07)
	Unemployed	5.25(2.70)	8.83(3.43)	4.08(2.87)	3(1.70)
	Employed	6.33(4.06)	9.51(4.80)	5.51(3.38)	4.42(1.65)
	Statistics	t=6.06	t=5.14	t=0.825	t=2.653
	p value	0.01*	0.674	0.483	0.053
Health self-awareness	Not at all	4(5.65)	11.50(9.19)	6.50(9.19)	4(0.00)
	Poor	4.40(4.56)	8.60(7.46)	5.20(4.65)	2.60(2.60)
	Moderate	5.52(3.71)	11.17(4.39)	5.35(3.81)	4.05(2.17)
	Well	4.43(3.34)	8.66(3.96)	5.76(3.19)	4.17(1.53)
	Very well	3.30(2.67)	6.95(3.10)	3.40(2.21)	3.20(1.60)
	Statistics	t=1.363	t=3.534	t=1.707	t=1.624
	p value	0.253	0.010*	0.155	0.175
Smoking habit	Yes	9.14(4.03)	4.17(3.61)	5.25(2.82)	4.57(1.59)
	No	10.01(4.67)	4.76(3.37)	5.15(3.90)	3.76(1.87)
	Ex-smoker	7.42(4.22)	4.61(3.66)	4.95(3.41)	3.14(1.93)
	Statistics	t=2.574	t=0.255	t=0.044	t=3.872
	p value	0.081	0.775	0.957	0.024*

Table 6.continued

Characteristics	Categories	Mean "Personal life" (SD)	Mean "Procedural issues"(SD)	Mean "Facing challenges" (SD)	Mean "Psychological load" (SD)
Stage of cancer	In situ	8.41(4.66)	4.91(2.96)	5.83(3.84)	3.66(1.68)
	I	8.78(4.75)	2.91(3.15)	4.83(3.51)	3.91(2)
	IIA	9.38(3.66)	5(3.16)	5(2.73)	3.92(1.60)
	IIB	10.41(5.16)	6.16(3.83)	3.75(3.69)	3.08(2.19)
	IIIA	11.20(3.58)	6.70(3.68)	6.40(3.62)	5(1.33)
	IIIB	9.25(2.87)	6.25(3.68)	5.25(2.21)	3.75(2.06)
	Statistics	t=0.781	t=3.618	t=0.881	t=1.244
	p value	0.566	0.0005*	0.497	0.295
Type of surgery	mastectomy	3.44(2.59)	9.59(4.30)	5.17(3.84)	3.72(1.81)
	lumpectomy	5.02(3.690	8.34(4.85)	5.12(3.37)	3.72(1.81)
	Statistics	t=0.22	t=-1.266	t=0.279	t=-0.469
	p value	0.039*	0.235	0.953	0.638
PSS score	Pearson'srho	0.373	0.389	0.301	0.155
	p value	0.000*	0.000*	0.002*	0.024*
HADS-A	Pearson'srho	0.627	0.447	0.502	0.484
	p value	0.000	0.000	0.000	0.000
HADS-D	Pearson'srho	0.310	0.384	0.459	0.339
	p value	0.002*	0.000*	0.000*	0.001*

Level of significance <0.05

Table 7. Associations between NDBCSS total score and other study measurements

Characteristics	Categories	Mean NDBCSS total score	Characteristics	Categories	Mean NDBCSS total score (SD)
			Health		
PSS score	Pearson'srho	0.400	**self-awareness**	Not at all	27(22.62)
	p value	0.000*		Poor	21.40(17.79)
				Moderate	26.05(10.50)
HADS-A score	Pearson'srho	0.612		Well	22.35(9.03)
	p value	0.000*		Verywell	16.20(6.33)
				Statistics	t=3.251
HADS-D score	Pearson'srho	0.468		p value	0.015*
	p value	0.000*			

Level of significance <0.05

Contribution of authors

1) Study concept: Charalampopoulou Maria
2) Study design: Charalampopoulou Maria, Darviri Christina
3) Data analysis:Charalampopoulou Maria
4) Data interpretation: Charalampopoulou Maria, Darviri Christina
5) Manuscript preparation: Charalampopoulou Maria
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