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Symptom cluster of emotional distress, fatigue and cognitive difficulties among young and older breast cancer survivors: The mediating role of subjective stress

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ABSTRACT

Objectives: To examine the nature of the symptom cluster of emotional distress, fatigue, and cognitive difficulties in young and older breast cancer survivors (BCS); To assess the mediating role of subjective stress and coping strategies (emotional control and meaning-focused coping) in the association between age and symptom cluster. **Materials and Methods:** Participants were 170 BCS, stages I-III, 1–12 months post-chemotherapy, filled-out the Fatigue, Emotional Control, Meaning—focused Coping, Emotional Distress and the Cognitive Difficulties Questionnaires. Statistical analyses included tests for difference between-groups Pearson correlations and Structural Equation Modeling for the assessment of the study model.

Results: Older BCS (aged 60–82) reported lower levels of emotional distress ($M = 0.87$, $SD = 0.87$), fatigue ($M = 3.85$, $SD = 2.38$), and cognitive difficulties ($M = 1.17$, $SD = 1.07$) compared to the younger BCS (aged 24–59) (emotional distress $M = 1.17$, $SD = 0.85$, fatigue $M = 5.02$, $SD = 2.32$, and cognitive difficulties $M = 1.66$, $SD = 1.23$, $p < .01$ – $.05$). The older survivors reported lower levels of subjective stress and used more emotional control strategies compared to the younger BCS. The empirical model had good fit indices ($\chi^2 = 27.60$, $p = 0.20$, $\chi^2/df = 1.26$; CFI = 0.98; TLI = 0.98; NFI = 0.95; RMSEA = 0.04 (90% CI = 0.00, 10) and showed that subjective stress, but not coping strategies, mediated the effect of age on symptom cluster severity.

Conclusions: Lower levels of subjective stress, but not coping strategies, mediated the association of age with the symptom cluster of emotional distress, fatigue and cognitive difficulties. Further research is needed to explore differences in subjective stress by age.

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1. Introduction

Until recent years, breast cancer survivors (BCS), aged 60 and older, have been excluded from the majority of clinical and psycho-social studies [1,2]. Therefore, knowledge about the effects of the disease and the treatments on the physical, mental and cognitive state of older women, compared to younger women, is limited [2].

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Symptoms of emotional distress (depression and anxiety), fatigue, and cognitive difficulties persist over time in BCS after chemotherapy, impairing survivors' quality of life [3–7]. In addition, a substantial percent of survivors also reported fatigue and distress levels far beyond the clinically significant cutoff scores (64% for fatigue and 25% for depression) [8]. Reports of cognitive difficulties over time vary among studies - from no difficulties at all to a prevalence of difficulties among 36% of the BCS samples [9].

These symptoms, of emotional distress, fatigue and cognitive difficulties, were previously suggested to be referred to as a symptom cluster [10,11] defined as a group of co-occurring symptoms that interact with each other, and the symptoms often share a common origin [12,13]. In the case of the triad of emotional distress, fatigue and cognitive difficulties in BCS, these symptoms may originate from the chemotherapy treatment or the chronic

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inflammatory state often observed post-chemotherapy [13]. A symptom cluster may have a greater adverse cumulative impact on the individual than each of the individual symptoms [12]; therefore, symptom clusters need to be studied. However, differences in symptom cluster patterns in older and younger BCS have not been previously studied.

Most of the studies that compared levels of each of the individual symptoms between younger and older cancer survivors reported higher levels of emotional distress and fatigue among younger compared to older BCS [14]. Several studies have also reported more cognitive difficulties among young compared to older BCS [15], while still other studies reported either no differences or more cognitive difficulties among the older BCS [15,16]. However, in many of the studies that reported lower levels of difficulties, especially in regard to fatigue and distress among older survivors, a substantial percent of the older survivors had not received chemotherapy [17]. Nevertheless, a few studies that compared levels of emotional symptoms in older and younger BCS who received chemotherapy reported higher levels of symptoms of depression and anxiety among the younger cancer survivors [8,18–20]. Other studies reported non-linear relations between age and emotional distress among patients and cancer survivors [21–23].

According to the cognitive model of coping with stress, emotional reactions to a stressor (e.g., cancer diagnosis and treatments) are, to a large extent, affected by the subjective perceptions of the stressful situation (i.e., stress appraisals) and the coping strategies employed to cope with this stressor [24]. Coping strategies represent the cognitive and behavioral efforts that a person mobilizes in order to deal with a stressful situation [25]. Most of the prior studies that assessed coping strategies used the classical categorization method, dividing coping into two categories: problem-focused and emotion-focused coping strategies, suggested by Lazarus and Folkman [25]. Since previous studies failed to find consistent differences between younger and older individuals regarding the usage patterns of these coping strategies [26], these studies cannot adequately explain the differences in the levels of symptoms in older compared to younger adults. In contrast, more consistent differences related to age were reported regarding the coping strategies of emotion control and meaning-focused coping.

Emotion control is conceptualized as the individual's conscious efforts to influence which emotions they experience, when they experience them, and how these emotions are experienced or expressed [27]. Studies indicate that older adults use more emotional control strategies than younger individuals [28–30] which, in turn, are associated with enhanced well-being among older adults [31,32]. However, contrasting results were found regarding the relation between emotional control and distress in patients with cancer or survivors [33,34]. Meaning-focused coping strategy is defined as cognitive efforts made to manage the meaning of the given situation [35]. In this process, the individual draws on values, beliefs, and goals to modify the meaning of a stressful situation. Meaning-focused coping has been linked to various aspects of positive adjustment in many different situations [36,37] and was proposed to be especially useful in cases of chronic stress [37] or uncontrollable stressors such as cancer [38].

The present study examined the expression of symptom cluster in relation to coping with stress. Specifically, the first aim of this study was to examine the differences between young and older BCS in relation to levels of the distress-fatigue-cognitive difficulties symptom cluster. The second aim was to examine the role of subjective stress and coping strategies as mediators of the associations between age and the symptom cluster. In contrast to many previous studies involving older women, included BCS who both received and did not receive chemotherapy in the same sample—our study sample consisted of younger and older women, all one to twelve months post adjuvant chemotherapy.

2. Materials and Methods

2.1. Participants and Procedure

Prior to commencing the study, authorization was obtained from the Institutional Review Board at each participating medical center, from Rambam Health Care Campus, No. 0354-10-RMB; from Assaf Harofeh Medical Center, No. 119/13; and from Meir Medical Center, No. MMC-0230-13.

Participants were 120 BCS aged 20–59, and 50 BCS aged 60–82. The current study is part of a larger study assessing associations between post treatment symptoms and levels of cytokines within a longitudinal design, which is still running. The present sample consists of all participants who completed questionnaires at baseline. This was a multi-center study; participants were recruited at three main oncology institutes in northern and central Israel, with no statistically significant differences in demographic or medical characteristics of participants according to the treatment center. Participants were consecutively sampled, i.e., all participants answering the inclusion criteria were asked to participate. Inclusion criteria were a diagnosis of breast cancer stages I–III and one–twelve months post-chemotherapy with no current evidence of disease and without a previous diagnosis of cancer. Exclusion criteria were: dementia or a mental illness (according to medical files) and not having sufficient Hebrew or Arabic. Patients with co-morbidities that could directly affect levels of fatigue, such as autoimmune diseases, fibromyalgia, The human immunodeficiency virus (HIV), Hepatitis C, heart failure, cardiovascular diseases, or anemia were also excluded from the study.

The sample size calculation was based on Cohen [39], using GPower 3.1 software, according to which the minimum group size for group comparison tests, assuming a medium effect size of 0.3, at power 0.80 and $\alpha = 0.05$, is 50 participants per group. Based on Satorra and Saris [40], assuming a medium effect size (0.3) at power 0.80, $\alpha = 0.5$, and 22 degrees of freedom, the minimum sample size required is 80.

Questionnaires were administered in Hebrew and Arabic (following back translation). The overall response rate was 84.7%. Details of the disease and treatments were collected from the patients' files: cancer stage, surgery, radiotherapy, time since diagnosis, time since end of chemotherapy and chronic diseases. Biological therapy (targeted therapy) is an intravenous administration of Trastuzumab (Herceptin), a recombinant monoclonal antibody that inhibits the proliferation of tumor cells that overexpress HER2.

2.2. Questionnaires

Participants filled-out their personal and medical details, including age, marital status, number of children, employment status, income, and stage of cancer. ER/PR status, type of chemotherapy, endocrine therapy, and biologic therapy were not available in the database.

The Fatigue Symptom Inventory (FSI) [41] is a fourteen-item questionnaire that measures the severity of, Cancer Related Fatigue (CRF) symptoms and its perceived interference, rated on an eleven-point scale. Severity assessment consists of four items (e.g., "Please rate your level of fatigue on average this past week"). Perceived interference of fatigue during the past week consists of seven items. Mean scores of the severity and interference of CRF subscales were calculated as suggested before [41]; higher scores indicated a higher level of CRF. The internal reliability was $\alpha = 0.96$. The correlation between severity items and perceived items was $r = 0.86$, $p = 0.001$.

The Subjective Stress Scale is a one-item measure used to assess how the disease affects patients' stress level. Participants were asked to describe how often they felt stressed in the past week, using a ten-point Likert scale that ranged from zero="not at all" to ten = "extremely".

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