ORIGINAL ARTICLE

UDC: 618.19-006
DOI: https://doi.org/10.2298/VSP190501024N

What contributes the most to the breast cancer patients' quality of life during therapy – clinical factors, functional and affective state, or social support?

Šta najviše doprinosi kvalitetu života pacijentkinja tokom terapije karcinoma dojke – klinički faktori, funkcionalni i emocionalni status ili socijalna podrška?

Ivana Novakov*, Svetlana Popović-Petrović*†, Sonja Ilinčić-Zlatar*,
Milanka Tatić*†, Mirjana Ševo‡

***Oncology Institute of Vojvodina, Sremska Kamenica, Serbia; †University of Novi Sad, Faculty of Medicine, Novi Sad, Serbia; ‡Institute for Pulmonary Diseases of Vojvodina, Sremska Kamenica, Serbia**

Abstract

Background/Aim. As significant advances in cancer treatment have occurred over the past decades, the crucial questions in oncology nowadays are not related only to the treatment of the illness but also to the quality of life (QOL) of patients. The aim of our study was to explore which set of determinants (clinical, functional, affective, or social) has the greatest impact on explaining QOL in women who live with the diagnosis of breast cancer. **Methods.** The research was conducted on 64 women (with a mean age of 58.36 ± 11.30) while undergoing radiation therapy at the Oncology Institute of Vojvodina, Serbia. Quality of Life Instrument – Breast Cancer Patient Version (QOL-BC) questionnaire was used for evaluation of physical, psychological, social, spiritual, and general well-being, the Upper Extremity Functional Index (UEFI) was applied for the assessment of the upper extremity function, the Depression, Anxiety, and Stress Scale-21 Items (DASS-21) was used for measuring symptoms of depression, anxiety, and stress, the Medical Outcomes Survey, Social Support Survey (MOS-SSS) served for evaluation of social support; demographic and clinical data of patients were also collected. **Results.** Analysis of Variance (ANOVA) with repeated measures [$F(2.03, 127.80) = 20.24$, $p < 0.001$] showed that in our sample, physical QOL was significantly better from all other domains, while social QOL was significantly lower from both physical and psychological aspect. A hierarchical regression analysis [$F(8, 55) = 7.16$, $p < 0.001$, $R^2 = 0.51$] showed that patients who received adjuvant chemotherapy and experienced high levels of stress and poor social support usually had diminished general QOL. Introduction of affective-related variables [$\Delta R^2 = 0.16$, $p(\Delta F) < 0.01$] and social support [$\Delta R^2 = 0.05$, $p(\Delta F) < 0.05$] led to a significant increase in proportion of explained variance over and above the clinical and functional variables. **Conclusion.** Our results indicate that psychological and social resources are more important in predicting QOL compared to clinical and functional factors. At the same time, the social, psychological, and spiritual well-being of patients is significantly worse compared to the physical QOL, meaning that there is still much left to be done regarding the progress from a purely somatic to a holistic approach in the treatment of breast cancer.

Key words:
breast neoplasms; drug therapy; neoadjuvant therapy; psychology; social support; quality of life; radiotherapy; surveys and questionnaires

Apstrakt

Uvod/Cilj. Pošto je tokom decenija došlo do značajnog napretka u lečenju raka, ključna pitanja u onkologiji danas se ne odnose samo na lečenje bolesti, već i na kvalitet života pacijentkinja. Zbog toga je cilj ovog istraživanja bio da se ispita koji skup determinanti (klinički faktori, funkcionalno stanje, afektivni status ili socijalna podrška) u najvećoj meri doprinosi predviđanju kvaliteta života kod žena koje žive sa dijagnozom raka dojke. **Metode.** U istraživanju su učestvovale 64 žene (prosečne životne dobi od 58,36 ± 11,30 godine) tokom zračne terapije na Institutu za onkologiju Vojvodine. Upitnik *Quality of Life Instrument – Breast Cancer Patient Version* (QOL-BC) primenjen je za procenu fizičkog, psihičkog, socijalnog, duhovnog i opšteg kvaliteta života, *Upper Extremity Functional Index* (UEFI) je upotrebljen za procenu funkcije gornjih ekstremiteta, *Depression, Anxiety, and Stress Scale-21 Items* (DASS-21) korišćen je za procenu simptoma depresije, anksioznosti i stresa, *Medical Outcomes Survey, Social Support Survey* (MOS-SSS) služio je za procenu

---

Correspondence to: Ivana Novakov, Oncology Institute of Vojvodina, Put doktora Goldmana 4, 21 204 Sremska Kamenica, Serbia. E-mail: novakov.ivana@onk.ns.ac.rs

socijalne podrške, a prikupljeni su i demografski i klinički podaci pacijentkinja. **Rezultati.** Primenom testa analize varijanse (ANOVA) sa ponovljenim merenjima [F(2,03, 127,80) = 20,24, $p < 0,001$] nađeno je da je fizički kvalitet života pacijentkinja bio značajno bolji u odnosu na ostale domene, dok je socijalni kvalitet života bio značajno lošiji u odnosu na fizički i psihološki aspekt. Hijerarhijska regresiona analiza [F(8, 55) = 7,16, $p < 0.001$, $R^2 = 0,5$] pokazala je da su ispitanice koje su primile adjuvantnu hemioterapiju, i iskusile povišen nivo distresa i lošiju socijalnu podršku, imale smanjen generalni kvalitet života. Uvođenje varijabli povezanih sa afektivnim stanjem [$\Delta R^2 = 0.16$, $p(\Delta F) < 0.01$] i socijalnom podrškom [$\Delta R^2 = 0.05$, $p(\Delta F) < 0.05$] dovelo je do značajnog porasta u proporciji objašnjene varijanse, povrh kliničkih i funkcionalnih faktora. **Zaključak.** Naši rezultati ukazuju na to da psihološki i socijalni resursi imaju važniju ulogu u predviđanju kvaliteta života u poređenju sa kliničkim i funkcionalnim faktorima. Istovremeno, socijalno, psihološko i duhovno blagostanje pacijentkinja bilo je značajno lošije u poređenju sa fizičkim kvalitetom života, što znači da još mnogo toga treba da bude preduzeto u cilju napretka od dominantno somatskog, ka holističkom pristupu u lečenju karcinoma dojke.

Ključne reči:
dojka, neoplazme; lečenje lekovima; lečenje, neoadjuvantno; psihologija; socijalna podrška; kvalitet života; radioterapija; ankete i upitnici.

Introduction

Breast cancer (BC) is considered the most common type of cancer in women both worldwide [1, 2] and in Serbia [3]. As significant advances in cancer treatment have occurred over the past decades, and the survival rate is getting increasingly extended, crucial questions in oncology nowadays are not related only to the treatment and control of the illness but also to the emotional and psychological well-being and the quality of life (QOL) of patients. Knowing that breast cancer treatment is a very demanding and stressful process, often accompanied by uncertainty, assessing QOL is very important since patients are faced with a wide range of unpleasant experiences, which presumably tend to diminish different aspects of their functioning, both in the short term and in the long run.

Previous research, which focused on QOL as an important outcome measure, showed that clinical and demographic variables such as stage of the disease, adjuvant chemotherapy, marital status, and educational level might be important determinants of QOL [4]. Some authors found that single women and those with lower levels of education had poorer scores on QOL measures [5]. Younger age has also been found to predict lower QOL in breast cancer patients [5–7]. Furthermore, receiving chemotherapy [8], additional comorbid conditions [9, 10], and arm problems due to axilla surgery [11–13] are likely to affect the deterioration of QOL in patients treated for breast cancer. Axillary lymph node dissection, which results in several upper-limb symptoms and certain restrictions of daily activities, may be related to compromised body image, impaired functioning, and decreased QOL [14, 15]. One study that included a wide range of demographic and clinical factors revealed that arm dysfunction, comorbidity, and age were some of the strongest predictors of QOL among breast cancer patients [13]. The same study indicated that marital, educational, and employment status were significantly related to QOL, but to a lesser extent compared to previously mentioned variables [13].

However, findings regarding socio-demographic and clinical data are not always consistent. While some authors, for example, have stated that application of chemotherapy or radiotherapy significantly affects patients' QOL [16, 17], others have found no alterations in QOL regarding tumor severity and treatment type [18, 19]. In addition, some authors have shown that socio-demographic and treatment variables were only to a moderate extent related to QOL, while psycho-social variables showed a more convincing and consistent relationship with QOL measures [20]. Thus, age, chemotherapy, and time passed from the diagnosis were not related to any of the QOL outcomes, whilst psycho-social factors such as partner relationships, sexual functioning, body image, coping strategies, etc. showed a significant connection to QOL and well-being [20].

Given that the experience of breast cancer and its treatment is perceived as intensively stressful, facing the diagnosis can lead to psychological reactions such as denial, fear, uneasiness, anger, sadness, despair, and hopelessness. Patients with breast cancer diagnosis are at high risk of developing psychiatric comorbidities, especially depression and anxiety. In one recent study, it has been shown that, from 152 breast cancer patients, 38.2% could be classified as depressed, while 32.2% were found to be anxious [21]. Other authors have found that almost 50% of women with breast cancer manifested depression, anxiety, or both, one year following the diagnosis; 25% of them reported symptoms two, three, and four years after the diagnosis, and finally, 15% of women had symptoms five years following the diagnosis [18]. Furthermore, it has been found that 41% of newly diagnosed breast cancer patients experienced high levels of distress, while 11% had a major depressive disorder [22]. These findings clearly suggest that the affective state of breast cancer patients is at apparent risk and should be taken into account as an important factor in the better understanding of QOL determinants.

In addition, it is known that adequate social support is of outstanding importance when it comes to dealing with cancer diagnosis and demanding oncological treatment. Some studies have found that social support (which involves tangible support, emotional informational support, affectionate support, and positive social interaction) was related to better QOL and acted as a moderator between symptoms of depression and QOL [23]. It has also been shown that a decrease in social support quantity and quality is associated with increased symptoms of depression, stress, and negative effect in breast cancer patients [24]. According to the previous findings, social support quality is a more important predictor of well-being than social support quantity [25]. What's more, the quality and quantity of social support among women with breast cancer were shown to be related to posttraumatic growth, which is considered to be one of the positive well-being outcomes [26, 27].

Although there is a large body of literature regarding breast cancer patients' QOL, it remains unclear which group of factors has the strongest impact on different QOL domains, especially when it comes to women who live with the diagnosis of breast cancer in Serbia. Therefore, the main aim of this research was to offer a more comprehensive understanding of the contribution that different clusters of factors may have on diverse aspects of QOL in breast cancer patients. More specifically, the aim of our study was to explore which set of determinants (such as clinical factors, functional condition, affective state, and social support) had the greatest impact in explaining specific domains of QOL (physical, psychological, social, and spiritual) in patients. As some authors emphasize [13], a comprehensive approach to understanding the QOL in breast cancer patients could be useful to all members of the medical team by highlighting which problems should be prioritized and addressed in order to improve different aspects of life satisfaction in patients.

Methods

Study design and procedure

This cross-sectional research was conducted with the approval of the Ethics Committee of the Oncology Institute of Vojvodina, Serbia. Based on the principles of voluntary participation, the data were collected from patients at the beginning of their entry or stay at the Clinic for Radiotherapy within the Oncology Institute of Vojvodina. All participants were informed about the main goals of the research. Before filling in the questionnaires, all participants signed informed consent. The assessment period lasted approximately 45 min to 1 h, which also included a short break for refreshment. A research assistant was available all the time while participants were filling in the questionnaires, helping them in the case of need and reminding them to check if they had answered all the questions, due to which the problem of missing data has been overcome.

Sample

The research was conducted on 64 women, from 33 to 79 years [mean (M) age = 58.36, standard deviation (SD) = 11.30 years], while undergoing radiation therapy at the Oncology Institute of Vojvodina. Patients took part in the research within the period of 2 to 13 months following the breast cancer surgery (M = 5.39, SD = 2.62 months). Criteria for inclusion in the study were that participants had never been diagnosed with breast cancer before (or any other malignant disease) and that the presence of metastatic changes was not detected at the time of psychological assessment. In terms of educational level, 26.6% of participants completed elementary school, 54.7% completed secondary school, 7.8% had a college degree, while 11% had a university degree. Women mainly reported that they live in a city (64.1%). Besides, 26.6% of participants were employed, 25% unemployed, and 48.4% were retired. Considering marital status, 71.9% of participants had a partner, while 28.1% were single, divorced, or widowed. Finally, 85.9% of women had children. The data about clinical variables assessed in our research are presented in Table 1.

Table 1

Clinical variables in the study population

Clinical variables	Patients, n (%)	
	yes	no
Neoadjuvant chemotherapy	12 (18.8)	52 (81.3)
Adjuvant chemotherapy	32 (50)	32 (50)
Nonmalignant comorbid conditions	40 (62.5)	24 (37.5)

Instruments

A demographic and clinical data questionnaire was designed in order to collect data about the age of the participants, their educational level, working, marital, and birth status, as well as the place of residence. Information about clinical data, such as the number of months that passed after the surgical treatment, receiving neoadjuvant and/or adjuvant chemotherapy, and finally, the presence of any nonmalignant comorbid conditions, was also assessed.

Quality of Life Instrument – Breast Cancer Patient Version (QOL-BC) [28] scale is based on earlier versions of the QOL instrument, constructed by researchers at the City of Hope National Medical Center. The scale consists of 46 items representing four domains – physical, psychological, social, and spiritual well-being. Items are presented on a 10-point scale (from 0 = worst to 10 = best outcome). Participants are instructed to indicate the degree to which they agree or disagree with every statement. The physical aspect of QOL includes information about nausea, constipation, appetite, menstrual changes/fertility, sleep, aches/pain, and fatigue. Psychological well-being includes a sense of usefulness, happiness/satisfaction, control/coping, anxiety/depression, concentration/memory, overall perception of QOL, changes in appearance and self-concept, distress of diagnosis and treatment, and finally, fear of recurrence/tests. Social well-being refers to family distress, personal relationships, support, employment, home activities, sense of isolation, financial burden, and sexuality. The spiritual aspect contains a sense of hope and life purpose, (positive) spiritual change, religious/spiritual activity, and experience of uncertainty [29–33].

The Upper Extremity Functional Index (UEFI) [34] is a 20-item self-reporting scale. The instrument is used as a measure of upper extremity dysfunction. Items refer to everyday activities such as cleaning, dressing, driving, lifting a bag, preparing food, etc. Participants should report if they have any difficulties related to listed activities. The answers are rated on a five-point Likert scale (from 0 = extreme difficulty to 4 = no difficulty performing the task). The maximum possible score is 80. The higher the score, the better the upper extremity function. The instrument has shown good reliability [34].

Depression, Anxiety, and Stress Scale - 21 items (DASS-21) [35] is an instrument that contains three self-report scales which measure the emotional states of depression, anxiety, and stress. Each of the three scales consists of 7 items presented on a 4-point Likert scale, ranging from “do not apply to me at all“ to “applied to me very much or most of the time“. The depression scale covers dysphoria, hopelessness, depreciation of life, self-devaluation, lack of interest, anhedonia, and apathy. The anxiety scale includes information about autonomic nervous system arousal, tremor, situational anxiety, and subjective experience of anxious affect. The stress scale assesses difficulty relaxing, nervous arousal, and being easily agitated, irritable, and impatient. Three separate scores can be calculated by summing the items which belong to the same subscale [35].

Serbian translation of The Medical Outcomes Study Social Support Survey - Serbian translation (MOS-SSS) [36] is prepared according to the original version of MOS-SSS [37]. This scale was developed within The Medical Outcomes Study [38], whose goal was to explore the QOL in patients suffering from chronic diseases such as hypertension and diabetes. The scale consists of 19 items whose measure perceived social support. Items are classified into 4 sub-scales: 1) *emotional support* (the availability of a person who understands us and our problems, who is ready to listen, and with whom we can share our worries) / *informative support* (availability of a person whom we can ask for advice or information), 2) *instrumental or practical support* (availability of a person who can help us when we are sick), 3) *affective support* (availability of a person who shows us love and attention), and 4) *positive social interactions* (availability of a person with whom we can enjoy and relax) [36]. Participants are asked how often every type of support has been available to them when needed. Items are presented on a five-point Likert scale (from 1 = never to 5 = always). In addition, the scale contains one question which refers to structural social support. Here, participants should write how many close friends and relatives they have with whom they can feel comfortable. To this question, participants should respond by writing a number [36].

Statistical analysis

For statistical data processing, the IBM SPSS Statistics 21.0 software was used. After considering the descriptive data and correlation analysis for all variables in our research, we examined whether there were any statistically significant differences in the representation of four domains of QOL in our sample. Following the equalization of means according to the number of items by every subscale, and after checking for normality of distributions (we considered as normal data the measuring according to George and Mallery [39]), the One-way ANOVA with repeated measures was performed for QOL across four subscales. The Mauchly's test $[\chi^2(5) = 43.29$, $p < 0.001]$ indicated a violation of sphericity, therefore, the Greenhouse-Geisser method was used for correction.

Besides, we tested whether there were some important differences between the participants in the four domains and overall QOL regarding demographic data. Due to the small sample size (and thus assumed compromised normality), we decided to use nonparametric tests (Mann-Whitney U-test and Kruskal-Wallis test).

In order to answer our main research question – which sets of variables are the most important in predicting different aspects of QOL in breast cancer patients – a hierarchical regression analysis was applied. Since some of the predictors correlate highly with one another (Table 2), the data were checked for multicollinearity. For all predictors, the obtained VIF value was in an acceptable range, indicating that the problem of multicollinearity was not present. Furthermore, the data were analyzed for heteroscedasticity, which could also be excluded. Five hierarchical regression analyses were performed, with four

Table 2

Correlations between measures of quality of life (QOL), depression, anxiety, stress, social support (quantity and quality) and upper extremity function

Variables	Age (1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
Physical QOL (2)	0.10										
Psychological QOL (3)	-0.14	**0.66****									
Social QOL (4)	-0.03	**0.47****	**0.52****								
Spiritual QOL (5)	**-0.25***	0.07	0.22	-0.24							
General QOL (6)	-0.13	**0.77****	**0.95****	**0.63****	**0.32****						
Depression (7)	0.07	**-0.30***	**-0.51****	**-0.56****	0.05	**-0.52****					
Anxiety (8)	-0.00	**-0.42****	**-0.53****	**-0.61****	0.11	**-0.56****	**0.75****				
Stress (9)	-0.15	**-0.43****	**-0.58****	**-0.50****	0-.04	**-0.60****	**0.73****	**0.80****			
Social support quantity (10)	-0.14	0.03	0.06	0.09	0.24	0.12	-0.09	-0.02	-0.02		
Social support quality (11)	-0.03	**0.30***	**0.31***	0.22	0.20	**0.36****	**-0.31***	-0.17	-0.23	0.18	
Upper extremity function (12)	-0.19	**0.36****	**0.45****	**0.46****	-0.01	**0.47****	**-0.58****	**-0.65****	**-0.53****	**0.34***	0.18

***$p < 0.05$; **$p < 0.01$.**

domains and the overall QOL as criterion variables, while eight predictors were the same across all models and were always introduced in the same order. The first block of predictors consisted of clinical variables, such as receiving neoadjuvant and/or adjuvant chemotherapy and the presence of any nonmalignant comorbid conditions. Functional status, i.e., upper extremity function, was entered in the second step of the model. The third block consisted of the variables related to the affective state – indicators of depression, anxiety, and stress. In the final step, the perceived quality of social support was introduced.

Results

The descriptive statistical indicators and Cronbach's alpha coefficients for continuous variables in our research are presented in Table 3. Values of skewness and kurtosis indicate that distributions of data measured by different scales do not deviate importantly from normal [39]. Cronbach's alpha coefficients demonstrated that the reliability of the entire QOL-BC instrument was good, and the same went for the psychological QOL subscale. Physical and social QOL subscales manifested acceptable reliability, while the spiritual domain had questionable internal consistency (probably due to one reversely scored item, which turned out to compromise the reliability of this subscale). The reliability of subscales from DASS-21 varied from acceptable to good, while MOS-SSS and UEFI showed excellent reliability.

The Pearson's correlation was used in order to determine the relationship between variables. In Table 2, we can see that the age of participants correlated significantly only with spiritual QOL [r = -0.25, $p < 0.05$] (the older the person, the lower the spiritual aspect of QOL). Furthermore, it could be noticed that physical, psychological, social, and general QOL correlated significantly with the majority of other variables, such as depression, anxiety, stress, quality of social support, and indicators of functional status. However, it is important to note that correlation coefficients whose value is less than 0.5 are not of greater clinical significance. Finally, the spiritual aspect of QOL and social support expressed through quantity manifested low and nonsignificant correlations with almost all the above-mentioned variables. Therefore, the latter was not included in the hierarchical regression analysis.

Repeated measures ANOVA showed that the overall difference between the means on four aspects of QOL was statistically significant [F(2.03, 127.80) = 20.24, $p < 0.001$, $\eta p^2 = 0.24$]. Furthermore, we were interested in exploring which subscales differ one from another, therefore, the Bonferroni *post hoc* test was performed. The physical QOL was significantly better than all other domains. The psychological aspect was significantly worse than the physical but better than the social segment. The social QOL was significantly lower from both the physical and psychological domain, while the spiritual aspect was worse only compared to the physical QOL. Means for all subscales and the results of pairwise comparisons are shown in Figure 1.

Table 3

Descriptive statistics and reliability coefficients for all scales

Variables	Mean	Standard Deviation	Skewness	Kurtosis	Cronbach's α
Physical QOL	59.61	12.48	-0.51	-0.35	0.72
Psychological QOL	140.05	34.48	-0.32	-0.05	0.88
Social QOL	50.00	13.94	-0.64	0.15	0.71
Spiritual QOL	43.73	12.62	0.00	-0.15	0.64
General QOL	293.39	55.31	-0.52	0.43	0.89
Depression	5.11	4.77	1.06	0.32	0.88
Stress	6.34	4.77	0.63	-0.20	0.89
Anxiety	3.75	3.64	1.06	0.51	0.77
Social support quality	82.17	11.54	-1.71	2.13	0.97
Upper extremity function	59.92	15.84	-0.65	-0.21	0.95

QOL – quality of life.

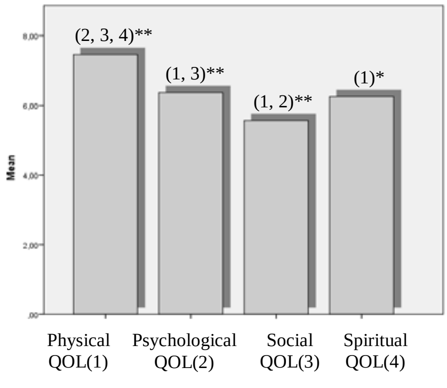

Fig. 1 – Means for physical, psychological, social, and spiritual quality of life (QOL) and results of pairwise comparisons ($p < 0.001$; * $p = 0.01$).**

When examining the marital status, no significant differences were found on physical, psychological, social, or general QOL. However, the Mann-Whitney U-test for independent samples showed that women who had a partner differed significantly on spiritual well-being (Mann-Whitney U = 279.5, $p = 0.04$), achieving better scores (mean rank = 35.42) compared to single women (mean rank = 25.03).

Results of the hierarchical regression analysis presented in Table 4 show that for physical QOL, all steps, except the first one, resulted in statistically significant models. The introduction of upper extremity function in the second step, F(4.59) = 4.00, $p < 0.01$, led to statistically significant increase in explained variance [$\Delta R^2 = 0.14$, $p(\Delta F) < 0.01$] with adjuvant chemotherapy ($p = 0.03$) and functional status ($p < 0.01$) as significant predictors. However, with the inclusion of depression, anxiety, and stress symptoms, functional status lost its significance, and adjuvant chemotherapy remained the only relevant predictor ($p = 0.04$). In the last step, a significant increase in explained variance occurred due to the introduction of social support quality [$\Delta R^2 = 0.05$, $p(\Delta F) < 0.05$]. The whole model [F(8.55) = 3.64, $p < 0.01$] explains around 35% of criterion variance, with adjuvant chemotherapy ($p = 0.03$) and perceived quality of social support ($p = 0.05$) being the only significant predictors. Our results indicated that women who did not receive adjuvant chemotherapy and had the perception of better social support were more likely to have increased scores in the physical domain of QOL.

As for the psychological aspect of QOL, in Table 4, it can be seen that all steps, except the first one, yield significant models. In the second step, where the introduction of functional status occurred, significant increase in the proportion of explained variance was detected [$\Delta R^2 = 0.20$, $p(\Delta F) < 0.001$] with adjuvant chemotherapy ($p = 0.01$) and upper extremity function ($p < 0.01$) as significant predictors. However, in the next step, when variables related to the affective state were entered, a significant increase in explained variance occurred again [$\Delta R^2 = 0.16$, $p(\Delta F) < 0.01$] with adjuvant chemotherapy ($p < 0.01$) and stress ($p = 0.03$) being now the only significant predictors. No further increase in explained variance was detected with the introduction of perceived quality of social support. The complete model [F(8.55) = 6.78, $p < 0.001$] explains around 50% of criterion's variance. Adjuvant chemotherapy ($p < 0.01$) and stress ($p = 0.03$) again turned out to be the only significant predictors. In other words, those women who underwent adjuvant chemotherapy and experienced higher levels of stress are more likely to have worse psychological QOL.

Results of the hierarchical regression analysis for social QOL, which are presented in Table 5, demonstrated again that significant models were obtained in all steps, except in the first one. Statistically significant model [F(4.59) = 4.81, $p < 0.01$] and relevant increase in the proportion of explained variance were obtained in the second step [$\Delta R^2 = 0.19$, $p(\Delta F) < 0.001$] when functional status was introduced, with upper extremity function as the only significant predictor ($p < 0.01$). When depression, anxiety and stress were entered [F(7.56) = 6.25, $p < 0.001$], another increase in the proportion of explained variance occurred [$\Delta R^2 = 0.19$,

Table 4

Hierarchical regression for physical and psychological quality of life (QOL)

Physical QOL				Psychological QOL		
Model	β	p	Predictors	β	p	Model
1	0.10	0.44	Neoadjuvant chemotherapy	0.02	0.86	1
F(3, 60) = 1.48	-0.26	0.04	Adjuvant chemotherapy	-0.32	0.01	F(3, 60) = 2.35
$p = 0.23$, $R^2 = 0.07$	0.04	0.77	Comorbid conditions	-0.04	0.74	$p = 0.08$, $R^2 = 0.10$
2	0.06	0.58	Neoadjuvant chemotherapy	-0.02	0.88	2
F(4, 59) = 4.00	-0.26	0.03	Adjuvant chemotherapy	-0.32	0.01	F(4, 59) = 6.40
$p < 0.01$, $R^2 = 0.21$	0.17	0.18	Comorbid conditions	0.11	0.34	$p < 0.001$, $R^2 = 0.30$
$\Delta R^2 = 0.14$ $p(\Delta F) < 0.01$	0.40	0.00	Upper extremity function	0.47	0.00	$\Delta R^2 = 0.20$ $p(\Delta F) < 0.001$
3	0.08	0.48	Neoadjuvant chemotherapy	0.02	0.86	3
F(7, 56) = 3.37	-0.24	0.04	Adjuvant chemotherapy	-0.31	0.00	F(7, 56) = 7.04
$p < 0.01$	0.16	0.21	Comorbid conditions	0.08	0.44	$p < 0.001$
$R^2 = 0.30$	0.21	0.17	Upper extremity function	0.18	0.19	$R^2 = 0.47$
$\Delta R^2 = 0.08$	0.14	0.45	Depression	-0.15	0.34	$\Delta R^2 = 0.16$
$p(\Delta F) = 0.10$	-0.20	0.39	Anxiety	0.02	0.93	$p(\Delta F) < 0.01$
	-0.27	0.20	Stress	-0.39	0.03	
4	0.10	0.36	Neoadjuvant chemotherapy	0.03	0.74	4
F(8, 55) = 3.64	-0.24	0.03	Adjuvant chemotherapy	-0.32	0.00	F(8, 55) = 6.78
$p < 0.01$	0.10	0.40	Comorbid conditions	0.04	0.70	$p < 0.001$
$R^2 = 0.35$	0.18	0.22	Upper extremity function	0.16	0.24	$R^2 = 0.50$
$\Delta R^2 = 0.05$	0.23	0.21	Depression	-0.08	0.62	$\Delta R^2 = 0.03$
$p(\Delta F) < 0.05$	-0.23	0.30	Anxiety	-0.01	0.97	$p(\Delta F) = 0.08$
	-0.26	0.20	Stress	-0.39	0.03	
	0.24	0.05	Social support - quality	0.18	0.08	

Table 5

Hierarchical regression for social and general quality of life (QOL)

Social QOL				General QOL		
Model	β	p	Predictors	β	p	Model
1	0.11	0.37	Neoadjuvant chemotherapy	0.04	0.72	1
$F(3, 60) = 1.19$	-0.18	0.15	Adjuvant chemotherapy	-0.27	0.04	$F(3, 60) = 1.71$
$p = 0.32$, $R^2 = 0.06$	-0.11	0.40	Comorbid conditions	-0.07	0.59	$p = 0.17$, $R^2 = 0.08$
2	0.08	0.50	Neoadjuvant chemotherapy	0.005	0.97	2
$F(4, 59) = 4.81$	-0.18	0.12	Adjuvant chemotherapy	-0.26	0.02	$F(4, 59) = 6.21$
$p < 0.01$, $R^2 = 0.25$	0.04	0.73	Comorbid conditions	0.09	0.43	$p < 0.001$, $R^2 = 0.30$
$\Delta R^2 = 0.19$	0.46	0.00	Upper extremity function	0.49	0.00	$\Delta R^2 = 0.22$
$p(\Delta F) < 0.001$						$p(\Delta F) < 0.001$
3	0.07	0.48	Neoadjuvant chemotherapy	0.04	0.72	3
$F(7, 56) = 6.25$	-0.16	0.12	Adjuvant chemotherapy	-0.25	0.01	$F(7, 56) = 6.79$
$p < 0.001$	0.10	0.38	Comorbid conditions	0.07	0.53	$p < 0.001$
$R^2 = 0.44$	0.09	0.52	Upper extremity function	0.20	0.15	$R^2 = 0.46$
$\Delta R^2 = 0.19$	-0.26	0.12	Depression	-0.11	0.51	$\Delta R^2 = 0.16$
$p(\Delta F) < 0.01$	-0.44	0.03	Anxiety	-0.04	0.86	$p(\Delta F) < 0.01$
	0.09	0.63	Stress	-0.38	0.04	
4	0.08	0.44	Neoadjuvant chemotherapy	0.06	0.55	4
$F(8, 55) = 5.48$	-0.16	0.12	Adjuvant chemotherapy	-0.26	0.01	$F(8, 55) = 7.16$
$p < 0.001$	0.08	0.48	Comorbid conditions	0.01	0.90	$p < 0.001$
$R^2 = 0.44$	0.08	0.56	Upper extremity function	0.17	0.20	$R^2 = 0.51$
$\Delta R^2 = 0.005$	-0.23	0.18	Depression	-0.01	0.95	$\Delta R^2 = 0.05$
$p(\Delta F) = 0.49$	-0.46	0.03	Anxiety	-0.07	0.72	$p(\Delta F) < 0.05$
	0.09	0.63	Stress	-0.38	0.03	
	0.08	0.49	Social support - quality	0.25	0.02	

$p(\Delta F) < 0.01$]. However, functional status was no longer relevant, and only symptoms of anxiety significantly predicted social QOL ($p = 0.03$). The introduction of social support in the last step did not lead to the significant increase in variance explained. When all predictors were included [F(8.55) = 5.48, $p < 0.001$], the model explained around 44% of criterion's variance, with anxiety remaining again the only significant predictor in the model ($p = 0.03$). In other words, women who experienced stronger symptoms of anxiety were more likely to have diminished social QOL.

For spiritual QOL, no significant models in any of the four steps were obtained.

Finally, hierarchical regression analysis for general QOL (Table 5) yields statistically significant models in all steps, except in the first one. In the second step [F(4.59) = 6.21, $p < 0.001$], significant increase in the proportion of explained variance occurred [$\Delta R^2 = 0.22$, $p(\Delta F) < 0.001$] due to the introduction of the functional status, with adjuvant chemotherapy ($p = 0.02$) and upper extremity function ($p < 0.01$) as significant predictors. The third step of the analysis brought again the significant increase in the variance explained [$\Delta R^2 = 0.16$, $p(\Delta F) < 0.01$], where stress ($p = 0.04$), along with the adjuvant chemotherapy ($p = 0.01$), turned out to be a statistically significant predictor, while functional status lost its significance. In the last step [F(8.55) = 7.16, $p < 0.001$], further increase in explained variance occurred due to the introduction of social support [$\Delta R^2 = 0.05$, $p(\Delta F) < 0.05$], with adjuvant chemotherapy ($p = 0.01$), stress ($p = 0.03$), and social support ($p = 0.02$) being significant predictors. The coefficient of determination indicated that the proportion of explained variance of the criterion was around 51%. Results showed that patients who received adjuvant chemotherapy and experienced high levels of stress and poor social support tend to have diminished general QOL.

Discussion

Since QOL nowadays is one of the core concepts in cancer treatment, a better understanding of factors that may contribute to its improvement is of great importance. Therefore, the main goal of our research was to explore which sets of variables contribute the most to the prediction of various aspects of QOL in breast cancer patients.

Although the process of oncological treatment is very challenging and involves overwhelming subjective reactions to its side effects, our results demonstrated that breast cancer patients, paradoxically, reported that their physical aspect of QOL was significantly better compared to all other domains. Psychological and spiritual aspects were significantly diminished compared to physical QOL. However, the social segment seems to be the most compromised. This finding once again sets light on the well-known fact that the experience of breast cancer diagnosis and its treatment largely exceeds physical level and disrupts not only psychological and spiritual but also social well-being. Perhaps disease-related reactions of family members, available support, personal relationships, sexuality, work, finances, etc. are the most threatened segments in our socio-cultural background that frequently remain in the shadow of concern about the physical health of the patients. This finding points to the fact that our healthcare system still focuses the most on the physical aspects of the disease, while other domains might remain overlooked, meaning that additional changes are needed in the direction of the holistic approach to breast cancer treatment. The scarce outcome in the social aspect of QOL might also be culturally-specific and it might be the result of inadequate information. Unfortunately, it might also be the result of prejudices that are still widespread about malignant diseases in our society, as well as of yet traditionally burdened cultural context in which women live, and the specific socio-economic situation in this region.

Our results demonstrated that, at the time of assessment which took part during the radiation therapy, the previously received adjuvant chemotherapy was an important determinant of physical, psychological, and general QOL, manifesting the reverse relationship with QOL indicators. This finding is pretty much expected, and it goes in line with both previous empirical results [40, 41] and generally known subjective reports of patients about their experiences during the treatment. Chemotherapy may lead to treatment-related somatic symptoms and changes in body image, resulting in adverse relations with different aspects of QOL. Although it was expected that neoadjuvant chemotherapy and additional health problems would affect the quality of patients' life, our results demonstrated that only adjuvant chemotherapy was related to QOL measures, at least in this period of assessment. It may be that recently experienced adverse chemotherapy effects mask previously felt discomfort. However, clinical factors included in the analysis were never sufficient by themselves to get a significant prediction of any QOL aspect.

When it comes to the contribution of functional status, our findings indicate that its inclusion always led to significant models and an increase in the proportion of explained variance. The better the upper limb function, the better physical, psychological, social, and general QOL is. These findings are strongly in accordance with the previous literature [42, 43], knowing that upper extremity disfunction and related limitations (with or without lymphedema) are one of the most limiting complications following breast cancer treatment. At first sight, it seems that functional status together with information about received adjuvant chemotherapy may constitute a satisfying model for the prediction of different aspects of QOL. Nevertheless, whenever symptoms of depression, anxiety, and stress were introduced, functional status lost its predictive significance, indicating that the emotional state of participants might be more powerful in predicting QOL in breast cancer. However, this could also be the result of the fact that the impaired affective state of patients is strongly interrelated to (or even possibly the consequence of) the compromised function of upper limbs, and consequently, restricted daily activities.

Our findings demonstrated that variables related to the emotional state of participants significantly predicted psychological, social, and general QOL, over and above clinical and functional factors. Heightened levels of distress during the treatment predict the worst psychological and general QOL, while symptoms of anxiety are significant in predicting poor social well-being. The notion that symptoms of distress or affective disorders have the reverse relationship with different indicators of QOL is anticipated and goes in line with previous literature [44-47]. It is expected for symptoms of anxiety and distress to intensify in transition times of diagnosis and treatment course, coexisting with decreased QOL indicators [48]. Nevertheless, from our results, it can be seen that symptoms of depression did not significantly predict any of the QOL measures, which appears to be unanticipated at first glance. However, if we notice that the majority of QOL-BC items, especially those contained in the psychological, and partially social subscale, are focused on (health) anxiety, fear (of recurrence), stress, and sense of control, it is reasonable that symptoms of anxiety and stress would be dominant predictors of QOL. Another less expected finding is that anxiety symptoms are the only significant predictors of social QOL, while perceived social support is not. It is known that an increased level of anxiety can affect individuals' social and work functioning [49, 50]. Moreover, it is possible that anxiety is strongly bonded to the social subscale of QOL-BC, whose items are aimed at worries related to finances, disrupted activities at home and work, compromised sexuality, concern for the health of close family members, etc. Probably all those facets of the social aspect of QOL are more saturated with uncertainty (which is the core component of vulnerability to anxiety) than with the quality of social support measured with MOS-SSS.

Another less anticipated result is that perceived quality of social support significantly predicts physical and general QOL, but not psychological and social aspects, which would be more expected. Quality of social support might be important for physical QOL, probably due to emotional/informative and instrumental/practical support, which could be crucial for coping with physical symptoms, difficulties, and limitations. An additional important observation is that, at least in this period of assessment, social support matters more in explaining the physical QOL than the presence of functional complications, or some clinical factors such as, for example, the existence of comorbidity. The earlier research has already shown that social support is substantial for health-related QOL in breast cancer patients [23, 26]. Thus, one longitudinal study indicated that positive emotional and informational support provided by a partner is especially important in maintaining health-related QOL [51]. Our results showed not only that social support is relevant for physical and general QOL but also that it is quality, not quantity of support that matters, which is in accordance with previous findings [25].

In earlier studies, a significant relationship had been found between religiosity/spirituality and better physical and functional status, reduced symptoms of psychopathology, greater emotional well-being, and improved social support [52–55]. However, our study did not show such results. No significant correlations between the spiritual aspect of QOL and levels of stress, anxiety, depression, social support (quantity and quality), and functional status were detected. What's more, from all QOL-BC subscales, the spiritual aspect manifests the lowest correlation with the total score and no significant correlations with the other three domains, meaning that it might be somehow the most distinctive construct. It also seems that clinical, functional, affective, and social factors analyzed in our study are not so prominent in explaining spiritual QOL in breast cancer. However, in review on spirituality and well-being of cancer patients, Visser et al. [56] point out that although most of the studies report positive relation between spirituality and well-being, the majority of them utilized spirituality questionnaires which contained items related to well-being itself, possibly leading to an artificial increase in the observed relationship. The spirituality subscale of QOL-BC does not contain related items to other well-being domains, so this could be one of the plausible explanations for low and nonsignificant correlations with other examined variables. On the other hand, as spirituality is a multidimensional concept, its different aspects (i.e., sense of meaning in life and active religious practices) may correlate differently with other physical and psychosocial variables. And yet, our research showed that age and marital status could be relevant when it comes to the spiritual aspect of QOL. Obtained results indicate that older patients and those who are single manifest lower spiritual QOL, which is inconsistent with previous studies showing that younger age is a risk factor for poor QOL in breast cancer patients [5-7]. It is probable that the process of aging, loneliness, possible loss of a partner (a significant part of single women in our sample were widowed) and dependence, bring to the foreground existential issues and loss of meaning, with which patients have difficulty coping. Hence, those women undergoing breast cancer treatment who are older and single are especially vulnerable in the context of uncertainty, hope, the meaning of life, and the capacity to grow after the crisis. These results could help target and include vulnerable patients in supportive programs for fostering spiritual well-being, as an important resource for adjustment and healing [57].

Given that our study is cross-sectional, the observation of temporal changes in QOL during and after the treatment would be recommended for future research. Therefore, the longitudinal design with a larger sample and more complex statistical approach is highly desirable in order to overcome some of the disadvantages of our study. Moreover, the inclusion of a wider range of variables, such as coping mechanisms, doctor-patient communication, type of surgical intervention, etc., would contribute to a more sophisticated understanding of this topic. Our results generally support the notion already detected in other studies that psychological and social resources are more important in predicting different aspects of quality of life in breast cancer patients, compared to clinical, demographical, and functional factors [20, 58].

Conclusion

While adjuvant chemotherapy turned out to be a powerful predictor of the physical, psychological, and general quality of life, clinical factors by themselves could not explain the quality of life outcomes, whilst functional status always lost its significance with the inclusion of psychological and social support measures, indicating that the latter are superior in determining different quality of life domains. At the same time, the social, psychological, and spiritual well-being of our patients is significantly worse compared to the physical quality of life, meaning that there is still much left to be done in the process of moving the focus from a purely somatic to a holistic approach in the treatment of breast cancer.

Additionally, it seems that for different aspects of patients' well-being during the treatment, training in coping skills, with a focus on reducing symptoms of distress and affective disorders, as well as fostering social and communicational skills, would be a target of highest priority for psycho-oncologists.

REFERENCES

1. *Vardar Yağlı N, Şener G, Arıkan H, Sağlam M, Inal Ince D, Savcı S*, et al. Do Yoga and aerobic exercise training have impact on functional capacity, fatigue, peripheral muscle strength, and quality of life in breast cancer survivors? Integr Cancer Ther 2015; 14(2): 125–32.
2. *Pinto M, Gimigliano F, Tatangelo F, Megna M, Izzo F, Gimigliano R*, et al. Upper limb function and quality of life in breast cancer related lymphedema: a cross-sectional study. Eur J Phys Rehabil Med 2013; 49(5): 665–73.
3. Cancer Registry of Central Serbia, Cancer incidence and mortality in central Serbia 2015. Belgrade, Serbia: Institute of Public Health of Serbia „Dr Milan Jovanović Batut“; 2017. Report No. 17. Available from: http://www.batut.org.rs/download/publikacije/Incidencija%20i%20mortalitet%20od%20raka%202015.pdf [cited 2019 March 18]
4. *Irvine D, Brown B, Crooks D, Roberts J, Browne G.* Psychosocial adjustment in women with breast cancer. Cancer 1991; 67(4): 1097–117.
5. *King MT, Kenny P, Shiell A, Hall J, Boyages J.* Quality of life three months and one year after first treatment for early stage breast cancer: influence of treatment and patient characteristics. Qual Life Res 2000; 9(7): 789–800.
6. *Hopwood P, Haviland J, Mills J, Sumo G, Bliss JM.* The impact of age and clinical factors on quality of life in early breast cancer: an analysis of 2208 women recruited to the UK START Trial (Standardisation of Breast Radiotherapy Trial). Breast 2007; 16(3): 241–51.
7. *Parker PA, Youssef A, Walker S, Basen-Engquist K, Cohen L, Gritz ER*, et al. Short-term and long-term psychosocial adjustment and quality of life in women undergoing different surgical procedures for breast cancer. Ann Surg Oncol 2007; 14(11): 3078–89.
8. *Wöckel A, Schwentner L, Krockenberger M, Kreienberg R, Janni W, Wischnewsky M*, et al. Predictors of the course of quality of life during therapy in women with primary breast cancer. Qual Life Res 2017; 26(8): 2201–8.
9. *Repetto L, Ausili-Cefaro G, Gallo C, Rossi A, Manzione L.* Quality of life in elderly cancer patients. Ann Oncol 2001; 12(Suppl 3): S49–S52.
10. *Ahn SH, Park BW, Noh DY, Nam SJ, Lee ES, Lee KM*, et al. Health-related quality of life in disease-free survivors of breast cancer with the general population. Ann Oncol 2007; 18(1): 173–82.
11. *Erickson VS, Pearson ML, Ganz PA, Adams J, Kahn KL.* Arm edema in breast cancer patients. J Natl Cancer Inst 2001; 93(2): 96–111.

12. *Kwan W, Jackson J, Weir LM, Dingee C, McGregor G, Olivotto IA.* Chronic arm morbidity after curative breast cancer treatment: prevalence and impact on quality of life. J Clin Oncol 2002; 20(20): 4242–8.
13. *Engel J, Kerr J, Schlesinger-Raab A, Eckel R, Sauer H, Hölzel D.* Predictors of quality of life of breast cancer patients. Acta Oncol 2003; 42(7): 710–8.
14. *Hormes JM, Bryan C, Lytle LA, Gross CR, Ahmed RL, Troxel AB*, et al. Impact of lymphedema and arm symptoms on quality of life in breast cancer survivors. Lymphology 2010; 43(1): 1–13.
15. *Collins LG, Nash R, Round T, Newman B.* Perceptions of upper-body problems during recovery from breast cancer treatment. Support Care Cancer 2004; 12(2): 106–13.
16. *Härtl K, Engel J, Herschbach P, Reinecker H, Sommer H, Friese* K. Personality traits and psychosocial stress: quality of life over 2 years following breast cancer diagnosis and psychological impact factors. Psychooncology 2010; 19(2): 160–9.
17. *Brunault P, Toledano A, Aguerre C, Suzanne I, Garaud P, Trzepidur-Edom M,* et al. Impact of late treatment-related radiotherapy toxicity, depression, and anxiety on quality of life in long-term breast cancer survivors. Bull Cancer 2012; 99(5): 589–98.
18. *Burgess C, Cornelius V, Love S, Graham J, Richards M, Ramirez A.* Depression and anxiety in women with early breast cancer: five year observational cohort study. BMJ 2005; 330(7493): 702–5.
19. *Reich M, Lesur A, Perdrizet-Chevallier C.* Depression, quality of life and breast cancer: a review of the literature. Breast Cancer Res Treat 2008; 110(1): 9–17.
20. *Avis NE, Crawford S, Manuel J.* Quality of life among younger women with breast cancer. J Clin Oncol 2005; 23(15): 3322–30.
21. *Tsaras K, Papathanasiou IV, Mitsi D, Veneti A, Kelesi M, Zyga S*, et al. Assessment of depression and anxiety in breast cancer patients: prevalence and associated factors. Asian Pac J Cancer Prev 2018; 19(6): 1661–9.
22. *Hegel MT, Moore CP, Collins ED, Kearing S, Gillock KL, Riggs RL*, et al. Distress, psychiatric syndromes, and impairment of function in women with newly diagnosed breast cancer. Cancer 2006; 107(12): 2924–31.
23. *Huang CY, Hsu MC.* Social support as a moderator between depressive symptoms and quality of life outcomes of breast cancer survivors. Eur J Oncol Nurs 2013; 17(6): 767–74.
24. *Fong AJ, Scarapicchia TMF, McDonough MH, Wrosch C, Sabiston CM.* Changes in social support predict emotional well-being in breast cancer survivors. Psychooncology 2017; 26(5): 664–71.
25. *Cohen S, Underwood L, Gottlieb B.* Social support measurement and intervention: a guide for health and social scientists. New York: Oxford University Press; 2000.
26. *McDonough MH, Sabiston CM, Wrosch C.* Predicting changes in posttraumatic growth and subjective well-being among breast cancer survivors: the role of social support and stress. Psychooncology 2014; 23(1): 114–20.
27. *Sabiston CM, McDonough MH, Crocker PR.* Psychosocial experiences of breast cancer survivors involved in a dragon boat program: exploring links to positive psychological growth. J Sport Exerc Psychol 2007; 29(4): 419–38.
28. *Ferrell BR, Dow KH, Grant M.* Quality of Life Instrument - Breast Cancer Patient Version (QOL-BC). Measurement Instrument Database for the Social Sciences; 2012. [cited 2019 March 12] Available from: http://www.midss.org/sites/default/files/qol-bc.pdf
29. *Ferrell BR, Grant M, Funk B, Garcia N, Otis-Green S, Schaffner MLJ.* Quality of life in breast cancer. Cancer Practice 1996; 4(6): 331-40.
30. *Dow KH, Ferrell BR, Leigh S, Ly J, Gulasekaram P.* An evaluation of the quality of life among long-term survivors of breast cancer. Breast Cancer Res Treat 1996; 39(3): 261–73.
31. *Ferrell BR, Grant M, Funk B, Otis-Green S, Garcia N.* Quality of life in breast cancer. Part I: physical and social well-being. Cancer Nurs 1997; 20(6): 398–408.
32. *Ferrell BR, Grant M, Funk B, Otis-Green S, Garcia N.* Quality of life in breast cancer. Part II: psychological and spiritual well being. Cancer Nurs 1998; 21(1): 1–9.
33. *Ferrell BR, Grant M, Funk B, Otis-Green S, Garcia N.* Quality of life in breast cancer survivors: implications for developing support services. Oncol Nurs Forum 1998; 25(5): 887–95.
34. *Stratford PW, Binkley JM, Stratford DM.* Development and initial validation of the Upper Extremity Functional Index. Physioter Can 2001; 52(281): 259–67.
35. *Lovibond PF, Lovibond SH.* The structure of negative emotional states: comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. Behav Res Ther 1995; 33(3): 335–43.
36. *Jovanović V, Gavrilov-Jerković V.* Validity of a Serbian translation of the Medical Outcomes Study Social Support Survey (MOS-SSS). Primenjena Psihologija 2015; 8(3): 245–64. (Serbian)
37. *Sherbourne CD, Stewart AL.* The MOS social support survey. Soc Sci Med 1991; 32(6): 705–14.
38. *Tarlov AR, Ware JE, Greenfield S, Nelson EC, Perrin E, Zubkoff M.* The Medical Outcomes Study. An application of methods for monitoring the results of medical care. JAMA 1989; 262(7): 925–30.
39. *George D, Mallery M.* SPSS for Windows step by step: a simple guide and reference, 17.0 update. 10th ed. Boston: Allyn & Bacon; 2010.
40. *Lorusso D, Bria E, Costantini A, Di Maio M, Rosti G, Mancuso A.* Patients' perception of chemotherapy side effects: expectations, doctor–patient communication and impact on quality of life – an Italian survey. Eur J Cancer Care (Engl) 2017; 26(2): doi: 10.1111/ecc.12618.
41. *Sommariva S, Pongiglione B, Tarricone R.* Impact of chemotherapy-induced nausea and vomiting on health-related quality of life and resource utilization: a systematic review. Crit Rev Oncol Hematol 2016; 99: 13–36.
42. *Dawes DJ, Meterissian S, Goldberg M, Mayo NE.* Impact of lymphoedema on arm function and health-related quality of life in women following breast cancer surgery. J Rehabil Med 2008; 40(8): 651–8.
43. *Chachaj A, Małyszczak K, Pyszel K, Lukas J, Tarkowski R, Pudełko M,* et al. Physical and psychological impairments of women with upper limb lymphedema following breast cancer treatment. Psychooncology 2010; 19(3): 299–305.
44. *Gold M, Dunn LB, Phoenix B, Paul SM, Hamolsky D, Levine JD*, et al. Co-occurrence of anxiety and depressive symptoms following breast cancer surgery and its impact n quality of life. Eur J Oncol Nurs 2016; 20: 97–105.
45. *Fasoi-Barka GG, Kelesi-Stauropoulou MN, Koutsopoulou-Sofikiti VE.* Study for the change of health related quality of life in women with early stage breast cancer, one year after the diagnosis. Rostrum of Asclepius 2010; 9: 76–99.
46. *Montazeri A, Vahdaninia M, Harirchi I, Ebrahimi M, Khaleghi F, Jarvandi S.* Quality of life in patients with breast cancer before and after diagnosis: an eighteen months follow-up study. BMC Cancer 2008; 8: 330.
47. *Andritsch E, Dietmaier G, Hofmann G, Zloklikovits S, Samonigg H.* Global quality of life and its potential predictors in breast cancer patients: an exploratory study. Support Care Cancer 2007; 15(1): 21–30.
48. *Charalambous A, Kaite CP, Charalambous M, Tistsi T, Kouta C.* The effects on anxiety and quality of life of breast cancer patients following completion of the first cycle of chemotherapy. SAGE Open Med 2017; 5: 2050312117717507.
49. *Plaisier I, Beekman AT, de Graaf R, Smit JH, van Dyck R, Penninx BW.* Work functioning in persons with depressive and anxiety

disorders: the role of specific psychopathological characteristics. J Affect Disord 2010; 125(1–3): 198–206.

50. *Lou Z, Li Y, Yang Y, Wang L, Yang J.* Affects of anxiety and depression on health-related quality of life among patients with benign breast lumps diagnosed via ultrasonography in China. Int J Environ Res Public Health 2015; 12(9): 10587–601.
51. *Leung J, Pachana NA, McLaughlin D.* Social support and health-related quality of life in women with breast cancer: a longitudinal study. Psychooncology 2014; 23(9): 1014–20.
52. *Matthews DA, Larson DB, Barry CP.* The faith factor: an annotated bibliography of clinical research on spiritual subjects, volume 1. Rockville, MD: National Institute for Healthcare Research; 1993.
53. *Matthews DA, Larson DB.* The faith factor: an annotated bibliography of clinical research on spiritual subject, volume 3: enhancing life satisfaction. Washington, DC: National Institute for Healthcare Research; 1995.
54. *Weaver AJ, Flannelly KJ.* The role of religion/spirituality for cancer patients and their caregivers. South Med J 2004; 97(12): 1210–4.
55. *Rippentrop AE, Altmaier EM, Burns CP.* The relationship of religiosity and spirituality to quality of life among cancer patients. J Clin Psychol Med Settings 2006; 13(1): 29.
56. *Visser A, Grassen B, Vingerhoets A.* Spirituality and well-being in cancer patients: a review. Psychooncology 2010; 19(6): 565–72.
57. *Cotton SP, Levine EG, Fitzpatrick CM, Dold KH, Targ E.* Exploring the relationships among spiritual well-being, quality of life, and psychological adjustment in women with breast cancer. Psychooncology 1999; 8(5): 429–38.
58. *Brunault P, Champagne AL, Huguet G, Suzanne I, Senon JL, Body G*, et al. Major depressive disorder, personality disorders, and coping strategies are independent risk factors for lower quality of life in non-metastatic breast cancer patients. Psychooncology 2016; 25(5): 513–20.

Received on May 1, 2019.
Revised on March 13, 2021.
Accepted on March 16, 2021.
Online First March, 2021.