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Original Scientific Paper

IMPACT OF BODY COMPOSITION ON THE QUALITY OF LIFE OF PREMENOPAUSAL PATIENTS WITH EARLY STAGE BREAST CANCER DURING CHEMOTHERAPY

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SUMMARY – Body composition has been studied relatively recently as part of oncology trials in different types of tumors. There are numerous studies that define the impact of chemotherapy side effects on the quality of life (QoL) of breast cancer patients, however, there are few studies that analyze the impact of body composition on the QoL of premenopausal patients in the course of cytotoxic treatment. The study was performed on a sample of premenopausal patients treated with neoadjuvant or adjuvant AC chemotherapy for early-stage breast cancer at Day Hospital of the Department of Medical Oncology, University Hospital for Tumors in Zagreb. The study included 68 patients, median age 46.6 years. Analysis of the QoL questionnaires and their association with body composition indicated several interesting results. At the beginning of treatment, most pronounced was the connection between body composition and physical and sexual functioning and hair loss, while in subsequent treatment cycles the effect on other QoL subdomains, in particular fatigue and diarrhea, was more pronounced. In conclusion, we found body composition to have a significant impact on certain QoL subdomains during treatment.

Key words: *Body composition; Quality of life; Breast cancer; Premenopausal women; Chemotherapy*

Introduction

Breast cancer is the most common malignancy and the most common cause of death from malignant disease in women in Croatia and Europe[1,2]. In almost 80% of patients, it is detected at an early stage when the goal of oncology treatment is long-term survival without disease recurrence[1]. Patients with an increased risk of disease recurrence (with clinically advanced stage of the disease or with molecular-genetically high-risk subtype of tumor) are candidates for preoperative (neoadjuvant) or postoperative (adjuvant) chemotherapy, usually based on anthracycline.

Body composition has been studied relatively recently as part of oncology trials in different types of tumors in the context of the metabolism of different anticancer drugs, assessment of response to treatment and its toxicity, and consequently the overall prognosis of the disease depending on the proportion of each body component[3–5]. There are numerous studies that clearly define the impact of chemotherapy and its side

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effects on the quality of life (QoL) of breast cancer patients, however, there are few studies that analyzed the impact of body composition on chemotherapy tolerance, as well as on the QoL of premenopausal patients in the course of cytotoxic treatment.

Patients and Methods

The study was performed on a consecutive sample of patients treated with neoadjuvant or adjuvant chemotherapy for early-stage breast cancer at the Day Hospital of the Department of Medical Oncology, University Hospital for Tumors in Zagreb between December 2018 and April 2019. All patients were premenopausal (study allowed inclusion of patients who had their last menstrual cycle within one year before treatment initiation). All patients received four cycles of AC chemotherapy (doxorubicin + cyclophosphamide) every three weeks, before or after the surgery. In all patients, the total dose of doxorubicin administered was 240 mg/m^2 and cyclophosphamide 2400 mg/m^2.

All patients gave their informed consent prior to their inclusion in the study.

During each visit, patients filled out standardized QoL questionnaires (EORTC QLQ-C30 and QLQ-B23). A physician performed anthropometric measurement including height and weight measurement used to calculate body surface area, which is necessary for calculating the dose of cytotoxic drugs for each patient. After that, patient body composition was estimated using Tanita BC-420MA analyzer.

Data analysis

Data were presented as mean and standard deviation for numerical data, or number and percentage for categorical data. Testing was performed with Pearson's correlation coefficient. All analyses were performed in R, with the level of significance set at $p<0.05$.

Results

The study included 68 patients, median age 46.6 (range 29-55) years. Patient characteristics are shown in Table 1.

Analysis of the QoL questionnaires and their association with body composition indicated several interesting results (Tables 2-5). At the beginning of treatment, most pronounced was the connection between body composition and physical and sexual functioning and hair loss (Table 2). In the second cycle, significant QoL result included financial problems (Table 3), while in subsequent treatment cycles other variables began to significantly affect QoL subdomains, in particular fatigue and diarrhea (Table 5).

Table 1. Descriptive statistics of the patient sample analyzed

Variable	Value
Age (years); mean ± SD[a] [range]	46.6±6.6 [29.0-55.0]
Height (cm); mean ± SD[a] [range]	164.7±5.5 [153.0-177.0]
Localization; n (%)	
Locoregional disease	36 (52.9)
Local disease	32 (47.1)
Biological subtype of tumor:	
Luminal A	2 (2.9)
Luminal B HER2 neg.	28 (41.2)
Luminal B HER2 pos.	22 (32.4)
Non-luminal HER2 pos.	5 (7.4)
Triple negative	9 (13.2)
Neoadjuvant chemotherapy:	
Yes	29 (42.6)
No	39 (57.4)

Table 2. Correlation of body composition variables with subdomains of QLQ-C30 and QLQ-B23 questionnaires – first measurement

	Body mass index	Body fat percentage	Visceral fat index	Skeletal muscle percentage
QL2, Global health status	-0.17 (0.195)	-0.13 (0.309)	-0.21 (0.096)	0.10 (0.453)
PF, Physical function	**-0.27 (0.033)**	-0.19 (0.138)	**-0.34 (0.006)**	0.20 (0.125)
RF2, Role function	-0.06 (0.656)	0.02 (0.874)	-0.06 (0.646)	-0.06 (0.638)
EF, Emotional function	0.10 (0.441)	0.05 (0.728)	0.12 (0.381)	0.01 (0.936)
CF, Cognitive function	0.22 (0.089)	0.22 (0.082)	0.21 (0.106)	-0.17 (0.192)
SF, Social function	0.05 (0.700)	-0.01 (0.960)	0.04 (0.793)	-0.04 (0.775)
FA, Fatigue	-0.07 (0.601)	-0.16 (0.208)	-0.04 (0.771)	0.17 (0.194)
NV, Nausea/vomiting	-0.12 (0.349)	-0.09 (0.493)	-0.03 (0.824)	0.12 (0.380)
PA, Pain	-0.03 (0.827)	-0.03 (0.822)	0.11 (0.423)	0.02 (0.895)
DY, Dyspnea	-0.06 (0.640)	-0.11 (0.398)	0.01 (0.945)	0.15 (0.246)
SL, Insomnia	-0.15 (0.237)	-0.16 (0.218)	-0.13 (0.305)	0.20 (0.115)
AP, Appetite loss	-0.14 (0.278)	-0.17 (0.200)	-0.07 (0.608)	0.07 (0.599)
CO, Constipation	-0.03 (0.829)	-0.07 (0.631)	0.05 (0.714)	0.09 (0.479)
DI, Diarrhea	0.17 (0.192)	0.11 (0.408)	0.13 (0.306)	-0.09 (0.503)
FI, Financial problems	0.05 (0.753)	0.02 (0.892)	-0.07 (0.622)	0.03 (0.837)
BRBI, Body image	0.05 (0.749)	0.02 (0.920)	0.09 (0.502)	0.06 (0.675)
BRSEF, Sexual functioning	-0.19 (0.181)	-0.25 (0.079)	**-0.41 (0.002)**	**0.32 (0.020)**
BRSEE, Sexual enjoyment	-0.27 (0.207)	-0.29 (0.169)	**-0.48 (0.019)**	0.29 (0.173)
BRFU, Future perspective	0.02 (0.920)	0.07 (0.595)	0.13 (0.324)	-0.05 (0.705)
BRCT, Systemic therapy	0.02 (0.903)	-0.05 (0.730)	0.06 (0.690)	0.05 (0.712)
BRRT, Breast symptoms	0.14 (0.292)	0.07 (0.624)	0.06 (0.665)	-0.09 (0.520)
BRSY, Arm symptoms	0.10 (0.454)	-0.01 (0.977)	0.01 (0.940)	-0.01 (0.966)
BRHL, Hair loss	-0.24 (0.076)	**-0.30 (0.027)**	-0.26 (0.057)	**0.30 (0.030)**

Statistically significant results are bold.

Table 3. Correlation of body composition variables with subdomains of QLQ-C30 and QLQ-B23 questionnaires – second measurement

	Body mass index	Body fat percentage	Visceral fat index	Skeletal muscle percentage
QL2, Global health status	-0.04 (0.769)	-0.11 (0.383)	-0.07 (0.601)	0.10 (0.442)
PF, Physical function	-0.09 (0.508)	-0.07 (0.618)	-0.12 (0.373)	0.06 (0.680)
RF2, Role function	0.03 (0.828)	-0.03 (0.833)	-0.03 (0.852)	0.02 (0.918)
EF, Emotional function	-0.02 (0.928)	-0.08 (0.570)	0.01 (0.952)	0.07 (0.574)
CF, Cognitive function	0.06 (0.668)	0.06 (0.664)	0.07 (0.598)	-0.06 (0.661)
SF, Social function	0.12 (0.336)	0.05 (0.686)	0.20 (0.111)	-0.07 (0.593)
FA, Fatigue	-0.02 (0.879)	0.03 (0.859)	0.02 (0.915)	-0.01 (0.941)
NV, Nausea/vomiting	0.12 (0.341)	0.24 (0.053)	0.17 (0.176)	-0.23 (0.062)
PA, Pain	0.13 (0.306)	0.20 (0.105)	0.15 (0.238)	-0.20 (0.112)
DY, Dyspnea	0.03 (0.812)	0.06 (0.666)	-0.03 (0.812)	-0.06 (0.667)
SL, Insomnia	-0.11 (0.393)	-0.11 (0.394)	-0.11 (0.406)	0.11 (0.398)
AP, Appetite loss	0.09 (0.470)	0.22 (0.084)	0.23 (0.071)	-0.23 (0.072)
CO, Constipation	0.15 (0.247)	0.17 (0.183)	0.02 (0.892)	-0.16 (0.199)
DI, Diarrhea	0.16 (0.220)	0.04 (0.759)	0.10 (0.423)	-0.04 (0.756)
FI, Financial problems	**0.04 (0.008)**	0.01 (0.989)	-0.08 (0.549)	0.01 (0.995)
BRBI, Body image	-0.01 (0.947)	-0.05 (0.691)	-0.01 (0.952)	0.04 (0.749)
BRSEF, Sexual functioning	-0.08 (0.602)	-0.20 (0.137)	**-0.36 (0.007)**	0.21 (0.132)
BRSEE, Sexual enjoyment	-0.18 (0.388)	-0.17 (0.430)	-0.38 (0.065)	0.18 (0.411)
BRFU, Future perspective	0.01 (0.955)	-0.01 (0.983)	0.07 (0.601)	0.02 (0.908)
BRCT, Systemic therapy	0.02 (0.893)	0.06 (0.649)	0.05 (0.731)	-0.05 (0.700)
BRRT, Breast symptoms	0.24 (0.058)	0.23 (0.072)	0.23 (0.068)	-0.22 (0.076)
BRSY, Arm symptoms	0.17 (0.177)	0.18 (0.170)	0.14 (0.278)	-0.18 (0.147)
BRHL, Hair loss	-0.09 (0.486)	-0.05 (0.727)	-0.11 (0.426)	0.03 (0.848)

Statistically significant results are bold.

Table 4. Correlation of body composition variables with subdomains of QLQ-C30 and QLQ-B23 questionnaires – third measurement

	Body mass index	Body fat percentage	Visceral fat index	Skeletal muscle percentage
QL2, Global health status	-0.17 (0.188)	-0.10 (0.458)	-0.15 (0.262)	0.10 (0.472)
PF, Physical function	-0.09 (0.488)	-0.04 (0.761)	-0.20 (0.113)	0.04 (0.769)
RF2, Role function	-0.05 (0.690)	0.02 (0.912)	-0.02 (0.932)	-0.02 (0.890)
EF, Emotional function	-0.01 (0.976)	-0.05 (0.711)	0.02 (0.906)	0.05 (0.722)
CF, Cognitive function	0.01 (0.946)	-0.06 (0.673)	-0.08 (0.570)	0.06 (0.680)
SF, Social function	0.13 (0.322)	0.02 (0.901)	0.13 (0.309)	-0.02 (0.885)
FA, Fatigue	-0.09 (0.514)	-0.15 (0.241)	-0.08 (0.562)	0.15 (0.235)
NV, Nausea/vomiting	0.18 (0.158)	0.23 (0.077)	0.17 (0.178)	-0.22 (0.081)
PA, Pain	-0.01 (0.938)	0.03 (0.838)	0.02 (0.882)	-0.03 (0.849)
DY, Dyspnea	-0.16 (0.208)	-0.18 (0.162)	-0.12 (0.373)	0.18 (0.157)
SL, Insomnia	0.01 (0.986)	-0.08 (0.525)	-0.09 (0.506)	0.09 (0.524)
AP, Appetite loss	0.18 (0.158)	0.11 (0.396)	0.25 (0.047)	-0.11 (0.413)
CO, Constipation	0.08 (0.569)	0.12 (0.363)	0.01 (0.995)	-0.12 (0.366)
DI, Diarrhea	0.10 (0.475)	0.09 (0.495)	0.13 (0.329)	-0.09 (0.504)
FI, Financial problems	-0.23 (0.077)	-0.19 (0.159)	-0.29 (0.024)	0.19 (0.155)
BRBI, Body image	-0.03 (0.857)	-0.15 (0.252)	-0.02 (0.903)	0.15 (0.252)
BRSEF, Sexual functioning	-0.01 (0.954)	-0.15 (0.296)	**-0.28 (0.040)**	0.15 (0.305)
BRSEE, Sexual enjoyment	-0.32 (0.138)	-0.26 (0.244)	-0.37 (0.086)	0.26 (0.244)
BRFU, Future perspective	0.02 (0.921)	-0.01 (0.971)	0.03 (0.849)	0.01 (0.970)
BRCT, Systemic therapy	0.10 (0.445)	0.10 (0.434)	0.17 (0.199)	-0.10 (0.440)
BRRT, Breast symptoms	0.09 (0.518)	0.17 (0.184)	0.14 (0.287)	-0.17 (0.185)
BRSY, Arm symptoms	-0.03 (0.819)	-0.05 (0.715)	-0.06 (0.641)	0.05 (0.712)
BRHL, Hair loss	0.04 (0.798)	0.07 (0.603)	0.01 (0.981)	-0.07 (0.608)

Statistically significant results are bold.

Table 5. Correlation of body composition variables with subdomains of QLQ-C30 and QLQ-B23 questionnaires – fourth measurement

	Body mass index	Body fat percentage	Visceral fat index	Skeletal muscle percentage
QL2, Global health status	-0.14 (0.291)	0.02 (0.924)	-0.17 (0.214)	0.02 (0.934)
PF, Physical function	0.16 (0.235)	**0.31 (0.018)**	0.07 (0.608)	-0.28 (0.034)
RF2, Role function	0.11 (0.440)	0.12 (0.389)	0.09 (0.504)	-0.11 (0.435)
EF, Emotional function	0.11 (0.423)	0.12 (0.398)	0.15 (0.275)	-0.11 (0.444)
CF, Cognitive function	0.04 (0.804)	0.05 (0.727)	0.04 (0.778)	-0.04 (0.773)
SF, Social function	0.19 (0.165)	0.18 (0.188)	0.20 (0.153)	-0.18 (0.201)
FA, Fatigue	**-0.36 (0.005)**	**-0.46 (<0.001)**	**-0.34 (0.010)**	**0.44 (<0.001)**
NV, Nausea/vomiting	-0.04 (0.764)	-0.03 (0.876)	-0.04 (0.763)	0.02 (0.891)
PA, Pain	-0.10 (0.456)	-0.05 (0.726)	-0.05 (0.734)	0.04 (0.779)
DY, Dyspnea	-0.11 (0.435)	-0.21 (0.119)	-0.10 (0.479)	0.20 (0.139)
SL, Insomnia	0.07 (0.627)	-0.07 (0.642)	0.01 (0.999)	0.05 (0.759)
AP, Appetite loss	0.05 (0.715)	-0.07 (0.648)	0.20 (0.134)	0.06 (0.657)
CO, Constipation	0.04 (0.809)	0.12 (0.392)	0.07 (0.634)	-0.14 (0.304)
DI, Diarrhea	0.19 (0.156)	0.17 (0.227)	**0.27 (0.040)**	-0.20 (0.150)
FI, Financial problems	-0.12 (0.406)	-0.08 (0.602)	-0.22 (0.113)	0.08 (0.598)
BRBI, Body image	0.11 (0.424)	0.15 (0.277)	0.19 (0.178)	-0.13 (0.347)
BRSEF, Sexual functioning	-0.09 (0.552)	-0.13 (0.404)	-0.28 (0.051)	0.14 (0.339)
BRSEE, Sexual enjoyment	-0.22 (0.341)	-0.21 (0.354)	-0.41 (0.058)	0.22 (0.343)
BRFU, Future perspective	0.12 (0.414)	0.16 (0.243)	0.20 (0.154)	-0.16 (0.251)
BRCT, Systemic therapy	-0.16 (0.236)	-0.13 (0.333)	-0.08 (0.561)	0.11 (0.413)
BRRT, Breast symptoms	-0.06 (0.664)	-0.11 (0.415)	-0.06 (0.660)	0.09 (0.533)
BRSY, Arm symptoms	0.04 (0.799)	-0.05 (0.741)	0.03 (0.845)	0.02 (0.925)
BRHL, Hair loss	0.12 (0.410)	0.09 (0.535)	0.17 (0.262)	-0.09 (0.538)

Statistically significant results are bold.

Discussion

Analysis of the results of body composition measurements in correlation with QoL showed the impact of body composition on certain QoL subdomains during treatment. At the beginning of the study (first measurement), patients with higher body mass and increased visceral fat index showed worse physical performance than other patients; it was especially apparent on the last measurement (Table 5). This result was not related to the use and impact of systemic antineoplastic treatment, but suggested general physical condition of patients before treatment initiation and the potential impact of chemotherapy. The relationship between higher body mass/increased body fat and poorer physical functioning is well described in numerous studies[6-8].

Throughout the study, sexual functioning in patients with higher visceral fat index was significantly reduced. Changes in sexual functioning during treatment of malignant disease are caused by several factors, and in the context of the relationship between reduced sexual functioning and body composition, it can be assumed that patients with a higher percentage of fat have an additionally impaired image of their own body, and this has been shown to significantly affect sexual functioning and sexual desire[9,10]. Studies conducted on healthy subjects showed a clear correlation between increased body fat level and reduced sexual functioning[11,12].

Later in the study, we observed an interesting pattern (see Tables 2-5); patients with a higher percentage of body fat and visceral fat index were significantly more tired than patients who had a higher percentage of muscle mass. Greater muscle mass suggests more physical activity in patients before the diagnosis of the disease and onset of treatment, i.e., lifestyle habits that entail more movement or physical training. Fatigue in breast cancer patients is often associated with other symptoms such as menopausal symptoms, sleep disorders and pain[13-15]. However, physical activity levels were shown to be significantly associated with fatigue in breast cancer patients, so that patients who were physically inactive reported more fatigue as a side effect as opposed to active ones[16,17]. Based on this fact, several interventional studies were designed in which the impact of exercise on different QoL domains was studied, including fatigue, and the results showed a significant reduction in fatigue in the group of patients who exercised compared to those who did not[18,19]. We can assume that our patients, who were physically active before the diagnosis of the disease, kept a similar lifestyle to some extent after diagnosis of the disease, which was clearly reflected in the less reported fatigue in this group of patients.

This research had some limitations including unrandomized design, which could have led to significant deviation of the results, small sample size, and most importantly, individual characteristics of each patient which may significantly affect the studied parameters. The psychological profile of an individual patient, individual coping mechanisms, social status, marital status, and support within the family and social community, reproductive status, religious and spiritual beliefs play a significant role in the perception of the disease and treatment. Those parameters can indirectly but significantly affect changes in global QoL and its subdomains.

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Sažetak

UTJECAJ SASTAVA TIJELA NA KVALITETU ŽIVOTA PREMENOPAUZALNIH BOLESNICA S RANIM STADIJEM RAKA DOJKE TIJEKOM KEMOTERAPIJE

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Sastav tijela se počeo proučavati relativno nedavno u sklopu onkoloških ispitivanja u različitim vrstama tumora. Postoje brojne studije koje definiraju utjecaj nuspojava kemoterapije na kvalitetu života bolesnika oboljelih od raka dojke, međutim, malo je studija koje su analizirale utjecaj sastava tijela na kvalitetu života premenopauzalnih bolesnica tijekom citotoksičnog liječenja. Studija je provedena na uzorku premenopauzalnih bolesnica liječenih neoadjuvantnom ili adjuvantnom kemoterapijom po protokolu AC za rani stadij raka dojke u Dnevnoj bolnici Zavoda za internističku onkologiju Klinike za tumore u Zagrebu. U istraživanju je sudjelovalo 68 bolesnica, medijan dobi od 52,6 godina. Analiza upitnika kvalitete života i njihova povezanost sa sastavom tijela ukazali su na nekoliko zanimljivih rezultata. Na početku liječenja najizraženija je bila veza između sastava tijela i fizičkog i seksualnog funkcioniranja te gubitka kose, dok je u kasnijim ciklusima liječenja utjecaj na druge poddomene kvalitete života, osobito umor i proljev, bio više izražen. Zaključno, sastav tijela ima značajan utjecaj na određene poddomene kvalitete života u tijeku kemoterapijskog liječenja.

Ključne riječi: *Sastav tijela; Kvaliteta života; Rak dojke; Premenopauzalne žene; Kemoterapija*