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Associations of Nutritional Status, Oxidative Parameters and Quality of Life of Breast Cancer Patients Before, During and After Chemotherapy

Meme Kanseri Hastalarının Kemoterapi Öncesinde, Sırasında ve Sonrasında Beslenme Durumu, Oksidatif Parametreler ve Yaşam Kalitesi İlişkisi

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** This study was produced from the doctoral thesis named "Evaluation of Nutritional Status, Some Biochemical Parameters and Quality of Life in Breast Cancer Patients During Chemotherapy".*

ABSTRACT

Aim: *Monitoring the nutritional status of cancer patients is crucial. We aimed to assess the associations between nutritional status, oxidative parameters and quality of life before, during, and after chemotherapy (CT) in breast cancer patients.*

Material and Method: *Clinical, anthropometric, demographic, quality of life, laboratory (i.e., blood oxidative marker level) and dietary intake data of breast cancer patients who planned to have two cycles of CT were recorded. All collected data were compared between pre-CT, mid-CT, and post-CT time points.*

Results*: Fifty women who were diagnosed with breast cancer and would start CT treatment were included in the study. Post-CT body weight and BMI was significantly lower than the pre-CT values ($p<0.001$). They both turned back to pre-CT levels at the end of CT with a decrease in total daily caloric and macronutrient intake. Consumption of specific food groups such as milk or yogurt, cheese, eggs, and sugar significantly decreased compared to their pre-CT consumption levels ($p<0.001$, $p<0.001$, $p=0.017$, and $p=0,01$). Blood oxidative stress marker analysis revealed a significant reduction in GPx levels with CT ($p=0.007$). Analysis of the quality-of-life scores revealed that post-CT scores were significantly higher than the pre-CT scores while the life quality was lowest in the mid-CT period.*

Conclusion*: Breast cancer patients have a lower dietary intake during CT, which is associated with a lower intake of specific food groups. Adequate caloric intake and antioxidant intake should be recommended to these patients during CT via dietary counseling to maintain healthy anthropometric measures and oxidative hemostasis.*

Keywords*: Breast cancer, Chemotherapy, Nutritional status, Oxidative stress, Quality of life*

ÖZET

Amaç: *Meme kanserli hastalarda kemoterapi (KT) öncesi, sırası ve sonrasında beslenme durumu, oksidatif parametreler ve yaşam kalitesi arasındaki ilişkileri değerlendirilmesi amaçlandı.*

Gereç ve Yöntem: *KT planlanan meme kanserli hastaların klinik, antropometrik, demografik, yaşam kalitesi, kan oksidatif belirteç düzeyi ve diyet alım verileri kaydedildi. Toplanan tüm veriler, KT öncesi, KT ortası ve KT sonrası zaman noktaları arasında karşılaştırıldı.*

Bulgular: *Çalışmaya meme kanseri tanısı konan ve KT tedavisine başlanacak 50 kadın dahil edildi. KT sonrası vücut ağırlığı ve beden kütle indeksi, KT öncesi değerlerden anlamlı derecede düşüktü ($p<0,001$). Her ikisi de KT'nin sonunda toplam günlük kalori ve makro besin alımında bir düşüşle KT öncesi seviyelere döndüler. Belirli gıda gruplarının tüketimi, KT öncesi tüketim düzeylerine göre önemli ölçüde azaldı ($p<0,001$). Kan oksidatif stres belirteç analizi, KT ile glutatyon peroksidaz düzeylerinde önemli bir azalma olduğunu ortaya koydu ($p=0,007$). Yaşam kalitesi puanlarının analizi, KT sonrası puanların KT öncesi puanlardan anlamlı derecede yüksek olduğunu, KT ortasında ise en düşük olduğunu ortaya koydu.*

Sonuç: *Sağlıklı antropometrik ölçümler, oksidatif denge ve yaşam kalitesi sağlamak için bu hastalara KT sırasında diyet danışmanlığı yoluyla yeterli enerji alımı ve antioksidan alımı önerilmelidir.*

Anahtar Kelimeler: *Meme kanseri, Kemoterapi, Beslenme Durumu, Oksidatif stres, Yaşam kalitesi*

INTRODUCTION

Breast cancer is the most commonly encountered malignancy in women (Sung et al., 2021). It is a significant cause of morbidity and mortality. According to the World Health Organization (WHO), there were 2.3 million women diagnosed with breast cancer and 685000 deaths globally in 2020 (Sung et al., 2021). In Turkey, 24175 women were newly diagnosed with breast cancer in 2020, and this number is expected to double in 2025, making breast cancer a significant healthcare problem (WHO,2020).

Despite its relatively high incidence, the exact etiology of breast cancer is not known. However, many epidemiological risk factors have been associated with this disease's initiation and progression (Sun et al., 2017). The epidemiological studies revealed that multiple environmental, hormonal, anthropometric, and genetic factors participate in breast cancer development. Among these risk factors, dietary intake is crucially important as it is the best-known route of exposure to carcinogens and also the one that can be modified with counseling and patient education (Rojas & Stuckey, 2016; Sun et al., 2017). Furthermore, obesity, another healthcare problem related to diet, is known to increase breast cancer risk exponentially (Fortner, Katzke, Kühn, & Kaaks, 2016).

It is known that dietary intake and metabolism of specific nutrients may change in patients with breast cancer due to disease-related processes (Picon-Ruiz, Morata-Tarifa, Valle-Goffin, Friedman, & Slingerland, 2017). Besides, most of these patients are treated with chemotherapy (CT), which often causes nausea, vomiting, diarrhea, and appetite loss (Kaya & Pekcan, 2021). For this reason, the quality of life of (QoL) a person who cannot be fed regularly due to the intensity of nausea and vomiting during chemotherapy decreases. As a result, fatigue, weakness, and cachexia arise as they cannot get the nutrients they need to take (Neo, Fettes, Gao, Higginson, & Maddocks, 2017). These alterations in dietary intake may impact patient compliance, treatment success, and overall patient survival.

Additionally, dietary factors might be related to the generation of reactive oxygen species (ROS) and oxidative stress (De Cicco et al., 2019). Oxidative stress can result in cellular damage and mutations leading to breast cancer (De Cicco et al., 2019). Since breast cancer CT is associated with significant oxidative stress-related side effects due to damage of the cells of the untargeted tissues and organs such as bone marrow, skin, stomach, and bowels, it was suggested that increasing the daily intake of antioxidants through the diet may help alleviate these side effects (Fisusi & Akala, 2019). In addition, quality of life is an important outcome parameter in oncology patients (Lopes et al., 2018). This prospective study aimed to assess the anthropometric measures, dietary intake, oxidative stress, and QoL parameters and their relationships with each other before, during, and after CT in newly diagnosed breast cancer patients.

MATERIAL and METHOD

Research Type

This descriptive and cross-sectional study was conducted in Tekirdag Namik Kemal University Training and Research Hospital, Department of Medical Oncology between January 2018 and April 2019.

Study Population

The population of the study consists of all female patients who applied to the medical oncology department in one year, were diagnosed with breast cancer, and were started on chemotherapy. Assuming a standard deviation of ±10 in the study, the minimum sample size required to be taken with 80% power and 5% error was deemed sufficient to be formed with at least 44 people. Sample size calculations G*Power v. It was made in the 3.0.10 package program. Initially, 64 female patients aged 30-65 years diagnosed with breast cancer were included in the study. However, 14 patients were excluded from the study due to the reasons for discontinuing or refusing the treatment and continuing the treatment in another institution. Therefore, the study sample consisted of 50 patients aged 30-65 years, who were recently diagnosed with breast cancer, were scheduled for chemotherapy, and could be followed throughout the entire treatment.

Data Collection Tools

The relevant data were retrieved from patient folders, including pathology and radiological imaging reports. Eligible patients were recruited before the initiation of CT. Women who had mental disabilities, previous history of cancer, or chronic diseases were excluded. Additionally, women who were pregnant or lactating during the

study period were omitted. Written informed consent was obtained before participation in the study. Demographic data, education levels, and clinical data, including menopausal status, past medical history, and family history, were recorded for all study participants. Anthropometric data and dietary intake data of the study participants were collected, and their blood samples were obtained at three distinct time points; one day before initiation of CT (i.e., pre-CT), after the completion of the first three months of CT (mid-CT) and at the end of CT (post-CT).

Anthropometric Assessment: Height (cm), weight (kg), waist, and hip circumferences (cm) of the study participants were measured before, during, and after CT. Height and weight measurements were utilized to calculate the body mass index (BMI) (kg/m2). The waist-to-hip ratio (WHR) was calculated by simply dividing the waist circumference by the hip circumference.

Dietary Intake Assessment: Dietary intake was assessed at 3 study time points by a validated semi-quantitative food frequency questionnaire (Männistö, Virtanen, Mikkonen, & Pietinen, 1996). A nutritionist performed all questionnaires. Pictures and household utensils of different sizes (spoons, mugs, and plates) were shown to the participants to determine the amount of daily dietary intake in a standardized fashion, and the portion sizes and consumption frequencies were recorded. These amounts were then converted to grams and milliliters. Macronutrient intake was classified as carbohydrates, protein, fat, and fiber. Additionally, 16 subgroups were composed for more detailed analysis; milk-yogurt, cheese, red meat, chicken, fish, other delicatessen products, eggs, legumes, oilseed, bread, other grains, vegetables, fruits, vegetable oil, butter, and sugar. None of the breast cancer patients in this study received any dietary treatment or advice before or during the study period; however, they were all recommended to comply with routine healthy eating habits.

Biochemical Analysis: The blood samples were obtained from all patients one day before initiation of CT after completing the first three months of CT and at the end of CT. These samples were centrifuged at 5000 rpm for 5 minutes, and the sera were kept in -80 ˚C freezers until biochemical analysis.

Total antioxidant status (TAS), total oxidant status (TOS), glutathione peroxidase (GPx) and nitric oxide (NO) levels were analyzed. Commercially available ELISA assay kits were used (Sunred Biological Technology Co., Ltd, Shanghai, China, and Cusabio Technology LCC., US- Kit numbers CSB-E09496h, CSB-EL022399HU, CSB-E01N0092 and KTE60839 for TAS, TOS, GPx and NO, respectively) according to the manufacturer's protocol.

The QoL Measurements: The QoL of breast cancer patients in this study cohort was examined using the EORTC QoL Questionnaire (Guzelant et al., 2004; Lopes et al., 2018). This questionnaire consisted of 30 questions. These questions were divided into three main sections; general health score, functional score, and symptom-related score. The first 28 questions in the questionnaire were scaled in a Likert type. On the other hand, the last two questions included the general health score, and the patient was asked to mark a score between 1 and 7 for grading her status. Turkish adaptation of this questionnaire and its validity and reliability studies have been undertaken by Guzelant and colleagues (Guzelant et al., 2004).

Ethics Consideration

The study project was reviewed and approved by the Tekirdağ Namık Kemal University Non-Invasive Clinical Research Ethics Committee (Date: 07.08.2017 and No: 2017/68/07/03).

Data Analysis

Statistical analyses were carried out using the Statistical Package for Social Sciences software (SPSS 17.0, IBM Corporation, Armonk, NY, USA). Shapiro-Wilk test was performed to determine whether the data were normally distributed. The sample size was calculated with G*Power by examining similar studies (De Vries et al., 2017, Nwozo, Solomon, Abimbola, Kikelomo, 2013). Descriptive statistics were given as means and standard deviations or medians of continuous numeric variables, while categorical variables were given as numbers and percentages. Whether there was a statistically significant difference among the pre-CT, mid-CT, and post-CT parameters, including patient weight, BMI, and hip circumference were evaluated by multivariate analysis of variance (i.e., Wilks Lambda test). A p-level of less than 0.05 was considered statistically significant. If the Wilks Lambda test results were significant; the follow-up times that caused the difference was determined by the Bonferroni corrected multiple-

comparison test.

Relationships with anthropometric measurements such as waist circumference and WHR, CT phase, oxidative parameters, macronutrients and foods were examined using the Friedman test. The Bonferroni test was used for further analysis when the Friedman test showed a significant difference. The correlation between anthropometric measurements and oxidative stress indicators was investigated using Spearman's rank correlation test. Bonferroni correction was performed to control the type 1 error in the correlation analysis. A p-value of less than 0.0167 was regarded as statistically significant.

RESULTS

Table 1. Demographic and Clinical Characteristics of the Study Group

Characteristics Groups		Number of Patients	Percentage
Age (years)			
	30-39	5	10
	40-49	23	46
	50-59	15	30
	60-69	7	14
Age (years) X ± SD	**50.1 ± 8.5 years**		
Education Level			
	Low	36	72
	Medium	9	18
	High	5	10
Smoking Status			
	Current	2	4
	Former	21	42
	Never	27	54
Family History of Breast Cancer			
	Yes	16	32
	No	34	68
Menstrual Status			
	Premenopausal	19	38
	Postmenopausal	31	62
Number of Children			
	No Children	4	8
	1 Child	10	20
	2 Children	29	58
	≥3 Children	7	14

Patient Characteristics

The baseline characteristics of the study patients (n=50) are displayed in Table 1. The mean age was 50.1 ± 8.5 years. Most patients (n=36; 72%) received primary school education only, while 9 (18%) received secondary school education. Two patients (4%) were current smokers, 21 (42%) were ex-smokers, and 27 (54%) had never smoked. Sixty-eight percent of patients had no family member with breast cancer, whereas 32% had at least one family member diagnosed with breast cancer. Overall, 38% of the study participants were classified as premenopausal, and 62% were categorized as postmenopausal. The mean number of childbirths was 1.8 in the entire cohort. Most of the study patients (58%) had two children at the time of diagnosis.

Anthropometric Assessment

The mean pre-CT weight of the study patients was 68.94 ± 12.63 kg (Table 2). The mid-CT and post-CT weight measurements were 67.48 ± 12.22 and 68.76 ± 12.75 kg. During the first cycle of CT, there was a mean reduction of 1.46 kg of body weight. Statistical analysis revealed that the mean pre-CT body weight was significantly higher than the mean mid-CT body weight ($p<0.001$). On the other hand, an increase was detected in the mean body weight during the second cycle of CT. It was found that the mean post-CT body weight was significantly higher than the mean mid-CT values ($p<0.001$). Nevertheless, there was not any significant difference between the mean pre-CT and post-CT body weights of our study patients ($p>0.999$). The mean pre-CT BMI was 27.64 ± 4.97 kg/m2 in the entire cohort. Thirty-four percent of the patients were overweight, and 36% were obese as per baseline measurements. The mean mid-CT BMI was significantly lower than the pre-CT value ($p<0.001$). The BMI levels turned back to the pre-CT values at the end of CT ($p>0.999$). Analysis of anthropometric measures revealed that the patients' mean hip circumference decreased 1.9 cm during the first cycle of CT and the difference between mean pre-CT and mid-CT hip circumferences were statistically significant ($p<0.001$). Mean hip circumference increased by 1.5 cm during the second cycle of CT, and the difference between mean mid-CT and post-CT hip circumference values was also statistically significant ($p<0.001$). There was no significant difference between the pre-CT and post-CT hip circumference measurements ($p>0.999$). Waist circumference showed significant differences between the pre-CT (93.42 ± 13.64 cm) and mid-CT (92.54 ± 13.23 cm) and also between mid-CT and post-CT (93.44 ± 13.92 cm) measurements ($p=0.013$, $p=0.049$). Nevertheless, there was not any significant difference between the pre-CT and post-CT values ($p>0.05$). As such, there was no

statistically significant difference in WHRs ($p>0.05$).

Table 2. Pre-CT, Mid-CT and Post-CT Anthropometric Measurements of the Study Patients

Anthropometric Measures	Pre-CT	Mid- CT	End- CT	*P-value*	*P¹*	*P²*	*P³*
Body Weight (kg)	68.94 ± 12.63	67.48 ± 12.22	68.76 ± 12.75	< 0.001*	< 0.001	> 0.999	< 0.001
BMI (kg/m^2)	27.64 ± 4.97	27.04 ± 4.79	27.55 ± 4.94	< 0.001*	< 0.001	> 0.999	< 0.001
Waist (cm)	93.42 ± 13.64	92.54 ± 13.23	93.44 ± 13.92	0.004**	0.013	> 0.999	0.049
Hip (cm)	106.8 ± 10.44	104.90 ± 9.86	106.04 ± 9.92	< 0.001*	< 0.001	> 0.999	< 0.001
Wais- to-Hip Ratio	0.88 ± 0.09	0.88 ± 0.09	0.88 ± 0.09	0.607**	-	-	-

CT: Chemotherapy
* Analysis of variance in repeated measures, Wilks' Lambda test
** Friedman test
P¹ Comparisons between chemotherapy onset and mid-chemo
P² Comparisons between the start of chemotherapy and the end of chemotherapy
P³ Comparisons between mid-chemotherapy and end of chemotherapy

Table 3. Dietary Intake of the Study Patients Immediately Before, During and After CT

Macronutrient and Food Groups	Pre-CT	Mid-CT	End-CT	*P-value**	*Multiple comparisons***		
					P¹	*P²*	*P³*
Energy (kcal)	2011 ± 232.9	1648.3 ± 163.6	2034 ± 224.1	< 0.001	< 0.001	> 0.999	< 0.001
Carbohydrates (g)	237.7 ± 39.8	181.9 ± 32.4	241.7 ± 38.6	< 0.001	< 0.001	> 0.999	< 0.001
Carbohydrates (%)	47.1 ± 7.6	43.2 ± 6.3	47.5 ± 6.1	< 0.001	0.003	> 0.999	< 0.001
Protein (g)	77.7 ± 16.5	63.8 ± 11.7	74.9 ± 11.2	< 0.001	< 0.001	> 0.999	< 0.001
Protein (%)	15.8 ± 3.1	15.8 ± 2.6	15.1 ± 2.3	0.113	-	-	-
Fat (g)	93.9 ± 23.7	80.5 ± 14.3	96 ± 21.3	< 0.001	< 0.001	> 0.999	< 0.001
Fat (%)	45.9 ± 8.4	43.9 ± 6.5	42.5 ± 7.3	0.003	0.013	> 0.999	0.021
Fiber (g)	27.0 ± 9.4	21.6 ± 6.3	26.3 ± 6.9	< 0.001	< 0.001	> 0.999	< 0.001
Milk yogurt (g)	307.08 ± 168.12	234.03 ± 99.79	261.72 ± 100.1	< 0.001	0.043	0.750	0.581
Cheese (g)	47.68 ± 13.18	37.68 ± 19.63	42.08 ± 18.04	< 0.001	< 0.001	0.038	0.044
Red meat (g)	51.14 ± 31.05	48.28 ± 29.69	50.42 ± 30.46	0.135	-	-	-
Chicken (g)	46.82 ± 31.23	41.94 ± 30.57	43.10 ± 30.28	0.156	-	-	-
Fish (g)	30.56 ± 26.12	22.54 ± 17.61	23.58 ± 18.41	0.022	0.042	0.094	0.340
Otr. delicatessen products (g)	5.28 ± 11.25	3.60 ± 7.21	4.04 ± 7.58	0.068	-		-
Eggs (g)	43.90 ± 18.10	39.14 ± 18.77	41.36 ± 17.92	0.017	0.016	0.421	0.277
Legumes (g)	31.50 ± 28.13	30.36 ± 26.79	31.94 ± 26.05	0.066	-	-	-
Oil seed (g)	29.84 ± 19.60	28.80 ± 19.80	25.86 ± 16.90	0.049	0.0502	0.044	0.135
Bread (g)	181.20 ± 82.59	168.0 ± 74.02	170.24 ± 68.44	0.076	-	-	-
Other grains (g)	61.64 ± 53.91	53.56 ± 29.68	56.12 ± 28.01	0.097	-	-	-
Vegetables (g)	252.56 ± 94.47	240.36 ± 81.27	241.06 ± 77.04	0.174	-	-	-
Fruits (g)	343.32 ± 167.67	335.50 ± 164.61	338.62 ± 139.82	0.368	-	-	-
Vegetable oil (g)	32.60 ± 18.59	29.96 ± 15.97	29.40 ± 15.28	0.067	-	-	-
Butter (g)	5.28 ± 4.59	4.78 ± 4.54	4.68 ± 4.48	0.152	-	-	-
Sugar (g)	32.16 ± 23.25	27.62 ± 21.25	26.30 ± 19.02	0.010	0.024	0.007	0.483

CT: Chemotherapy *Friedman test, ** Dunn-Bonferroni test.
P¹ Comparisons between chemotherapy onset and mid-chemotherapy,
P² Comparisons between the start of chemotherapy and the end of chemotherapy,
P³ Comparisons between mid-chemotherapy and end of chemotherapy

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Dietary Intake Assessment

At the study onset, mean energy and macronutrient intakes were recorded (Table 3). Mean pre-CT energy intake was 2011 ± 232.9 kcal/day with 237.7 ± 39.8 g/day of carbohydrates, 77.7 ± 23.7 g/day of fat, and 93.9 ± 23.7 g/day of fat consumption. On average, fiber constituted 27.0 ± 9.4 g/day in the pre-CT diet. Our analysis elucidated that the patients' mean energy intake was

significantly lower during the first cycle of CT compared with the pre-CT period ($p<0.001$). A significant decline in all macronutrient components and fiber contributed to this difference.

Interestingly, the decline in energy intake recovered during the second cycle of CT. The mean post-CT daily energy intake was calculated as 2030 ± 224.1 kcal/day. The increase in mean daily carbohydrate (241.7 ± 38.6 g/day) intake had a dominant role in this recovery. Although the amount of daily protein and fat intake increased during the second cycle of CT ($p<0.001$), the daily consumption percentage of protein did not change significantly ($p=0.113$).

Overall, among all three measurements, a significant change was detected in the consumption of milk, yogurt and cheese products when the intake of specific food subgroups was analyzed ($p<0.001$, $p<0.001$). The decrease in mean daily cheese intake was statistically significant when the pre-CT intake was compared with the mid-CT intake ($p<0.001$) (Table 3).

Daily cheese consumption was calculated as 47.68 ± 13.18, 37.68 ± 19.63, and 42.08 ± 18.04 g before, during, and after CT. According to multiple comparisons, the difference in daily cheese consumption was statistically significant when pre-CT, mid-CT, and post-CT levels were compared ($p<0.001$, $p=0.038$, $p=0.044$). Other food subgroups with significantly different consumption amounts between study time points were fish, eggs, oilseeds, and sugar ($p=0.022$, $p=0.017$, $p=0.049$, $p=0.010$). While pre-CT mean daily fish consumption was 30.56 ± 26.12 g, it decreased to 22.54 ± 17.61 g at the mid-CT time point ($p=0.022$). The amount of egg consumption also showed a statistically significant decrease between pre-CT (43.90 ± 18.1 g) and mid-CT (39.14 ± 18.77 g) time points ($p=0.017$). Our analysis also revealed a significant reduction in the mean daily consumption of oilseeds when pre-CT levels were compared with post-CT levels ($p=0.044$). Mean daily sugar consumption was calculated as 32.16 ± 23.25 g immediately before, 27.62 ± 21.25 g in the middle of, and 26.3 ± 19.02 g immediately after CT.

Biochemical Analysis

The pre-CT, mid-CT, and post-CT levels of oxidative stress markers are shown in Table 4. No statistically significant difference was detected in TAS, TOS, and NO levels when levels measured at different study time points were compared ($p>0.05$). The mean pre-CT GPx level was 23.13 ± 39.79 ng/mL, while mid-CT and post-CT levels were 19.62 ± 34.18 and 18.39 ± 33 ng/mL; comparative analysis revealed that the difference between these GPx levels was statistically significant ($p=0.007$).

A correlation analysis was implemented between the oxidative stress marker levels and anthropometric measurements (Table 5). A statistically significant and inverse correlation was found between body weight and TAS at the beginning of CT ($r=-0.384$, $p=0.006$). A statistically significant and inverse correlation was also found between TAS and hip circumference measurements ($r=-0.358$, $p=0.011$). A similar inverse correlation was found between pre-CT waist circumferences, WHRs, and GPx levels ($r=-0.386$, $p=0.006$ and $r=-0.374$, $p=0.007$). Another statistically significant and inverse correlation was detected between pre-CT waist circumferences and NO levels ($r=-0.365$, $p=0.009$). There was no significant correlation between other parameters and anthropometric measurements as per Bonferroni correction ($p>0.0167$).

The QoL Measurements

The pre-CT, mid-CT, and post-CT scores of QoL are shown in Table 6. The pre-CT, mid-CT, and post-CT functional health scores were 68.22 ± 15.53, 57.73 ± 10.26, and 78.49 ± 8.14. A statistically significant difference was detected between the pre-CT and post-CT scores ($p=0.002$). While the mean pre-CT symptom score was 34.26 ± 14.99, this score increased to 38.21 ± 14.72 in the mid-CT period; however, this increase was not statistically significant ($p> 0.05$). On the other hand, the mean symptom score decreased to 21.74 ± 10.51 in the post-CT assessment, and this difference was statistically significant ($p<0.001$). While the pre-CT general health status score was 61.83 ± 23.81, it increased to 43.50 ± 18.23 in the mid-CT and 80.83 ± 12.17 in the post-CT period. This change was statistically significant ($p<0.001$).

Table 4. Serum Oxidative Stress Parameter Levels of the Study Patients Immediately Before, During and Immediately After CT

CT: Chemotherapy, TAS: Total antioxidant status, TOS: Total oxidant status, GPx: Glutathione peroxidase, NO: Nitric oxide

Oxidative Stress Parameters	Pre-CT	Mid-CT	End-CT	*P-value**	*Multiple comparisons***		
					P¹	*P²*	*P³*
TAS(U/ml)	67.32 ± 43.27	68.58 ± 41.81	61.62 ± 42.98	0.095	-	-	-
TOS (U/mL)	3.48 ± 5.48	2.56 ± 3.53	2.28 ± 3.04	0.020	0.216	0.021	>0.999
GPx (ng/ml)	23.13 ± 39.79	19.62 ± 34.18	18.39 ± 33.62	0.007	> 0.999	0.010	0.043
NO (µmol/L)	91.55 ± 160.88	78.58 ± 131.85	65.89 ± 100.89	0.078	-	-	-

*Friedman test, ** Dunn-Bonferroni test.
P¹ Comparisons between chemotherapy onset and mid-chemotherapy,
P² Comparisons between the start of chemotherapy and the end of chemotherapy,
P³ Comparisons between mid-chemotherapy and end of chemotherapy

Table 5. Association of Anthropometric Measurements and Oxidative Stress Parameters at the Beginning of Chemotherapy

	Weight		BMI		Waist		Hip		Waist-to-Hip Ratio	
	r	*P**	*r*	*P**	*r*	*P**	*r*	*P**	*r*	*P**
TAS	-0.384	**0.006**	-0.215	0.134	-0.315	0.026	-0.358	**0.011**	-0.120	0.407
TOS	-0.373	**0.008**	-0.212	0.140	-0.347	**0.014**	-0.332	0.018	-0.174	0.226
GPx	-0.287	0.043	-0.187	0.192	-0.386	**0.006**	-0.221	0.123	-0.374	**0.007**
NO	-0.259	0.070	-0.182	0.207	-0.365	**0.009**	-0.281	0.048	-0.311	0.028

TAS: Total antioxidant status, TOS: Total oxidant status, GPx: Glutathione peroxidase, NO: Nitric oxide, BMI: Body mass index.
*Spearman correlation test (according to Bonferroni Correction, the results for p<0.0167 were considered statistically significant)

Table 6. Quality of Life Scores of the Study Patients Immediately Before, During and After CT

QoL scores	Pre-CT	Mid-CT	End-CT	*P-value**	*Multiple comparisons***		
					P¹	*P²*	*P³*
Functional score	68.2 ± 15.5	57.7 ± 10.3	78.5 ± 8.1	**<0.001**	**<0.001**	**0.002**	**<0.001**
Symptom score	34.3 ± 15.0	38.2 ± 14.7	21.7 ± 10.5	**<0.001**	>0.999	**<0.001**	**<0.001**
General health score	61.8 ± 23.8	43.5 ± 18.2	80.8 ± 12.2	**<0.001**	**0.004**	**<0.001**	**<0.001**

CT: Chemotherapy, QoL: Quality of life, *Friedman test, ** Dunn-Bonferroni test.
P¹ Comparisons between chemotherapy onset and mid-chemotherapy,
P² Comparisons between the start of chemotherapy and the end of chemotherapy,
P³ Comparisons between mid-chemotherapy and end of chemotherapy

DISCUSSION

Breast cancer is an extensive health problem, and its incidence increases yearly, especially in developing countries (Sung et al., 2021). Favorable outcomes can be achieved with early diagnosis and treatment based on current guidelines (Rojas & Stuckey, 2016; Sun et al., 2017; WHO). In line with this, the estimated 5-year survival rate was reported to be over 60%, much higher than other types of cancers (Maajani et al., 2019). Despite its high incidence, the exact etiology of breast cancer remains unknown. However, breast cancer is a multifactorial disease and genetic mutations and environmental factors contribute to its pathogenesis (Rojas & Stuckey,

2016; Sun et al., 2017). Some variables, such as weight, menopausal state, parity, smoking status, diet, and family history, were related to breast cancer risk. Among these parameters, weight and diet can be influenced by both the treatment (i.e., CT) and the disease itself (De Vries et al., 2017).

Considering this fact, we investigated the changes in dietary habits and anthropometric measures and their relationship with oxidative stress markers levels and quality of life in our study patients who were all treated by CT for breast cancer. It is important to note that oxidative processes are involved in the carcinogenesis of breast cancer and the mechanisms of action of breast cancer CT agents (Gorrini, Harris, & Mak, 2013).

Most women with breast cancer are treated with CT (Maughan, Lutterbie, & Ham, 2010). Treatment with cytotoxic chemotherapeutic drugs is usually associated with obnoxious symptoms, which may directly affect dietary intake and lead to food aversion, which may cause significant weight loss (Najafi et al., 2019). We observed significant weight loss during the first cycle of CT, which recovered during the second cycle. Overall, no significant weight change was recorded when the pre-CT and post-CT measurements were compared in our cohort. Contrarily, Rockenbach et al. reported a significant increase in the body weights and BMIs of 40 breast cancer patients who received CT (Rockenbach et al., 2011). However, Nwozo et al. reported no significant weight or BMI change during CT in their cohort of 30 breast cancer patients (Nwozo, Solomon, Abimbola, & Kikelomo, 2013).

The potential relationship between anthropometric measures and breast cancer risk has been studied extensively (Al-Ajmi, Lophatananon, Ollier, & Muir, 2018; Flanagan et al., 2018). In their population-based case-control study, which included 1233 breast cancer patients and 1241 controls, Friedenreich et al. found a significant correlation between WHR and breast cancer risk (Friedenreich, Courneya, & Bryant, 2002). Similarly, in the current study, more than half of the women before chemotherapy were observed to be slightly obese and obese. Also, this study showed a statistically significant and inverse correlation between body weight and pre-CT TAS. Additionally, another statistically significant and inverse correlation was found between TAS and hip circumference. They also denoted that pre-CT waist circumference and WHR measurements were inversely correlated with the pre-CT GPx and NO levels. These results imply a disruption in the antioxidant hemostasis with obesity and a high WHR, which plays an essential role in cancer pathogenesis. This finding may explain the increased risk of breast cancer in patients with a high WHR and central obesity. In this study, no significant changes were recorded in the patients' WHRs during CT cycles.

Although it would be reasonable to suggest that CT could affect breast cancer patients' daily dietary intake, inconsistent findings were reported in the literature. While some researchers showed that daily dietary intake significantly decreased during CT cycles, others reported no change or a significant increase in this parameter (De Cicco et al., 2019; Fabian, Kimler, & Hursting, 2015).

This variation can be ascribed to the difference in the methods used for measuring dietary intake. In our study cohort, body weight and BMI alterations were correlated with the patients' total caloric intake and macronutrient consumption. A significant decrease was recorded in total caloric intake during the first CT cycle while it turned back to the pretreatment levels in all macronutrient groups.

Since most studies focused on energy and macronutrient intake but not on food subgroups, it is unclear whether changes in dietary intake during CT were due to changes in the intake of specific food subgroups (Najafi et al., 2019; Rockenbach et al., 2011). De Vries et al. studied 117 newly diagnosed breast cancer patients and 88 controls to observe the impact of CT on the dietary intake of specific food subgroups. They stated that -during CT- breast cancer patients consumed significantly fewer legumes, pastry, meat, and cheese than women without cancer (De Vries et al., 2017). To these findings, our study demonstrated a significant reduction in daily milk-yogurt, egg, sugar, and cheese product intake in breast cancer patients during CT.

It is widely accepted that nutritional factors can be directly related to the generation of ROS, trigger oxidative stress, cause damage in DNA and consequently increase the risk of progression and recurrence in patients with breast cancer (Braakhuis, Campion, & Bishop, 2016). Oxidative stress further disrupts mitochondrial function, which results in more extensive ROS production in a pathological positive feedback loop. Interestingly, the mechanisms of action of some breast cancer CT agents are similar (Fisusi

& Akala, 2019). These agents induce cancer cell apoptosis by increasing the amount of ROS in these cells. Nevertheless, excess production of ROS can also damage healthy cells. Therefore, a diet rich in antioxidants is vital for reducing the risk of disease progression and recurrence (Braakhuis et al., 2016). Our study revealed that TAS declined during CT, but this decline was not statistically insignificant.

The reduction of GPx level was especially significant when pre-CT and post-CT levels were compared. Glutathione peroxidase is a selenoenzyme that catalyzes the reduction of various hydroperoxides and protects the cell from oxidative damage (Lubos, Loscalzo, & Handy, 2011). Its decline indicates that the anti-oxidative defense mechanisms are impaired.

Chemotherapy creates many physiological side effects such as pain, insomnia, nausea, loss of appetite, fatigue and hair loss (Lopes et al., 2018). In general, the quality of life of cancer patients is reduced by these side effects of chemotherapy. In this study, similar to other studies in the literature, it was found that the quality of life of the patients decreased during chemotherapy and that the quality of life increased after the treatment (Wang, Yin, & Jia, 2019). Nutritional counseling provided from the beginning of chemotherapy may have positive effects on quality of life, along with anthropometric measurements and oxidative parameters.

Limitations

This study has some weaknesses. First, our dataset did not include the physical activity levels of the study patients. Physical activity levels can affect weight, BMI, and the oxidative system. It is known that regular physical activity strengthens the antioxidant defense mechanisms. Second, the sample size was limited due to the long treatment period and some patients discontinuing the treatment for various reasons (such as discontinuation of treatment, death, or change in the treatment protocol). Finally, our results were based on the assumption that the information given by our study patients regarding their food consumption was reliable.

Despite these weaknesses, we conclude that increased oxidative stress and excessive ROS increase in the body during CT may impact the treatment response and long-term outcomes in breast cancer treatment. A balanced diet rich in antioxidant nutrients can positively affect breast cancer treatment's effectiveness and reduce the oxidative damage caused by cancer treatment. Patients must preserve their ideal weight during treatments. Thus, nutritional counseling should be given to breast cancer patients immediately after the CT is planned.

CONCLUSION

Consequently; the data obtained show that the nutritional status, anthropometric measurements, oxidative parameters and quality of life of breast cancer patients can change during the chemotherapy process and the relationships between these variables. It is possible to say that both adequate and balanced nutrition increases the quality of life during the chemotherapy period, and that the nutritional status of cancer patients with a higher quality of life during chemotherapy is better. Nutrition education to be provided for cancer patients before chemotherapy starts will increase their adaptation to new conditions against possible complications of treatment. Detailed information about dietary changes and nutritional status of patients undergoing chemotherapy can help modify recommended guidelines during chemotherapy. In addition to the literature, these data have the potential to contribute to future studies on adequate and balanced nutrition during and after the treatment of breast cancer.

Ethics Committe Approval
Ethics committee approval was received for this study from the Tekirdağ Namık Kemal University Non-Invasive Clinical Research Ethics Committee (Date: 07.08.2017 and No: 2017/68/07/03).
Author Contributions
Idea/Concept: A.S.K, A.A.M.; Design: A.S.K, T.Y.; Supervision/Consulting: A.A.M., T. Y., S.G.; Analysis and/or Interpretation: A.S.K., A.Y., S.G.; Literature Search: A.S.K, A.Y.; Writing the Article: A.S.K.; Critical Review: A.A.M, T.Y.
Peer-review
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Conflict of Interest
The authors have no conflict of interest to declare.
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