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The Effects of Individual Diet Therapy on Food Intake, Quality of Life, and Related Serum Proteins in Patients with Breast Cancer: A Randomized Clinical Trial

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ABSTRACT

Background: In cancer patients, weight loss due to malnutrition has a significant impact on the patients' treatment and quality of life. This study aimed to determine the appropriate therapeutic strategy to control the side effects of chemotherapy in patients with breast cancer to improve their health, quality of life, and nutritional status.

Methods: In our prospective study, we examined gastric cancer patients who were Seventy patients undergoing chemotherapy were included and randomly divided into intervention (n=35) and control groups (n=35). The intervention group received an individualized diet according to their nutritional needs for eight weeks, and the control group received dietary advice on the side effects of chemotherapy. Malnutrition, nutritional barriers, and patients' quality of life were evaluated by PG-SGA, nutritional barriers, and QLQ-C30 questionnaires. Serum proteins were also assessed at the beginning and the end of the study.

Results: The patients' mean age was 50.91±1.72 years in the intervention group and 51±1.35 in the control group. According to the PG-SGA questionnaire classification, 68.5% of patients had malnutrition at baseline. In the intervention group, the mean score of PG-SGA decreased, which indicated an improvement in patients' nutritional status. Increased scores in the functional section of QLQC30 and a decrease in the symptom section of this questionnaire indicated the improved quality of life in patients undergoing treatment at the end of the intervention. Albumin (P<0.001) and hemoglobin (P<0.001) levels increased in the intervention group, while there were no significant changes in these variables of the control group. Serum levels of ferritin did not show significant changes in either the intervention or the control group.

Conclusion: Identifying nutritional barriers in breast cancer patients and individual diet therapy based on these barriers and nutritional needs reduces nutritional barriers. Consequently, malnutrition would decline, and the quality of life may enhance in these patients.

Keywords: Breast Cancer, Diet Therapy, Malnutrition, Chemotherapy, Randomized Clinical Trial



INTRODUCTION:

Cancer is one of the leading causes of death worldwide. As a non-communicable disease, it is the second leading cause of death after cardiovascular disease (CVD) in developed countries (1). Breast cancer is responsible for 33% of all cancers in women and 20% of deaths from cancer. The incidence of breast cancer increases with age, although it decreases slightly after menopause (2). The low incidence of breast cancer in Asian women is attributed to their traditional lifestyle. However, rapid socioeconomic development and sociocultural changes, including fewer offspring, higher childbearing age, and shorter lactation, lead to changes in lifestyle and increased risk of breast cancer in Asia (3, 4).

Breast cancer treatments, including chemotherapy, have various side effects, leading to weakness, fatigue, increased nutritional needs, and reduced nutrient intake that may eventually lead to malnutrition (5). The prevalence of eating disorders depends on various factors, including the type of cancer and its treatment. For example, weight can be affected by edema, dehydration, tumor growth, type of cancer, social conditions of the patient, type of clinical complaint, food intake, and physical activity (6). In cancer patients, weight loss due to malnutrition is a common phenomenon that significantly impacts the treatment, follow-up, patient's survival, and quality of life. Malnutrition and protein deficiency can aggravate hair loss in patients (7). Weight loss of at least 5% compared to pre-disease weight has been reported in one-third of breast cancer patients. In addition to the impact of weight loss on increased mortality, malnutrition is associated with a prolonged hospital stay, increased risk of unplanned hospitalization, increased disability and increased overall care costs (8). As a result, using a standard nutritional assessment tool and a standard nutritional intervention approach is required to manage and prevent cancer-induced cachexia

in patients with cancer undergoing chemotherapy (9). In 2014, the American Institute for Cancer Research reported that diet, exercise, and weight management play a pivotal role in breast cancer patients' survival (10, 11). Findings from the Nurses' Health Study showed that a high-fat diet during adulthood was associated with an average increase in breast cancer risk in premenopausal women (12, 13). There is also evidence that high levels of fruit and vegetable consumption may be associated with a reduced risk of breast cancer (14). Obesity after menopause increases the risk of breast cancer (15, 16). The risk of postmenopausal breast cancer is 1.5 times higher in overweight women and about two times higher in obese women. The risk of breast cancer is probably related to increased estrogen levels because adipose tissue is the largest estrogen source in women after menopause. Obesity is also a risk factor for type 2 diabetes, which is associated with an increased risk of postmenopausal breast cancer (17, 18). Therefore, a proper diet before, during, and after treatment will help the patient feel better and survive longer.

There is evidence of using different dietary components on cancer patients' pain index, which is acclaimed by the McGill Pain Questionnaire. Khosravi et al. translated the questionnaire to Persian form and confirmed its validity and reliability (19).

The prevalence of cancer in the country is increasing, and cancer treatment consequences have a remarkable impact on the quality of patients' lives. There are almost no studies on the effect of proper individual diet on the consequences of chemotherapy in Iran. Thus, this study aimed to evaluate the effect of individual diet therapy on the consequences of chemotherapy and quality of life as well as serum proteins, including ferritin, albumin, and hemoglobin, in breast cancer patients.

METHODS:

Participants

Seventy breast cancer patients under chemotherapy

treatment were recruited from Motahari clinic, Shiraz, Iran. Subjects were randomly assigned into two groups (intervention for eight weeks or control) using random allocation software. Thirty-five patients per group were computed as necessary. The inclusion criteria were as follows: women with breast cancer, over 18 years, willing to participate in the study, stable, undergoing chemotherapy one to three times, not having any diseases such as CVD, diabetes, or neurodegenerative disease, not following particular treatment regimen and lack of metastatic breast cancer. All participants provided written informed consent before participation and procedure. The study was confirmed by the ethics committee of Shiraz University of Medical Sciences (ethics number: 94-01-84-10828).

Study Design

This study was an eight-week, double-blind, randomized, placebo-controlled clinical trial. The allocation was performed by a nutritionist with no clinical involvement in the study. All physicians and technicians remained blinded until the end of the analysis. Compliance was monitored through a weekly phone call.

Anthropometric measures

At the beginning and end of the trial, anthropometric indices were measured. After an overnight fast with subjects standing without shoes and wearing light clothing, body weight was measured to the nearest 0.1 kg, using Seca Electronic Weighing Scale (Seca, Hamburg, Germany). Height was recorded using a non-stretch tape measure (Seca, Hamburg, Germany) in a standing position without shoes to the nearest 0.1 cm accuracy. BMI was calculated by dividing weight (kg) by height squared (m²).

Dietary intake

Dietary intake was estimated using a 3-day 24-hour dietary recall at the baseline, midpoint, and endpoint of the trial and analyzed using Nutritionist 4 software (First Databank Inc., San Bruno, CA, USA), modified

for Iranian foods.

Intervention

Patients were given a specific diet that is calculated based on the amount of energy and protein requirement and the side effects of chemotherapy (diarrhea and constipation, nausea and vomiting, oral ulcers, anorexia, and changes in taste, early satiety, dry mouth, difficulty in chewing, and devouring food). The amount of energy and protein is based on a case study of cancer patients undergoing chemotherapy in Korea in 2015 (energy: 30-35 kcal/kg; and protein: 1.2-1.6 gr/kg). The calorie division of macronutrients in the basic regimens was also determined as follows: In 1600 calorie diet: 48.37 % carbohydrate, 20.12% protein, and 31.49 % fat. In 1800 calorie diet: 48.66 % carbohydrate, 20.55 % protein, and 30.79 % fat. In 2000 calorie diet: 51.3 % carbohydrate, 19.7 % protein, and 29 % fat. In this study, we attempted to reduce chemotherapy side effects through proper diet and provide recommendations for side effects. Also, pamphlets containing routine nutritional recommendations were given to the control group simultaneously as the intervention group.

Blood Sampling and Biochemical Measurements

Seven milliliters (7 ml) fasting blood samples were collected from all patients at the baseline and endpoint of the study, put into serum separation vacutainers, and allowed to clot for 10 minutes. Serum samples were collected using centrifugation at 3000 RPM for 10 minutes at room temperature, then were quickly frozen and stored at -80°C until analyzed. Albumin, ferritin, and hemoglobin were measured.

Nutritional barriers and the quality of life

The patients completed three questionnaires containing nutritional barriers, PG-SGA, and EORTC-QLQ-C30. The purpose of this study was to identify nutritional and malnutrition barriers and quality of life in patients, their relationship with food intake, and the consequences of chemotherapy. The Nutrition Barriers

Questionnaire consists of 17 questions, separately on each of the outcomes and nutritional barriers, including patient appetite, difficulty in chewing and swallowing food, heartburn, sore throat, nausea and vomiting, dry mouth, weakness, fatigue, changes in taste and smell, premature satiety, changes in weight, dietary hatred, depression, oral ulcers, diarrhea, and constipation. The questionnaire was completed through face-to-face interviews. Concerning nutritional barriers, the scoring for each barrier is qualitative and based on the severity of the complication.

The PG-SGA questionnaire consists of two parts: 1) Medical history, including weight changes, changes in dietary intake, the persistence of gastrointestinal symptoms for more than two weeks, and changes in functional capacity; and 2) Physical examinations, including the evaluation of subcutaneous fat gain due to musculoskeletal disorders such as knee edema and ascites. For each scoring section (0–4), scores were aggregated at the end of the part, depending on symptom levels and nutritional status. Scores above nine indicated nutritional intervention requirements.

The EORTC-QLQ-C30 Quality of Life Questionnaire consists of 30 questions consisting of two parts: Functional (Physical, Emotional, Cognitive, Social, Role Playing) and Symptoms (Fatigue, Nausea and Vomiting, Pain, Dyspnea, Sleep Reduction, Appetite Reduc-

tion, Constipation, diarrhea, and financial problems). Scoring in each part ranged from 0 to 100. Higher scores in the functional part indicated better status, while in the symptom part, higher scores indicating more problems in the patient.

Statistical Analyses

Data were analyzed using SPSS software version 17.0 (SPSS Inc., Chicago, IL, USA), and results are expressed as mean (±SD). The normality of data distribution was assessed by a one-sample Kolmogorov-Smirnov test. Baseline variables in the two groups were compared using an independent sample t-test for quantitative variables and a chi-square test for qualitative variables. Within-group differences were analyzed using a paired sample t-test. For identifying any differences between the two groups after the intervention, an analysis of covariance (ANCOVA) was used. Results were considered statistically significant at $p < 0.05$.

RESULTS:

The mean age in the control and intervention group was 51 ± 1.35 and 50.91 ± 1.72 , respectively. The anthropometric characteristics of patients are shown in **Table 1**. The mean weight was 65.67 ± 11.98 and 70.16 ± 15.91 in the control and the intervention group, respectively. There were no statistically significant differences between the groups regarding weight, height,

Table 1. Anthropometric indices of control and intervention groups at the baseline

Index	Intervention group (n=35) mean ±SD	Control group (n=35) mean ±SD	P-value*
Weight (kg)	67.65 ±11.98	70.16 ±15.91	0.45
Height (cm)	163.40 ±6.10	161 ±7.60	0.15
BMI	25.39 ±4.55	27.07 ±5.47	0.16

Table 2. Mean scores of the questionnaires at the beginning of the study

	Diet therapy group (n=35)	Control group (n=35)	P-value*
PG-SGA	19.34±4.81	16.94±5.93	0.06
Functional scale	55.26±10.50	61.10±14.03	0.53
Symptom scale	52.44±12.74	50.95±16.31	0.67
Global scale	46.64±13.44	50.21±14.64	0.29

*Independent sample T-Test, values less than 0.05 considered significant.

and BMI.

The variables were evaluated by an independent sample t-test.

According to the PG-SGA questionnaire classification, 68.5% of the patients had malnutrition at baseline. About the patients' appetite, 11 had a good appetite, 17 had a low or moderate appetite, and 42 had a poor appetite."in its latest global review

The scores obtained from the PG-SGA and QLQ30 questionnaires were compared between the groups at

the beginning of the intervention (**Table 2**).

As shown, the mean scores did not show a significant difference between the control group and the intervention group before the treatment.

Table 3 shows changes in the score of PG-SGA and QLQC30 questionnaires during the eight-week study in both groups under singular and control treatment diets.

As shown, scores of the QLQC30 and PG-SGA questionnaires in the treatment group showed a significant

Table 3. Comparison of mean changes in the scores obtained by the questionnaires

Variable	Group						P-value**	
	Diet therapy			Control				
	Before	After	P-value*	Before	After	P-value		
PG-SGA	0.10	17.91±4.88	16.94±5.93	<0.001	14.82±4.19	19.34±4.81	0.06	
QLQ-C30	Functional scale	0.02	58.28±12.01	61.10±14.03	<0.001	61.80±10.83	55.26±10.50	0.53
	Symptom scale	0.94	51.02±15.78	50.95±16.31	<0.001	42.82±11.04	52.44±12.74	0.67
	Global Scale	0.19	48.28±12.45	50.21±14.64	<0.001	60.21±11.27	46.64±13.44	0.29

*Paired T-Test **Independent sample T-Test, values less than 0.05 considered significant.

change during the eight-week intervention. Still, in the control group, only the QLQC30 scores showed a significant difference after eight weeks.

The comparison between the two groups indicated that the QLQC30 questionnaire had no significant difference at the end (Table 4). Although, the PG-SGA

questionnaire, the QLQC30 symptom, and the world-scale were significantly different. The comparison between the two groups indicated that the QLQC30 questionnaire had no significant difference at the end. However, the PG-SGA questionnaire, the QLQC30 symptom, and the world-scale were significantly dif-

Table 4. Nutrition barriers in the two groups at the beginning and end of the study

Variable		Group						P-value**
		Diet therapy			Control			
		Before	After	P-value*	Before	After	P-value	
Oral inflammation	Yes	23 (65.71)	6 (17.14)	<0.001	16 (45.71)	24 (68.57)	0.03	<0.001
	No	12 (34.28)	29 (82.85)		19 (54.28)	11 (31.42)		
Changes in the sense of taste and smell	Yes	31 (88.57)	13 (37.4)	<0.001	25 (71.42)	26 (74.28)	0.1	0.002
	No	4 (11.42)	22 (62.85)		10 (28.57)	9 (25.71)		
Depression	Yes	17 (48.57)	14 (40)	0.54	12 (34.28)	18 (51.42)	0.33	0.1
	No	18 (51.42)	21 (60)		23 (65.71)	17 (48.57)		
Diarrhea	Never	17 (48.57)	24 (68.57)	0.03	23 (65.71)	13 (37.4)	0.01	0.003
	Sometimes	6 (18.14)	10 (28.57)		7 (20)	14 (40)		
	Often	12 (34.28)	1 (1.75)		5 (14.28)	8 (22.85)		
Constipation	Never	19 (54.28)	27 (77.14)	<0.001	21 (60)	16 (45.71)	0.12	0.003
	Sometimes	8 (22.85)	8 (22.85)		5 (14.28)	13 (37.4)		
	Often	8 (22.85)	0 (0)		9 (25.71)	6 (17.14)		
Dysphagia	Never	11 (31.42)	17 (48.57)	0.007	18 (51.42)	15 (42.85)	0.12	0.56
	Sometimes	16 (45.71)	11 (31.42)		11 (31.42)	11 (31.42)		
	Often	8 (22.85)	7 (20)		6 (17.14)	9 (25.71)		

Table 4. Continue...

Variable		Group						P-value**
		Diet therapy			Control			
		Before	After	P-value*	Before	After	P-value	
Appetite	Never	4 (11.42)	5 (14.28)	<0.001	4 (11.42)	2 (5.71)	0.18	0.003
	Sometimes	9 (25.7)	24 (68.57)		9 (25.71)	15 (42.85)		
	Often	22 (62.85)	6 (17.14)		22 (62.85)	18 (51.24)		
Heartburn	Never	11 (31.42)	10 (28.57)	0.11	15 (42.85)	14 (40)	0.39	0.75
	Sometimes	15 (42.85)	21 (60)		11 (31.42)	14 (40)		
	Often	9 (25.71)	4 (11.42)		9 (25.71)	7 (20)		
Nausea	Never	4 (11.42)	8 (22.85)	<0.001	4 (11.42)	3 (8.57)	0.03	0.001
	Sometimes	7 (20)	26 (74.28)		9 (25.71)	19 (54.28)		
	Often	24 (68.57)	1 (1.75)		22 (62.85)	13 (37.4)		
Vomiting	Never	17 (48.57)	23 (65.71)	0.01	19 (54.28)	18 (51.42)	0.20	0.24
	Sometimes	13 (37.4)	11 (31.42)		12 (32.28)	16 (45.71)		
	Often	5 (14.28)	1 (1.75)		4 (11.42)	1 (1.75)		
Weakness and fatigue	Never	0 (0)	0 (0)	0.28	0 (0)	0 (0)	0.1	
	Sometimes	5 (14.28)	5 (14.28)		6 (17.14)	7 (20)		
	Often	30 (85.71)	30 (85.71)		29 (82.85)	28 (80)		
Dry mouth	Never	2 (5.71)	2 (5.71)	<0.001	1 (1.75)	4 (11.42)	0.07	0.79
	Sometimes	4 (11.42)	4 (11.42)		10 (28.57)	20 (57.14)		
	Often	29 (82.85)	29 (82.85)		24 (68.57)	11 (31.42)		
Early satiety	Never	11 (31.42)	15 (42.85)	0.28	8 (22.85)	10 (28.57)	0.31	0.39
	Sometimes	17 (48.57)	12 (34.28)		18 (51.42)	17 (48.57)		
	Often	7 (20)	8 (22.85)		9 (25.71)	8 (22.85)		

ferent.

Table 5 shows that the level of serum albumin and hemoglobin in the intervention group significantly decreased. In contrast, the ferritin level did not change significantly during the eight weeks. The comparison between the two groups showed a significant difference in all biochemical parameters except ferritin at the end of the study.

DISCUSSION:

The prevalence of breast cancer is increasing dramatically, and previous studies have shown that chemotherapy affects physical health and quality of life in breast cancer patients. According to previous studies, side effects of chemotherapy interfere with proper nutrition, increase malnutrition, reduce the quality of life, and increase mortality in these patients. In the present

study, we investigated the effects of an individual diet on chemotherapy outcomes and quality of life in breast cancer patients.

Some nutritional factors, including oral inflammation, changes in taste and smell, diarrhea, constipation, anorexia, nausea, weakness, fatigue, and dryness of mouth are the most prevalent side effects among patients and are considered influencing factors on patients' food intake. These are challenges to proper nutrition that, if left unaddressed, lead to malnutrition.

A similar study conducted in Iran in 2010 by Khushnesh et al. revealed that anorexia, dry mouth, nausea, and depression were major nutritional complaints that led to reduced food intake in cancer patients. This is similar to the data obtained from the present study. Important differences of our data with previous studies are the selection of patients with common cancers (gastro-

Table 5. Comparison of changes in biochemical parameters of study subjects between the two groups

Variable	Group						
	Intervention			Control			
	Before N=35 mean ±SD	After N=35 mean ±SD	P-value ^a	Before N=35 mean ±SD	After N=35 mean ±SD	P-value	P-value ^b
Alb (gr/dl)	4.06±0.23	4.14±0.24	0.001	4.18±0.35	4.12±0.30	0.45	0.014
Hb (gr/dl)	11.66±1.74	12.21±1.21	0.001	11.84±1.58	11.91±1.19	0.38	0.003
Ferritin (ng/ml)	126.29±229.25	122.72±218.04	0.30	69.36±56.11	72.62±55.59	0.26	0.19

P-values less than 0.05 are considered significant.

a. The variables were evaluated by paired sample t-test.

b. Changes in variables after the intervention were evaluated in both groups by an independent sample t-test.

intestinal, lung, blood, breast, genitourinary cancers) and patients with no specific type of cancer (20-22). Another similar study in the Netherlands in 1997 showed that nausea and vomiting were the most common side effects of nutritional chemotherapy (23). This study differs from the present study in the following points: This study used a self-reporting questionnaire to evaluate adverse events, divided them into two categories of physical and non-physical symptoms, and also examined the prevalence of complications by age and sex. In addition to our nutritional barriers questionnaire, other validated nutritional questionnaires such as PGA-SGA and QLQ-C30 were also used to assess patients' nutritional status and quality of life. This study showed that using an individual diet resulted in a significant reduction in symptoms and nutritional barriers. This study also showed that adherence to appropriate diet during chemotherapy leads to the preservation of patients' weight and prevention of malnutrition and improvement of their clinical status. Evidence has shown that anorexia and inadequate nutrition lead to malnutrition in patients and affect patients' quality of life, health status, and mortality.

A 2010 study by Gupta and Liz showed that improved nutrition over time is associated with better survival in patients with ovarian cancer (24). A critical component in assessing a patient's nutritional status is a detailed diet history and gathering information on patients' nutritional behaviors, which is crucial in identifying factors that may reduce a patient's nutrient intake (25, 26). Participants in the present study were also filled participation form at the beginning of the study. At the end of the eighth week, the Nutrition Barrier Questionnaire, Quality of Life, PG-SGA, and 24-hour recalls (baseline, end of the fourth week, and end of the eighth week) were completed. Based on previous studies, dietary interventions, including modified diets following the patients' side effects, improve the calorie increasing and protein intake (27).

It is well accepted that many malignancies are associated with a metabolic effect on the host. However, the level of metabolism affected by the vast differences in individual responses, cancer type, and the combination of treatments is challenging. A 1985 meta-analysis reported required calories in the absence of surgery or infection in cancer patients for maintenance of $1.15 \times$ BEE and storage and anabolism of $1.15 \times$ BEE (28). In patients with weight loss, calorie deficiency was also estimated at approximately 250–450 kcal per day with significant variations based on the disease's stage and severity (29-31). The protein needed to achieve a positive nitrogen balance for people with proper nutrition, mild stress is 0.8-1 g/kg IBW. In patients with mild to moderate reduction in protein with metabolic stress, the required protein is 1.5-2 g/kg IBW (32, 33). In the present study, energy and protein levels were considered 30-30 kcal/kg and 1.2-1.6 gr/kg, respectively, based on the results of recent studies performed on chemotherapy patients. Diets were also adjusted based on nutritional needs and nutritional barriers.

In the QLQ-C30 questionnaire, a higher score in the functional part indicates the patient's better status, and a higher score in the symptom section indicates more problems in patients. In the present study, after the individual diets, patients had higher scores in the functional part, a lower score in the symptom part, and an increase in the overall quality of life score, indicating an improvement in patients' status at the end of eight weeks. Patients with cancer due to chemotherapy problems have a lower quality of life than healthy individuals. Using the QLQ-C30, Jarmstad et al. compared the quality of life among five groups of people with various diseases (cancer, heart disease, physical illness such as arthritis, chronic diseases such as diabetes, and visual or hearing impairment) and a group of people with no health problems. The results showed that cancer patients scored lower in the functional part of the questionnaire in terms of cognitive, physical, social,

functional, and overall quality of life compared to the other groups (34, 35). If not diagnosed and not given proper nutritional support and anticancer therapies, it can lead to increased appetite, weight loss, muscle loss, impaired immune response, increased infections, bed wounds, and decreased quality of life (36). Nirenberg and Raynard also suggested that malnutrition may lead to increased risk of complications, decreased response and tolerance to treatment, poor quality of life, reduced survival, and higher health care costs (37, 38). One of the problems in assessing the prevalence of malnutrition is that there is no specific definition. Its prevalence can vary based on the index used. Body mass index (BMI) is one of the valid nutritional status measures with the highest correlation with fat in adults (39). However, the BMI of cancer patients with malnutrition may be in the normal or overweight range, with body fat making the lean mass reduction uncertain. Therefore, BMI is not a sensitive indicator of protein-energy malnutrition, as it does not differentiate between fat and muscle depletion (40). Another limiting factor in applying BMI is fluid retention, which leads to a false increase in body weight.

Otter's PG-SGA questionnaire is one of the ultimate tools for assessing nutritional status in cancer patients. The PG-SGA questionnaire is an easy-to-use nutritional assessment tool to identify and prioritize malnutrition in cancer patients (41, 42). In addition to measuring BMI, in this study, the PG-SGA questionnaire was used to assess patients' nutritional status and make a more accurate assessment of their nutritional status. In the PG-SGA questionnaire, patients are divided into three levels of optimal nutrition, mild to moderate malnutrition and severe malnutrition based on weight loss, dietary intake, and symptoms of nutritional complaints, performance, and physical examinations (9). Patients' PG-SGA scores decreased after the individual treatment regimen, indicating an improvement in the patients' nutritional status, which was not observed in

the control group, and PG-SGA scores were increased. Individuals with moderate malnutrition were 33 at the beginning of the study, which decreased to 15 after eight weeks of study.

Furthermore, the number of patients in optimal nutrition status increased from 22 to 53 at the end of the intervention. Also, 15 patients had severe malnutrition at the beginning of the study. At the end of the eight weeks, they achieved better nutritional status by maintaining weight, lowering nutritional barriers, and improving quality of life. At the end of the intervention, only two patients had severe malnutrition.

Studies have demonstrated that albumin is the best malnutrition predictor in various age groups and the most valid biochemical index applicable for protein status assessment. However, some believe that the long half-life of albumin (21 days) limits its effectiveness in monitoring fast-food changes and makes it a poor indicator of nutritional status (43, 44). It is worth noting that nutritional status and protein intake were significantly correlated with serum levels of liver protein, albumin. Studies have also shown that serum albumin levels are associated with morbidity and mortality. Therefore, it is a useful indicator in malignant patients. Serum protein provides indirect information about visceral protein levels, indicating less liver synthesis due to low intake (45). In this line, Marrine et al. reported a significant correlation between low serum albumin levels and low dietary protein intake in patients (46). Gaura et al. conducted a study in 2007 on 45 cancer patients and reported that a protein-containing diet increased serum hepatic proteins, indicating an increase in protein synthesis (47). In this regard, the present study showed that patients with 1.2-1.6 gr/kg protein in diet had higher serum albumin levels than the control group at the end of eight weeks, indicating the importance of dietary protein intake on albumin. Albumin is not only a nutrition marker but also carries medicines in these patients.

Another essential serum protein in cancer patients is ferritin, which acts as a buffer against iron deficiency and iron overload. In this regard, studies have shown that serum ferritin is abundant in tumor cells, and the increased expression levels can help to detect malignant tumors. Also, serum ferritin as a positive acute-phase protein is increased in some cases, including chronic diseases, inflammation, and malignancy. Findings indicate that ferritin expression is elevated in many malignancies, such as colon cancer, breast cancer, colorectal cancer, lung cancer, and prostate cancer (48). High serum ferritin levels in cancer patients depend on a multifactorial mechanism that includes growth and proliferation, increased necrosis, tumor cell lysis, ferritin release, and accumulation of ferric ions in reticuloendothelial cells, and consequently increased ferritin synthesis (49). One of the most common consequences of increasing iron in the body is promoting cancer cells because it is a strong oxidizer and mutagen, an inhibitor of white blood cells, and a nutrient for the rapid growth of cancer cells (50). However, the present study did not show any effect of individual diet on ferritin levels, which may be due to the nature of the disease itself on serum ferritin levels. Patients in this study were similar to those with low hemoglobin levels indicating anemia in these patients. In this regard, Kitano et al. study showed that most patients with cancer undergo anemia during treatment (51). As the present study showed, patients undergoing individual diet achieved normal hemoglobin levels at the end of eight weeks. Because many chemotherapeutic agents affect erythropoietin and may cause erythropoiesis, it may cause a high prevalence of anemia in these patients. Similarly, Barret lee et al. reported that cancer patients with low hemoglobin levels before starting treatment had a higher risk of developing anemia after chemotherapy (52).

This is the first study to evaluate individual diet therapy on breast cancer patients in Iran to the best of our

knowledge. However, there are some limitations such as small sample size, lack of inflammatory factors measurement, and lack of prolonged follow-up. Thus, it is suggested to consider these limitations in future studies. Also, it is suggested to evaluate the individual diet therapy effects on other cancers.

CONCLUSION:

The results of the present study showed that identifying nutritional barriers in patients with breast cancer and individual diets based on these barriers and also based on the patient's need for energy and protein reduced the nutritional barriers affecting dietary intake and, consequently, reduced malnutrition, increased quality of life in these patients.

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CONFLICT OF INTERESTS:

The authors declare that there is no conflict of interest associated with this work.

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REFERENCES:

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. *CA: a cancer journal for clinicians*. 2015;65(1):5-29.
2. DeSantis CE, Ma J, Goding Sauer A, Newman LA, Jemal A. Breast cancer statistics, 2017, racial disparity in mortality by state. *CA: a cancer journal for clinicians*. 2017;67(6):439-48.
3. Agarwal G, Pradeep P, Aggarwal V, Yip C-H, Cheung PS. Spectrum of breast cancer in Asian women. *World journal of surgery*. 2007;31(5):1031-40.
4. Yip C-H. Breast cancer in Asia. *Cancer Epidemiology: Springer*; 2009. p. 51-64.
5. Binkley JM, Harris SR, Levangie PK, Pearl M, Guglielmino J, Kraus V, et al. Patient perspectives on breast cancer treatment side effects and the prospective surveillance model for physical rehabilitation for women with breast cancer. *Cancer*. 2012;118(S8):2207-16.

6. O'Brien KM, Whelan DR, Sandler DP, Weinberg CR. Eating disorders and breast cancer. *Cancer Epidemiology and Prevention Biomarkers*. 2017;26(2):206-11.
7. Darga LL, Magnan M, Mood D, Hryniuk WM, DiLaura NM, Djuric Z, editors. Quality of life as a predictor of weight loss in obese, early-stage breast cancer survivors. *Oncology nursing forum*; 2007.
8. Bodai BI, Tusso P. Breast cancer survivorship: a comprehensive review of long-term medical issues and lifestyle recommendations. *The Permanente Journal*. 2015;19(2):48.
9. Ottery FD. Definition of standardized nutritional assessment and interventional pathways in oncology. *Nutrition*. 1996;12(1):S15-S9.
10. Adamsen L, Midtgaard J, Rorth M, Borregaard N, Andersen C, Quist M, et al. Feasibility, physical capacity, and health benefits of a multidimensional exercise program for cancer patients undergoing chemotherapy. *Supportive care in cancer*. 2003;11(11):707-16.
11. Abazari O, Divsalar A, Ghobadi R. Inhibitory effects of oxali-Platin as a chemotherapeutic drug on the function and structure of bovine liver catalase. *Journal of Biomolecular Structure and Dynamics*. 2020;38(2):609-15.
12. Linos E, Willett WC, Cho E, Frazier L. Adolescent diet in relation to breast cancer risk among premenopausal women. *Cancer Epidemiology and Prevention Biomarkers*. 2010;19(3):689-96.
13. Abbasi M, Asadi A, Musavi H. Association of Liver Aminotransferases with Lipid Profile in Patients with Type II Diabetes Mellitus. *Medical Laboratory Journal*. 2019;13(6):11-6.
14. Wu A, Yu M, Tseng C, Pike M. Epidemiology of soy exposures and breast cancer risk. *British journal of cancer*. 2008;98(1):9-14.
15. Fund WCR, Research AIfC. Food, nutrition, physical activity, and the prevention of cancer: a global perspective: Amer Inst for Cancer Research; 2007.
16. Abazari O, Divsalar A, Ghobadi R. Inhibitory effects of oxali-Platin as a chemotherapeutic drug on the function and structure of bovine liver catalase. *Journal of Biomolecular Structure and Dynamics*. 2019:1-7.
17. La Vecchia C, Giordano SH, Hortobagyi GN, Chabner B. Overweight, obesity, diabetes, and risk of breast cancer: interlocking pieces of the puzzle. *The oncologist*. 2011;16(6):726.
18. Abbasi M. Investigation of the lipid profile in patients with subclinical hypothyroidism. *Archives of Medical Laboratory Sciences*. 2017;3(4).
19. Khosravi M, Sadighi S, Moradi S, Zende del K. Translation, Adaptation and Reliability of Persian-McGill Pain Questionnaire (P-MPQ) in Iranian Cancer Patients. *Basic & Clinical Cancer Research*. 2014;6(3):12-7.
20. Khoshnevis N, Shahid Sales S, Alizadeh M, MirSadraei M, Akbari, Mohammad Esmail. Nutritional assessment of cancer patients by PG-SGA questionnaire in Cancer Research Center (CRC) of Shahid Beheshti University of Medical Sciences, Tehran, Iran, 2010. *Pejouhesh dar Pezeshki (Research in Medicine)*. 2012;36(3):132-8.
21. Abazari O, Shafaei Z, Divsalar A, Eslami-Moghadam M, Ghalandari B, Saboury AA. Probing the biological evaluations of a new designed Pt (II) complex using spectroscopic and theoretical approaches: Human hemoglobin as a target. *Journal of Biomolecular Structure and Dynamics*. 2016;34(5):1123-31.
22. Mirzaei A, Abbasi M, Sepehri S, Mirzaei M. The Effects of Allium porrum and Medicago sativa on Iron Concentration in Thalassemia Serums. *Life Science Journal*. 2013;10(11s).
23. de Boer-Dennert M, De Wit R, Schmitz P, Djontono J, v Beurden V, Stoter G, et al. Patient perceptions of the side-effects of chemotherapy: the influence of 5HT3 antagonists. *British journal of cancer*. 1997;76(8):1055-61.
24. Gupta D, Lis CG. Pretreatment serum albumin as a predictor of cancer survival: a systematic review of the epidemiological literature. *Nutrition journal*. 2010;9(1):69.
25. Laky B, Janda M, Bauer J, Vavra C, Cleghorn G, Obermair A. Malnutrition among gynaecological cancer patients. *European journal of clinical nutrition*. 2007;61(5):642-6.
26. Abazari O, Shafaei Z, Divsalar A, Eslami-Moghadam M, Ghalandari B, Saboury AA, et al. Interaction of the synthesized anticancer compound of the methyl-glycine 1, 10-phenanthroline platinum nitrate with human serum albumin and human hemoglobin proteins by spectroscopy methods and molecular docking. *Journal of the Iranian Chemical Society*. 2020:1-14.
27. Nadalin W, Waitzberg D. Nutritional intervention improves the caloric and proteic ingestion of head and neck cancer patients under radiotherapy. *Nutricion hospitalaria*. 2005;20(5):320-5.
28. Dempsey DT, Mullen JL. Macronutrient requirements in the malnourished cancer patient. How much of what and why? *Cancer*. 1985;55(S1):290-4.
29. Charney P. Nutrition screening vs nutrition assessment: how do they differ? *Nutrition in Clinical Practice*. 2008;23(4):366-72.
30. Bozzetti F. Nutritional assessment from the perspective of a clinician. *Journal of Parenteral and Enteral Nutrition*. 1987;11:115S-21S.
31. Abbasi M, Abazari OO. Probing the Biological evaluations of a new designed Palladium (II) complex using spectroscopic and theoretical approaches: Human Hemoglobin as a Target. *Archives of Medical Laboratory Sciences*. 2018;3(3).
32. Long CL, Schaffel N, Geiger JW, Schiller WR, Blakemore WS. Metabolic response to injury and illness: estimation of energy and protein needs from indirect calorimetry and nitrogen balance. *Journal of Parenteral and Enteral Nutrition*. 1979;3(6):452-6.

33. Abbasi M, Namjoo AR, Khamesipour F. Ethanol effects on histobiochemical parameters of suckling pups borned from alcoholic rat mothers. *Comparative Clinical Pathology*. 2016;25(4):833-9.
34. Hjermstad M, Fayers P, Bjordal K, Kaasa S. Using reference data on quality of life—the importance of adjusting for age and gender, exemplified by the EORTC QLQ-C30 (+ 3). *European Journal of Cancer*. 1998;34(9):1381-9.
35. Asadi A, Nezhad DY, Javazm AR, Khanicheragh P, Mashouri L, Shakeri F, et al. In vitro Effects of Curcumin on Transforming Growth Factor- β -mediated Non-Smad Signaling Pathway, Oxidative Stress, and Pro-inflammatory Cytokines Production with Human Vascular Smooth Muscle Cells. *Iranian Journal of Allergy, Asthma and Immunology*. 2019:1-10.
36. van Bokhorst-de van der Schueren MA. Nutritional support strategies for malnourished cancer patients. *European Journal of Oncology Nursing*. 2005;9:S74-S83.
37. Nitenberg G, Raynard B. Nutritional support of the cancer patient: issues and dilemmas. *Critical reviews in oncology/hematology*. 2000;34(3):137-68.
38. Abbasi M, Namjoo A. Low dose effects of ethanol on suckling rats: Enzymes activity, histological alterations and growth parameters. *Journal of Shahrekord Uuniversity of Medical Sciences*. 2013;15.
39. Mahan LK, Escott-Stump S. Krause's food, nutrition, & diet therapy: Saunders Philadelphia; 2004.
40. Gil KM, Frasure HE, Hopkins MP, Jenison EL, von Gruenigen VE. Body weight and composition changes in ovarian cancer patients during adjuvant chemotherapy. *Gynecologic oncology*. 2006;103(1):247-52.
41. Vincent I, De Vita J, Hellmann S, Rosenberg A. Principles and Practice of oncology. Lippincott, Williams and Wilkins; 2001.
42. Bauer J, Capra S. Comparison of a malnutrition screening tool with subjective global assessment in hospitalised patients with cancer—sensitivity and specificity. *Asia Pacific journal of clinical nutrition*. 2003;12(3).
43. Sun L-C, Chu K-S, Cheng S-C, Lu C-Y, Kuo C-H, Hsieh J-S, et al. Preoperative serum carcinoembryonic antigen, albumin and age are supplementary to UICC staging systems in predicting survival for colorectal cancer patients undergoing surgical treatment. 2009;9(1):288.
44. Shafaei Z, Abazari O, Divsalar A, Ghalandari B, Poursoleiman A, Saboury AA, et al. Effect of a Synthesized Amyl-Glycine1, 10-Phenanthroline Platinum Nitrate on Structure and Stability of Human Blood Carrier Protein, Albumin: Spectroscopic and Modeling Approaches. *Journal of fluorescence*. 2017;27(5):1829-38.
45. Fuhrman MP, Charney P, Mueller CMJJotADA. Hepatic proteins and nutrition assessment. 2004;104(8):1258-64.
46. Marín MC, Gómez CC, Castillo RR, Lourenço TN, García MH, Loria VK, et al. Nutritional risk evaluation and establishment of nutritional support in oncology patients according to the protocol of the Spanish Nutrition and Cancer Group. 2008;23(5):458-68.
47. Guerra LT, Rosa ARPd, Romani RF, Gurski RR, Schirmer CC, Kruel CDPJNhMV, no. 2 , p. 241-242. Serum transferrin and serum prealbumin as markers of response to nutritional support in patients with esophageal cancer. 2009.
48. Shi H-B, Li X-D, Jiang J-T, Zhao W-Q, Ji M, Wu C-PJJocr, et al. Serum ferritin is elevated in advanced non-small cell lung cancer patients and is associated with efficacy of platinum-based chemotherapy. 2014;10(3):681.
49. Lorenzi M, Lorenzi B, Vernillo RJIjobm. Serum ferritin in colorectal cancer patients and its prognostic evaluation. 2006;21(4):235-41.
50. Beckman L, Van Landeghem G, Sikstrom C, Wahlin A, Markevarn B, Hallmans G, et al. Interaction between haemochromatosis and transferrin receptor genes in different neoplastic disorders. 1999;20(7):1231-3.
51. Kitano T, Tada H, Nishimura T, Teramukai S, Kanai M, Nishimura T, et al. Prevalence and incidence of anemia in Japanese cancer patients receiving outpatient chemotherapy. 2007;86(1):37-41.
52. Ludwig H. Prevalence and incidence of anemia and risk factors for anemia in patients with cancer. *Recombinant Human Erythropoietin (rhEPO) in Clinical Oncology: Springer*; 2008. p. 189-206.