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REDUCED BODY MASS INDEX BUT NOT FAT MASS IN ANTHRACYCLINE-BASED CHEMOTHERAPY OF LOCALLY ADVANCED BREAST CANCER PATIENTS

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Abstract

Background: *Breast cancer is a cancer disease with the highest proportion of new cases and the proportion of deaths it causes is quite high at 6.9%. Cancer patients who use anthracycline-based chemotherapy experience loss of body weight, muscle, body cell mass, distribution of extracellular fluid expansion and reduced intracellular air. This study was to determine the change of the Body Mass index (BMI) and body composition of patients with locally advanced breast cancer (stage IIIA, IIIB and IIIC) who had undergone anthracycline-based chemotherapy.*
Methods: *This anthracycline-based observational analytical study of pre and post chemotherapy was conducted with a cross-sectional approach. Subjects were measured height by microtoise; weight, body composition, daily calorie intake (DCI) and basal metabolic rate (BMR) as measured by Bioelectrical Impendance Analysis (BIA).*
Results: *47 locally advanced breast cancer patients underwent anthracycline-based chemotherapy. Based on the Wilcoxon statistical test, 6 variables with a 95% confidence level ($p<0.05$) showed a decrease in the value 5 variables, namely BMI, total body water (TBW), visceral fat, skeletal muscle mass and skeletal bone mass. Meanwhile, body fat showed a p value=0.224. The changes of variable confounding, DCI decrease ($p=0.004$), but BMR increase not significantly ($p=0.795$).*
Conclusion: *There is an effect of chemotherapy on nutritional status of BMI, TBW, visceral fat, skeletal muscle mass and bone mass in patients with locally advanced breast cancer who underwent anthracycline-based chemotherapy, which may the result of the calorie intake decreased, but not on body fat.*
Keywords: *anthracycline-based chemotherapy, bioelectrical impedance analysis, BMI, body composition, daily calorie intake.*

Introduction

Breast cancer is the most common malignancy in women in developed countries and the second leading cause after cervical cancer in developing countries and constituted 29% of all cancers diagnosed each year. According to GLOBOCAN data in 2020, it is known that breast cancer is a cancer disease with the highest percentage of new cases, which is 11.7% and the percentage of deaths from breast cancer is 6.9%, noted that 16.7% of Indonesia's population, or as many as 58,256 people suffered from breast cancer.[1,2,3]

Breast cancer therapy can be classified into surgery, radiotherapy, and hormonal therapy. Chemotherapy is a treatment process using drugs that aims to destroy or slow the growth of cancer cells. Side effects vary

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depending on the drug regimen given. According to the National Cancer Institute, side effects of anthracycline-based chemotherapy include nausea, vomiting, diarrhea, stomatitis, alopecia, susceptibility to infection, thrombocytopenia, neuropathy, myalgia. Cancer patients do not experience overall weight loss but also loss of musce and body cell mass (BCM), and changes in fluid distribution with extracellular expansion and reduced intracellular air. Managing nutritional needs based solely on weight can be misleading, as it does not reflect body composition.[1,4,7]

The Bioelectrical Impedance Analysis (BIA) is an objective, easy-to-use, and technical tool that can be used to measure changes in body composition. This examination is quite easy and inexpensive to apply to patients undergoing outpatient or inpatient treatment. The purpose of this study is to analyse the effect of chemotherapy on body composition of locally advanced breast cancer patients who have undergone anthracycline-based chemotherapy.

Materials and Methods

This research is a cohort study of pre and post chemotherapy to determine changes in BMI and nutritional status. The subjects of the study were local advanced breast cancer patients who would undergo treatment in the form of anthracycline-based chemotherapy at the Polyclinic of Oncology Surgery, Dr. Hasan Sadikin Hospital Bandung between August 2021 to May 2022. The sample size of the study was set at a total of 47 patients, calculated using a sample size determination in health studies issued by WHO.

The inclusion criteria were: women at least 18 years old when they were first diagnosed; suffered from stage IIIA, IIIB, or IIIC breast cancer based on AJCC 2002 breast cancer staging criteria; underwent anthracycline-based chemotherapy (FAC regimen) used doxocorubicin 6 cycle doses of 60mg/LPT, cyclophosphamide doses of 600 mg/LPT, and 5 Fluoro Uracil doses of 600 mg/LPT for the first time at RSUP Dr. Hasan Sadikin Bandung; and willing to participate in the study. The exclusion criteria were subjects with a history or currently had cancer other than breast cancer in the last 5 years and subjects with Diabetes Mellitus, pregnancy and other chronic diseases.

Body composition assessment include body fat (BF), visceral fat, total body weight (TBW), skeletal muscle mass (SMM), skeletal bone mass (SBM), basal metabolic rate (BMR), and daily calorie intake (DCI) was collected by using Tanita BC-730. BMR and DCI assessed as variable confounding. Nutritional status assessed

by body mass index (BMI) according to WHO criteria.

The statistical analysis to determine the correlation of chemotherapy with nutritional status BMI and body composition used the Wilcoxon non-parametric with 95% confidence interval level. P value ≤0.05 is statistically significant or meaningful, and p value >0.05 is insignificant or statistically insignificant.

Research Results

Characteristic of 47 research subjects are presented in Table 1. The range age of the study was 26 until 79 years. The most stage obtained in this study was stage IIIC 57.4%. There was a preliminary examination obtained body weight with a median of 59 kg. This study also calculated the height in subjects with a Median of 155 cm. For the BMI results, the study obtained a median of 24.7 and a BMI range of 14.3 to 39.5. This showed that the mean BMI in the study subjects was overweight.

Table 1. Characteristic of Research Subjects

Variable	Amount (n=47)
Age (years)	
Mean	49.4
Median	48
Range (min-max)	26-79
Stages of breast cancer	
Stage III A	7 (14.9%)
Stage III B	13 (27.7%)
Stage III C	27 (57.4%)
Weight (kg)	
Mean	60.2
Median±Std	59 kg ±13.42
Range	30-96
Height (cm)	
Mean	155.1
Median±Std	155 cm ± 6.38
Range	136-170
BMI (kg/m^2)	
Mean	25.4
Median±Std	24.7 ± 4.91
Range	14.3-39.5

Notes: BMI=body mass index

Table 2. Changes of Body Mass Index, Total Body Weight, Body Fat, Skeletal Muscle Mass, Visceral Fat Level, Skeletal Bone Mass after Anthracycline Chemotherapy

Variable	Chemotherapy		P-value
	Before n=47	After n= 47	
Body Mass Index			
Median±Std	24,70±4,91	23,10±4,63	**< 0.01***
Range (min-max)	14.30-39,50	13,10-36,80	
Total Body Weight			
Median±Std	47,00%±8,00	45,00%±4,98	**< 0.01***
Range (min-max)	34.00%-73,00%	36,00%-54,00%	
Body Fat			
Median±Std	35,00%±7,86	34,00%±7,91	**0.224****
Range (min-max)	13,00%-53,00%	11,00%-49,00%	
Skeletal Muscle Mass			
Median±Std	60.07%±11.09	54.40%±9,72	**< 0.01***
Range (min-max)	30.06%-80,57%	21.12%-74,94%	
Visceral Fat Level			
Median±Std	7,00±2,53	6,00±2,30	**< 0.01***
Range (min-max)	1,00-14,50	2,00-13,00	
Skeletal Bone Mass			
Median±Std	2,00 kg±0,38	2,00 kg±0,35	**0.025***
Range (min-max)	0,90 kg-3,60 kg	0,90 kg-2,90 kg	

P value was tested using Wilcoxon test, *p≤ 0.01 means very significant, **p> 0.05 means insignificant

Changes of body mass index, total body weight, body fat, skeletal muscle mass, visceral fat level, skeletal bone mass after anthracycline chemotherapy presented in Table 2. Based on the results above, there were an effect of chemotherapy on BMI and body composition (TBW, body fat, visceral fat, skeletal muscle mass and skeletal bone mass) in locally advanced breast cancer patients undergoing anthracycline-based chemotherapy, except for body fat.

The changes of DCI and BMR as variable confounding after anthracycline chemotherapy presented in Table 3. There was a change in DCI after the administration of anthracycline chemotherapy, significantly (p=0.004). In contrast, there was increased of BMR but not statistically significant (p=0.795).

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Table 3. Changes of Daily Calorie Intake and Basal Metabolic Rate after Anthracycline Chemotherapy

Variable	Chemotherapy		P value
	Before N=47	After N= 47	
Daily Calorie Intake			
Median±Std	1,510kkal±399,8	1,235kkal±280,5	**< 0.01***
Range (min-max)	649kkal-2569kkal	878kkal-2178kkal	
Basal Metabolic Rate			
Median±Std	4,356±788	4,458±838,1	**0.795****
Range (min-max)	2714-6312	2567-6138	

P value was tested using Wilcoxon test, *p≤ 0.01 means very significant, **p> 0.05 means insignificant

Discussion

This study was conducted to determine the effect of anthracycline chemotherapy on nutritional status BMI and body composition. The results showed that there was an influence of anthracycline chemotherapy on body composition in several parameters. We measured several parameters of body composition such as total body water, skeletal muscle mass, skeletal mass, body fat and visceral fat level. Body composition assessed in our study subjects decreased statistically significantly compared to before getting anthracycline chemotherapy. This is in accordance with research conducted by Cotogni et al. which the nutritional status in cancer patients who received chemotherapy was decreases in total body water and body fat. Cotogni et al. said the main reason was because the toxicity of chemotherapy caused a decrease in appetite in people with chemotherapy.

Shachar et al. shows that cancer patients who were given chemotherapy such as anthracyclines and taxans would result in a decrease in body fat levels and a decrease in skeletal bone mass and skeletal muscle with no significant weight loss. Similar with our study, there was a decrease in the skeletal muscle mass and skeletal bone mass caused by the chemotherapy process. Justa et al. in 2019 stated that after chemotherapy, there was a decrease in lean mass body composition but an increase in fat period. Accordance with our study, body fat did not change significantly, but other body compositions decreased statistically significant. Taufik et al. stated that there were changes in body composition that could be calculated by BIA in chronic severe disease patients. There

was a decrease in body mass such as skeletal bone mass, skeletal muscle mass and also a decrease in total body water. This condition was caused by the burden of chronic severe diseases that resulted in an increase in metabolism that broke down energy stores in the body (skeletal bone mass, skeletal muscle mass), this might also appear in breast cancer patients.

Talima et al. showed changes of BMI in breast cancer patients who had been given chemotherapy in Egypt. In this study, one of the causes of weight loss was the toxicity of chemotherapy itself. Most of the studies suggest that there was an incidence of weight change in breast cancer patients. Most agreed that this was caused by the toxicity of chemotherapy which resulted in a decrease in appetite, a decrease in intake directly and the presence of an imbalance of the metabolism system in the body of a cancer survivor. Custodio et al. stated that chemotherapy would have an effect on impaired consumption of micro and macro nutrients which would result in disturbances in nutritional status.

The research conducted by Van De Berg et al., obtained different results from our study. Van De Berg et al. found that body composition improved during the chemotherapy period such as an increase in total body water, skeletal muscle mass and skeletal bone mass. This was likely due to the ability of chemotherapy drugs to retain fluids which resulted in an increase in body weight. The same thing was conveyed by Vivosky et al. which found that patients who received chemotherapy experienced an increase in body weight, some of the possible causes due to a decrease in physical activity in breast cancer patients with decrease in body metabolism which resulted in an increase in body weight.

In our study, variable confounding such as basal metabolic rate and daily calorie intake was also taken. The changes in body composition not only occurred due to anthracycline chemotherapy but also due to a decrease in daily calorie intake. Custodio et al. also stated that there was a decrease in calorie intake, and nutrition in the form of macro and micronutrients in patients who were carried out chemotherapy. This stated that the possibility of decreased appetite as the effect of toxicity and anthracycline was the caused a decrease in calorie intake, this is in line with our study. Basal metabolic rate did not change in our study which stated that there was no significant metabolic change to make BMR as a confounding variable. However, it turned out that our study showed a significant decrease BMI due to the administration of anthracycline chemotherapy.

In our study, the decrease in BMI was accompanied in detail with a decrease in body composition, except fat mass, whereas, BMI has been used to indicate obesity, or fat accumulation, so, the decrease in BMI is more due to the composition of fat-free mass, and not fat mass. BMI measurements cannot detect in detail changes in body composition.

Conclusion

There was an effect of chemotherapy on nutritional status of BMI and body composition (TBW, visceral fat level, skeletal muscle mass and skeletal bone mass) in patients with locally advanced breast cancer who underwent anthracycline-based chemotherapy, except for body fat.

Competing Interest

The authors declare that there are no competing interests related to the study.

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