ORIGINAL ARTICLE

Nutrition, Metabolism, and Prevention of NCDs

Nutritional Status, Muscle Mass, and Body Fat Percentage in Patients with Breast Cancer Undergoing Adjuvant Chemotherapy

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ABSTRACT

Aims: To evaluate alterations in weight, body composition, and nutritional parameters, and to identify the clinical, anthropometric, and dietary determinants of these changes among patients with breast cancer (BC) treated with adjuvant chemotherapy (AC).

Methods: This study involved a cohort of 252 BC patients treated with AC. Anthropometric measurements were collected using standardized equipment and body composition was evaluated via bioelectrical impedance analysis (BIA). Clinical data were retrieved from the hospital's information system. Adherence to the Mediterranean Diet (MedDiet) was evaluated using a validated food frequency questionnaire.

Results: Post-AC, 29.3% and 22.7% of patients experienced moderate/high weight gain (WG ≥ 5%) and moderate/severe weight loss (MSWL ≥ 5%), respectively. The prevalence of patients with low muscle mass (LMM) and sarcopenic obesity increased from 11.5% and 2.8% pre-treatment to 15.1% and 7.9% post-treatment, respectively. Younger women (aged 24 – 39 years) exhibited reduced odds of experiencing MSWL (OR = 0.31, 95%CI: 0.08 – 1.20) and LMM (OR = 0.19, 95%CI: 0.02 – 1.61) compared to those aged ≥ 60 years. Patients with BC stages I and II were associated with increased odds of WG (OR = 2.10, 95%CI: 0.44 – 9.89; and OR = 2.13, 95%CI: 0.46 – 9.68, respectively). Relative to obese individuals, normal-weight/underweight individuals exhibited a significantly higher likelihood of WG (OR = 2.29; 95%CI: 1.03 – 5.08) and MSWL (OR = 3.23, 95%CI: 1.19 – 8.80), but a lower likelihood of LMM (OR = 0.33, 95%CI: 0.13 – 0.87). The Anthracycline-Taxane and Monoclonal-antibodies-Taxane regimens were associated with higher odds of MSWL (OR = 3.64, 95%CI: 0.35 – 36.98, and OR = 2.63, 95%CI: 1.03 – 6.72, respectively). Low and moderate adherence to the MedDiet were independently associated with an elevated risk of both WG and MSWL.

Conclusions: A substantial proportion of patients with BC experience significant weight fluctuation or deterioration in muscle mass following AC. These adverse outcomes are modulated by patient age, cancer stage or duration, baseline BMI, the specific chemotherapy regimen employed, and MeDiet adherence.

Keywords: Adjuvant chemotherapy; Body composition; Body Mass Index; Breast cancer; Mediterranean diet; Weight change.

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1 INTRODUCTION

Breast cancer (BC) constitutes the most frequently diagnosed malignancy and remains the leading cause of cancer-related mortality among women worldwide (Bray *et al.,* 2018; Wilkinson *et al.,* 2022), accounting for approximately 2.26 million new cases and 685,000 reported deaths in 2020 (Wilkinson *et al.,* 2022; WHO, 2024b). Over the last two decades, several high-income countries have achieved substantial decline in annual BC mortality rates. However, the 40% reduction in breast cancer mortality observed in high-income countries since the 1980s has not yet been replicated across the majority of low- and middle-income countries (LMICs). This disparity is attributable to several factors, including delayed diagnosis, insufficient diagnostic and therapeutic infrastructure, and restricted healthcare access (WHO, 2024b).

In Morocco, a lower-middle-income country in North Africa, cancer ranks as the second leading cause of mortality (14%) after cardiovascular diseases (38%) (WHO, 2018). BC represents the most prevalent cancer type nationally, with 12,756 (20.1%) of all newly diagnosed cancers and 4,044 (10.9%) cancer-related deaths in 2022 (Bray *et al.,* 2024).

Therefore, the prevention and rigorous control of BC and its associated risk factors must be established as critical priorities within public health strategies in Morocco as well as in other LMICs.

Adjuvant chemotherapy is a cornerstone of BC treatment, playing a vital role in reducing the risk of recurrence and improving survival outcomes. Nevertheless, the systemic toxicity inherent to chemotherapy is frequently associated with deleterious changes in patient weight, body composition, nutritional status, and dietary intake (Custódio *et al.,* 2016; Pedersen *et al.,* 2017; Pedersini *et al.,* 2021; Van den Berg *et al.,* 2017). These physiological and behavioral shifts can affect treatment efficacy and quality of life, potentially escalating the predisposition to co-morbidities such as cardiovascular diseases and diabetes (De Kruif *et al.,* 2019; Godinho-Mota *et al.,* 2021; Ramos da Silva *et al.,* 2021; Ryan *et al.,* 2019). Thus, understanding the extent and nature of weight fluctuations, body composition alterations, and modifications in dietary habits induced by chemotherapy, is crucial for developing targeted public health interventions to optimize the overall care of BC patients during and following therapy.

The current study aimed to investigate, for the first time to the best of our knowledge, the changes in weight, nutritional status, body composition, and dietary habits and associated factors in Moroccan BC patients undergoing AC. By exploring these factors, we endeavor to provide healthcare researchers and professionals with the necessary evidence base to develop effective interventions that improve the clinical outcomes for BC patients, enhance the quality of life, and reduce the risk of secondary morbidities for BC patients.

2 Material and Methods

2.1 Study Design and Participants

This is a prospective observational study conducted at the Sidi Mohamed Ben Abdellah National Institute of Oncology (NIO), between March 2023 and June 2024. Patients with confirmed stages I to III breast cancer (BC) who attended the NIO's day hospital for adjuvant chemotherapy (AC) were invited to participate in the study. Exclusion criteria included patients (1) with metastatic BC, (2) who were not candidate for AC, (3) who did not provide a written informed consent, and (4) whose medical records on initial admission and post-chemotherapy were not available through the hospital inpatient system.

The minimum sample size (n) required for this study was calculated using the Cochran's formula (1977) (Cochran, 1977):

$$n = \frac{z^2 * p * (1 - p)}{m^2}$$

Where:

z = 1.96 (the confidence level according to the normal distribution for a 95% confidence interval).
p = 19.3% (the estimated proportion of patients who would experience weight gain (≥ 5%) after AC, assuming that BC patients are more likely to gain weight than lose it during AC (Van den Berg *et al.,* 2017) and using the average proportion of BC patients that gained weight in two previous studies conducted by (Mutschler *et al.*, 2018) (17.3%) and (Yang *et al.*, 2022) (21.3%).
m = 0.05 (the tolerated margin of error (5%).

Considering the health status of the target population, study duration, and expected response rate, we anticipated a 20% drop-out rate after completing all AC sessions. The final sample size was N = 290.

2.2 Data collection

2.3.1 Sociodemographic and Clinical Data

Data collection was performed at two key time points: at the patient's admission for the first AC session and again at the final AC session. The duration between these points varied (3, 6, or 8 months, depending on the regimen duration for each patient).

A standardized questionnaire was employed to collect sociodemographic information. Clinical data, including time elapsed since referral to the oncology center (in months), cancer stage, type and duration of chemotherapy were extracted from the hospital's medical records.

Patients' menopausal status was categorized based on age: those under 50 years old were classified as premenopausal, and those 50 years or older were classified as postmenopausal (Heideman *et al.*, 2009).

The administered chemotherapy regimens were categorized into three groups: 1) Anthracyclines based schedules combined with Taxane, 2) Monoclonal antibodies combined with Taxane, and 3) Alkylating agents. More details regarding the chemotherapy regimens are summarized in the supplementary material Supplement Table 1.

2.3.2 Anthropometric Assessment and Body Composition Analysis

Anthropometric measurements were performed employing standardized protocols and calibrated instrumentation. Body Mass Index (BMI) was calculated at the ration of body weight to the squared of height (kg/m²). Based on the WHO criteria, patients were classified into four categories: underweight (BMI < 18.5 kg/m²), normal weight (18.5 kg/m² ≤ BMI < 25.0 kg/m²), overweight (25.0 kg/m² ≤ BMI < 30.0 kg/m²), and obese (BMI ≥ 30.0 kg/m²) (WHO, 2024a).

Body composition was assessed using bioelectric impedance analysis (BIA) following standardized procedures with a multifrequency impedance analyzer (Nutriguard-MS, Germany) (Lukaski *et al.,* 1985). Measurements were performed while patients lay in a supine position, using four self-adhesive electrodes placed on the dorsal surfaces of the right hand and foot, as per the manufacturer's instructions. Previous studies utilizing BIA for body composition evaluation in cancer patients (Jager-Wittenaar *et al.,* 2014) estimated fat-free mass (FFM) using Geneva's equation, which relies on resistance (R50) and reactance (Xc50) values measured at a frequency of 50 kHz (Kyle *et al.,* 2001):

- $FFM\ (Kg) = -4.104 + (0.518 \times (height\ (cm))^2 / R50kHz) + (0.231 \times weight\ (kg)) + (0.130 \times Xc50kHz) + (4.229 \times sex\ [men = 1, women = 0])$ (a)

The following formulas were employed to determine fat mass (FM), body fat percentage (BF%), and fat-free mass index (FFMI):

- $FM\ (Kg) = Weight\ (Kg) - FFM\ (Kg)$ (b)
- $BF\% = (FM / Weight) \times 100$ (c)
- $FFMI = FFM/Height2$ (d)

Excess body fat levels were defined based on body fat percentage (BF%) thresholds for women (20-39 years: > 32%; 40-59 years: > 33%; 60-79 years: > 35%) (Gallagher *et al.,* 2000).

Nutritional parameters associated with AC among women were assessed using the GLIM (Global Leadership Initiative on Malnutrition) criteria: (1) low BMI: < 20 kg/m² for individuals under 70 years, or < 22 kg/m² for those over 70 years; (2) weight loss within the last 6 months (moderate malnutrition: > 5%; severe malnutrition: > 10%); (3) low muscle mass or low FFMI: < 15 kg/m². Individuals with both low muscle mass (Cederholm *et al.,* 2019) and excess body fat (Gallagher *et al.,* 2000) were classified as having sarcopenic obesity.

2.3.3 Dietary Habits

Adherence to the Mediterranean diet (MedDiet) was assessed using the KIDMED questionnaire (Serra-Majem *et al.,* 2003), which includes 16 items reflecting key principles of the MedDiet. Although initially validated in children and adolescents, this index has also been applied in adult and elderly populations (Couto *et al.,* 2011; Grosso *et al.,* 2017). Each positive dietary behavior is scored +1 and each negative behavior −1, yielding a total score ranging from −4 to 12. In this study, adherence was categorized as low (≤ 3), moderate (4 – 7), or high (≥ 8), in line with previous research.

2.3.4 Ethical Considerations

The study protocol adhered to the ethical principles outlined in the World Medical Association Declaration of Helsinki and was approved by the Biomedical Research Ethics Committee of the Faculty of Medicine and Pharmacy in Rabat (Certificate number: 99/22). We obtained written informed consent from all participants.

2.3.5 Statistical Analysis

Statistical analyses were conducted using the Statistical Package for Social Sciences (SPSS) version 22.0. The Kolmogorov-Smirnov test was applied to evaluate the normality of variables' distribution. Descriptive statistics are reported as mean (± standard deviation (SD)) for continuous variables that were normally distributed, and as proportions (95% confidence interval) for categorical variables. Comparisons between various groups were performed using the Student *t*-test (parametric) or Wilcoxon signed-rank test (non-parametric) for continuous variables and the Chi-square test or Kruskal-Wallis test for categorical variables. Binary logistic regression analysis was employed to examine the associations of weight gain, weight loss, and low muscle mass with age, education level, menopausal status, cancer stage, time since referral to oncology center (months), weight status, body fat level, chemotherapy type and duration, and adherence to the Mediterranean diet. A p-value < 0.05 was considered statistically significant.

3 Results

A total of 290 patients diagnosed with stages I-III BC who met the inclusion criteria were included in the study. At the end of June 2024, 38 (13.1%) patients were lost to follow-up. The final sample comprised 252 patients aged 52.25 ± 0.68 years. The majority (52.4%) of them were illiterate, 65.1% were overweight or obese, and 59.1% were post-menopausal. Most of patients (75.8%) were referred to the oncology center within the last 12 months, 81.3% had clinical stage I or II breast cancer, and 63.5% received Anthracycline with Taxane as their chemotherapy regimen (Table 1).

Table 2 presents variations in body weight and body composition measurements from the beginning to the end of AC. A significant increase was observed in weight, BMI, fat mass (FM), body fat percentage (BF%), and fat mass index (FMI), while fat-free mass (FFM), fat-free mass percentage (FFM%), and fat-free mass index (FFMI) significantly decreased ($p < 0.001$).

From baseline to the last session of AC, 20.6% and 8.7% of patients experienced moderate and high weight gain, respectively, while 17.9% and 4.8% of them presented moderate and severe weight loss, respectively. Over the same period, the proportion of patients with low BMI, low muscle mass, and sarcopenic obesity also increased from 7.1%, 11.5%, and 2.8% to 8.7%, 15.1% and 7.9%, respectively (Table 3).

Logistic regression analysis showed that younger patients (24 – 39 years) were less likely to experience weight gain, moderate/severe weight loss, and muscle mass reduction than those aged 60 years or older (OR = 0.57, 95%CI: 0.19 – 1.71; OR = 0.31, 95%CI: 0.08-1.20; and OR = 0.19, 95%CI: 0.02 – 1.61, respectively). Odds of weight gain were higher among women with stages I and II of the disease than those with stage III (OR = 2.10, 95%CI: 0.44-9.89; and OR = 2.13, 95%CI: 0.46 – 9.68, respectively).

Similarly, patients who were referred to the oncology center within the last 6 months or within 6 – 11 months prior to AC were less likely to experience moderate/severe weight loss compared to those referred earlier (OR = 0.29; 95% CI: 0.10 – 0.85 and OR = 0.40; 95% CI: 0.16 – 1.02, respectively). Compared to obese individuals, normal-weight/underweight and overweight individuals had increased likelihood of weight gain (OR = 2.29; 95%CI: 1.03 – 5.08, and OR = 1.36, 95%CI: 0.65 – 2.87, respectively) and moderate/severe weight loss (OR: 3.23; 95%CI: 1.19 – 8.80, and OR = 2.63, 95%CI: 1.03 – 6.72, respectively). Patients treated with Anthracycline based regimen with Taxane and Monoclonal antibodies with Taxane were more than twice as likely to experience moderate/severe weight loss than those treated with Alkylating agents (OR = 3.64, 95%CI: 0.35 – 36.98, and OR = 2.63, 95%CI: 1.03 – 6.72, respectively). Low adherence to the MedDiet were associated with an increased risk for both weight gain and weight loss compared to high adherence to the MedDiet (Table 4a).

Table 1. Baseline Characteristics of the Study Population (N = 252)

Variables	N/n	Mean ± SD or proportion (95% CI)
Age groups (years)	252	52.25 ± 0.68
24 – 39	30	11.9 (7.9 – 16.3)
40 – 59	155	61.5 (55.6 – 67.5)
≥ 60	67	26.6 (21.4 – 32.1)
Education level		
None (Illiterate)	132	52.4 (46.0 – 58.7)
Primary	55	21.8 (17.1 – 27.0)
Secondary	38	15.1 (10.7 – 19.8)
University	27	10.7 (6.8 – 14.7)
BMI categories		27.07±0.40
Underweight	7	2.8 (0.8 – 4.8)
Normal weight	81	32.1 (26.2 – 38.1)
Overweight	91	36.1 (29.8 – 42.1)
Obese	73	29.0 (23.0 – 35.3)
Menopausal status		
Pre-menopausal	103	40.9 (34.8 – 47.0)
Post-menopausal	149	59.1 (52.6 – 64.8)
Cancer stage		
I	84	33.3 (27.4 – 39.3)
II	121	48.0 (41.7 – 54.0)
III	47	18.7 (13.9 – 23.8)
Time since referral to oncology center (months)		
<6	83	32.9 (20.2 – 29.4)
6-11	108	42.9 (27.3 – 37.4)
≥12	61	24.2 (13.9 – 22.3)
Drug class		
Anthracycline with Taxane	160	63.5 (42.2 – 52.8)
Monoclonal antibodies with Taxane	78	31.0 (18.2 – 27.0)
Alkylating agents	14	5.6 (2.3 – 6.7)
Chemotherapy duration (months)		
3	53	21.0 (16.2 – 26.5)
6	150	59.5 (53.4 – 65.6)
8	49	19.5 (14.6 – 24.5)

Note: Data are presented as mean ± standard deviation (SD) for continuous variables, and as proportion (95% confidence interval) based on 1000 bootstrap samples for categorical variables.

Table 2. Changes in weight, BMI, and body composition in women with BC after AC

Variables	Mean ± SD	*p*-value *
Weight (Kg)		
Pre-treatment	69.40 ± 0.86	**< 0.001**
Post-treatment	71.03 ± 0.90	
Changes (%)	1.18 ± 0.51	
BMI (Kg/m²)		
Pre-treatment	27.07 ± 0.40	**< 0.001**
Post-treatment	27.62 ± 0.34	
Changes (%)	1.19 ± 0.52	
FFM (Kg)		
Pre-treatment	45.18 ± 0.40	**< 0.001**
Post-treatment	44.02 ± 0.39	
Changes (%)	-2.44 ± 0.37	
FFM%		
Pre-treatment	65.41 ± 0.56	**< 0.001**
Post-treatment	63.24 ± 0.59	
Changes (%)	-2.17 ± 0.32	
FFMI (Kg/m²)		
Pre-treatment	17.56 ± 0.13	**< 0.001**
Post-treatment	17.10 ± 0.13	
Changes (%)	-2.64 ± 0.34	
FM (Kg)		
Pre-treatment	25.15 ± 0.60	**< 0.001**
Post-treatment	27.02 ± 0.65	
Changes (%)	7.15 ± 1.29	
BF%		
Pre-treatment	34.58 ± 0.56	**< 0.001**
Post-treatment	36.75 ± 0.59	
Changes (%)	6.32 ± 1.08	
FMI		
Pre-treatment	9.79 ± 0.24	**< 0.001**
Post-treatment	10.52 ± 0.26	
Changes (%)	**7.15 ± 1.28**	

Abbreviations: BMI: Body mass index; FFM: Fat-free mass; FFM%: Fat-free mass percentage; FFMI: Fat-free mass index; FM: Fat mass; BF%: Body fat percentage; FMI: Fat mass index. Adherence to the Mediterranean diet based on the KIDMED scores: Low (≤ 3); Moderate (4 – 7); High (≥ 8) (Serra-Majem *et al.*, 2003).

4 Discussion

This study aimed to explore changes in body weight, body composition, and nutritional status, and associated factors in

BC patients undergoing AC during a period of three, six, or eight months. After treatment, patients experienced a significant decrease in FFM mean (-2.44 ± 0.37%) and a significant increase in FM mean (+7.15 ± 1.29%), while their mean BMI has only risen slightly (+1.19± 0.52%). Overall, our findings are consistent with previous studies that demonstrated similar significant fluctuations in FFM and FM among BC patients receiving AC (Jung *et al.,* 2020; Van den Berg *et al.,* 2018). However, as these changes do not result in significant fluctuations in BMI, they may be overlooked in clinical practice. This emphasizes the importance of assessing body composition rather than relying only on anthropometric measurements.

From the first to the last session of AC, 20.6% and 8.7% of patients experienced moderate and high weight gain, respectively. Our results are consistent with previous studies (Pedersini *et al.,* 2023; Van den Berg *et al.,* 2017) that reported a significant weight gain during chemotherapy in women with BC. Several mechanisms contribute to weight gain and body composition changes during adjuvant chemotherapy. Pharmacological factors, such as corticosteroids like dexamethasone, can induce fluid retention, stimulate appetite, and alter glucose metabolism, promoting weight gain (Vargas-Meza *et al.,* 2017; Martínez *et al.,* 2025). Hormonal changes, including chemotherapy-induced ovarian failure and menopause, also reduce estrogen levels, favoring fat accumulation and lean mass loss (Molinelli *et al.,* 2024). Behavioral factors, such as fatigue, decreased physical activity, and increased intake of energy-dense foods due to nausea, taste alterations, or dysgeusia, further exacerbate fat gain (De Kruif *et al.,* 2021; Pellegrini *et al.,* 2023). Additionally, gut microbiota dysbiosis and systemic inflammation may also contribute to these metabolic alterations (Walker *et al.,* 2023). Further research is warranted to better understand whether the weight gain is predominantly attributed to fat mass or fat-free mass, as these factors can have different clinical implications in BC patients during AC.

Conversely, 17.9% and 4.8% of patients experienced moderate weight loss and severe weight loss, respectively, highlighting the more common concern of weight loss during cancer treatment. These findings are aligned with earlier studies that have shown a higher prevalence of weight loss in cancer patients, particularly those undergoing chemotherapy, due to several factors such as reduced appetite, nausea, vomiting, and metabolic changes associated with the disease and treatment (Ryan *et al.,* 2019; Cespedes Feliciano *et al.,* 2017). Severe weight loss can be a critical concern as it may lead to malnutrition, lower treatment tolerance, severe chemotherapy-related toxicity and poorer overall prognosis (Wopat *et al.,* 2023; Olfa *et al.,* 2024). Thus, our findings underscore the need for public health interventions throughout AC to prevent weight loss and related adverse health consequences.

Another interesting finding of our study is the significant rising proportion of patients with low BMI, low muscle mass, and sarcopenic obesity, which went from 7.1%, 11.5%, and 2.8% at the start of AC to 8.7%, 15.1%, and 7.9%, respectively, at the end of the treatment. These findings suggest that, while some patients gained weight, there was also a shift towards a higher incidence of sarcopenic obesity and

Table 3. Changes in Patients' Indicators of Nutritional Status Before and After Treatment (AC)

Nutritional characteristics	Pre-treatment n (%)	Post-treatment n (%)	*p*-values *
BMI categories [a]			
Without low BMI	234 (92.5)	230 (90.9)	**< 0.001**
With low BMI	18 (7.1)	22 (8.7)	
Weight-change categories [b]			
Weight-stability	-	6 (2.4)	-
Low weight gain (<5%)	-	67 (26.5)	-
Moderate weight gain (5 – 10%)	-	52 (20.6)	-
High weight gain (> 10%)	-	22 (8.7)	-
Low weight-loss (< 5%)	-	48 (19.0)	-
Moderate weight-loss (5 – 10%)	-	45 (17.9)	-
Severe weight-loss (> 10%)	-	12 (4.8)	-
Muscle mass (MM) categories [c]			
Normal MM	223 (88.5)	214 (84.9)	**< 0.001**
Low MM	29 (11.5)	38 (15.1)	
Sarcopenic obesity (SO) [d]			
Without SO	245 (97.2)	232 (92.1)	**0.001**
With SO	**7 (2.8)**	**20 (7.9)**	

Note: **p*-value using the Chi-square test. [a] Low BMI: < 20 if < 70 years, or < 22 if > 70 years (Cederholm *et al.,* 2019). [b] Weight loss: Low: < 5%; Moderate: 5 – 10%; Severe: > 10% (Cederholm *et al.,* 2019). [c] Low muscle mass or low fat-free mass index (FFMI, kg/m^2): < 15 kg/m^2 for women (Cederholm *et al.,* 2019). [d] A condition with both excess body fat levels (Jou *et al.,* 2021) and low muscle mass (Cederholm *et al.,* 2019).

Table 4a. Factors Associated with Weight Gain and Moderate/Severe Weight Loss among BC Patients Following AC

Variables	Weight gain		Moderate/severe weight loss [e]	
	OR (95%CI) [i]	*p-value* [i]	OR (95%CI) [i]	*p-value* [i]
Age groups (years)				
24 – 39	0.57 (0.19 – 1.71)	0.320	0.31 (0.08 – 1.20)	**0.091**
40 – 59	0.65 (0.19 – 1.71)	0.296	0.44 (0.18 – 1.08)	**0.076**
≥ 60	Ref.		Ref.	
Education level				
< primary	1.39 (0.74 – 2.61)	0.299	1.28 (0.61 – 2.71)	**0.505**
≥ primary	Ref.		Ref.	
Menopausal status				
Pre-menopausal	0.89 (0.47 – 1.69)	0.742	0.67 (0.31 – 1.45)	**0.315**
Post-menopausal	Ref.		Ref.	
Cancer stage				
I	2.10 (0.44 – 9.89)	0.348	0.68 (0.31 – 1.48)	**0.338**
II	2.13 (0.46 – 9.68)	0.328	0.83 (0.43 – 1.62)	**0.597**
III	Ref.		Ref.	
Time since referral to oncology center (months)				
< 6	1.11 (0.45 – 2.74)	0.812	0.29 (0.10 – 0.85)	**0.024**
6 – 11	0.72 (0.31 – 1.70)	0.465	0.40 (0.16 – 1.02)	**0.056**
≥ 12	Ref.		Ref.	
Weight status				
Normal weight/underweight	2.29 (1.03 – 5.08)	0.043	3.23 (1.19 – 8.80)	**0.022**
Overweight/	1.36 (0.65 – 2.87)	0.418	2.63 (1.03 – 6.72)	**0.043**
Obese	Ref.		Ref.	
Body fat levels				
Without excess	5.28 (2.51 – 11.08)	<0.001	4.05 (1.75 – 9.39)	**0.001**
With excess [&]	Ref.		Ref.	
Chemotherapy duration (months)				
3	0.53 (0.20 – 1.35)	0.184	0.82 (0.27 – 2.46)	**0.728**
6	1.44 (0.63 – 3.29)	0.385	1.23 (0.46 – 3.28)	**0.679**
8	Ref.		Ref.	
Drug class				
Anthracycline based regimen with Taxane	1.05 (0.27 – 4.07)	0.944	3.64 (0.35 – 36.98)	**0.274**
Monoclonal antibodies with Taxane	0.43 (0.10 – 1.73)	0.237	2.87 (0.27 – 29.71)	**0.377**
Alkylating agents	Ref.		Ref.	
Adherence to the MedDiet				
Low	2.13 (0.68 – 6.65)	0.193	2.37 (0.67 – 8.35)	**0.671**
Moderate	1.19 (0.48 – 2.92)	0.704	1.40 (0.29 – 6.62)	**0.178**
High	**Ref.**		**Ref.**	

[e] Moderate and severe weight loss: ≥ 5% of weight loss (Cederholm *et al.*, 2019). [f] Low muscle mass or low fat-free mass index (FFMI, kg/m^2): < 15 kg/m^2 for women (Cederholm *et al.*, 2019). [i] Crude odds ratio (OR) and 95% confidence interval (95%CI) using logistic regression. [&] Excess body fat levels: 20 – 39 years > 32%; 40 – 59 years: > 33%; 60 – 79 years: > 35% for women (Jou *et al.*, 2021).

muscle alteration during treatment. Sarcopenic obesity, a condition characterized by the simultaneous presence of increased body fat and reduced muscle mass, can present a complex clinical challenge. Previous studies have shown that sarcopenic obesity is strongly associated with adverse clinical outcomes, higher chemotherapy toxicity, poorer compliance with oncological treatments, and increased risk of mortality in mortality in cancer patients (Bozzetti, 2017; Gao *et al.*, 2022). On the other hand, the increased proportion of patients with low muscle mass may be associated with the mitotoxic effects of chemotherapeutics on skeletal muscle (Guigni *et al.*, 2018), which may contribute to muscle wasting, a common issue in cancer patients that worsens with the severity and duration of treatment and may have detrimental clinical consequences (Aversa *et al.*, 2017). The implementation of validated therapeutic interventions aimed at addressing these effects on muscle mass could help reduce the disease's burden on patients (Bozzetti, 2017).

Our results showed that younger women (24 – 39 years and 40 – 59 years) tended to be less likely to experience weight gain, moderate/severe weight loss, and muscle mass loss compared to those aged 60 years or older. However, these observed associations were not statistically significant, and the apparent "protective" effect of younger age should be interpreted as descriptive only. This suggests that age may play a role in body composition changes during adjuvant chemotherapy, but further studies are required to confirm this. However, previous studies reported that younger patients

may have a higher likelihood of weight gain (Yeo *et al.,* 2017; Kim *et al.,* 2013; Makari-Judson *et al.,* 2007).

These discrepancies could be partly explained by differences in educational and socioeconomic status, since younger patients are generally more likely to access healthcare facilities, adopt preventive measures, and maintain healthier lifestyles. In line with this, our study also found that patients with lower education levels were at an increased risk of both weight gain and moderate/severe weight loss compared to those with higher education attainment. These findings underline the complex interplay between age, education, and socioeconomic status in shaping weight and body composition outcomes during chemotherapy.

Moreover, menopausal status appears to be another key determinant. In our cohort, pre-menopausal status tended to have a protective effect against weight gain and moderate/severe weight loss, whereas it was associated with a higher risk of muscle mass loss compared to post-menopausal status. In line with previous studies, post-menopausal women have been reported to have a higher risk of weight gain (Nyrop *et al.,* 2019; Trédan *et al.,* 2010; Winkels *et al.,* 2014), as well as higher mean body fat percentage and lower mean muscle mass compared to their pre-menopausal peers (Jung *et al.,* 2020). Considered together, these results highlight the importance of considering both age and menopausal status when addressing chemotherapy-induced changes in weight and body composition. Future interventions should therefore integrate menopausal-specific strategies to mitigate adverse metabolic effects during and after adjuvant chemotherapy.

Our results demonstrated that women with stages I or II of BC were more likely to gain weight compared to those with stage III. Patients whose disease was diagnosed within the last 12 months preceding AC also were less likely to have moderate/severe weight loss than those diagnosed earlier. These results are consistent with earlier studies indicating that women with early-stage BC have higher odds of weight gain during treatment (Ee *et al.,* 2020; Gandhi *et al.,* 2019). Other studies have found that even when a patient's weight remains stable during treatment, weight gain persists for years after diagnosis (Ee *et al.,* 2020; Vagenas *et al.,* 2015; Van den Berg *et al.,* 2017). Thus, our findings underscore the importance of additional interventions to encourage healthy eating habits and regular physical activity to prevent weight gain and negative changes in body composition during and beyond AC, particularly in women with stages I and II breast cancer.

Normal weight/underweight and normal body fat levels were associated with significantly increased risk of weight gain, moderate/severe weight loss, and reduced risk of low muscle mass compared to obesity and excess body fat levels, respectively. These findings are partly aligned with earlier studies (Makari-Judson *et al.,* 2007; Nissen *et al.,* 2011; Pedersini *et al.,* 2023; Trédan *et al.,* 2010) suggesting that women with a normal BMI at baseline are more likely to experience weight gain and change in body composition with gain in fat mass and loss in lean body mass during chemotherapy. However, Van den Berg et al. reported in a recent meta-analysis that individuals with higher baseline BMI are more likely to gain weight during treatment (Van den Berg *et al.,* 2017). The weight gain observed in women who were underweight or normal weight was probably characterized by an increase in fat mass and a decrease in muscle mass, suggesting the onset of sarcopenic obesity (Williams *et al.,* 2017). Although our findings should be interpreted with caution, in the light of the possible role of other confounding factors, they underscore the importance of healthcare interventions among BC patients undergoing AC to tackle excess body fat and weight gain which have a significant impact on the disease's progression, recurrence, and mortality (Hurtado *et al.,* 2024).

Patients receiving an Anthracycline-based regimen with Taxane and Monoclonal antibodies with Taxane were more likely to experience moderate/severe weight loss than those treated with Alkylating agents. This may be due to the combined impact of abnormal nutritional status and chemotherapy regimen. It should be noted that the majority (65.1%) of participants were overweight or obese (Table 1) and they might have a vitamin D deficiency, which has recently been found to affect more than 74% of Moroccan women and to be associated with obesity indicators (Mehdad *et al.,* 2022). For instance, a recent study demonstrated that severe deficiency of vitamin D and Anthracycline-Taxane regimen are associated with cachexia, a condition that causes significant weight loss and muscle loss (Hutajulu *et al.,* 2025). Our results also can be explained by the extended duration of treatment with these AC regimens and their associated side effects such as fatigue and change in eating habits due to altered taste and smell. Indeed, fatigue occurring during and following oncological treatment was found to be significantly associated with moderate-severe weight loss (Wang *et al.,* 2013), which may lead to a deterioration in nutritional status and quality of life among BC patients (Álvaro Sanz *et al.,* 2020). Nevertheless, a meta-analysis showed that significant reduction in physical activity and basal metabolic rate that occurs during chemotherapy can disrupt energy balance and contribute to weight gain in BC patients (Van den Berg *et al.,* 2017). Further studies are needed to explore the relationship between chemotherapy regimens and changes in weight and body composition in large samples of women with BC undergoing AC.

There is growing evidence that higher adherence to the Mediterranean Diet (MedDiet) among BC patients may result in (i) a reduced risk of cancer recurrence, (ii) lower overall cancer mortality, and (iii) a decreased incidence of

other comorbidities, such as cardiovascular diseases, therefore improving metabolic health and promoting longevity (Castelló *et al.,* 2017; Schwingshackl *et al.,* 2017). The present study showed that low adherence to the MedDiet is associated with a greater risk of both weight gain and weight loss compared to high adherence to the MedDiet. This may be due to an imbalance in energy intake, with patients potentially consuming more processed foods, refined sugars, and unhealthy fats that could increase the risk of weight gain. On the other hand, low adherence to this diet may not provide sufficient caloric intake or macronutrient balance, which could contribute to unintended weight loss. Other factors, including poor dietary habits and psychological factors, such as stress or emotional eating, may also lead to inconsistent dietary choices that disrupt energy balance, which can further contribute to weight fluctuations. Thus, it has been suggested that monitoring dietary and lifestyle behaviors of BC patients before and after chemotherapy, with providing simple recommendations based on MedDiet principles and regular physical activities based on the international guidelines, is effective in preventing weight gain in women with normal weight and promoting weight loss in overweight and obese women (Pedersini *et al.,* 2023). Further longitudinal studies are needed to explore the underlying mechanisms of the relationship between various adherence levels to the MedDiet and body weight fluctuations.

Study limitations

The current study investigation is subject to some limitations that warrant acknowledgment. First, the restriction of a single-center design necessarily limits the generalizability of the findings to a larger population. Second, while bioelectrical impedance analysis is a practical and widely implemented method, it carries a potential for measurement bias in accurately estimating body composition and its changes over time (Talma *et al.,* 2013). Third, the study cohort comprised patients with heterogeneous cancer stages and undergoing various chemotherapy regimens (each associated with distinct side effects), which complicate the interpretation of the results and their comparison with those of other studies. Fourth, critical data on potential confounding factors —specifically biochemical markers, detailed energy and macronutrient intake, objective physical activity levels, and socioeconomic status—were not collected. These factors are commonly associated with changes in weight and body composition. Fifth, the study lacked long-term follow-up assessment after completion of adjuvant chemotherapy (AC). Given that weight gain may persist or even intensify in the years following treatment cessation, future longitudinal studies are warranted to explore long-term trajectories of weight and body composition change in breast cancer patients. Finally, the reliance on self-reported dietary habits for assessing adherence to the MedDiet introduces the risk of information bias. Furthermore, while the KIDMED questionnaire was applied in this adult populations, its original development and validation focused on children and adolescents, which may compromise its precision in assessing MedDiet adherence among adults.

5 Conclusion

In conclusion, the present investigation revealed significant alterations in weight status and body composition measurements among BC patients following AC. This study draws attention to the considerable proportion of patients who exhibited adverse body composition profiles post-AC, specifically low BMI (8.7%), sarcopenic obesity (7.9%), or low muscle mass (15.1%). Furthermore, approximately, 30% and 23% of the cohort experienced moderate/high weight gain and moderate/severe weight loss, respectively. The observed outcomes were found to be associated with several key demographic and clinical factors, including age, educational level, menopausal status, cancer stage, time since referral to the oncology center, BMI, specific chemotherapy regimen utilized, and degree of MedDiet adherence. Although further research is essential to elucidate the mechanisms underlying these associations, our findings underscore the necessity for systematic monitoring of weight and body composition measurements throughout the AC period. Moreover, the implementation of early dietary and behavioral interventions is also warranted to prevent excessive weight gain, severe weight–muscle depletion and nutritional status alterations in BC patients undergoing AC, with particular emphasis on those women classified as underweight or normal weight at baseline.

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