RESEARCH ARTICLE

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Severe Deficiency of Vitamin D and Anthracycline-Taxane Regimen are associated with Cachexia Following Breast Cancer Chemotherapy: A Single Center Assessment Using Two Consensus-Based Criteria

Susanna Hilda Hutajulu[1]*, Sofi Aresy[2], Yufi Kartika Astari[3], Juan Adrian Wiranata[3,4], Herindita Puspitaningtyas[5], Dian Caturini Sulistyoningrum[6], Kartika Widayati Taroeno-Hariadi[1], Johan Kurnianda[1], Ibnu Purwanto[1], Mardiah Suci Hardianti[1]

Abstract

Background: Cancer cachexia in breast cancer (BC) patients is not commonly reported, particularly in Indonesia. This study assessed the prevalence of cachexia in local patients with BC receiving chemotherapy, and the associated factors. **Methods:** This cross-sectional study included 160 BC patients who started chemotherapy between July 2018 and June 2022. We collected data including age, body mass index, comorbidity, stage, surgery type, chemotherapy information, neutrophil-to-lymphocyte ratio, albumin, vitamin D, C-reactive protein, and the presence of chemotherapy-induced nausea and vomiting. We used the Fearon and Evans criteria to define the outcomes of cachexia. A multivariate logistic regression test was used to determine the factors related to the cachexia status following chemotherapy. **Results:** During and after chemotherapy, 61 participants (38.1%) and 32 participants (20%) experienced cachexia based on Fearon and Evans criteria, respectively. All the patients had a deficient vitamin D concentration at baseline and vitamin D below median value (8.94 ng/mL) was classified as severe deficiency. Vitamin D severe deficiency was associated with an increased risk of cachexia (OR 2.47, 95%CI 1.19–5.11, p=0.014 for Fearon; and OR 2.47, 95%CI 1.03–5.92, p=0.043 for Evans), as well as anthracycline-taxane regimen based on Fearon criteria only (OR 4.35, 95%CI 1.39–13.53, p=0.011). **Conclusion:** Our findings demonstrated that vitamin D severe deficiency and anthracycline-taxane regimen were associated with cachexia occurrence among BC patients following chemotherapy. Strategies and further investigation are warranted to reduce cachexia occurrence, along with nutritional support during chemotherapy.

Keywords: Cachexia- breast neoplasms- chemotherapy- Indonesia

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Introduction

Breast cancer is the most prevalent cancer in Indonesia, accounting for 30.1% of all cancers in females. In 2022, it was responsible for 14.4% of all cancer deaths, ranking third after lung and liver cancer [1]. The five-year overall survival rate is generally adverse, at 48-51% across all stages and only 12% for metastatic cases [2, 3].

Cancer cachexia is among the primary causes of mortality in various cancer types and responsible for 20-40% of cancer deaths in those with advanced stage [4]. Cachexia is a multifactorial illness characterized by body weight loss at least 5%, the gradual loss of skeletal muscle mass, and inflammation, that is not entirely reversible with conventional nutritional support and leads to increased functional impairment [5]. It may evolve along the course of cancer disease, even before diagnosis or treatment initiation [6]. Patients with cachexia often receive a lower

*[1]Division of Hematology and Medical Oncology, Department of Internal Medicine, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada/Dr. Sardjito General Hospital Yogyakarta, Indonesia. [2]Division of Endocrinology and Metabolic, Department of Internal Medicine, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada/Dr Sardjito General Hospital, Yogyakarta, Indonesia. [3]Division of Hematology and Medical Oncology, Department of Internal Medicine, Dr. Sardjito General Hospital Yogyakarta, Indonesia. [4]Academic Hospital, Universitas Gadjah Mada, Yogyakarta, Indonesia. [5]Doctorate Program of Health and Medical Science, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia. [6]Department of Nutrition and Health, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia. *For Correspondence: susanna.hutajulu@ugm.ac.id. Susanna Hilda Hutajulu and Sofi Aresy have equal contribution in this study.*

initial chemotherapy dosage and have more frequent and severe dose-limiting effects compared with weight-stable patients [7].

Cachexia has been commonly reported in the liver (50.1%), pancreatic (45.6%), head and neck (42.3%), lung (37.2%), and gastric cancers (33.3%) [8]. Although not frequently reported, the occurrence of cachexia in breast cancer patients is not rare (20- 33%) [9, 10], especially in those with advanced disease [4]. Breast cancer patients with weight loss leading to a body mass index (BMI) loss experience more than a two-fold increased risk in overall survival than those with a stable weight [11].

Several risk factors of cancer cachexia have been studied in different types of cancer. These include age [12], gender [13], lifestyle (smoking and alcohol consumption) [13], nutritional status [14], comorbidity [12, 15], stage [13], Eastern Cooperative Oncology Group (ECOG) Performance Status [12], pre-treatment inflammatory biomarkers such as neutrophil-to-lymphocyte ratio (NLR) and C-reactive protein (CRP) [16], and treatment modalities such as radiotherapy [13], surgery [12], and chemotherapy [12]. Chemotherapy-induced nausea has been associated with a lower energy intake that may also lead to cancer cachexia [17]. Low vitamin D levels were also observed to be more prevalent in advanced cancer patients with cachexia [18].

In Indonesia, only a few local publications regarding cancer cachexia are available [19, 20], and only one study applied to patients with breast cancer [20]. The influencing factors of cachexia are also rarely analyzed, including the vitamin D level, despite its impact on cancer cachexia being highlighted in recent years [20, 21]. Therefore, this study aims to determine the occurrence of cachexia in Indonesian breast cancer patients, and investigate the associated factors.

Materials and Methods

Study participants and design

This cross-sectional study included participants who were registered in a prospective cohort study on chemotherapy toxicity in breast cancer patients, which aimed to recruit a minimum of 200 patients between July 2, 2018, and June 15, 2022. In the main study, patients who visited and had their first-line chemotherapy treatment at the Hematology and Medical Oncology Division, "Tulip"/ Integrated Cancer Clinic, Dr Sardjito General Hospital, Yogyakarta, Indonesia, were included. The participants were women ≥18 years old, with histopathologically confirmed breast cancer, who had a good to moderate performance status according to the ECOG Performance Status scale (≤2). Patients with a terminal illness or severe cardiac failure were excluded. In these cases, chemotherapy was used as a neoadjuvant, adjuvant, or palliative treatment (with or without surgery). In the present study, we included patients who had at least three cycles of chemotherapy. Patients with incomplete anthropometric data were excluded. From a total of 214 patients who met the inclusion criteria in the main study, 160 were finally recruited into the present study. The study was authorized by the Medical and Health Research & Ethics Joint Committee, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada (reference number: KE/FK/0417/EC/2018). All patients provided written informed consent.

Data collection and key variables

We gathered data from the main study's database on demographic, anthropometric, and clinical data, and treatment details between September 30, 2021, and February 20, 2023. Age was categorized as below and over the median (52 years old). Other data included the presence of comorbidity and the cancer stage (early-stage/ stage I-II and advanced-stage/stage III-IV), based on the 8th edition American Joint Committee on Cancer (AJCC) staging system. We also obtained data on the pre-treatment neutrophil-to-lymphocyte ratio (NLR) (≤1.64 vs >1.64), albumin (≤4.45 vs >4.45 g/dl), vitamin D (quantified using the enzyme-linked immunosorbent assay (ELISA), ≤8.94 vs >8.94 ng/ml), and C-reactive protein (CRP) level (≤4.96 vs >4.96 mg/l) that were categorized based on each median value. Vitamin D levels were defined as sufficient (≥30 ng/ml), insufficient (20.0–29.9 ng/ml), and deficient (<20 ng/ml) [22]. Due to a low median value of vitamin D in our participants, we further define vitamin D level below the median value (8.94 ng/ml) as severely deficient.

Treatment details included history of surgery (mastectomy and without mastectomy), chemotherapy settings (adjuvant/neoadjuvant and palliative), and the chemotherapy regimen. Among the 160 patients receiving chemotherapy, 129 (80.6%) received anthracycline-taxane combination regimen, 13 (8.1%) received an anthracycline-based regimen, 16 (10.0%) received a taxane-based regimen, and two patients (1.3%) received capecitabine regimen. The information about the type and total dosage of chemotherapy was presented in Supplementary Table 1. We included anthracycline-taxane regimen (yes and no) in the final analysis. The anthropometric status was determined using BMI (<18.5 kg/m^2 for underweight, 18.5 to 24.9 kg/m^2 for normal, 25 to 29.9 kg/m^2 for overweight, and ≥30 kg/m^2 for obese, based on World Health Organization (WHO) BMI cut-off for Asian populations), body weight, and upper left arm circumference. These parameters were measured before, in the middle, at the end of chemotherapy, and at one, two, three, and six months after chemotherapy ended. We also tracked the documented occurrence of chemotherapy-induced toxicities from the study's database on nausea and vomiting (CINV) that were collected based on the Common Terminology Criteria for Adverse Events (CTCAE) version 4. We then categorized the data into two classes (no CINV and mild symptoms vs. moderate to severe symptoms).

Definitions of cachexia

We used two consensus-based criteria to define the outcomes of cachexia. The first definition was a cancer-specific framework of cachexia from an international panel of experts in clinical cancer cachexia research by Fearon et al. [5]. It defines cancer cachexia as weight loss of >5% over the past six months (in the absence of simple starvation), or BMI of <20 kg/m^2 and any degree of weight

loss >2%, or appendicular skeletal muscle index consistent with sarcopenia (males <7.26 kg/m^2; females <5.45 kg/m^2) and any degree of weight loss >2% [5]. The second definition was a more general framework of cachexia as described by Evans et al. It defines cachexia as weight loss of at least 5% (edema-free) in 12 months or less in the presence of underlying illness (in cases where weight loss cannot be documented, a BMI of <20.0 kg/m^2 is sufficient) plus at least three of the following criteria: decreased muscle strength (lowest tertile), fatigue (physical and/or mental weariness resulting from exertion; an inability to continue exercise at the same intensity with a resultant deterioration in performance), anorexia (limited food intake, i.e. total caloric intake less than 20 kcal/kg body weight/day; <70% of usual food intake, or poor appetite), low fat-free mass index (defined by lean tissue depletion with mid-upper arm muscle circumference of less than a 10th percentile for age and gender), and abnormal biochemistry (increased inflammatory markers CRP >5.0 mg/l, IL-6 >4.0 pg/ml, anemia <12 g/dl, or low serum albumin <3.2 g/dl) [23]. We used CRP, hemoglobin, and albumin levels as biochemistry parameters to assess the cachexia status before chemotherapy, according to Evans criteria. However, during and after chemotherapy completion, we only used hemoglobin levels, since CRP and albumin levels were not routinely checked.

Statistical analysis

Data on the patient's baseline characteristics were presented as mean and standard deviation (SD) or median and interquartile range (IQR) for continuous data, and frequency for categorical data. We presented the incidence of cachexia cumulatively after chemotherapy completion based on Fearon and Evans criteria, and also before chemotherapy initiation based on Evans criteria. The incidence of cachexia before and after chemotherapy was analyzed with McNemar test. Bivariate and multivariate logistic regression test analyzed the clinicopathologic, laboratory, and treatment risk factors for both cachexia definitions. A p-value <0.05 was considered significant. We used STATA software version 17 (Stata Corp., College Station, TX) for our statistical analyses.

Results

Patients' characteristics

From 214 participants recruited for the main study, 54 patients were excluded due to having less than three chemotherapy cycles (19), having more than 12 months duration between their cancer diagnosis and cachexia occurrence (7), or had incomplete data (28) (Figure 1). Finally, a total of 160 subjects aged from 32 to 75 years old were included in the present study. Cases were dominated by those with a normal BMI (90, 56.3%), having at least one comorbid condition (89, 55.6%), with an advanced stage (103, 64.4%), undergoing mastectomy (130, 81.3%), receiving adjuvant/neoadjuvant chemotherapy (127, 79.4%), and with anthracycline-taxane regimen (129, 80.6%) (Table 1).

Table 1. Baseline Characteristics of Study's Subjects (N=160)

Variables	Frequency (%)
Age (years)	
Mean ± SD	51.9 ± 8.64
BMI (kg/m^2)	
<18.5	15 (9.4)
18.5–24.9	90 (56.3)
25–29.9	43 (26.9)
≥30	12 (7.5)
Comorbidity	
No	71 (44.4)
Yes	89 (55.6)
Stage	
I–II	57 (35.6)
III–IV	103 (64.4)
Surgery	
Mastectomy	130 (81.3)
Non-mastectomy	
Core biopsy	17 (10.6)
Lumpectomy	13 (8.1)
Chemotherapy setting	
Adjuvant/neoadjuvant	127 (79.4)
Palliative	33 (20.6)
Chemotherapy regimen	
Anthracycline-taxane combination	129 (80.6)
Anthracycline-based	13 (8.1)
Taxane-based	16 (10.0)
Capecitabine	2 (1.3)
Baseline NLR	
Median (IQR)	1.64 (1.45–1.89)
Baseline albumin (g/dl) (n=149)	
Median (IQR)	4.45 (4.10–4.73)
Baseline vitamin D (ng/ml) (n=143)	
Median (IQR)	8.94 (6.39–10.78)
Baseline CRP (mg/l) (n=136)	
Median (IQR)	4.96 (1.46–11.15)

SD, Standard Deviation; BMI, Body Mass Index; NLR, Neutrophil-to-Lymphocyte Ratio; IQR, Interquartile Range; CRP, C-reactive protein

Cachexia incidence before and after chemotherapy

At baseline nine patients (6%) had cachexia and a total of 20% of patients had persistent or evolved into cachexia after chemotherapy, based on Evans criteria (Table 2). Overall, in any observation period during and

Table 2. Cachexia based on Evans criteria before and after Chemotherapy (N=152)

		After chemotherapy (n(%))	
		Cachexia	No cachexia
Before chemotherapy (n (%))	Cachexia	1 (0.7)	8 (5.3)
	No cachexia	30 (19.7)	113 (74.3)

p-value=0.0004 (McNemar test)

Table 3. Factors associated with Cancer Cachexia based on Fearon's Criteria

Variable	Fearon Cachexia (%)	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age					
>52 years	50.8	Ref			
≤52 years	49.2	0.84 (0.44–1.59)	0.592		
Comorbidity					
No	52.5	Ref			
Yes	47.5	0.59 (0.31–1.12)	0.107		
Stage					
I-II	36.1	Ref			
III-IV	63.9	0.97 (0.49–1.89)	0.927		
Surgery					
Non-mastectomy	24.6	Ref			
Mastectomy	75.4	0.55 (0.24–1.22)	0.141		
Chemotherapy settings					
Adjuvant/neo-adjuvant	80.3	Ref			
Palliative	19.7	0.91 (0.41–2.01)	0.815		
Anthracycline-taxane regimen					
No	8.2	Ref		Ref	
Yes	91.8	3.99 (1.44–11.04)	0.008	4.35 (1.39–13.53)	0.011
CINV					
None to mild	88.5	Ref			
Moderate-severe	11.5	0.67 (0.26–1.74)	0.414		
NLR					
≤1.64	59.0	Ref			
>1.64	41.0	0.56 (0.29–1.08)	0.085		
Albumin (g/dl)					
>4.45	48.2	Ref			
≤4.45	51.8	1.05 (0.54–2.06)	0.876		
Vitamin D (ng/ml)					
>8.94	35.3	Ref		Ref	
≤8.94	64.7	2.49 (1.23–5.05)	0.011	2.47 (1.19–5.11)	0.014
CRP (mg/l)					
≤4.96	49.0	Ref			
>4.96	51.0	1.06 (0.53–2.15)	0.858		

OR, Odds Ratio; CI, Confidence Interval; Ref, Reference; CINV, Chemotherapy-induced nausea & vomiting; NLR, Neutrophil to Lymphocyte Ratio; CRP, C-reactive protein.

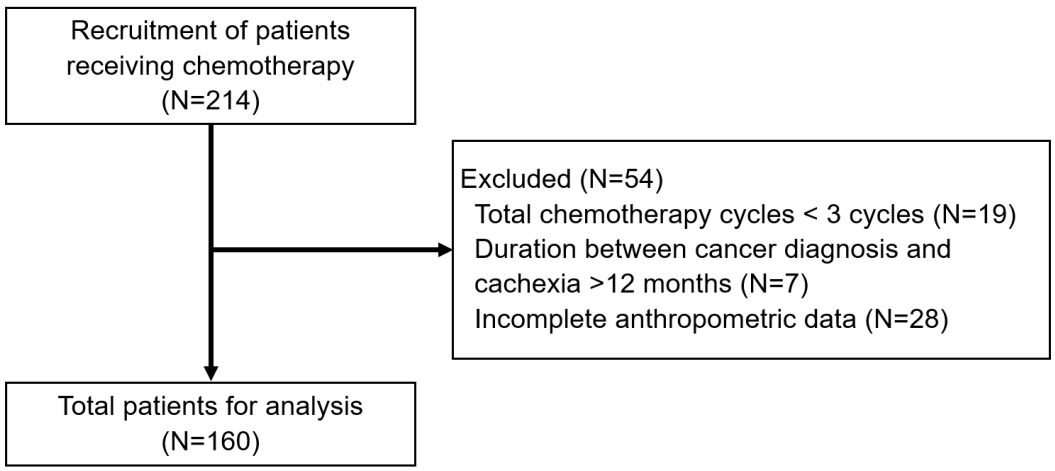

Figure 1. Flow Diagram for the Study's Recruitment, Inclusion and Analysis Process.

Table 4. Factors associated with Cancer Cachexia based on Evans' Criteria

Variable	Evans Cachexia (%)	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age					
>52 years	56.3	Ref			
≤52 years	43.7	0.66 (0.30–1.45)	0.305		
Comorbidity					
No	46.9	Ref			
Yes	53.1	0.88 (0.40–1.92)	0.750		
Stage					
I-II	31.3	Ref			
III-IV	68.7	1.28 (0.56–2.92)	0.564		
Surgery					
Non-mastectomy	28.1	Ref			
Mastectomy	71.9	0.50 (0.20–1.23)	0.134		
Chemotherapy settings					
Adjuvant/neo-adjuvant	78.1	Ref			
Palliative	21.9	1.09 (0.43–2.82)	0.845		
Anthracycline-taxane regimen					
No	0	Omitted			
Yes	100				
CINV					
None to mild	78.1	Ref			
Moderate-severe	21.9	1.96 (0.73–5.27)	0.182		
NLR					
≤1.64	50.0	Ref			
>1.64	50.0	1.01 (0.47–2.20)	0.968		
Albumin (g/dl)					
>4.45	48.3	Ref			
≤4.45	51.7	1.04 (0.46–2.33)	0.931		
Vitamin D (ng/ml)					
≤8.94	32.1	Ref		Ref	
>8.94	67.9	2.47 (1.03–5.92)	0.043	2.47 (1.03–5.92)	0.043
CRP (mg/l)					
≤4.96	42.9	Ref			
>4.96	57.1	1.43 (0.62–3.32)	0.398		

OR, Odds Ratio; CI, Confidence Interval; Ref, Reference; CINV, Chemotherapy-induced nausea & vomiting; NLR, Neutrophil to Lymphocyte Ratio; CRP, C-reactive protein.

after chemotherapy, a total of 61 participants (38.1%) and 32 participants (20%) fulfilled the criteria of cachexia, based on Fearon and Evans criteria, respectively.

Factors associated with cancer cachexia

Table 3 showed the bivariate and multivariate analyses of demographic, clinicopathologic, and treatment characteristics associated with cachexia based on Fearon criteria. Having a pre-treatment vitamin D severe deficiency and receiving anthracycline-taxane regimen were associated with an increased risk of cachexia (OR 2.47, 95%CI 1.19–5.11, p=0.014 and OR 4.35, 95%CI 1.39–13.53, p=0.011). Meanwhile, based on Evans criteria, having a vitamin D severe deficiency before chemotherapy was the only factor that independently associated with an increased risk of cachexia (OR 2.47, 95%CI 1.03–5.92, p=0.043) (Table 4).

Discussion

This is the first study in Indonesia that determine the extent of cachexia and explores its determinants in breast cancer cases. Being a country with breast cancer as the most predominant malignancy, data on the factors influencing cachexia might be useful for designing early interventional programs [4]. In our study, cachexia was found in 20.0% and 38.1% of cases using different criteria, and was significantly associated with pre-treatment vitamin D severe deficiency and the anthracycline-taxane regimen.

Choosing the diagnostic criteria for cachexia in cancer

patients remains arbitrary in both clinical and research settings. Fearon criteria have an emphasis on weight loss and sarcopenia, and are cancer-specific criteria. Meanwhile, Evans criteria are more generic and complex after incorporating chronic inflammation, anemia, protein depletion, anorexia, and fatigue. Due to having fewer variables, Fearon criteria can capture cancer cachexia earlier than Evans method, but tends to be over-rating [24]. Indeed, our study demonstrated a higher cachexia prevalence with Fearon criteria compared to Evans. While Fearon criteria suffice and are appropriate to identify cancer cachexia, Evans criteria need a more specific evaluation that may not be practical in daily settings [25]. However, cachexia diagnosis using Evans criteria may provide a better prognosticator of cancer mortality. In fact, more studies on various types of cancer used Fearon criteria than Evans. Specifically, based on Fearon criteria, cachexia occurrence in breast cancer was lower than that in gastrointestinal cancer (75%) and lung cancer (56%) [24].

Using Fearon criteria, the cachexia rate in our breast cancer patients (38.1%) was higher than that observed in Norway (11%) [12] with cases having higher BMI than our study's participants. In the Indonesian context, Sutandyo et al. observed higher rates of breast cancer cachexia than our findings (50%) [21]. More broadly, the prevalence of cachexia in our patients is also higher than that in previous studies using other classifications, such as in the United States and the European Union (23.5%, using various definitions) [8], South Korea (33.0%, using BMI, serum albumin, total lymphocyte counts and type of diet) [10], and France (20.5%, using BMI and age) [9]. Studies applying Evans criteria in breast cancer patients is very limited. An Indonesian study showed a similar rate of cachexia in breast cancer (30%) to ours, using the criteria [20].

The difference in cachexia proportion with previous studies might be caused by the difference in treatment spectrum from the included patients. All patients included in this study received chemotherapy, with and without a history of surgery and radiation therapy. Similar to ours, Kwon et al. and Kusuma et al. measured cachexia during and after chemotherapy completion [6, 20]. Meanwhile, the other studies did not specifically measure cachexia after treatment, although they provided data about the history of treatment (surgery, chemotherapy, and radiation).

In contrast to patients with pancreatic or lung cancer, who commonly suffer weight loss and have cachexia upon diagnosis [26], breast cancer patients frequently gain weight. One meta-analysis estimates that breast cancer patients during chemotherapy gain a mean of 2.7 kilograms in weight [27]. However, this meta-analysis was derived from studies mainly conducted in Western countries. Our study found that breast cancer patients lost up to five kilograms on average, with 40% experiencing weight loss and only 25.1% of subjects experiencing weight gain (Supplementary Table 2). These findings are similar to another study from Asian countries demonstrating that weight gain in breast cancer patients is not a dominant feature [28].

Using Evans criteria, an increased incidence of cancer cachexia was observed in our study from 6% before chemotherapy and 20% after chemotherapy. This phenomenon supported other study in head and neck cancer patients showing an increased incidence from 6.1% to 41% at the end of treatment. The increased occurrence might be due to the tumor itself or treatment aggressiveness. It is important to reassess cachexia status because persistent or newly evolved cancer cachexia during the first year after initial treatment was an important prognostic factor for survival [6].

Despite the fact that all of our participants had low vitamin D levels at baseline (median 8.94 ng/ml), we demonstrated a significant negative correlation of vitamin D with cachexia. Unlike ours, other studies from Indonesia with a higher median value for the vitamin D level (17.1 ng/ml) did not find any significant association [20, 21]. Others, however, observed an impact of vitamin D on proinflammatory cytokines production [29] and skeletal muscle strength and function [30], leading to cancer cachexia. In line with these, a correlation between the vitamin D level with muscle mass and handgrip strength in various types of cancer [21], and an improvement of muscle strength upon vitamin D treatment in metastatic prostate cancer, was also observed [31]. Furthermore, the vitamin D supplementation was associated with reduced risk of recurrence and mortality in patients with breast cancer [32, 33]. These indicate a need for further exploration of vitamin D relationship with cachexia, both in basic and clinical settings.

In our study, anthracycline-taxane regimen was significantly associated with an increased risk of cachexia based on Fearon definition. This finding supported previous report showing that patients experienced weight loss after anthracycline treatment and started to gain weight after taxane initiation [34]. Other study reported that weight gain was associated with a high number of taxane cycles [35]. Thus, we assumed that in the anthracycline-taxane regimen, anthracycline induced weight loss more profoundly. A basic study showed that doxorubicin caused hyperglycemia and insulin resistance mediated by AMPk inhibition, which led to muscle atrophy, weight loss, and anorexia, which was a part of cachexia syndrome [36]. In our patients, weight loss was more prominent than weight gain, which was associated with an increased risk of cachexia.

Since cancer cachexia leads to unfavourable survival rates, studies have investigated whether nutritional intervention might improve the outcomes. Dietary interventions such as diet consultation and oral or parenteral supplementation in cachectic cancer patients have been shown to significantly enhance performance scale and survival [37]. In addition, our findings on the association between low vitamin D levels and cachexia suggest vitamin D supplementation would improve and optimize the levels. Furthermore, nutritional supplementation can improve the efficacy of chemotherapy and radiotherapy while minimizing toxicity and optimizing outcomes [38]. At the least, addressing cancer cachexia can also alleviate weight loss- and eating-related distress, which improves the overall quality of life [39].

The American Society for Parenteral and Enteral Nutrition (ASPEN) [40] does not suggest that cancer patients get routine specialized parenteral or enteral nutrition. They do, however, advocate nutrition support for patients who are malnourished and are expected to be unable to intake and/or absorb appropriate nutrients for an extended length of time while getting active anticancer therapy. By recognizing the risk factors for cancer cachexia, as indicated by our findings, we may identify individuals at risk of malnutrition and initiate nutritional intervention early.

The strength of our study includes its prospective nature in data collection with sufficient follow-up time. The use of the CTCAE questionnaire with regular patient visits also facilitated capturing data on the symptoms associated with nutrition, such as nausea, vomiting, oral mucositis, and loss of appetite. Nevertheless, the presence of these symptoms has no significant association with cancer cachexia. The incorporation of vitamin D levels in the multivariable model has enriched the literature on the role of vitamin D in the development of cancer cachexia, yet warrants further exploration. Some limitations of this study should also be acknowledged. Firstly, this is a single-institution assessment, so the results may not represent the Indonesian breast cancer population. Secondly, since the observation started right before any chemotherapy program, the presence of cachexia long before this point could not be established. Patients recruited from the main study were carefully selected, with good performance and without poor comorbidities. Thus, cachexia prevalence in our study may be lower than the actual figure, if we included all patients receiving chemotherapy without selection. Further studies with a wider patient population and other clinical backgrounds need to be carried out to confirm our findings.

In conclusion, cachexia occurs in 20% and 38.1% of breast cancer patients in the local setting, using different criteria. Vitamin D severe deficiency and anthracycline-taxane regimen are associated with the risk of cachexia occurrence. The identified parameters can inform clinicians to stratify patients who may develop cancer cachexia following chemotherapy. Strategies and further investigation are needed to reduce the prevalence of cachexia, with nutritional support during chemotherapy programs.

Author Contribution Statement

Conceptualization: SHH, SA, MSH; data curation: SHH, YKA, HP, DCS; formal analysis: SHH, SA, YKA, JAW, DCS; investigation: SHH, SA, YKA, JAW, HP, MSH; resources and supervision: SHH, KWT, JK, IP, MSH; writing original draft: SHH, SA, YKA, JAW; review, editing, and approval of final draft: all authors.

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General

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Ethical declaration

The study was authorized by the Medical and Health Research & Ethics Committee, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada (reference number: KE/FK/0417/EC/2018) and all patients provided written informed consent.

Data availability

The datasets generated and analyzed during the current study are not publicly available because of privacy and ethical restrictions. Still, anonymized data are available from the corresponding author at reasonable request.

Conflict of interest

The authors declare no conflict of interest for this manuscript.

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