



# Cancer cachexia following breast cancer chemotherapy was associated with vitamin D concentration, clinical stage, and number of chemotherapy cycles

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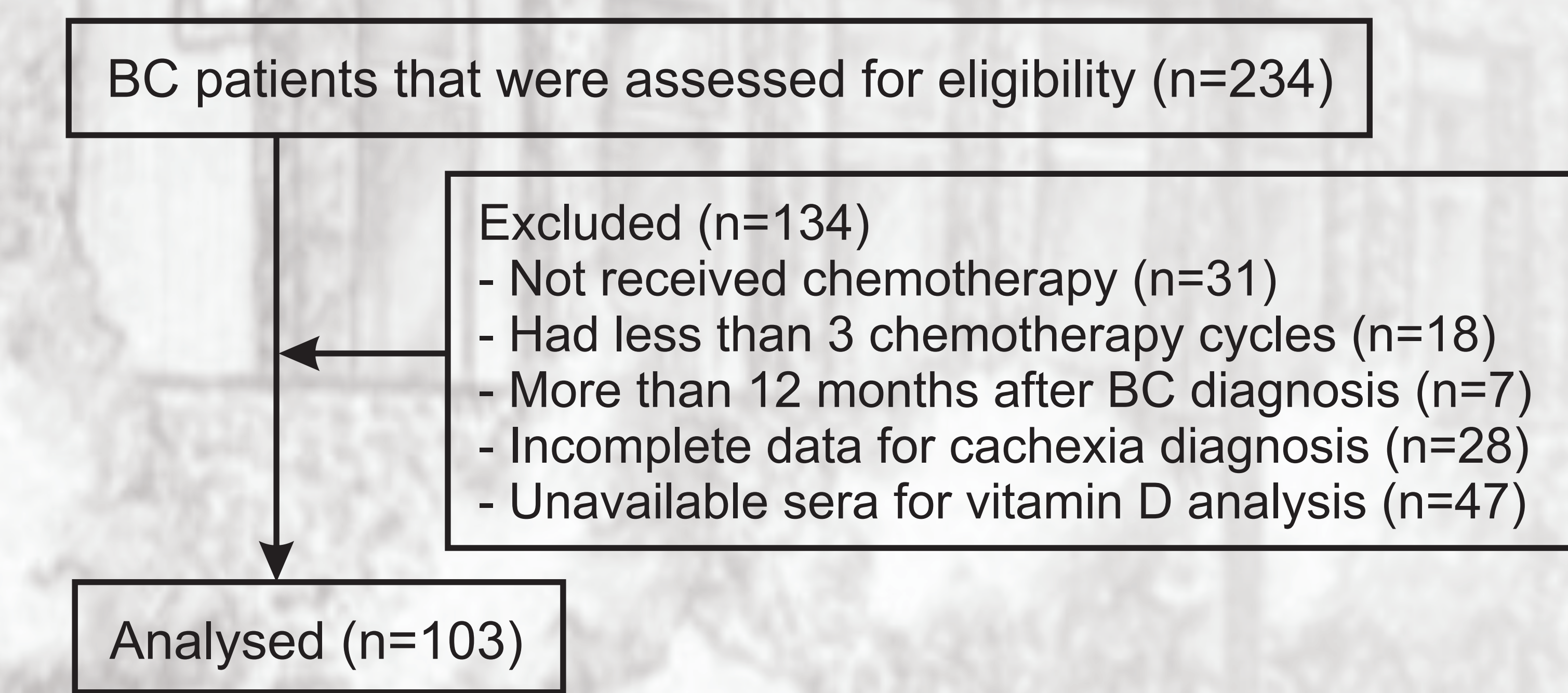
## BACKGROUND

Cancer cachexia has been rarely reported in Indonesian breast cancer (BC) patients.<sup>1</sup> We aimed to determine the prevalence and factors associated with cancer cachexia following chemotherapy in the local patients with breast cancer.

## METHODS

**Design:** pre-post observational analysis

**Study recruitment:**



**Cachexia definition:**

- weight loss of at least 5% or low BMI <20 kg/m<sup>2</sup>, and
- low muscle strength, fatigue, anorexia, low fat-free mass index, or abnormal biochemistry.<sup>2</sup>

**Analysis method of vitamin D:** ELISA

**Statistical analysis:**

- Baseline characteristics, vitamin D levels, and cachexia status were explored using descriptive analysis.
- Multivariate logistic regression test was used to determine factors related to cachexia status following chemotherapy.

## RESULTS

At baseline 4.9% of patients had cachexia and a total of 28.2% of patients had persistent cachexia or evolved into cachexia after chemotherapy program (Table 2). All patients had a deficient vitamin D concentration at baseline and after chemotherapy (Table 2).

**Table 1.** Baseline characteristics of study subjects (n=103)

Variables	Frequency (%)
Age (years, mean ± SD)	52.5 ± 9.1
BMI (kg/m <sup>2</sup> )	
<18.5	9 (8.7)
18.5–24.9	35 (34.0)
25–29.9	25 (24.3)
≥30	34 (33.0)
Comorbidity	
No	47 (45.6)
Yes	56 (54.4)
Stage	
I–II	37 (35.9)
III–IV	66 (64.1)
Surgery category	
Non-mastectomy	18 (17.5)
Mastectomy	85 (82.5)
Chemotherapy setting	
Adjuvant/neoadjuvant	81 (78.6)
Palliative	22 (21.4)
Chemotherapy cycle	
< 8 cycles	27 (26.2)
≥ 8 cycles	76 (73.8)

Abbreviations: SD=Standard Deviation; BMI=Body Mass Index; IQR=Interquartile Range

**Table 2.** Vitamin D level and cachexia status based on Evans criteria before and after chemotherapy (n=103)

	Before chemotherapy	After chemotherapy
Vitamin D level (ng/ml, median (IQR))	8.43 (4.90)	6.96 (4.48)
Cachexia status (frequency (%))		
No cachexia	98 (95.1)	74 (71.8)
Persistent/becoming cachexia	5 (4.9)	29 (28.2)

Abbreviations: IQR=Interquartile Range

Having persistent cachexia or becoming cachexia was significantly associated with late-stage presentation (OR 3.43, 95%CI 1.10–10.74, p=0.034), receiving more than eight chemotherapy cycles (OR 12.05, 95%CI 2.29–63.46, p=0.003) and higher post-chemotherapy vitamin D level (OR 4.60, 95%CI 1.56–13.56, p=0.006). Having a higher baseline vitamin D level was significantly associated with a lower risk of cachexia after chemotherapy (OR 0.33, 95%CI 0.11–0.95, p=0.040) (Table 3).

**Table 3.** Significant associated risk factors for having persistent or becoming cachexia (n=103)

Variable	Persist/Become Cachexia (%)	Adjusted OR	95% CI	p
Stage				
I–II	6 (5.8)	Ref		
III–IV	23 (22.3)	3.43	1.10–10.74	0.034
Chemotherapy cycle				
< 8 cycles	2 (1.9)	Ref		
≥ 8 cycles	27 (26.2)	12.05	2.29–63.46	0.003
Baseline vitamin D*	7.38 (6.90)	0.33	0.11–0.95	0.040
Post-chemotherapy vitamin D*	7.97 (4.08)	4.60	1.56–13.56	0.006

\*Vitamin D was in ng/ml (Median (IQR)). Abbreviations: OR=Odds Ratio; CI=Confidence Interval; Ref=Reference; IQR=Interquartile Range

## CONCLUSIONS

Cachexia often occurs in local BC patients. Late-stage presentation, receiving more than eight chemotherapy cycles and higher post-chemotherapy vitamin D level are associated with an increased risk of cachexia while having a higher baseline vitamin D level is associated with a reduced risk of cachexia. Strategies and further investigation are warranted to improve cachexia with nutritional support during chemotherapy.

## REFERENCES

1. Puspitaningtyas H, Sulistyoningrum DC, Witaningrum R, Widodo I, Hardianti MS, Hutajulu SH, et al. Vitamin D status in breast cancer following chemotherapy: A pre and post observational study in a tertiary hospital in Yogyakarta, Indonesia. PLoS ONE. 2022,17(6):e0270507.
2. Evans WJ, Morley JE, Argiles J. Cachexia: A new definition. Clinical Nutrition. 2008,27:793-799.

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