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The Effect of Body Mass Index on Survival in Breast Cancer

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Abstract

Background: Obesity is a well-known risk factor for breast cancer recurrence and poor prognosis. The objective of this study was to evaluate the effect of body mass index (BMI) on survival in breast cancer patients. **Methods:** We performed a retrospective analysis of 50 breast cancer patients treated in our hospital from January 2012 to December 2013. Patients were divided according to body mass index when diagnosed into: normal weight BMI < 25 Kg/m^2, over weight BMI ≥ 25 Kg/m^2 to < 30 Kg/m^2, obesity BMI ≥ 30 Kg/m^2. In this study the effect of body mass index on progression free survival (PFS) and overall survival (OS) was evaluated. **Results:** The disease free survival (DFS) and overall survival (OS) decreased in overweight and obese patients. Both overweight and obesity were predictors for increased risks of breast cancer relapse and mortality with a median disease free survival for overweight 29 mons and obese patients 11 mons and a median overall survival for overweight patients 49 mons and obese patients 39 mons. **Conclusion:** Obesity and overweight are associated with poorer disease free survival and overall survival in patients with breast cancer.

Keywords

Body Mass Index, Breast Cancer, Obesity, Overweight, Relapse, Mortality

1. Introduction

Obesity or overweight has become an emerging health concern worldwide with over 500 million adults were obese and 958 million were overweight in 2008, [1] [2] and overweight or obesity was also reported to be a risk factor for increased incidence of various forms of cancer [3] [4]. Breast cancer is the most common malignant neoplasm among women [5] and being overweight or obese in adults is associated with a greater risk of breast cancer. [6]. Also nowadays there is

widespread consensus on the importance of obesity or overweight as a negative prognostic factor for breast cancer [7] [8].

In 2004, Berclaz *et al.* [9] have reported that obesity or overweight is associated with a poor prognosis after breast cancer treatment, and other studies also suggested that obesity at the time of cancer diagnosis or pre-diagnosis is associated with poor prognosis for breast cancer patients [10] [11]. In addition, it has been shown that breast cancer patients with higher body mass index (BMI) estimated as obesity or overweight have a worse prognosis disease regardless of tumor subtype [12].

A review of 26 studies involved 29,460 women and showed that increased BMI was associated with adverse prognosis of breast cancer [13]. In a meta-analysis, it was reported that in patients with increased BMI, the risk of recurrence was 1.91 (95% CI, 1.52 - 2.40) at 5 years and the risk of death was 1.6 (95% CI, 1.38 - 1.76) at 10 years. These results showed that obese women have an increased risk of recurrence and death. In a prospective cohort study including 512 women with early-stage breast cancer (T1 - T3, N0 - N1, and M0), increased BMI was strongly associated with poor DFS and OS [14]. In many large cohort studies inverse association between increased BMI and breast cancer mortality was evident [15]. The adverse effect of obesity on breast cancer prognosis was detected both in pre and postmenopausal women [15]. However, there were controversial results regarding the association of obesity and survival in premenopausal women. In many studies there was inverse association between breast cancer risk and premenopausal women [16] [17].

Several mechanisms are suggested to explain the association between obesity and poor prognosis of breast cancer. The most widely discussed mechanisms are the effect of obesity on the hormonal status of women and tumor characteristics. However, up till now no study showed an exact underlying pathophysiological mechanism [15].

Therefore, in this study, we aimed to assess the effect of BMI on recurrence pattern and survival in breast cancer patients.

2. Patients and Methods

2.1. Patient Characteristics

This retrospective study analyzed the data of 50 breast cancer patients who were admitted at the department of clinical oncology, Assiut university hospital from January 2012 to December 2013. Patients who had body mass index values were included in the study. The patients who had metastatic disease at the time of diagnosis were excluded from the study. Body mass index was calculated as weight (Kg)/height 2 (m^2) and patients were classified into three categories: normal body weight BMI < 25 Kg/m^2, overweight BMI ≥ 25 to < 30 Kg/m^2 and obesity BMI ≥ 30 Kg/m^2.

Information of patients was obtained covering age, height, weight, menopausal status, history of contraception, pathology, grade, clinical stage, lymph vascu-

lar invasion, ER, PR, HER 2 and treatment (surgery, chemotherapy, radiotherapy and endocrine therapy).

All study participants provided written informed consent and the study protocol and procedures were approved by the ethics committee in our faculty.

2.2. Follow up

Follow-up has been maintained by reviewing clinical charts and by contacting patients via telephone. Events used for the analysis were mortality of breast cancer or relapse including local, regional and contralateral breast cancer or distant breast cancer recurrence. Survival status was censored at the date of last contact or 31 December 2018 (last follow-up). DFS defined as the time of diagnosis to development of first evidence of recurrence (distant metastasis or local regional recurrence) or date of the last follow-up. OS was defined as from the time of diagnosis to last follow-up or time of mortality.

2.3. Statistical Analysis

In our study, the associations between different BMI groups and clinic pathologic characteristics of breast cancer patients were analyzed by the chi-square test. Data were analyzed with the help of SPSS version 23 software, which included descriptive analysis. Mean was calculated for quantitative variables. Disease free survival and overall survival were calculated (Tables 1-12 and Figures 1-4).

Table 1. Demographic data.

Item	Descriptive
1-Age	49.72 ± 10.88
2-Weight	77.54 ± 18.16
3-Height	1.55 ± 0.05
4-BMI	31.97 ± 7.02
5-BMI status:	
• Normal	6 (12.0%)
• Overweight	18 (36.0%)
• Obesity	26 (52.0%)
6-Menopausal status:	
• Pre-menopausal	25 (50.0%)
• Post-menopausal	25 (50.0%)
7-History of contraceptive:	
• No	24 (48.0%)
• Yes	26 (52.0%)

Table 2. Clinical data.

Item	Descriptive
1-Pathology:	
• DCIS	1 (2.0%)
• IDC	46 (92.0%)
• ILC	3 (6.0%)

Continued

2-Grade:	
• 1	1 (2.0%)
• 2	39 (78.0%)
• 3	10 (20.0%)
3-N1:	
• 0	14 (28.0%)
• 1 - 5	18 (36.0%)
• 5 - 10	11 (22.0%)
• >10	7 (14.0%)
4-N2:	
• 0	5 (10.0%)
• 1 - 5	10 (20.0%)
• 5 - 10	30 (60.0%)
• >10	5 (10.0%)
6-Clinical stage:	
• I	2 (4.0%)
• IA	1 (2.0%)
• IIA	14 (28.0%)
• IIB	8 (16.0%)
• IIIA	10 (20.0%)
• IIIB	2 (4.0%)
• IIIC	9 (18.0%)
• IV	4 (8.0%)
7-Lymphovascular invasion:	
• No	32 (64.0%)
• Yes	18 (36.0%)
8-ER:	
• −ve	25 (50.0%)
• +ve	25 (50.0%)
9-PR:	
• −ve	27 (54.0%)
• +ve	23 (46.0%)
10-HER-2:	
• −ve	11 (22.0%)
• +ve	10 (20.0%)

Table 3. Surgery data.

Item	Descriptive
Surgery:	
• Breast conservative surgery (BCS)	20 (40%)
• Modified radical mastectomy (MRM)	30 (60%)

Table 4. Radical local & palliative radiotherapy & hormonal therapy data.

Item	Descriptive
Radical local radiotherapy:	
• No	16 (32.0%)
• Yes	34 (68.0%)
Palliative radiotherapy:	
• No	34 (68.0%)
• Yes	16 (32.0%)
Hormonal therapy-Tamoxifen (Tam):	
• No	30 (60.0%)
• Yes	20 (40.0%)

Continued

Duration of Tam	2.78 ± 1.85
Hormonal therapy-Aromatase inhibitors (AI):	
• No	31 (62.0%)
• Yes	19 (38.0%)
Duration of AI	2.87 ± 1.54
Herceptin:	
• Yes	1 (2.0%)
• No	49 (98.0%)

Table 5. Toxicity data.

Item	Descriptive
Toxicity:	
• No	45 (90.0%)
• Acute bronchitis	1 (2.0%)
• Cardio toxicity	1 (2.0%)
• Fungal infection	1 (2.0%)
• Neutropenia	1 (2.0%)
• Pancytopenia	1 (2.0%)

Table 6. Response data.

Item	Descriptive
Response:	
• Complete remission	45 (90.0%)
• Partial remission	5 (10.0%)

Table 7. Recurrence & Metastasis data.

Item	Descriptive
Recurrence:	
• Local recurrence	11 (22.0%)
• No recurrence	39 (78.0%)
Metastasis:	
• Yes	26 (52.0%)
• No	24 (48.0%)

Table 8. Relation between BMI and other variables.

Item	BMI < 25 "n = 6"	25 ≤ BMI <30 "n = 18"	BMI ≥ 30 "n = 26"	P-value
1-Age at diagnosis:				
• ≤36 yrs.	0	4 (22.2%)	2 (7.7%)	
• 36 - 65 yrs.	4 (66.7%)	14 (77.8%)	22 (84.6%)	P < 0.03
• ≥65 yrs.	2 (33.3%)	0	2 (7.7%)	
2-Menopausal:				
• Premenopausal	1 (16.7%)	11 (61.1%)	13 (50.0%)	P < 0.04
• Postmenopausal	5 (83.3%)	7 (38.9%)	13 (50.0%)	
3-Lymph node metastases:				
• 0	3 (50.0%)	7 (38.89%)	6 (23.07%)	
• 1 - 3	1 (16.67%)	5 (27.78%)	7 (26.9%)	P < 0.001
• ≥4	2 (33.3%)	6 (33.33%)	13 (50.0%)	

Continued

4-Clinical stage:				
• I	1 (16.7%)	0	2 (7.7%)	
• IA	0	0	1 (3.8%)	
• IIA	1 (16.7%)	5 (27.8%)	8 (30.8%)	
• IIB	0	2 (11.1%)	6 (23.1%)	P = 0.365 n.s
• IIIA	2 (33.3%)	7 (38.9%)	1 (3.8%)	
• IIIB	1 (16.7%)	0	1 (3.9%)	
• IIIC	1 (16.7%)	2 (11.1%)	6 (23.1%)	
• IV	0	2 (11.1%)	2 (7.7%)	
5-Lymphovascular invasion:				
• No	3 (50.0%)	11 (61.1%)	18 (69.2%)	P = 0.643 n.s
• Yes	3 (50.0%)	7 (38.9%)	8 (30.8%)	
6-ER:				
• −ve	4 (66.7%)	11 (61.1%)	10 (38.5%)	P = 0.230 n.s
• +ve	2 (33.3%)	7 (38.9%)	16 (61.5%)	
7-PR:				
• −ve	4 (66.7%)	12 (66.7%)	11 (42.3%)	P = 0.225 n.s
• +ve	2 (33.3%)	6 (33.3%)	15 (57.7%)	
8-HER-2:				
• −ve	2 (33.3%)	3 (16.7%)	6 (23.1%)	P = 0.375 n.s
• +ve	1 (16.7%)	2 (11.1%)	7 (26.9%)	
9-Toxicity:				
• No	6 (100%)	16 (100%)	23 (88.5%)	
• Acute bronchitis	0	0	1 (3.8%)	P < 0.03
• Cardio toxicity	0	0	1 (3.8%)	
• Fungal infection	0	0	1 (3.8%)	
• Neutropenia	0	1 (5.5%)	0	
• Pancytopenia	0	1 (5.5%)	0	

Table 9. Relation between Overall survival and BMI.

Item	BMI < 25 "n = 6"	25 ≤ BMI <30 "n = 18"	BMI ≥ 30 "n = 26"	P-value
Mean ± SE	58.16 ± 3.67	49.50 ± 4.73	39.83 ± 10.24	P < 0.001
Median	58	49	39	

Table 10. Relation between Progression free survival (PFS) and BMI.

Item	BMI < 25 "n = 6"	25≤ BMI <30 "n = 18"	BMI ≥ 30 "n = 26"	P-value
Mean ± SE	42.27 ± 6.12	38.76 ± 5.32	28.16 ± 10.30	P < 0.01
Median	38	29	11	

Table 11. Means and medians for survival time.

(a)

Mean[a]				Median			
Estimate	Std. error	95% confidence interval		Estimate	Std. error	95% confidence interval	
		Lower bound	Upper bound			Lower bound	Upper bound
38.760	3.724	31.462	46.058	35.000	7.071	21.141	48.859

[a]Estimation is limited to the largest survival time if it is censored.

(b)

Mean[a]				Median			
Estimate	Std. error	95% confidence interval		Estimate	Std. error	95% confidence interval	
		Lower bound	Upper bound			Lower bound	Upper bound
51.460	3.101	45.382	57.538	59.000	4.710	49.768	68.232

[a]Estimation is limited to the largest survival time if it is censored.

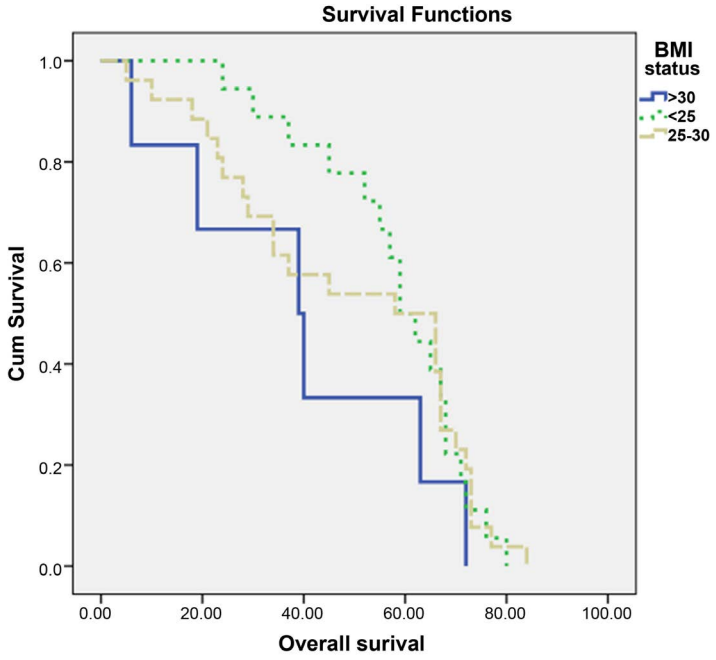

Figure 1. Relation between OS & BMI.

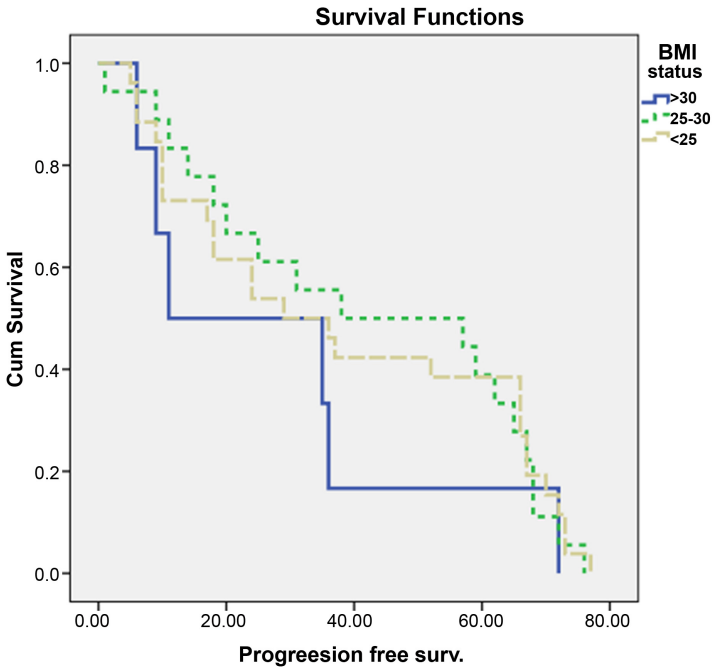

Figure 2. Relation between PFS & BMI.

Table 12. Relation between PFS & OS and BMI in premenopausal and postmenopausal patients.

Item	BMI < 25 "n = 1"	25 ≤ BMI <30 "n = 11"	BMI ≥ 30 "n = 13"	P-value
PFS premenopausal	41.90 ± 0.00	37.30 ± 12.48	35.21 ± 8.48	P < 0.03
PFS postmenopausal	42.85 ± 18.50	40.23 ± 16.64	26.80 ± 12.50	P < 0.01
OS premenopausal	57.27 ± 0.00	46.69 ± 13.27	40.25 ± 15.48	P < 0.04
OS postmenopausal	56.71 ± 13.31	50.46 ± 13.94	39.80 ± 18.31	P < 0.03

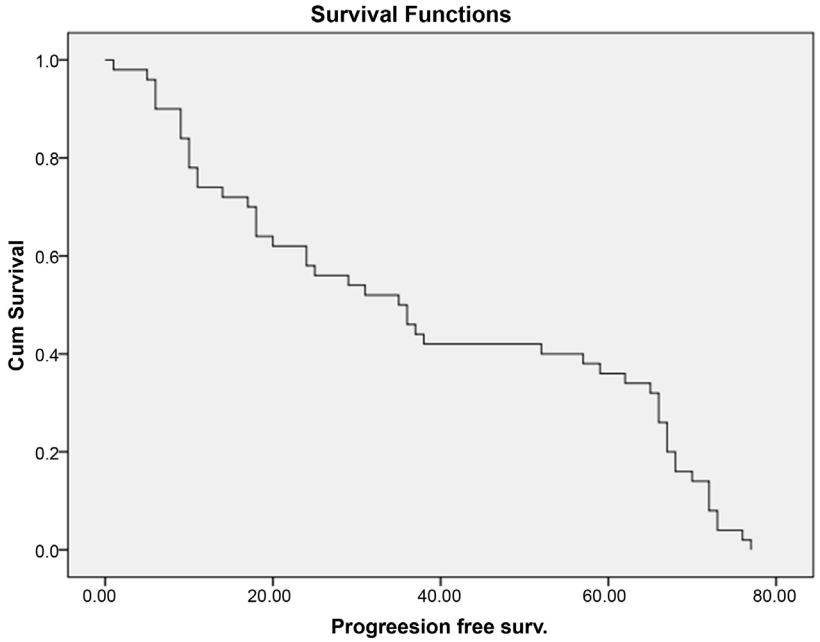

Figure 3. Progression free survery.

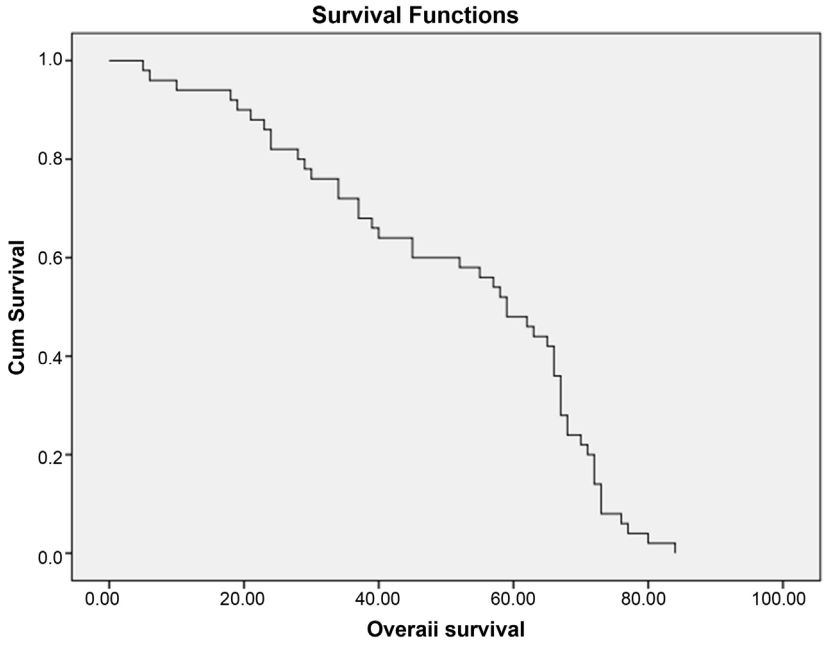

Figure 4. Overall survival.

3. Discussion

Obesity and overweight in adults have been reported to be associated with a greater risk of breast cancer, [6] [17] while the studies that evaluated influence of overweight and obesity on breast cancer survival have shown mixed findings [18] [19]. In an effort to address this gap, we conducted a retrospective study to make the relationship between obesity and breast cancer prognosis clear.

We also found that overweight and obesity were independent predictors for increased risks of breast cancer recurrence and death for the whole cohort. In a previous study from America, after 5-year follow-up, the authors calculated that hazard ratios (HR) for risks of relapse was 1.18 (95% CI 1.02 - 1.36) in overweight patients and breast cancer death was 1.23 (95% CI 1.00 - 1.52) in the obese group relative to the normal weight, while overweight did not affect recurrence and obesity wasn't a predictor for breast cancer mortality [18]. In a study including African patients, overweight was significantly related to breast cancer death (HR 2.903, 95% CI: 1.551 - 5.432) and relapse (HR 1.899, 95% CI: 1.05 - 3.433) by multivariable analysis [20]. Another study found that the risks of developing distant metastasis were significantly increased for Danish obese patients, while both obesity and overweight women had a higher risk of breast cancer death relative to normal-weight women [21]. However, Kawai *et al.* reported that obesity was an independent risk factor for breast cancer mortality (HR: 1.47; 95% CI: 1.11 - 1.93) but not for relapse, and overweight had no association with breast cancer prognosis [22]. Nevertheless, in another study from America, Kwan *et al.* in 2012 [23] observed that overweight or obesity was not associated with increased risk of relapse and breast cancer death compared to normal weight, a report from the Korean Breast Cancer Society demonstrated similar results [19].

Although the association between obesity/overweight and the prognosis of breast cancer patients remains controversial, it has been reported that impact of BMI on prognosis of breast cancer may relate to menopausal status [24].

In a stratified analysis, it was found that being overweight was associated with increased risks of breast cancer recurrence and death within 5 years after breast cancer diagnosis for postmenopausal but not for premenopausal women, and obesity was an independently poor predictor for breast cancer recurrence and death regardless to menopausal status [25]. Similar to the study, Reeves *et al.* in 2007 have reported that obesity and overweight were related to increased breast cancer progression and mortality primarily in British postmenopausal women. A meta-analysis of 82 studies that included 213,075 breast cancer patients demonstrated that obesity was associated with higher risk of breast cancer mortality (HR, 1.41; 95% CI, 1.29 - 1.53) in both premenopausal (HR, 1.75; 95% CI, 1.26 - 2.41) and postmenopausal (HR, 1.34; 95% CI, 1.18 - 1.53) women [26], similar results were found by Niraula *et al.* in 2012 [27]. A study from Japan found that obesity and overweight were associated with a nonsignificant higher risk of relapse and breast cancer mortality for premenopausal women, and obesity but

not overweight was associated with a significantly higher risk of breast cancer mortality for postmenopausal women (not for relapse) [22], results from a cohort study also suggest that obesity (not overweight) was an independent poor prognostic predictor for American postmenopausal breast cancer patients [28]. However, some authors [9] found that overweight or obesity is significantly associated with a shorter OS and DFS for premenopausal and perimenopause patients. Besides, another study including American breast cancer patients also demonstrated that overweight or obesity was positively associated with recurrence in premenopausal rather than postmenopausal women [24]. Moreover, some studies indicated that overweight is an independent prognostic factor for increased breast cancer death and relapse in premenopausal triple-negative breast cancer women, while similar results were not found in postmenopausal women [20] [29].

Our study found that overweight and obesity at diagnosis were related to poor prognosis of breast cancer irrespective of menopausal status, with worse progression free survival and overall survival in both pre and postmenopausal patients. The limitation of our study was the small sample size.

4. Conclusion

Our study shows that both overweight and obesity are associated with poorer DFS and OS in breast cancer patients. However, further studies with a larger sample size and more comprehensive design are urgently warranted.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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