

# Body Mass Index and Clinical Outcomes in Egyptian Women with Breast Cancer: A Multi-institutional Study

## ABSTRACT

**Purpose:** The aim of this work was to evaluate the association between body mass index (BMI) and clinical outcomes among Egyptian female breast cancer patients.

**Methods:** We reviewed the file registry of 629 patients with operable breast cancer regarding age, sex, height, weight, menopausal status, family history of breast cancer, tumor features, TNM arrangement, and treatment during the period from January 2006 to December 2012. In our studies, obesity was defined as a BMI of  $\geq 30$  kg/m<sup>2</sup>. The primary objective was to estimate the effect of body mass index on the clinical outcomes of breast cancer patients including DFS and OAS.

**Results:** A total of 629 patients with a mean age of 51.1 years. Stage III and Stage II presented 52% and 46.6% respectively. Overweight and obese patients represent 60.5% of all patient population. there was no association between tumor stage, grade or menopausal status and BMI. Patients with normal BMI showed a median survival of 95.3 months [ CI: 54.6,136.06]. This was significantly higher than overweight and obese patients ( $p = 0.001$ ). Nearly one-third of patients (29.1%) with normal BMI experienced disease relapse compared to 32.8% for overweight and obese patients, however, this was statistically not significant (0.097).

**Conclusion:** According to the results of this retrospective study, increased BMI may be associated with less favorable prognosis of breast cancer patients.

## 1. INTRODUCTION

Breast cancer is one of the most frequent cancers and is considered a chief reason of cancer mortality among females worldwide. It accounts for 25% of all cancer cases and 15% of all cancer deaths among females [1]. In Egypt; Breast Cancer is estimated to be the most common female cancer with a crude incidence rate of 35.8 per 100,000 [2].

The prevalence of obesity being overweight is defined by a high body mass index (BMI), which has been increasing regardless of sex, age or whether people live in developed or developing countries [3,4].

According to a study published in the lancet, Egypt is the seventh most overweight country in the world [5]. Obesity may increase the incidence of various human cancers, as reported in several epidemiological studies [6-9].

The underlying mechanisms that might elucidate the association between obesity and breast cancer survival are not recognized, Higher estradiol level that was produced in postmenopausal women by aromatization of androgens in the adipose tissues, and higher insulin level, a disorder public in obese women, are connected to poorer prognosis in breast cancer. Non-biological mechanisms could include chemotherapy under-dosing in obese women, suboptimal treatment, and obesity-related complications [1,10,11].

Several studies have examined the relationship between obesity and breast cancer consequences, while the results were different among all studies due to different factors like BMI cut-offs, the extent of disease, estrogen receptor status, menopausal status, mode of treatments [13-16].

A large- scale meta- analysis of 82 studies conducted by the World Cancer Research Fund and American Institute for Cancer Research (WCRF/AICR) that study the magnitude and the shape of the association between obesity, and the risk of mortality in women with pre and postmenopausal breast cancer, concluded that obese patients had poorer overall and breast cancer survival, for both pre- and postmenopausal patients [12].

Up to our knowledge, there are no studies investigating the association between body mass index (BMI) and breast cancer outcomes among Egyptian breast cancer ladies. The aim of this work was to evaluate the association between BMI and breast cancer outcomes for patients in Egypt.

## **2. PATIENTS AND METHODS**

### **2.1 Patients and Data Collection**

Between January 2006 and December 2012, Medical records of patients with invasive breast cancer who were treated at Clinical Oncology Department, Minia University and Clinical Oncology & Nuclear Medicine Department, Mansoura University were reviewed.

Eligibility criteria included female patients of 18 years or older, histologically proven invasive breast cancer, and height and weight were recorded in the database. Patients with distant metastasis or incomplete data were excluded. Data of patients were collected from their medical files.

Information on patients covering age, height and weight, menopausal status, , TNM classification, tumor grade and type of treatment (chemotherapy, endocrine therapy, and radiation therapy) were reviewed in patient's records. The TNM classification and histological classification

were registered according to the UICC staging [17] and WHO classification systems, [18] respectively. Information on ER/PR/HER2 was also taken. if at least 1% of nuclei in the tumor were immunohistochemically positive for ER or PR ER/PR, it was considered positive. An immunohistochemical HER2 score of 3 + and/or a positive FISH result was defined as overexpression.

The height and weight were measured at the time of diagnosis and were routinely documented in patients records in both hospitals. The BMI was calculated as weight divided by the square of height (kg/m<sup>2</sup>). According to World Health Organization's recommendations patients were categorized by BMI into five groups: underweight<18.5 kg/ m<sup>2</sup>; normal 18.5–24.9 kg/m<sup>2</sup>; overweight 25.0–29.9 kg/m<sup>2</sup>; obesity 30.0–34.9 kg/m<sup>2</sup>; and excess obesity ≥35 kg/m<sup>2</sup>. In our analyses, obesity was defined as a BMI of ≥30 kg/m<sup>2</sup>.

### **2.2 Statistical Analysis**

Disease free survival (DFS) was defined as the time from diagnosis until first relapse (locoregional, or distant), contralateral breast cancer, or death from any cause. overall survival (OAS); defined as the time from diagnosis until death from any cause. The DFS and OAS rates were calculated by the Kaplan–Meier method. All reported P value are two sided and  $p \leq 0.05$  was considered significant.

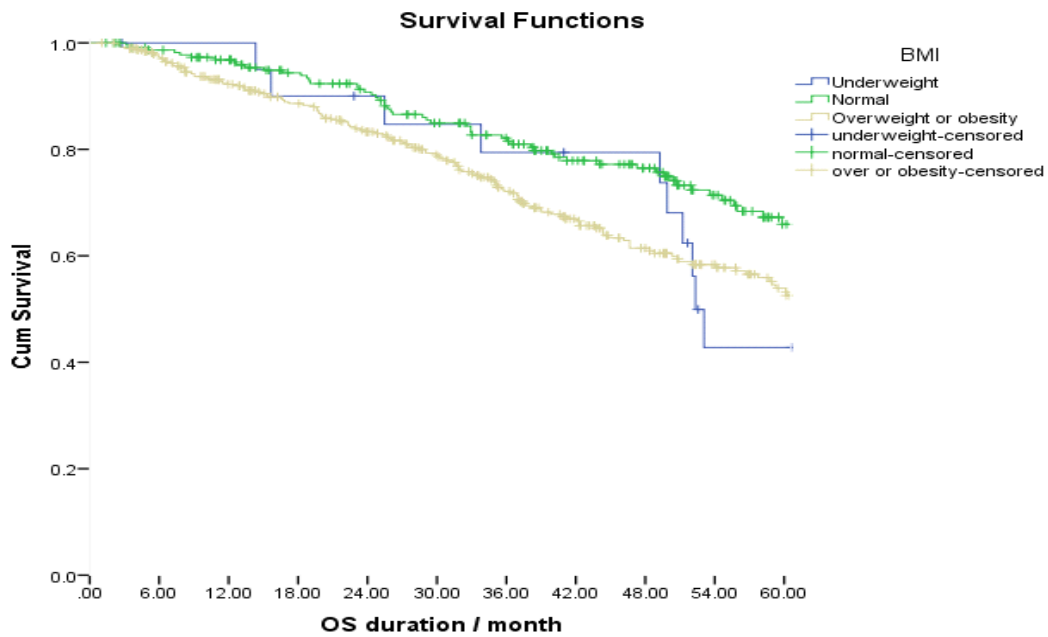
## **3. RESULTS**

### **3.1 Patient Characteristics**

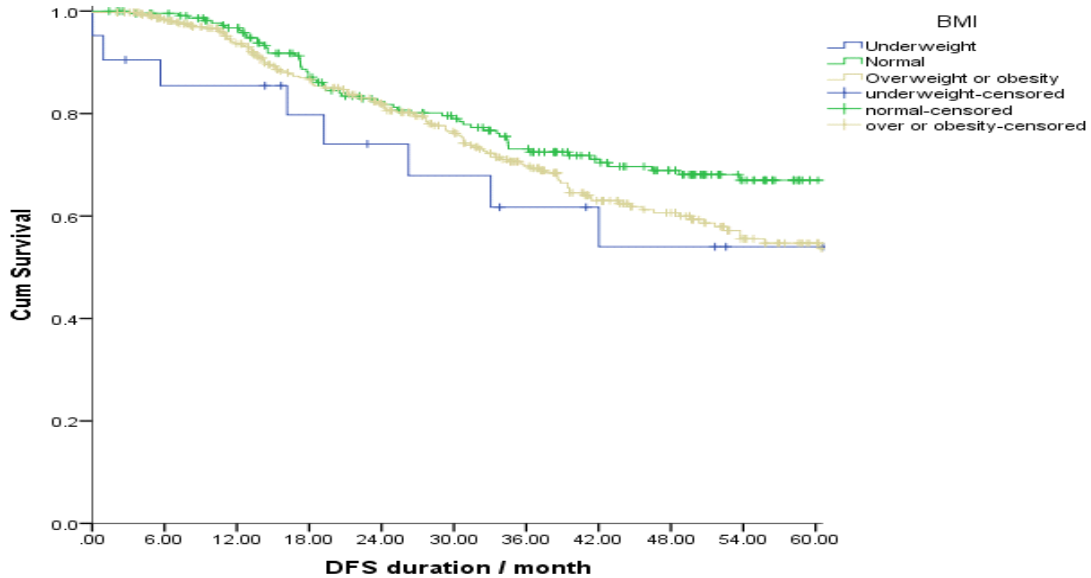
Table (1) illustrates patient characteristics. A total of 629 patients included in our study with a mean age of 51.1 years. Stage III and Stage II presented 52% and 46.6% respectively. Half of the cases were postmenopausal at the time of diagnosis (52.7%). ER and PR positive tumors represented 45.8% and 46% respectively. Overweight and obese patients represent 60.5% of all patient population compared to 36% and 3.5% for those with normal and underweight patients respectively.

Table 1. Patient characteristics

	Total N = 629		BMI								P value
			Underweight N = 21		Normal Weight N = 227		Overweight N = 180		Obese N = 201		
	N	%	N	%	N	%	N	%	N	%	
<b>Age (Years)</b>											
Mean (SD)	51.1(11.7)		46.5(13.1)		50.4(12.9)		49(10.7)		52.8(10.9)		
Median	50		45		49		48.5		50		
<b>Tumor Stage</b>											
Stage I	8	1.4	0	0	2	25	2	25	4	50	
Stage II											
Stage IIA	125	19.8	4	3.2	44	35.2	38	30.4	39	31.2	p =
Stage IIB	168	26.8	8	4.7	66	39.2	52	30.9	42	25.2	0.732
Stage III											
Stage IIIA	222	35.2	8	3.6	72	32.5	63	28.4	79	35.5	p =
Stage IIIB	106	16.8	1	1	43	40.5	25	23.5	37	35	0.443
<b>Menopausal Status</b>											
Premenopausal	298	47.3	12	4	120	40.2	94	31.6	72	24.2	p =
Postmenopausal	331	52.7	9	2.7	107	32.3	86	26	129	39	0.196
<b>Tumor grade</b>											
G I	6	1	0	0	4	66.7	0	0	2	33.3	p =
G II	555	88.1	20	3.6	197	35.5	164	29.5	174	31.4	0.486
G III	68	10.9	1	1.5	26	38.3	16	23.5	25	36.7	
<b>Hormonal Status</b>											
ER											
Positive	286	45.8	8	2.8	105	36.7	80	28	93	32.5	p =
Negative	126	19.9	1	2.4	44	34.9	36	27	45	35.7	0.941
Unknown	217	34.3	12	5.5	78	37.3	64	30	63	27.2	
<b>PR</b>											
Positive	288	46	5	2.5	105	36.4	82	27.8	96	33.3	P =
Negative	122	19.3	4	3.4	40	35.2	32	27	46	34.4	0.877
Unknown	219	34.7	12	5.5	82	37.4	66	30.1	59	27	



**Fig. 1. Overall survival of breast cancer patients**



**Fig. 2. Disease free survival of breast cancer patients**

**3.2 Clinical Features of Breast Carcinoma in Relation to BMI**

Patients with advanced breast cancer tumor stage composed half of all patients in our study (52%), of them those with high BMI were 62.1% (204/328) however the association between BMI

and advanced tumor stage was not statistically significant [p = 0.443]. Similarly, Stage II represented 46.6% of our cohort. Of them, those with high BMI composed 58.3% (171/293) however, this was statistically not significant. Overweight and obesity were more prevalent in postmenopausal women (57.6%) compared to

40.7% for premenopausal women but this was not statistically significant ( $p = 0.196$ ). Similarly, there was no association between tumor grade and BMI ( $p = 0.486$ ). Data were available regarding estrogen receptor status in nearly two thirds (65.8%) of patients (414/629). Overweight and obese patients composed 61% of all ER-positive tumors however this was not associated with BMI ( $p = 0.941$ ). About two-thirds of our study population (70.4%) have positive progesterone receptors. Obese and overweight patients presented a majority (61.3 %) of this population however the association between BMI and positive hormonal status was not proved to be significant ( $p = 0.877$ ).

### 3.3 Correlation between BMI and Survival

Regarding survival, there was 70% of breast cancer patients with normal BMI alive at the time of analysis. This compared to 58% were alive for overweight and obese patients. In fact, patients with normal BMI showed a median survival of 95.3 months [CI: 54.6,136.06]. This was significantly higher than overweight and obese patients ( $p = 0.001$ ). Nearly one-third of patients (29.1%) with normal BMI experienced disease relapse compared to 32.8% for overweight and obese patients, however, this was statistically not significant (0.097).

## 4. DISCUSSION

There are contradictory results about the role of obesity in the development of cancer. In some studies, high BMI is considered as a risk factor for breast cancer development and increased mortality [20-28].

On the other hand, other studies have reported that increased BMI may also be protective of mortality [29-33]. So according to these vague results, the rank of BMI as a prognostic element for breast Cancer continued undefined.

Our results are in the same line of the concept that BMI is an independent prognostic tool in breast cancer patients. BMI as a general independent factor does not have a significant influence on DFS but does have a significant effect on OS, with overweight and obese patients (heavier) patients showing worse survival. As shown in our result in which; Overweight and Obese patients had a bad consequence compared to normal and underweight patients as regard overall survival, patients with normal BMI showed a mean survival of 109 months and a

median survival of 95.3 months. This was significantly higher than overweight and obese patients ( $p = 0.001$ ), but no difference was seen in DFS. These results are consistent with prior studies that have exhibited a poorer OS with increasing weight including large scale meta-analysis of 82 studies that showed that obese patients had poorer overall breast cancer survival, for both pre- and postmenopausal patients. [12], and other authors in their researches support our findings as regard a bad impact of increasing body weight on the prognosis in these patients [22, 35].

Senie et al showed that obese patients showed low DFS [36]. Other studies did not explore an impact of obesity on OS or DFS [37]. While another study finds an effect of obesity on both OS or DFS [38].

In our study, there were no positive correlations between BMI and tumor features such as tumor stage, hormonal receptor and tumor grade These findings are inconsistent with earlier studies [22, 36, 39, 40] that shown a robust correlation between obesity and tumor size as in those trials most of the patients with obese BMI had tumors of  $\geq 2$  cm diameter compared to patients with normal BMI, this may be related to relatively small number of our patients.

## 5. LIMITATIONS

However, the data in the retrospective studies are almost always incomplete and accused of selection bias because it depends mainly on medical documentation. But, in reality, it reflects real-life oncologists' experience. Other limitations of our study are like a lack of data gathering on weight changes at the termination of adjuvant chemotherapy or during follow-up was not done; and the reporting of unplanned subgroup analysis. Also, the small sample size is an important limitation.

## 6. CONCLUSION AND RECOMMENDATIONS

In conclusion, this retrospective study reveals that BMI is an independent prognostic factor for OS in patients with operable breast cancer. Our study supports the indication that obese BMI denotes a poor risk factor for the consequence. With increasing obesity universal, more studies on alleviating the treatment of obese BC patients are required.

## STATEMENT OF ETHICS

The institutional review board of each participating center approved this multicenter retrospective study, and written informed consent was waived because of the retrospective design.

## COMPLIANCE WITH ETHICAL STANDARDS

**Ethical approval** all procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

This study protocol had ethical approval from Medical Research Ethics Committee, Faculty of Medicine, Mansoura University.

## INFORMED CONSENT

Retrospective review of de-identified patients using the Cancer Registry database in both Minia and Mansura University.

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