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ORIGINAL RESEARCH

Association Between Obesity and Clinicopathological Profile of Patients with Newly Diagnosed Non-Metastatic Breast Cancer in Saudi Arabia

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Purpose: Obesity is prevalent in Saudi Arabia and is associated with adverse clinical features and poor breast cancer (BC) outcomes. We determined the distribution of body mass index (BMI) and evaluated its association with disease characteristics and outcomes in women with non-metastatic BC.

Patients and Methods: We conducted a retrospective analysis of a prospectively collected database of consecutive patients treated for non-metastatic BC between 2002 and 2014. Patients were categorized into the following groups: underweight/normal weight (BMI <25 kg/m^2), overweight (BMI 25–29.9 kg/m^2), and obese (BMI ≥30 kg/m^2). Regression analysis was used to evaluate clinicopathological factors associated with BMI and clinical stage.

Results: A total of 2212 patients were enrolled. The median age was 45 years (interquartile range [IQR], 39–52 years), and the median BMI was 30 kg/m^2 (IQR, 26–34 kg/m^2). Most patients were premenopausal (63.6%), nearly half of the patients had stage III disease, and 11.2% were screen-detected. The prevalence of obesity was 53.4%, with a significant difference between the peri/premenopausal (49.4%) and postmenopausal (61.7%) groups ($p < 0.001$). Obese patients were more likely to be aged >40 years, be postmenopausal, have a history of oral contraceptive pills, have advanced-stage disease, and have undergone radiation therapy, and were less likely to have human epithelial growth factor 2 (HER2)+ disease than non-obese patients. Premenopausal obese women had fewer hormone receptor-positive and more triple-negative cancers than postmenopausal obese women did. Obesity, non-screening-detected BC, and HER+ status were independent prognostic factors for advanced-stage presentation.

Conclusion: The prevalence of obesity and its significant association with advanced BC justify the upscaling of screening services and instituting weight-reduction strategies.

Keywords: obesity, body mass index, non-metastatic breast cancer, clinical stage, Saudi Arabia

Introduction

Breast cancer (BC) in women has the highest global age-standardized incidence rate (ASR) per 100,000 persons per year and is the most common cause of death due to cancer worldwide,[1] including in Saudi Arabia (SA).[2] Although the ASR in the Saudi Kingdom is far less than the global figure (27.7 vs 89.9 per 100,000 persons per year, respectively),[3] over the past three decades, a sharp rise in local cancer incidence and mortality has been reported,[4,5] which is in concordance with the global transition cancer theory and changes in risk factors.[6] Obesity (body mass index [BMI] ≥30 kg/m^2) is a major global health problem, especially in wealthy or transitional economies. Between 1980 and 2015, its prevalence doubled in >70 countries, and the numbers continue to increase in most other nations,[7] thereby affecting 20–41% of the populations.[8] Among Saudi women, the prevalence of obesity has significantly increased over the past several decades

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(14.3% in 1975, 30% in 2001, and 41.2% in 2016),[9] and in conjunction with being overweight (BMI ≥25 kg/m^2), the prevalence is approximately 70%.[9] Excess body weight is associated with increased cancer incidence, and poor overall and BC-specific survival.[10,11] The disease characteristics of obesity include larger tumors, more positive nodes, higher tumor grades, more triple-negative disease in premenopausal women, and more hormone-positive tumors in postmenopausal women.[12–15] Ethnicity is associated with variations in age and tumor stage at diagnosis. Moreover, race, age, menopausal status, and BMI at diagnosis are associated with variations in the molecular subtype distribution.[16–21]

We observed a high rate of obesity and a high rate of adverse clinical features of non-metastatic BC at diagnosis in Saudi women. However, there are no data on BMI prevalence or the impact of BMI on BC. This study aimed to evaluate the BMI impact on non-metastatic BC among Saudi women and evaluate the associated factors with advanced clinical stage.

Patients and Methods

This retrospective study used data from consecutive patients with non-metastatic BC treated at the Oncology Center of the King Faisal Specialist Hospital and Research Center, Riyadh, between January 2002 and December 2014. The study protocol was approved by the Research Advisory Council of King Faisal Specialist Hospital and Research Centre. This study was conducted in accordance with the ethical principles of the Declaration of Helsinki (2000).

The data were obtained from a prospective BC database. Data on the following demographic and clinicopathological parameters were retrieved: age at the time of diagnosis, presentation (screen-detected or non-screen-detected), history of oral contraceptive pill (OCP) use, menopausal status, height, weight, tumor histology and grade, clinical tumor and nodal stages, estrogen receptor (ER) and progesterone receptor (PR) status, and human epithelial growth factor 2 (HER2) overexpression. Data on management, chemotherapy (adjuvant and neoadjuvant), surgery type, radiation therapy, hormonal therapy, and anti-HER2 therapy were also retrieved.

A specialized BC pathologist confirmed all pathology slides. ER- or PR-positive tumors were defined as tumor cells with ≥10% immunohistochemistry (IHC) staining for ER or PR. Tumors were defined as hormone receptor (HR)-positive if ER, PR, or both were positive. HER2 status was determined by IHC scoring as follows: 0 or +1, negative; +2, positive (confirmed by fluorescence in situ hybridization); and +3, positive. Tumor grade was determined based on the Nottingham histological score. Weight and height were measured and documented at the time of diagnosis. BMI was computed as weight divided by height^2 and expressed as kg/m^2. The patients were divided according to BMI classification as described by the World Health Organization: underweight, <18.5 kg/m^2; normal weight, 18.5–24.9 kg/m^2; overweight, 25–29.9 kg/m^2; and obese, ≥30 kg/m^2. BC was clinically staged according to the TNM staging system of the UICC/AJCC.

Statistical Analysis

Patient characteristics are expressed as frequencies for continuous variables and as medians with interquartile ranges (IQRs) for categorical variables. Continuous comparisons were performed using the Mann–Whitney *U*-test or Kruskal–Wallis test, and categorical variables were compared using the chi-squared test. Regression analysis was used to determine the factors associated with BMI and clinical stage. Covariates with a proven or potential association in previous studies were selected. Multicollinearity was avoided by including only variables with an intervariable correlation coefficient ≤0.7, tolerance ≥0.1, and variance inflation factor (VIF) <10. The covariates included were age, menopausal status, mode of presentation (screen-detected vs symptomatic), history of OCP use, histology, grade, clinical stage, chemotherapy, surgery, and radiation therapy. Hormonal and anti-HER2 therapy were not included because of high collinearity with ER/PR and HER2 status. In the final model, the VIF and tolerance of all included variables were <2.5 and >0.4, respectively. Disease-free survival and overall survival probabilities were plotted using the Kaplan–Meier estimator. Statistical computations were performed using IBM SPSS Statistics for Mac, version 27.0.

Results

The study enrolled 2212 women with non-metastatic BC, with the majority being premenopausal (63.6%). The median BMI was 30 kg/m^2 (IQR, 26–34 kg/m^2). At the time of diagnosis, 53.4% of patients were obese, 30.9% were overweight,

and 15.6% were normal weight/underweight. Table 1 shows patient demographics, clinicopathological characteristics, and management.

The median age at diagnosis was 45.7 ± 10.4 years (IQR, 39–52 years), with a significant difference between the BMI groups as follows: underweight/normal weight, 41 years (IQR, 34–50 years); overweight, 44 years (IQR, 37–50 years); and obese, 47 years (IQR, 40–53 years) ($p < 0.001$). The distribution of BMI of pre- and postmenopausal patients is shown in Figure 1.

Menopausal Status and Molecular Subtypes in Obese Patients

The molecular subtype distribution for all women stratified by obesity (BMI ≥30 kg/m^2) and menopausal status is illustrated in Figure 2A and B. Obese premenopausal patients demonstrated a lower rate of HR+/HER− (45.1% vs 53.5%) and a higher number of triple-negative tumors (24.5% vs 15.5%) than postmenopausal obese patients and almost similar rates of HER2-enriched subtypes (HR+, 15.6% vs 16.7%; HR−, 14.8% vs 14.3%; overall, 30.4% vs 31%; $p = 0.003$, Figure 2C). There was no significant difference in molecular subtype distribution in the non-obese group ($p = 0.10$, Figure 2D).

Factors Associated with Obesity

Table 2 presents the logistic regression of variables associated with obesity (BMI ≥30 kg/m^2). The factors independently associated with obesity were ≥40 years of age (odds ratio [OR], 1.90; 95% CI, 1.49–2.43; $p < 0.001$), history of OCP use (OR, 1.33; 95% CI, 1.05–1.67; $p = 0.01$), postmenopausal status (OR, 1.37; 95% CI, 1.06–1.76; $p = 0.01$), stage III vs stage I/II disease (OR, 1.25; 95% CI, 1.01–1.56; $p = 0.04$), radiation therapy (OR, 1.63; 95% CI, 1.22–2.209; $p = 0.001$), and HER2 overexpression (OR, 0.73; 95% CI, 0.59–0.92; $p = 0.008$). A subgroup analysis revealed that premenopausal obese women were more likely to present with a triple-negative molecular subtype (OR, 1.30; 95% CI 1.01–1.69; $p = 0.04$) and more advanced disease (stage III vs stage I/II) (OR, 1.27; 95% CI, 1.03–1.5; $p = 0.02$) than non-obese premenopausal women. In contrast, postmenopausal obese patients were only significantly associated with more stage III (OR, 1.45; 95% CI 1.05–2.01; $p = 0.02$) than non-obese postmenopausal women.

Factors Associated with Clinical Stage

Almost 50% of this cohort presented with stage III disease. The following factors were associated with advanced clinical stage (stage III vs stage I/II): obesity ($p = 0.001$), screen-detected tumors ($p = 0.01$), and molecular subtype ($p < 0.002$). The following factors were not associated with advanced stage at presentation: age ≤40 vs >40 years ($p = 0.14$), pre- vs postmenopausal status ($p = 0.33$), history of OCP use ($p = 0.11$), or tumor grade (G1 and G2 vs G3; $p < 0.11$). However, G3 was more strongly associated with advanced stage than G1 ($p = 0.04$). There was no significant association between overweight and clinical stage ($p = 0.33$).

Multivariate logistic regression revealed that screen-detected tumors were associated with less stage III vs stage I and II disease (OR, 0.69; 95% CI, 0.51–0.93; $p < 0.01$), and obese patients were at a greater risk of presenting with advanced disease (stage III vs I and II; OR, 1.52; 95% CI, 1.15–1.9; $p < 0.001$). In addition, in comparison to HR+/HER2− disease, the HR+/HER2+ subtype was associated more with advanced stage at diagnosis (OR, 1.46; 95% CI, 1.14–1.88; $p < 0.002$), as was the HR−/HER2+ subtype (OR, 1.54; 95% CI, 1.18–2.00; $p = 0.001$), whereas the triple-negative subtype did not reach statistical significance ($p = 0.09$).

The screen-detected tumors were associated with more stage I/II vs III in premenopausal women only, whereas HER2+ status and obesity were associated with advanced stage at diagnosis (stage III vs I/II) in pre- and postmenopausal women. However, the association of HER2+ with advanced stage at presentation was higher in premenopausal women (OR, 1.68; 95% CI, 1.33–2.11; $p < 0.001$) than in postmenopausal women (OR, 1.52; 95% CI, 1.08–2.13; $p < 0.01$), whereas the association of obesity with advanced stage was higher in postmenopausal women (OR, 1.46; 95% CI, 1.04–1.60; $p = 0.02$) than in premenopausal women (OR, 1.29; 95% CI, 1.04–1.60; $p = 0.01$).

Table 1 Patients' Demographic and Clinicopathological Characteristics and Management of the Study Group Stratified by BMI

Parameter	All		BMI (kg/m^2) Groups						P-value
			Normal Weight		Overweight		Obese		
	No.	%	No.	%	No.	%	No.	%	
No. of patients	2212	100	346	15.6	684	30.9	1182	53.4	<0.001
Age group, years									
≤40	717	32.4	166	48	253	37	298	25.2	<0.001
>40	1495	67.6	180	52	431	63	884	74.8	
Menopausal status									
Pre	1407	65.2	249	73.5	473	70.7	685	59.5	<0.001
Peri	62	2.9	9	2.7	13	1.9	40	3.5	
Post	690	32	81	23.9	183	27.4	426	37	
NA	53	2.0							
History of taking OCP	1164	70.9	148	61.7	369	70.3	647	73.8	0.001
Screen detected	247	11.2	40	12.4	72	10.5	135	11.4	0.67
Histology									
Invasive ductal carcinoma	1985	89.7	303	88.2	615	90.3	1067	90.2	0.94
Invasive lobular carcinoma	148	6.7	26	7.5	38	5.6	84	7.1	
Others	79	3.5							
Tumor grade									
G1	102	4.7	17	5.1	27	4.1	58	5	0.21
G2	970	45.1	162	48.4	286	43.3	522	45.2	
G3	877	40.8	117	34.9	285	43.2	475	41.1	
Gx	263	11.8	39	11.6	62	9.4	100	8.7	
ER									
Positive	1380	63	224	65.3	422	62.2	734	62.7	0.61
Negative	811	37	119	34.7	256	37.8	436	37.3	
Missing	21	<1							
PR									
Positive	1159	52.9	173	50.4	352	51.9	634	54.2	0.39
Negative	1032	47.1	170	49.6	326	48.1	536	45.8	
Missing	21	<1							
HER2									0.03
Positive	704	32.6	109	32.1	243	36.3	352	30.5	
Negative	1458	67.4	231	67.9	426	63.7	801	69.5	
Missing	50								

(*Continued*)

Table 1 (Continued).

Parameter	All		BMI (kg/m^2) Groups						P-value
			Normal Weight		Overweight		Obese		
	No.	%	No.	%	No.	%	No.	%	
Molecular profiles									0.24
ER/PR+/HER2–	1012	46.9	159	46.9	295	44.2	558	48.4	
ER/PR+/HER2+	380	17.6	64	18.9	131	19.6	185	16	
ER/PR-/HER2+	322	14.9	44	13	111	16.6	167	14.5	
ER/PR-HER2–	446	20.6	72	21.2	131	19.6	243	21.1	
Missing	52	2.3							
Clinical T stage									
T1	258	12.3	24	12.7	85	13.1	131	11.7	0.04
T2	887	42.3	155	46.8	291	44.9	441	39.4	
T3	511	24.3	75	22.7	149	23	287	25.6	
T4	443	21.1	59	17.8	123	19	261	23.3	
Tx	113	5							
Nodal stage									
N0	618	29	96	29	203	30.9	319	27.9	0.07
N1	968	45	165	49.8	295	44.9	508	44.4	
N2	376	17.6	55	16.6	111	16.9	210	18.4	
N3	169	7.9	15	4.5	48	7.3	106	9.3	
Nx	81	3.6							
Management									
Neoadjuvant chemotherapy	879	40.5	139	41.4	260	38.8	480	41.3	0.54
Type of breast surgery									
BCS	789	36.6	124	37.1	250	37.4	415	35.9	0.02
MRM	1188	55.1	183	54.7	343	51.4	662	57.4	
SSM	70	3.2	13	3.8	29	4.3	28	2.4	
SM	97	4.5	14	4.1	40	5.9	43	3.7	
Missing	10								
Axillary dissection	1860	85	283	84	568	83.8	1009	86.1	0.11
Adjuvant chemotherapy	1335	61.5	210	62.3	422	62.9	703	60.4	0.53
Radiation therapy	1795	82.8	258	77.2	545	81.2	992	85.2	0.001
Hormonal therapy	1355	63.4	212	63.3	417	63.3	726	63.6	0.92
Anti-HER2 therapy	548	25.3	87	25.7	181	27.1	280	24.1	0.37

Abbreviations: BCS, breast-conserving surgery; BMI, body mass index; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; IQR, interquartile range; MRM, modified radical mastectomy; NA, not available; OCP, oral contraceptive pill; PR, progesterone receptor; SM, simple mastectomy; SSM, skin-sparing mastectomy.

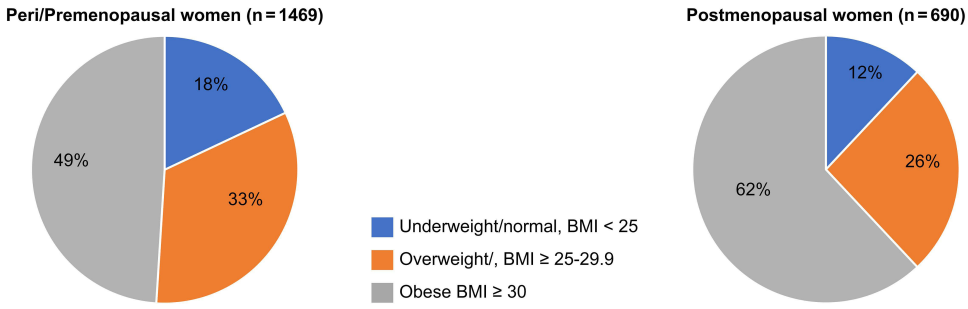

Figure 1 Pie charts demonstrating the distribution of body mass index (BMI) groups in peri/pre- and postmenopausal women ($p < 0.001$).

Survival Analysis

The median follow-up period was 39 months (IQR, 22–66 months), with 44 patients (2%) lost to follow-up. During this brief period, disease-free survival and overall survival did not differ significantly among the various BMI groups. However, there were significant differences among the women grouped by clinical stage (Figure 3A–D).

Discussion

We present the first study to examine the BMI distribution in Saudi women with newly diagnosed non-metastatic BC and clarify the association between BMI and clinicopathological characteristics and outcomes from the largest prospective database in SA. The results revealed that the prevalence of excess weight and obesity in newly diagnosed non-metastatic BC patients (84.4%) was higher than the prevalence in the general population of Saudi women (70.2%).[9] Obesity was less prevalent in premenopausal women (49.4%) than in postmenopausal women (61.7%).

Most newly diagnosed patients with non-metastatic BC were premenopausal (62%) and/or obese (53%), and nearly half presented with stage III disease. Only 11.2% of cases were screen-detected BC. Obesity in our patients was positively associated with an advanced clinical stage, regardless of menopausal status, and was associated with more triple-negative disease in premenopausal women. The following factors were independently associated with obesity: age ≥40 years, history of OCP use, postmenopausal status, HER2 overexpression, stage III vs stage I/II, and radiation therapy. The association between excess weight and adverse BC characteristics demonstrated in this study is comparable to that demonstrated in previous studies.[13–15,18,22–24] However, the higher prevalence of excess weight in Saudi women is associated with higher adverse pathological features. Independently, obesity, HER2-positive disease, and non-screen-detected tumors were associated with an advanced clinical stage. The higher prevalence of obesity and lower screening detection rate in our patients necessitates further research and encourages prompt intervention.

The vast majority of newly diagnosed BC patients have one risk factor at diagnosis.[25] The risk factors for BC in SA include a decrease in the age at menarche, increase in the age at marriage and first-time pregnancy, decrease in parity and breastfeeding duration, and obesity and physical inactivity.[26,27] Obesity is more prevalent in women than in men in SA,[28] and physical inactivity is especially widespread in women.[29]

Obesity is linked to BC pathogenesis through multiple mechanisms. It is associated with decreased blood flow and oxygenation of adipose tissue, upregulation of leptin levels and vascular endothelial growth factor via hypoxia-inducible factor-1, and inhibition of adiponectin expression. Circulating insulin and insulin-like growth factor-1 act as potent growth factors. Various processes increase aromatase-mediated estrogen production and stimulate the nuclear factor-kappa B pathway. These processes promote inflammation and trigger anti-apoptotic genes that facilitate BC proliferation, invasion, angiogenesis, and metastasis.[30–32]

The median age among Saudi non-metastatic BC patients at diagnosis was 45.7 years, which is in concordance with previous data from Arab countries (44.5–48.5 years),[33] Asia (47.3 years),[24] and the Caribbean region (49 years),[34] but lower than that in the United States (60 vs 63 years in black and white women, respectively).[35] Determining the reason for this apparent difference is beyond the scope of this study, but it could be attributed to the younger age structure of the population in these regions compared to that in the United States, which might be due to environmental and genetic

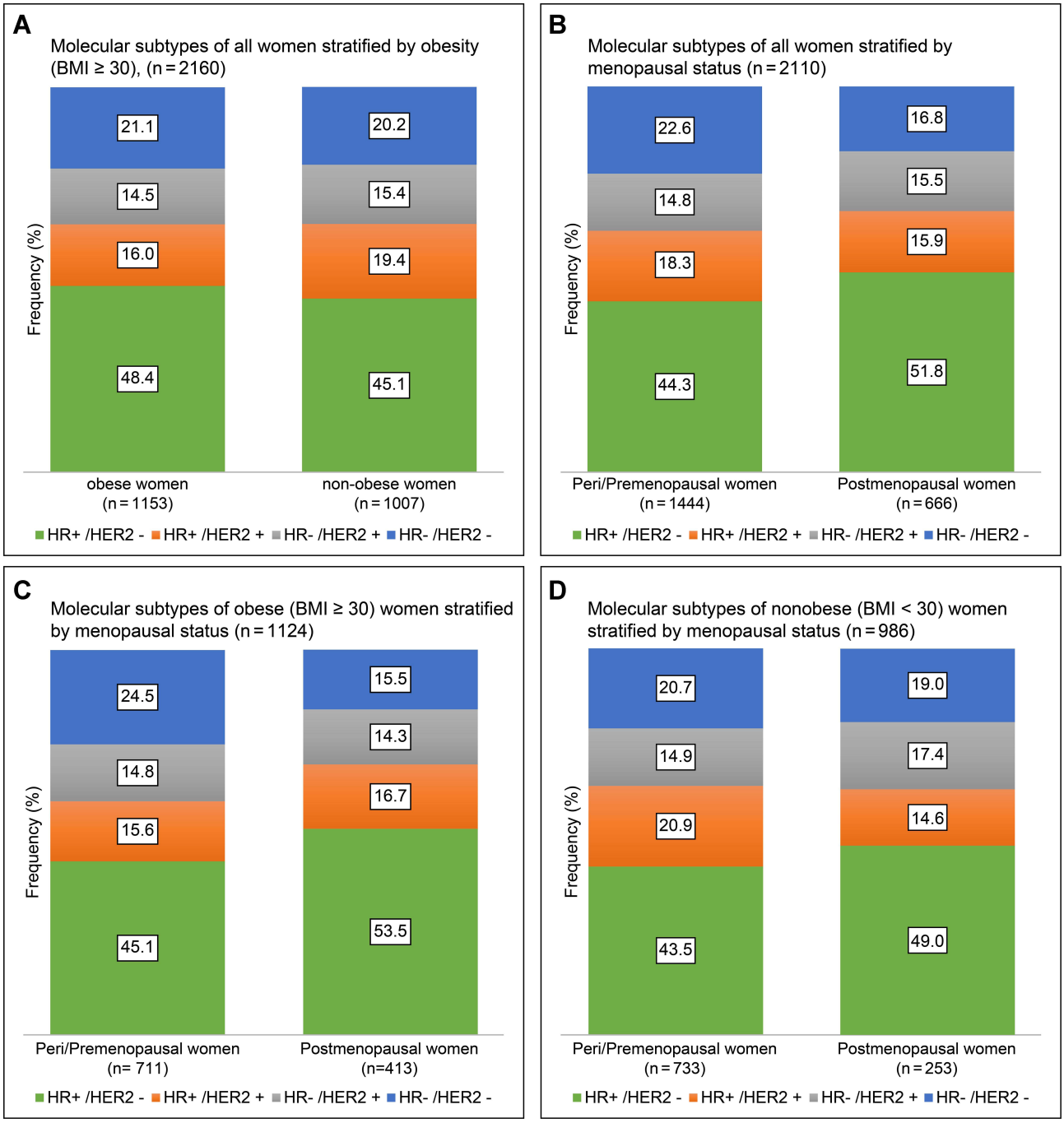

Figure 2 Bar graphs demonstrating molecular subtype distribution stratified by (**A**) obesity and (**B**) menopausal status in all patients and molecular subtype distribution in (**C**) obese and (**D**) non-obese women stratified by menopausal status in newly diagnosed non-metastatic breast cancer.

factors.[36] Furthermore, most of the Saudi women (62%) included in the study were premenopausal at diagnosis, which was higher than what was reported in a previous study from SA (49.7%)[37] and from Jourdan (44%).[14] However, both studies included metastatic disease, which we are not including here. In general, a BC diagnosis before the age of 50 years is higher in developing countries (47–56.9%) than in developed countries (16–21.5%).[38] The median age at diagnosis increased proportionally with an increase in BMI, which is in agreement with previous studies.[14,22]

We found that the rate of obesity was higher in older patients (age ≥40 years) than in younger patients (59.1% vs 41.6%; $p < 0.001$). Furthermore, age ≥40 years was an independent risk factor for obesity. However, age was not

Table 2 Regression Analysis of Variables Associated with Obesity (BMI ≥30 Kg/M^2)

Variables	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	P-value	OR	95% CI	P-value
Age, years						
≤40	1			1		
>40	2.03	1.69–2.43	<0.001	1.90	1.49–2.43	<0.001
Menopausal status						
Pre/perimenopause	1			1		
Postmenopause	1.65	1.37–1.99	<0.001	1.37	1.06–1.76	0.01
History of OCP	1.34	1.09–1.67	0.006	1.33	1.05–1.67	0.01
Screen detected	1.05	0.81–1.37	0.68			
ER+ vs ER-	0.97	0.82–1.12	0.97			
PR+ vs PR-	1.11	0.94–1.32	0.19			
HER2+ vs HER2-	0.82	0.68–0.98	0.03	0.73	0.59–0.92	<0.01
TN vs others	1.05	0.85–1.30	0.60			
Grade ≤II vs III	0.94	0.80–1.12	0.54			
Clinical stage I/II vs III	1.35	1.14–1.61	0.001	1.25	1.01–1.56	0.04
NAC vs no NAC	1.07	0.90–1.27	0.43			
MRM vs BCS	0.97	0.77–1.23	0.83			
Radiation vs no radiation	1.45	1.16–1.81	0.001	1.63	1.22–2.20	0.001
Axillary dissection	1.19	0.94–1.50	0.14			
ACT vs no ACT	0.90	0.76–1.07	0.27			

Abbreviations: ACT, adjuvant chemotherapy; BCS, breast conservative surgery; BMI, body mass index; CI, confidence interval; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; MRM, modified radical mastectomy; NAC, neoadjuvant chemotherapy; OR, odds ratio; PR, progesterone receptor; TN, triple-negative.

associated with an advanced clinical stage. Indeed, advanced tumor stage III vs stage I/II was more strongly associated with obesity, regardless of age and menopausal status.

This study also found an association between oral contraceptive use and obesity (BMI ≥30 kg/m^2) at BC diagnosis. A review of 49 clinical trials did not show a significant association between combination contraceptives and weight gain.[39] However, OCPs have been found to be a risk factor associated with BC in Arabian women.[40] In addition, the association between obesity and radiation therapy can be explained by the more advanced stages of BC among obese women in this population.

Three factors were independently associated with advanced clinical stage: obesity, HER2-positive disease, and non-screen-detected tumors. Interestingly, obesity was inversely associated with HER2+ disease (30.5% vs 34.9%), and both were independently associated with more advanced stage. However, we cannot exclude the aggressive influence of obesity on molecular subtypes, as we observed that in premenopausal women, obesity was associated with more triple-negative diseases (24.5% vs 20.7%). Screen-detected BC was not associated with obesity. However, both obesity and screen-detected BC were independently associated with the clinical stage. Therefore, the higher stage III disease in our patients cannot be explained by a low screening rate or factors related to screening only, such as lack of mammograms or mammogram inaccuracy in obese women, but is probably related more to the biological impact of obesity on BC

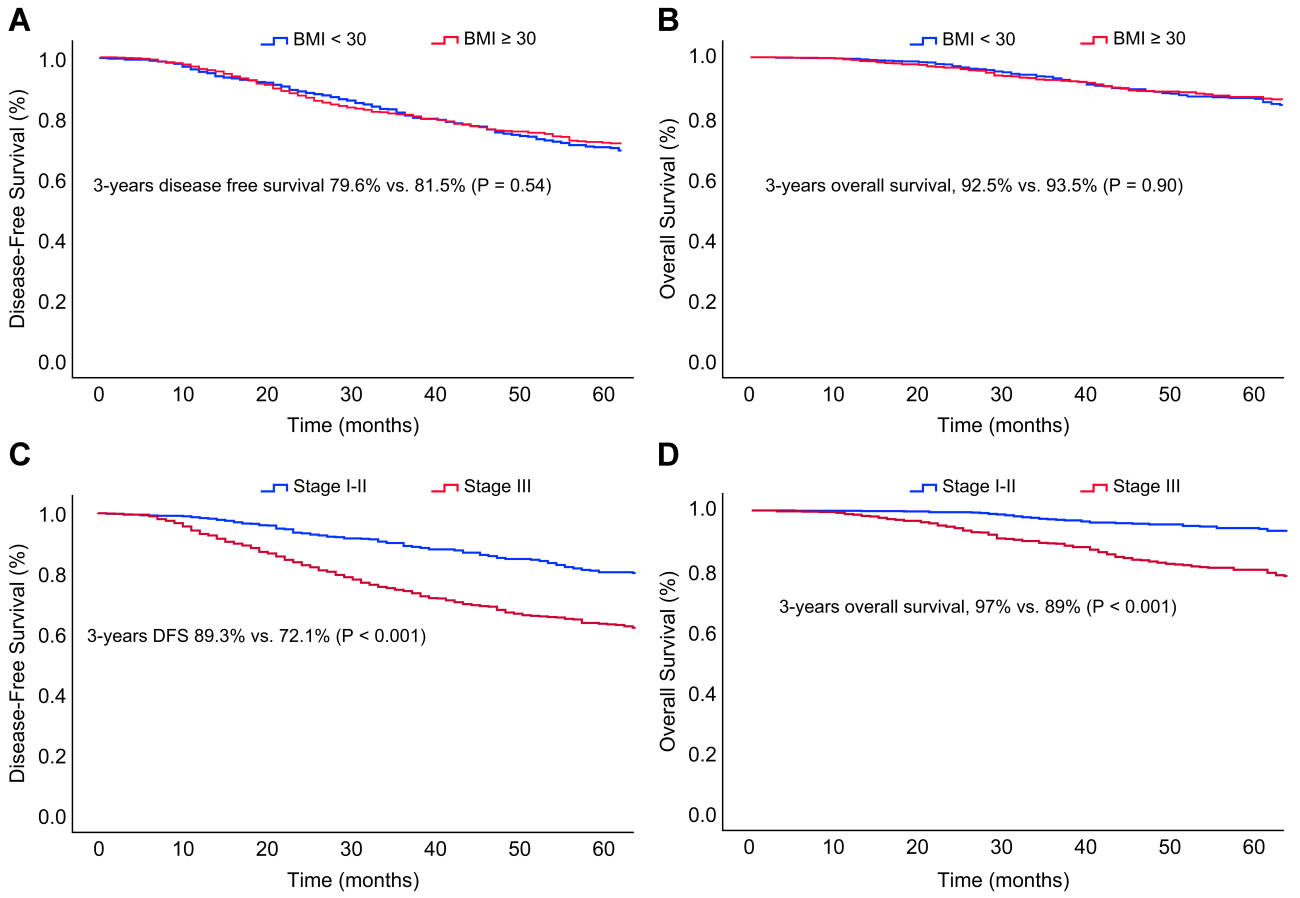

Figure 3 Kaplan–Meier curves of (**A**) disease-free survival and (**B**) overall survival stratified by obesity and (**C**) disease-free survival and (**D**) overall survival stratified by clinical stage (I and II vs III) in patients with non-metastatic breast cancer.

development, as explained earlier. However, some researchers have suggested that obesity is a potential barrier for screening compliance and effectiveness.[41–44] In contrast, other studies have shown no effect of obesity on screening compliance[45] and have reported that mammography use and accuracy are not the reasons for the higher clinical stage in obese patients.[46] Moreover, another study reported that obese women had higher sensitivity for screening mammography with similar specificity, regardless of their BMI group.[47] Delayed diagnosis of obese women has been reported as a reason for the advanced stage owing to the inability to feel the lumps because of breast size and embarrassment to seek medical help because of their body appearance.[48]

The rate of screen-detected tumors in our patients was far lower than has been reported internationally, 11.2% vs 22–36% and up to 48% in women aged >50 years.[49,50] The benefits of mammography screening have been evident since the mid-1980s based on results from randomized controlled trials; every 2–3 years, mammograms for women aged 40–74 years result in a one-third reduction in mortality from BC and a one-fourth reduction in advanced stage at diagnosis.[51] Given that BC incidence in SA has increased significantly in the last three decades and that the pattern is similar to that in the United States during the pre-screening mammography era,[26] intervention is warranted. National screening programs for BC in SA have not yet been established, and there is no widespread explicit action to overcome obesity. However, the Ministry of Health has promoted awareness for early BC detection[52] and provided obesity prevention and management guidelines.[53] The public acceptance of screening programs is encouraging;[54] however, 92% of women aged 50 years or older who participated in the Saudi Health Interview Survey 2013 reported never having had a mammogram, although mammography screening in SA is free.[55]

Obesity is a modifiable risk factor that merits further investigation and intervention to decrease its effects on the adverse features of BC. The inflammatory process in adipose tissue is reversible; research on interrupting the link between obesity and BC requires further work, and its impact on patients with BC is yet to be studied.[32]

In the present study, disease-free survival and overall survival were not affected by obesity, possibly because of the limited follow-up period. In a previous study, the significance of obesity on BC progression-free survival was observed after 5 years, and the risk of death increased after 10 years of follow-up.[56] Extended follow-up periods may provide greater insight into the effects of BMI on cancer recurrence and survival rates.

The strength of our study is that it targeted an unselected aggregate of women with non-metastatic BC from the largest prospectively collected database in SA, which makes the findings likely to be generalized in our region. Second, it provides a comprehensive and in-depth view of patient characteristics and healthcare system challenges in managing non-metastatic BC that necessitates prompt intervention in SA. We acknowledge that the duration of follow-up was relatively short for localized BC. Our facility is a broad-based referral center, and many patients continue their follow-up at local hospitals after completing their therapy.

Conclusion

The high prevalence of obesity and low screen-detection rate in SA significantly contributes to the high rate of adverse clinical features of non-metastatic BC in Saudi women. Given the significant increase in BC ASR in our population, these findings necessitate prompt intervention, including implementation of weight reduction strategies, a widespread mandatory screening program, and screening at earlier ages, particularly for obese women.

Data Sharing Statement

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Ethics Approval and Informed Consent

The study was approved by the Research Advisory Council (RAC) of King Faisal Specialist Hospital and Research Centre, Riyadh (RAC number 2051-029). The RAC committee at King Faisal Specialist Hospital and Research Centre, Riyadh, waived the requirement for informed consent. All methods were performed in accordance with relevant guidelines and regulations.

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Disclosure

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