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Original Research Article

## Lifestyle factors and breast cancer in a Moroccan population case-control study of the center Mohammed VI for cancer treatment

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### ABSTRACT

**Background:** The study aims to examine the association between lifestyle habits and breast cancer risk in a Moroccan population.

**Methods:** This is a case-control study conducted at the Mohammed VI Centre for cancer treatment in Casablanca.

**Results:** The results highlighted that family history of breast cancer (OR=5.73) and alcohol consumption (OR=3.76) were positively associated with breast cancer. Analysis of anthropometric parameters showed that the risk of developing breast cancer is estimated at 1.78 in overweight women and 2.39 in obese women compared to those of normal weight. The risk of developing breast cancer is estimated at 1.82 for women with a WC greater than 88 cm and 1.70 for women with a WHR greater than 0.85. At age 10, the risk is 1.60 for women with a large figure compared to women with a small figure. However, at age 40, the average body shape relative to the lean body was associated with a decreased risk of breast cancer. In addition, the data confirmed that physical activity participation decreases with age; in childhood and adolescence, women are more active while in post-menopause, women become moderately active. Being very active in childhood, peri-menopause and post-menopause seems to be a protective factor against the occurrence of breast cancer.

**Conclusions:** The study showed that the risk of breast cancer is potentially high in elderly women, overweight women and women with a family history of cancer. This risk was increased by behavioral factors such as toxic habits and physical inactivity.

**Keywords:** Anthropometric measurements, Breast cancer, Case-control study, Physical activity, Toxic habits

### INTRODUCTION

Breast cancer is the most common cancer in the female population. The main factors predicting breast cancer risk in women have been identified as: age, family history and genetic factors such as mutations in the BRCA1 and BRCA2 genes and other high-penetrance genes, such as

the p53 gene.<sup>1,2</sup> Over the past two decades, many surveys have examined the possible role of lifestyle factors, such as smoking and alcohol consumption, in increasing the risk of breast cancer.<sup>3-5</sup> According to Nkondjock and Stasiolek, physical inactivity and obesity are among the risk factors for this cancer.<sup>6,7</sup> Some of these behavioural risk factors can be easily modified, so their modification

can play an important role in breast cancer prevention.<sup>8</sup> The study aimed to evaluate breast cancer risk factors related to patients' lifestyle habits such as weight gain, smoking status, alcohol consumption, physical inactivity, among a Moroccan population in the Greater Casablanca region.

## METHODS

This is a case control study conducted at the Mohammed VI Centre in Casablanca for cancer treatment.

Participants are asked for prior informed consent to participate in the study. Explanations are given about the interest of the study, in compliance with the rules of the National Commission for the Control of Personal Data Protection. The newly diagnosed breast cancer patients at the centre were included in the study from January 2015 to December 2016. Controls free of all cancer diseases were included among the patients admitted to the dermatology and ophthalmology consultations at the Ibn Rochd University Hospital in Casablanca. Patients and controls were matched by age.

Data collection was done prospectively using a standardized, face-to-face questionnaire administered to patients. Data were collected on age at diagnosis, menopausal status, family history of cancer, and toxic habits (smoking status and alcohol consumption).

### *Anthropometric parameters*

Anthropometric parameters, patient weight and height were measured and the body mass index was calculated according to the formula

$$\text{BMI} = \text{weight (kg)} / \text{height (m)}^2$$

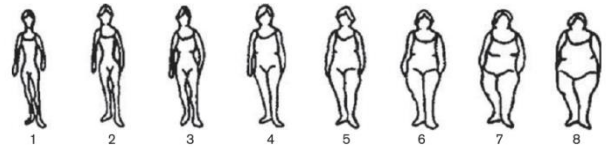
The data are analyzed and compared to the World Health Organization (WHO) classification [ $<25 \text{ kg/m}^2$  (normal weight),  $25\text{-}30 \text{ kg/m}^2$  (overweight),  $>30 \text{ kg/m}^2$  (obese)].

Waist and hip circumference, rounded to the nearest centimetre, were also collected and the waist and hip circumference ratio WHR [Waist circumference (cm)/hip circumference (cm)] was calculated. Waist circumference is the simplest criterion for assessing abdominal fat, which is directly implicated in breast cancer.

### *Evolution of corpulence over the life course*

For corpulence at different ages (between childhood and inclusion in the study), we used the female silhouettes on the Sorensen scale (Figure 1 as an indicator).<sup>9</sup> Women were asked to choose from eight silhouette drawings (numbered from 1 to 8, from the smallest to the largest) those that most closely resembled their silhouette at age 10, 20, 30 and 40.

From these eight silhouettes and in order to have enough subjects in each category for statistical analysis, groupings were made. At the age of 10, the "lean" category corresponds to figure 1, the "medium" category corresponds to Figure 2 and the "tall" category corresponds to figures 3 to 8. As for body size between 20 and 40 years of age, the "lean" category corresponds to silhouettes 1 and 2, the "medium" category corresponds to silhouette 3 and the "tall" category corresponds to silhouettes greater than or equal to 4.



**Figure 1: Sorensen silhouettes to assess body shape at different ages.**

However, this study has some limitations. The evaluation of body shape at different ages, using Sorensen shapes, requires long-term memory, which can lead to measurement errors. However, numerous studies showed that this information was reliable as an indirect indicator of the body's actual shape.<sup>11,12</sup>

### *Physical activity*

Data on physical activity were also collected. They cover activities related to professional tasks, walking and/or vigorous or moderate sporting activity

### *Statistical analysis*

A univariate analysis was conducted to identify factors associated with breast cancer. For this analysis, we used conditional logistic regression because it is a case-control study where age matching was done (one control for one case). The statistical analysis was done using the R software. The risk calculation quantifying the exposure/disease association was done by Odds Ratio (OR) and 95% confidence intervals (95% CI). The significance threshold has been set at 5%.

## RESULTS

During the study period, a total of 305 patients presenting for breast cancer managed at the Mohammed VI Centre for Cancer Treatment and 305 controls free of any cancer disease were included. Cases and controls are age-matched.

### *Age, menopausal status and family history of cancer*

The results obtained on associations between age, menopausal status, family history of cancer and breast cancer risk between cases and controls are shown in Table 1. The average age of all patients is 50.43 years, with a standard deviation of 11.21 years with extremes

ranging from 23 to 95 years. Regarding menopausal status, our results show that 56.1% of patients are menopausal vs. 55.4% of controls. No association was found between menopausal status and breast cancer risk (OR=1.05; 95% CI: 0.75 - 1.47; P trend = 0.56).

Family history of breast cancer was present in 20.33% of cases versus 4.26% of controls. Thus, the risk of developing breast cancer is estimated at 5.73 in women with a family history of breast cancer compared to those without (OR = 5.73; 95% CI: 3.07-10.67; P trend = 0.0001). As for the family history of other types of cancers, they were present in 25.57% of cases versus 9.2% of controls. The risk of developing breast cancer is estimated at 3.39 in women with a family history of other types of cancer compared to those without (OR=3.39; 95% CI: 2.13-5.41; P trend = 0.0001).

### **Toxic habits**

The results obtained on the associations between patients' toxic habits and breast cancer risk between cases and controls are shown in Table 2. The majority of patients in the study population (93.4%) were non-smokers versus 96% of controls, only a few patients reported being ex-smokers or smokers, with 4.3% and 2.3% respectively in cases versus 2% ex-smokers and 2% smokers in controls, or OR=1.19; 95% CI: 0.39-3.61; P trend = 0.1. In addition, only 18 cases investigated (5.9%) reported alcohol consumption versus 5 cases (1.6%) among controls. Thus, the risk of developing breast cancer is estimated at 3.76 for women who drink alcohol compared to those who do not (OR= 3.76; 95% CI: 1.37 - 10.26; P trend = 0.0001).

### **Anthropometric measurements**

The results regarding the association between anthropometric measurements in women with breast cancer compared to controls are presented in Table 3. The patients in our study measured an average of 1.62m, 76.42 kg and an average BMI of 29.06. In contrast, female controls averaged 1.62 m in height, 72.69 kg and

a BMI of 27.53, with a significant difference (p = 0.0001). There was no significant difference between cases and controls in size.

The BMI analysis found that 39% of cases were overweight compared to 35.7 in controls and 37.3% obese compared to 25.6 in controls. The risk of developing breast cancer is estimated at 1.78 in overweight women and 2.39 in obese women compared to those of normal weight (OR = 1.78; 95% CI: 1.20 - 2.64; P trend = 0.0001) and (OR = 2.39; 95% CI 1.58 - 3.61; P trend = 0.0001). For waist circumference (WC) distribution, our results show that 78.7% of patients have a WC greater than 88 cm versus 68.5% of controls. As for the waist-to-hip ratio (WHR), 65.6% of cases have a WHR greater than 0.85 versus 52.8% of controls. The risk of developing breast cancer is estimated at 1.82 in women with a TT greater than 88 cm and 1.70 in women with a WHR greater than 0.85 (OR = 1.82; 95% CI: 1.09 - 3.06; P trend = 0.02) and (OR = 1.70; 95% CI: 1.20 - 2.36; P trend = 0.001).

### **Evolution of corpulence over the life course**

The other objective of the work was to study the influence of the evolution of corpulence over the life course (from childhood to adulthood) on the occurrence of breast cancer in patients compared to controls. Most women chose silhouettes 1 and 2 to describe their body shape at age 10 (50% in breast cancer cases and 40% in controls; Figure 2). These proportions decrease drastically at age 20 (17.4% and 20%, respectively), to be almost nil at age 40. At age 10, Figure 2 is the most reported with 30.2% in cases versus 25.9% in controls with (p = 0.03). At the age of 20 years, silhouette 4 is the most frequent with 33.1% in patients compared to 28.9% in controls with an insignificant p (p = 0.15). At 40 years of age, figure 6 is the most frequently chosen with 27.3% in cases vs. 23.3% in controls (p = 0.002), Figures 7 and 8 were also reported by 15% of patients and only 9% of controls. Results regarding the association between lifetime body image perceptions in women with breast cancer compared to controls are presented in Table 4.

**Table 1: Associations between menopausal status, family history and breast cancer risk between cases and controls.**

Features and characteristics	Cases (%) N= 305	Control (%) N= 305	OR	95% CI	P trend
<b>Age</b>	50.43±11.21				
<b>Menopausal status</b>					
Pre-menopause	114 (37.4)	119 (39)		1	0.56
Peri-menopause	20 (6.6)	17 (5.6)	1.22	0.61 - 2.46	
Post-menopause	171 (56.1)	169(55.4)	1.05	0.75 - 1.47	
<b>Family history of breast cancer</b>					
No	243 (79.7)	292 (95.7)		1	0.0001
Yes	62 (20.3)	13 (4.3)	5.73	3.07-10.67	
<b>Family history of other types of cancer</b>					
No	227 (74.4)	277 (90.8)		1	0.0001
Yes	78 (25.6)	28 (9.2)	3.39	2.13-5.41	

**Table 2: Associations between toxic habits and breast cancer risk between cases and controls.**

Features and characteristics	Cases (%) N= 305	Control (%) N= 305	OR	95% CI	P trend
<b>Smoking status</b>					
Non-smoker	285 (93.4)	293 (96)		1	0.1
Smoker	7 (2.3)	6 (2)	1.19	0.39 - 3.61	
Ex-smoker	13 (4.3)	6 (2)	2.22	0.83 - 5.94	
<b>Alcohol consumer</b>					
No	287 (94.1)	300 (98.4)		1	0.01
Yes	18 (5.9)	5 (1.6)	3.76	1.37 - 10.26	

**Table 3: Associations between anthropometric measurements and breast cancer risk between cases and controls.**

Features and characteristics	Cases (%) N= 305	Control (%) N= 305	OR	95% CI	P trend
Average size	1.62±0.07	1.62±0.06			0.7
Average weight	76.42±14.03	72.69±13.26			0.001
Average BMI	29.06±5.12	27.53±4.56			0.0001
<b>Distribution of BMI</b>					
Normal weight	72 (23.7)	118 (39)		1	0.0001
Overweight	119 (39)	109 (35.7)	1.78	1.20 - 2.64	
Obese	114 (37.3)	78 (25.6)	2.39	1.58 - 3.61	
<b>Waist circumference distribution TT</b>					
WC < 80cm	27 (8.9)	43 (14.1)		1	0.02
80 <WC<88cm	38 (12.5)	53 (17.4)	1.14	0.60 - 2.15	
WC ≥ 88cm	240 (78.7)	209 (68.5)	1.82	1.09 - 3.06	
<b>Waist to hip ratio distribution RTH</b>					
WHR < 0.85	105 (34.4)	144 (47.2)		1	0.001
WHR ≥ 0.85	200 (65.6)	161 (52.8)	1.70	1.20 - 2.36	

**Table 4: Life-time distribution of silhouettes among breast cancer cases and controls.**

	Cases (%) N= 305	Control (%) N= 305	OR	95% CI	P trend
<b>Body image at age 10</b>					
Lean silhouette	47 (15.4)	63 (20.7)		1	0.03
Medium silhouette	79 (25.9)	92(30.2)	1.15	0.71 - 1.86	
Large silhouette	179(58.7)	150 (49.2)	1.60	1.03- 2.47	
<b>Body image at age 20</b>					
Lean silhouette	53 (17.4)	61 (20.0)		1	0.17
Medium silhouette	65 (21.3)	84 (27.5)	0.89	0.54 - 1.45	
Large silhouette	187 (61.3)	160 (52.5)	1.34	0.88 - 2.05	
<b>Body image at age 30</b>					
Lean silhouette	20 (6.6)	21(6.9)		1	0.30
Medium silhouette	37 (12.2)	57 (18.8)	0.68	0.32 - 1.42	
Large silhouette	247 (81.2)	226 (74.3)	1.14	0.60 - 2.17	
<b>Body image at age 40</b>					
Lean silhouette	10 (3.5)	7 (2.4)		1	0.03
Medium silhouette	21 (7.4)	47 (16.4)	0.31	0.10 - 0.93	
Large silhouette	251 (89.0)	233 (81.2)	0.75	0.28 - 2.01	

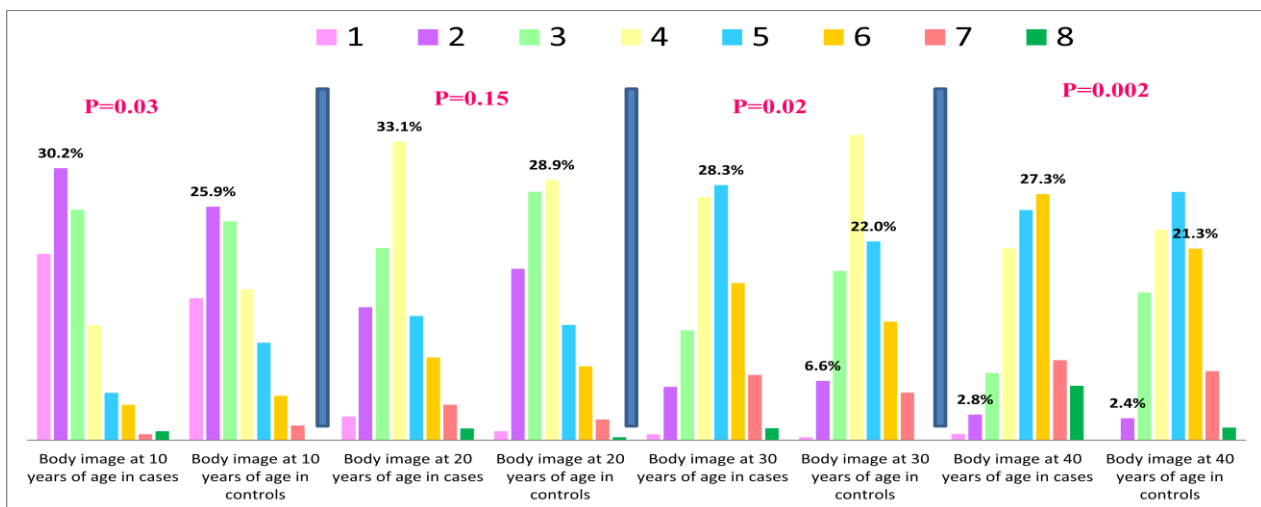
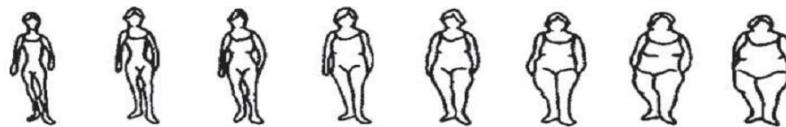
**Table 5: Associations between physical activity and breast cancer risk in cases and controls.**

	Cases (%) N= 305	Control (%) N= 305	OR	95% CI	P trend
<b>High intensity work</b>					
No	99 (32.5)	122 (40.0)		1	0.05
Yes	206 (67.5)	183 (60.0)	1.38	0.99 - 1.93	
<b>Moderate work intensity</b>					
					0.61

	Cases (%) N= 305	Control (%) N= 305	OR	95% CI	P trend
No	33 (10.8)	37 (12.1)		1	
Yes	272 (89.2)	268 (87.9)	1.13	0.69 - 1.87	
<b>Walking</b>					
No	61 (20.0)	53 (17.4)		1	0.40
Yes	244 (80.0)	252 (82.6)	0.84	0.55 - 1.26	
<b>High intensity sport</b>					
No	301 (98.7)	304 (99.7)		1	0.21
Yes	4 (1.3)	1 (0.3)	4.04	0.44 - 36.35	
<b>Moderate intensity sport</b>					
No	280 (91.8)	278 (91.1)		1	0.77
Yes	25 (8.2)	27 (8.9)	0.91	0.52 - 1.62	

**Table 6: Associations between lifetime physical activity and breast cancer risk in cases and controls.**

Physical activity	Cases (%) N= 305	Witnesses (%) N= 305	OR	95% CI	P trend
<b>Childhood</b>					
Not active	18 (5.9)	7 (2.3)		1	0.003
Moderately active	49 (16.1)	23 (7.5)	0.82	0.30 - 2.26	
Very active	238 (78)	274 (90.2)	0.33	0.13 - 0.82	
<b>Adolescence as an adult</b>					
Not active	10 (3.3)	4 (1.3)		1	0.07
Moderately active	87 (28.5)	57 (18.7)	0.61	0.81 - 2.04	
Very active	208 (68.2)	244 (80)	0.34	0.10 - 1.10	
<b>Peri-menopause</b>					
Not active	21 (6.9)	14 (4.6)		1	0.01
Moderately active	206 (67.5)	162 (53.1)	0.84	0.41 - 1.71	
Very active	78 (25.6)	129 (42.3)	0.40	0.19 - 0.83	
<b>Post-menopause</b>					
Not active	60 (35.1)	29 (17.2)		1	0.0001
Moderately active	106 (62.0)	122 (72.2)	0.42	0.25 - 0.70	
Very active	5 (2.9)	18 (10.7)	0.13	0.04 - 0.39	



**Figure 2: Distribution of body contour frequency at different ages among cases and controls.**



According to the results, there is an increase in body size over the course of a lifetime. At the age of 10, the leanest figure is the vast majority, while at the age of 40 more than 89% of women are at the tallest figure. A significant positive association has been established between the evolution of women's corpulence and the risk of developing breast cancer. This risk was estimated at 1.60 for women with a large figure compared to women with a lean figure (OR = 1.60; 95% CI: 1.03 - 2.47; P trend = 0.03). On the other hand, no association has been found between silhouettes at the age of 20, at the age of 30, and the risk of breast cancer. However, at age 40, the average body shape relative to the lean body was associated with a decreased risk of breast cancer (OR = 0.31; 95% CI: 0.10 - 0.93; P trend = 0.03).

### **Physical activity**

The results regarding the association between physical activity and breast cancer risk are presented in Table 5.

In our study, the practice of high-intensity labor was higher in patients with 67.5% versus 60% in controls (OR = 1.38; 95% CI: 0.99 - 1.93; P trend = 0.05). Moderate intensity labour is performed by 89.2% of patients vs. 87.9% of controls (OR = 1.13; 95% CI: 0.69 - 1.87; P trend = 0.61).

Concerning the practice of sports activities, 80% of cases walk versus 82.6% of controls (OR = 0.84; 95% CI: 0.55 - 1.26; P trend = 0.40). The practice of medium-intensity or high-intensity sports activity is low in both cases and controls, with respectively (8.2% of cases versus 8.9 of controls with OR=0.91; 95% CI: 0.52 - 1.62; P trend = 0.77) and (1.3% of cases versus 0.3 of controls with OR=4.04; 95% CI: 0.44- 36.35; P trend = 0.21). Thus, no association was found between high-intensity or moderate intensity work, medium-intensity or high-intensity sports activity and breast cancer risk.

The results regarding the association between lifetime physical activity and breast cancer risk are presented in Table 6.

The results show that physical activity decreases with age; in childhood and adolescence women are more active while in post-menopause women become moderately active. 78% of patients are very active during childhood vs. 90.2% of controls (OR = 0.33; 95% CI: 0.13 - 0.82; P trend = 0.003). In adulthood, 68.2% of cases vs. 80% of controls are active (OR = 0.34; 95% CI: 0.10 - 1.10; P trend = 0.07). In peri-menopause, only 25.6% of patients versus 42.3% of controls are active (OR = 0.40; 95% CI: 0.19 - 0.83; P trend = 0.01). In postmenopausal women, only 5 patients (2.9%) reported high activity versus 18 controls (10.7%) (OR = 0.13; 95% CI: 0.04 - 0.39; P trend = 0.0001) and 62% of cases versus 72.2 of controls reported moderate activity with OR = 0.40; 95% CI: 0.25 - 0.70; P trend = 0.0001. Indeed, being very active in childhood, peri-menopause

and post-menopause seems to be a protective factor against the occurrence of breast cancer.

## **DISCUSSION**

Over the past two decades, many surveys have examined the possible role of lifestyle factors, smoking, physical inactivity, alcohol consumption and obesity in the development of breast cancer. The objective of our case-control study is to describe and analyze the association between these factors and the risk of breast cancer in our Moroccan population.

### **Age, menopausal status and family history of cancer**

Age is the most important risk factor for breast cancer; the average age of our patients is 50.43±11.21. 56.1% of them are menopausal versus 55.4% of controls. No association was found between menopausal status and breast cancer risk (OR=1.05; 95% CI: 0.75 - 1.47; P trend = 0.56).

Family history of breast cancer has been reported as one of the most important risk factors for breast cancer.<sup>1,4,12</sup> The study confirms the important role of family history of breast cancer, which increases the risk in women with breast cancer (OR=5.73; 95% CI: 3.07-10.67; P trend = 0.0001). These results are relatively consistent with those of or who found a 3.5-fold increased risk of breast cancer in women aged 49 years.<sup>13-16</sup> Women at hereditary risk of breast cancer are a special population. On the one hand, their risk of breast cancer is extremely high. On the other hand, the young age of onset of their cancer is probably due to specific abnormalities in breast carcinogenesis, which means that the associated risk factors may differ from those identified in a sporadic context.

### **Toxic habits**

In the study, smoking is weakly found in the population; it does not seem to have any effect on the overall risk of developing breast cancer. This result is consistent with a collaborative analysis of 53 epidemiological studies and case-control studies.<sup>5,14,17</sup> However, other authors have found an increased relative risk of breast cancer for women who actively smoke.<sup>18-20</sup>

In addition, the study also indicates that alcohol consumption is a significant risk factor for breast cancer among women who drink alcohol compared to those who do not (OR = 3.76; 95% CI: 1.37 - 10.26; P trend = 0.0001). This finding has been noted in numerous studies that have shown that alcohol consumption is a moderate but consistent risk factor for breast cancer. Women who reported drinking alcohol increased their relative risk of breast cancer compared to those who reported no alcohol consumption (for example, OR = 1.32, 95% CI 1.19-1.45 for a consumption of 0.35 to 44 g per day of alcohol and OR = 1.46, 95% CI 1.33 to 1.61 for a daily intake ≥ 45 g, P trend <0.00001).<sup>4</sup> Alcohol influences estrogen and

folate metabolism, gene regulation and mutagenesis induction.

### ***Anthropometric measurements***

The results confirm that overweight is associated with an increased incidence of breast cancer. The risk of developing breast cancer is estimated at 1.78 in overweight women and 2.39 in obese women compared to those of normal weight. This positive association of breast cancer risk with the BMI index  $\geq 30$  kg/m<sup>2</sup> found in the study (OR=2.39) is higher than that reported by.<sup>13,21</sup> In the literature, the results for BMI are mixed.<sup>22</sup> Hu et al reported a decreased risk of breast cancer with BMI in non-menopausal women (RR = 0.45; 95% CI = 0.22 - 0.92 for a BMI  $\geq 23$  versus  $< 21$  kg/m<sup>2</sup>) and an increased risk in postmenopausal women (OR = 1.98 ; 95% CI = 0.86 - 4.55 for a BMI  $\geq 24$  versus  $< 21.5$  kg/m<sup>2</sup>).<sup>18</sup>

In the study, the risk of developing breast cancer is estimated at 1.82 in women with a WC greater than 88 cm and 1.70 in women with a WHR greater than 0.85 (OR=1.82; 95% CI: 1.09 - 3.06; P trend = 0.02) and (OR=1.70; 95% CI: 1.20 - 2.36; P trend = 0.001).

The results of reducing breast cancer risk before and after menopause, with an increase in WC, HC and WHR, are inconsistent in most previous studies conducted in high resource countries.<sup>23-27</sup> More recently, a study conducted in a multi-ethnic American population showed insignificant inverse associations between WHR and WC in women and breast cancer risk, (OR = 0.71, 95% CI = 0.46-1.11, for WHR  $> 0.85$  versus WHR  $\leq 0.77$ ; and OR=0.74, 95% CI = 0.47-1.17 for WC  $> 98$  cm versus WC  $\leq 78.7$  cm).<sup>28</sup> Overall, these results suggest that anthropometric factors may have different associations with breast cancer risk in women, perhaps due to ethnic variations in the distribution of body fat.

### ***Evolution of corpulence over the life course***

In order to clarify the relationship between adiposity and breast cancer, it was also necessary to take into account the history of corpulence by using Sorensen's silhouettes at different periods of life and its variations over time. To date, few studies have examined the relationship between body shape in young children and breast cancer risk in Moroccan women.

The analysis of our results showed a significant positive association between the evolution of women's corpulence and the risk of developing breast cancer. In the literature, studies have shown that the wide body shape relative to the constantly lean body shape is associated with a decreased risk of breast cancer (P trend=0.01).<sup>28,29</sup> However, several other studies conducted primarily in Western countries have shown that an increase in body fat (BMI, weight) in young people was associated with a lower risk of breast cancer in premenopausal women and

postmenopausal women.<sup>29-34</sup> The results highlight that at pre-adolescence, the risk of breast cancer is estimated at 1.60 for women with a large figure compared to women with a small figure (P trend = 0.03). In contrast, at age 40, the average body shape relative to the lean body shape was associated with a decreased risk of breast cancer (P trend = 0.03).

The biological mechanisms linking anthropometric parameters and breast cancer risk in postmenopausal women have been clearly established. It has long been known that overweight and obese adolescents have an earlier menarche than normal weight girls; early menarche is associated with a positive risk of breast cancer.<sup>35-37</sup> After cessation of ovarian activity, sex steroids, especially estrogens, remain synthesized mainly in adipose tissue. Obesity is then positively correlated with increased plasma testosterone and estradiol concentrations. Obesity also leads to insulin resistance, hyperinsulinemia and increased levels of bioavailable IGFI, an insulin-like growth factor involved in breast tissue development and tumour promotion.<sup>38</sup> This also results in a decrease in SHBG concentration, resulting in an overall increase in plasma levels of androgens and free estrogens.<sup>39-43</sup> Obesity also induces low-grade chronic inflammation leading to increased local and systemic cytokine levels.

These factors in turn can affect mitosis, apoptosis, cell senescence and angiogenesis [39]. Together, these hormonal and metabolic effects could facilitate tumor-promoting effects associated with a body shape of increasing shape throughout life and breast cancer risk. With respect to possible protective biological mechanisms, it has been postulated that, in premenopausal women, estradiol and progesterone levels are reduced in anovulatory cycles that occur more frequently in obese women than in thin women.<sup>44</sup>

These two hormonal effects may reduce hormone-dependent tumour growth in overweight and/or obese women, which partly explains the negative association between current anthropometric measurements (BMI, TT, and THR) and breast cancer risk observed in non-menopausal women.

### ***Physical activity***

Scientific evidence indicates that physical inactivity is the main known and modifiable health risk factor.<sup>45</sup> The study found that the risk of breast cancer was lower in highly active women compared to those who are inactive, regardless of menopausal status. This finding is consistent with the study by Kamarudin et al who found that breast cancer risk was significantly higher among inactive women (OR = 3.489) than among those who exercised regularly.<sup>46</sup> In addition, data from the study by Dallal et al showed a 20% reduction in the risk of invasive breast cancer in women with regular physical activity  $> 5$  hours/week.<sup>47</sup>

The role of physical activity is linked to various mechanisms of action. In the short term, muscle contraction involves energy and hormonal metabolism with consumption of energy substrates and increased insulin sensitivity, and in the long term physical activity modifies body composition, reducing fat mass and increasing muscle mass, a real generator of energy expenditure, necessary to limit the supply of energy substrates stimulating carcinogenesis, improve insulin sensitivity, modulate the ratio of adipokines, leptin and adiponectin, improve cellular immunity and block cell pathways favourable to cell proliferation and angiogenesis.<sup>48</sup>

## CONCLUSION

The results of this study provide additional evidence that lifestyle factors (obesity, physical inactivity, smoking, alcohol consumption) and a family history of breast cancer are associated with a high risk of breast cancer. This should encourage women to change their behaviour, especially with regard to toxic habits and physical inactivity that may increase their risk of breast cancer. It is also recommended that women maintain a normal weight and avoid increasing body weight throughout life.

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