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ORIGINAL RESEARCH

Association of Overweight and Inflammatory Indicators with Breast Cancer: A Cross-Sectional Study in Chinese Women

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Objective: This cross-sectional study aimed to explore the association of overweight and inflammatory indicators with breast cancer risk in Chinese patients.

Methods: Weight, height, and peripheral blood inflammatory indicators, including white blood cell count (WBC), neutrophil count (NE), lymphocyte count (LY), platelet count (PLT) and the concentration of hypersensitivity C-reactive protein (hsCRP), were collected in 383 patients with benign breast lumps (non-cancer) and 358 patients with malignant breast tumors (cancer) at the First Affiliated Hospital of Soochow University, China, from March 2018 to July 2020. Body mass index (BMI), neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) and systemic immune-inflammation index (SII) were determined according to the ratio equation. The correlations among overweight, inflammatory indicators, and the proportion of non-cancer or cancer cases were analyzed.

Results: BMI is associated with an increased breast cancer risk. Compared with non-cancer patients, the average WBC count, NE count, NLR, and level of hsCRP were significantly higher in cancer patients. The level of hsCRP was closely associated with the size of malignant breast tumors.

Conclusion: We conclude that overweight and high levels of hsCRP may serve as putative risk factors for malignant breast tumors in Chinese women.

Keywords: breast cancer, body mass index, overweight, chronic inflammation, inflammatory indicator

Introduction

Breast cancer is the most prevalent invasive cancer in women and the leading cause of cancer-related deaths in women around the world.[1–3] In China, breast cancer is also the most common cancer in women. In 2022, breast cancer will be China's fourth leading cause of death in women.[4] Therefore, it is of great significance to determine the putative-risk factors for breast cancer. Numerous studies aimed at enhancing the survival rate and prognosis of breast cancer patients have been reported. For instance, a novel approach has been developed to identify subtype-specific network biomarkers for predicting breast cancer survivability, achieving remarkable classification performance, and demonstrating potential clinical utility for personalized treatment strategies.[5] Moreover, an innovative method that combines high-dimensional embedding and residual neural networks has been introduced to accurately classify breast cancer Nottingham Prognostic Index (NPI) classes while identifying crucial prognostic biomarkers.[6]

It is well known that obesity has a huge impact on human health. The proportion of obese people who suffer from metabolic diseases such as diabetes, hypertension, hyperlipidemia and sleep apnea syndrome is significantly higher than that

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of nonobese people.[7] In recent years, many studies have shown that obesity is related to the occurrence of malignant tumors such as colorectal cancer, pancreatic cancer, bladder cancer and endometrial cancer.[8–14] Meanwhile, an increasing number of studies have revealed that obesity plays a significant role in promoting the onset and development of malignant tumors, poor prognosis, and drug resistance to anticancer therapy.[15,16] The production of insulin and insulin-like growth factors, adipocytokines, the inflammatory response, hypoxia, and oxidative stress are potential risk factors for obesity-related cancers.[17–23]

Obesity is linked to an increased incidence of breast cancer, a poor prognosis, an increased chance of disease recurrence, and increased mortality in postmenopausal women.[24–26] Comparing to non-obese patients, obese breast cancer patients exhibit significantly poorer overall survival rates. Additionally, obese breast cancer patients tend to have higher tumor grades, larger tumor diameters, and are more prone to lymph node involvement. Moreover, they are more likely to develop resistance to endocrine therapy and chemotherapy compared to non-obese patients.[27] In recent years, several studies have also found that obesity adversely affects the survival and prognosis of breast cancer patients. Obesity-related inflammation promotes the development of breast cancer.[28] The incidence of distant metastasis in obese breast cancer patients is significantly higher compared to normal-weight patients, regardless of pre- or post-menopausal status.[29] Furthermore, with the rapid advancement of gene chip and sequencing technologies, bioinformatics analysis has been widely utilized to identify potential biomarkers for diagnosis, treatment, and prognosis of various diseases. Previous studies have analyzed data from breast cancer patients in Gene Expression Omnibus (GEO) and The Cancer Genome Atlas Program (TCGA) databases using public microarray expression, revealing genetic differences between obese and non-obese breast cancer patients that are associated with cancer prognosis.[30]

Additionally, a number of observational studies have discovered that exercising to lose weight enhances breast cancer prognosis.[31] Studies have shown that overweight is an independent risk factor for breast cancer in postmenopausal women, especially in patients with hormone receptor-positive breast cancer.[32] The mechanism could be the production of inflammatory mediators and factors by obese patients' adipose tissues, which would then foster the invasion and metastasis of cancer.[33–35] However, uncertainty persists regarding the precise relationship between overweight and the clinical characteristics of Chinese breast cancer patients. Being overweight increases the risk of breast cancer in postmenopausal women; therefore, it is critical to identify straightforward markers that can predict risk and prognosis to prevent and cure breast cancer.

Tumor occurrence, development, and prognosis are all tightly correlated with inflammation, which also raises the risk of many malignancies.[36,37] Currently, it is thought that inflammatory substances, such as interleukin-6 (IL-6) and tumor necrosis factor (TNF-α), can trigger vascular growth factors, hence stimulating the development of blood vessels. On the other hand, it can enhance estrogen synthesis and aromatase activity, which will encourage the growth of breast cancer cells. Through the production of different cytokines, chemokines, and cytotoxic mediators, tumor cells also attract inflammatory cells. The proliferation and invasion of tumor cells are aided by this chain reaction between inflammatory and tumor cells, which encourages the growth of malignancies.[38,39]

In this cross-sectional study, we aimed to explore the association of overweight and inflammatory indicators with breast cancer risk in Chinese patients. We show that body mass index (BMI) is associated with an increased breast cancer risk. The average white blood cell count (WBC) and neutrophil count (NE), neutrophil-lymphocyte ratio (NLR), and level of hypersensitivity C-reactive protein (hsCRP) are significantly higher in cancer patients. The average hsCRP level is closely associated with the size of malignant breast tumors. These data suggest that overweight and high levels of hsCRP are associated with high breast cancer risk in Chinese patients. Our study provides pertinent clinical evidence for breast cancer therapy and prevention in the future.

Materials and Methods

Study Population

This is a cross-sectional study took place at the First Affiliated Hospital of Soochow University, China, from March 2018 to July 2020. We collected data from female breast tumor patients who underwent surgery. According to the following inclusion and exclusion criteria, 383 patients with benign breast lumps (non-cancer) and 358 patients with malignant breast tumors (cancer) were recruited for our study. Inclusion criteria of malignant breast tumors: a) all patients were diagnosed within one month; b) all patients were recruited after surgery; c) all patients were confirmed by postoperative

pathology. Exclusion criteria of malignant breast tumors: a) patients with preoperative chemotherapy, radiotherapy, endocrine or targeted therapy; b) patients with missing medical records; c) patients with secondary tumors or other malignant tumors; d) patients with acute infection. Inclusion criteria for benign breast lumps: a) all patients were diagnosed within one month; b) all patients were confirmed by postoperative pathology. The exclusion criteria for benign breast lumps were as follows: a) patients with malignant tumors, rheumatic diseases and inflammatory diseases; b) patients with missing data; and d) patients with acute infection. Figure 1 depicts the patient flow chart schematic. Table 1 provides a list of the patients' characteristics.

Data Collection

The height (meter, m) and weight (kg) of the patients were collected from medical records. The BMI of the patients was then determined using the following formula: BMI (kg/m^2)=weight (kg)/height^2 (m^2). According to the classification standards of Chinese adult BMI, subjects were divided into four categories: underweight below 18.5 kg/m^2, normal weight at 18.5–23.9 kg/m^2, overweight at 24–27.9 kg/m^2, and obese above 27.9 kg/m^2.[40,41] Because of the small number of underweight and obese subjects in this study, patients were divided into the nonoverweight group (BMI<24 kg/m^2, n=463) and the overweight group (BMI≥24 kg/m^2, n=278). Inflammatory indicators in the peripheral blood of these patients were collected, including white blood cell count (WBC), neutrophil count (NE), lymphocyte count (LY), and high-sensitivity C-reactive protein (hsCRP). Blood samples were collected before surgery. A sterile ethylenediaminetetraacetic acid (EDTA) tube was used to collect peripheral venous blood (5–7 mL). A hematology analyzer (Sysmex XE-2100, Sysmex) was used to assess hematological parameters within 30 minutes of sample collection. The concentration of hs-CRP was determined by immunonephelometric assay using a biochemistry analyzer (Hitachi 917, Roche). The neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII) were calculated according to the following formulas: NLR=neutrophil/lymphocyte; PLR=platelets/lymphocytes; SII=platelets×neutrophils/lymphocytes.

Statistical Analysis

Statistical analysis was performed with SPSS 25.0 software. The counting data were statistically described by frequency and composition ratio. For the measured data, a normality test should be carried out first. For data groups that were normally distributed and had uniform variance, a *t* test was used. For data groups that did not conform to a normal distribution, the Mann–Whitney *U*-test was used for comparisons between groups. For count or rank data, the chi-square test or Fisher's exact test was used. Spearman correlation analysis was used for binary data. The ROC curve was used to analyze the diagnostic efficacy of peripheral blood inflammatory indicators for breast cancer screening. The false discovery rate (FDR)-adjusted p-value was calculated by the Benjamin-Hochberg method. Multivariate logistic

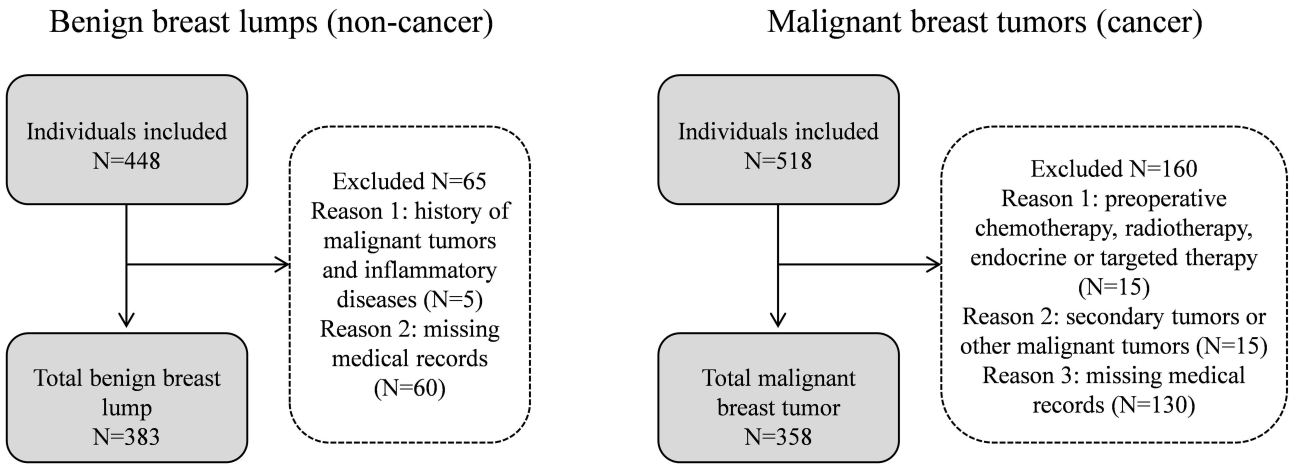

Figure 1 A patient flow diagram in accordance with the international Standards for Reporting of Diagnostic Accuracy Studies (STARD) guidelines.

Table 1 Clinical and Pathological Characteristics of 383 Non-Cancer Patients and 358 Cancer Patients

Variable	Non-Cancer Cases (n=383) n (%)	Cancer Cases (n=358) n (%)	P value	FDR
Age (years)				
≤30	66 (17.2)	8 (2.2)	<0.0001*	<0.0001*
31–60	287 (74.9)	226 (63.1)		
>60	30 (7.8)	124 (34.6)		
Menopause			0.0106*	0.0141*
No	285 (74.4)	164 (45.8)		
Yes	98 (25.6)	194 (54.2)		
Diabetes			0.0058*	0.0116*
No	371 (96.9)	314 (87.7)		
Yes	12 (3.1)	44 (12.3)		
BMI			0.1405	0.1405
<24 kg/m2	266 (69.5)	197 (55.0)		
≥24 kg/m2	117 (30.5)	161 (45.0)		
Tumor diameter (cm)	-			
<2		147 (41.1)		
2–5		190 (53.1)		
>5		21 (5.9)		
Histological grade	-			
Class I–II		180 (62.7)		
Class III		107 (37.3)		
Ki-67+ (%)	-			
<15		88 (24.6)		
15–30		141 (39.4)		
>30		129 (36.0)		
Lymph node metastasis	-			
No		217 (60.6)		
Yes		141 (39.4)		
Pathological staging	-			
Phase I		102 (28.5)		
Phase II		193 (53.9)		
Phase III		63 (17.6)		

(*Continued*)

Table 1 (Continued).

Variable	Non-Cancer Cases (n=383) n (%)	Cancer Cases (n=358) n (%)	P value	FDR
ER	-			
Negative		119 (33.2)		
Positive		239 (66.8)		
PR	-			
Negative		169 (47.2)		
Positive		189 (52.8)		
Vessel tumor emboli	-			
No		317 (88.5)		
Yes		41 (11.5)		
Pathological type	-			
Preinvasive carcinoma		25 (7.0)		
Invasive ductal carcinoma		295 (82.4)		
Invasive lobular carcinoma		8 (2.2)		
Mucinous adenocarcinoma		11 (3.1)		
Other types		19 (5.3)		
Molecular typing	-			
Luminal type a		116 (32.4)		
Luminal type b		76 (21.2)		
Triple negative		70 (19.6)		
Her2+HR+		47 (13.1)		
Her2+HR-		49 (13.7)		
Her2 grade	-			
0/1+		124 (40.5)		
2+		87 (28.4)		
3+		95 (31.0)		

Note: *P<0.05.
Abbreviations: ER, estrogen receptor; PR: progesterone receptor; Her2, human epidermal growth factor receptor 2.

regression analysis was used to determine the relationships between dependent and independent factors. P<0.05 indicates that the difference is statistically significant.

Results

The Association of Overweight on the Proportion of Non-Cancer Cancer Cases

A total of 383 non-cancer patients and 358 breast cancer patients were enrolled in the study. Non-cancer and cancer patients were divided into overweight (BMI≥24 kg/m^2, n=278) and nonoverweight (BMI<24 kg/m^2, n=463) groups. The difference in the proportion of non-cancer and cancer cases between the overweight and nonoverweight groups was

analyzed. The results showed that the proportion of cancer cases in the overweight group was significantly higher than that of non-cancer cases in the overweight group (161 cases, 57.9% vs 117 cases, 42.1%; $P<0.05$, Table 2).

The association between BMI and the proportion of non-cancer or cancer cases was further analyzed by Spearman correlation analysis. The proportion of non-cancer and cancer cases was significantly correlated with BMI, with a correlation coefficient of 0.149, showing a moderate positive correlation ($P<0.001$, Table 3).

Postmenopausal weight gain is one of the putative-risk factors for breast cancer. Meanwhile, overweight usually leads to diabetes and other complications. To determine whether these factors were independent putative-risk factors for breast cancer, multivariate logistic regression analysis was conducted using parameters including the presence/absence of overweight, menopause, or diabetes. The results showed that there were significant differences in BMI, menopause and diabetes ($P<0.05$, Table 4). This result suggests that overweight is an independent putative-risk factors for breast cancer along with menopause and diabetes.

Correlation Between BMI and Inflammatory Indicators in Peripheral Blood

In all patients, the overweight group exhibited a significantly higher average number of WBCs at 5.91 (4.98–6.97) $\times 10^9$/L compared to the nonoverweight group at 5.11 (4.34–6.04) $\times 10^9$/L. Similarly, the overweight group showed a markedly elevated average number of NE at 3.59 (2.83–4.37)$\times 10^9$/L, in contrast to the nonoverweight group at 3.00 (2.42–

Table 2 The Correlation of Overweight on the Proportion of Non-Cancer or Cancer Cases

	Non-Cancer (%)	Cancer (%)	Total	χ^2	*P* value
BMI			741	16.422	<0.001*
<24 kg/m^2	266 (57.5)	197 (42.5)	463		
≥24 kg/m^2	117 (42.1)	161 (57.9)	278		

Note: *$P<0.05$.

Table 3 Correlation Between BMI and the Proportion of Non-Cancer or Cancer Cases

			BMI	Non-Cancer or Cancer
Spearman Rho	BMI	Correlation coefficient	1.000	0.149
		P value		<0.001*
		Number	582	582

Note: *$P<0.05$.

Table 4 Multivariate Logistic Regression Analysis of Putative-Risk Factors for Breast Cancer

Variable	B	SE	Wald χ^2	*P* value	FDR	OR	95% CI
BMI	0.412	0.162	6.430	0.011*	0.011*	1.510	1.098–2.076
Menopause	1.068	0.163	42.729	<0.001*	<0.001*	2.910	2.112–4.008
Diabetes	1.025	0.348	8.685	0.003*	0.005*	2.788	1.410–5.513

Note: *$P<0.05$.

3.81)×10^9/L. Moreover, LY counts were notably higher in the overweight group at 1.72 (1.40–2.14)×10^9/L compared to the nonoverweight group at 1.61 (1.27–1.93)×10^9/L. Additionally, PLT counts were significantly elevated in the overweight group at 230 (193–273)×10^9/L compared to the nonoverweight group at 216 (181–257)×10^9/L. Furthermore, the concentration of hsCRP was markedly higher in the overweight group at 1.21 (0.68–2.81) mg/L compared to the nonoverweight group at 0.50 (0.26–0.98) mg/L. The NLR was also significantly elevated in the overweight group at 2.08 (1.57–2.68) compared to the nonoverweight group at 1.89 (1.47–2.50). Similarly, the SII was notably higher in the overweight group at 460.60 (345.79–604.39)×10^9/L compared to the nonoverweight group at 403.65 (289.49–566.73)×10^9/L. These differences were all statistically significant (P<0.05, Table 5). There was no significant difference in PLR between the overweight group and the nonoverweight group (P>0.05, Table 5).

Comparison of Inflammatory Indicators in the Peripheral Blood of Non-Cancer and Cancer Patients

In cancer patients, the average number of WBCs was 5.52 (4.67–6.57)×10^9/L, significantly exceeding that observed in non-cancer patients, which measured 5.27 (4.46–6.38)×10^9/L. Similarly, the average NE count in cancer patients reached 3.31 (2.65–4.23)×10^9/L, markedly surpassing that of non-cancer patients, which stood at 3.03 (2.45–3.95)×10^9/L. Moreover, the concentration of hsCRP in cancer patients registered 0.74 (0.39–1.78) mg/L, notably higher compared to non-cancer patients, whose hsCRP level measured 0.63 (0.27–1.32) mg/L. Additionally, the NLR in cancer patients reached 2.01 (1.59–2.68), showing a significant increase in contrast to non-cancer patients, who displayed an NLR of 1.87 (1.43–2.51). The differences were statistically significant (P<0.05). LY, PLT, PLR, and SII were not significantly different between non-cancer and cancer patients (P>0.05, Table 6).

Overweight and High Levels of hsCRP are Associated with High Breast Cancer Risk

The area under the receiver operating characteristic (ROC) curve (AUC) of BMI was 0.600. When the Youden index was the largest, the corresponding optimal cut-off value was 24.57 kg/m^2, with a sensitivity of 39% and a specificity of 77%. The area under the curve (AUC) of WBC was 0.544. When the Youden index was the largest, the corresponding optimal cut-off value was 4.95×10^9/L, with a sensitivity of 68% and a specificity of 42%. The area under the curve (AUC) of NE was 0.560. When the Youden index was the largest, the corresponding optimal cut-off value was 2.96×10^9/L, with a sensitivity of 67% and a specificity of 48%. The area under the curve (AUC) of hsCRP was 0.569. When the Youden index was the largest, the corresponding

Table 5 Correlation Between BMI and Peripheral Blood Inflammatory Indicators

	Nonoverweight Group Median (25%-75%) BMI<24 kg/m^2	**Overweight Group Median (25%-75%) BMI≥24 kg/m^2**	**Z score**	***P* value**	**FDR**
WBC (10^9/L)	5.11 (4.34–6.04)	5.91 (4.98–6.97)	−6.973	<0.001*	<0.001*
NE (10^9/L)	3.00 (2.42–3.81)	3.59 (2.83–4.37)	−6.387	<0.001*	<0.001*
LY (10^9/L)	1.61 (1.27–1.93)	1.72 (1.40–2.14)	−3.678	<0.001*	<0.001*
PLT (10^9/L)	216 (181–257)	230 (193–273)	−2.904	0.004*	0.005*
hsCRP (mg/L)	0.50 (0.26–0.98)	1.21 (0.68–2.81)	−10.550	<0.001*	<0.001*
NLR	1.89 (1.47–2.50)	2.08 (1.57–2.68)	−2.704	0.007*	0.008*
PLR	135.14 (106.80–172.07)	132.08 (105.05–160.33)	−1.241	0.215	0.215
SII (10^9/L)	403.65 (289.49–566.73)	460.60 (345.79–604.39)	−3.447	0.001*	0.002*

Note: *P<0.05.

Table 6 Comparison of Inflammatory Indicators in the Peripheral Blood of Non-Cancer and Cancer Patients

	Non-Cancer Median (25%-75%)	Cancer Median (25%-75%)	Z score	*P* value	FDR
WBC (10^9/L)	5.27 (4.46–6.38)	5.52 (4.67–6.57)	−2.057	0.040*	0.072
NE (10^9/L)	3.03 (2.45–3.95)	3.31 (2.65–4.23)	−2.838	0.005*	0.011*
LY (10^9/L)	1.66 (1.30–2.03)	1.64 (1.33–1.93)	−0.732	0.464	0.597
PLT (10^9/L)	223 (184–263)	219 (186–259)	−0.438	0.661	0.744
hsCRP (mg/L)	0.63 (0.27–1.32)	0.74 (0.39–1.78)	−3.245	0.001*	0.005*
NLR	1.87 (1.43–2.51)	2.01 (1.59–2.68)	−2.837	0.005*	0.011*
PLR	133.65 (105.58–170.00)	134.57 (105.91–164.33)	−0.183	0.855	0.855
SII (10^9/L)	404.87 (309.12–556.61)	444.26 (321.03–603.96)	−1.868	0.062	0.093
BMI (kg/m^2)	22.27(20.576–24.435)	23.44(21.50–25.78)	−4.722	<0.001*	<0.001*

Note: *P<0.05.

optimal off-cut value was 0.34 mg/L, with a sensitivity of 81% and a specificity of 32%. The area under the curve (AUC) of the NLR was 0.560. When the Youden index was the largest, the corresponding optimal truncation value was 1.85, with a sensitivity of 62% and a specificity of 49% (Table 7 and Figure 2). All the results were statistically significant, indicating that overweight, high WBC count, NE count, hsCRP level, and NLR are effective putative-risk factors for breast cancer.

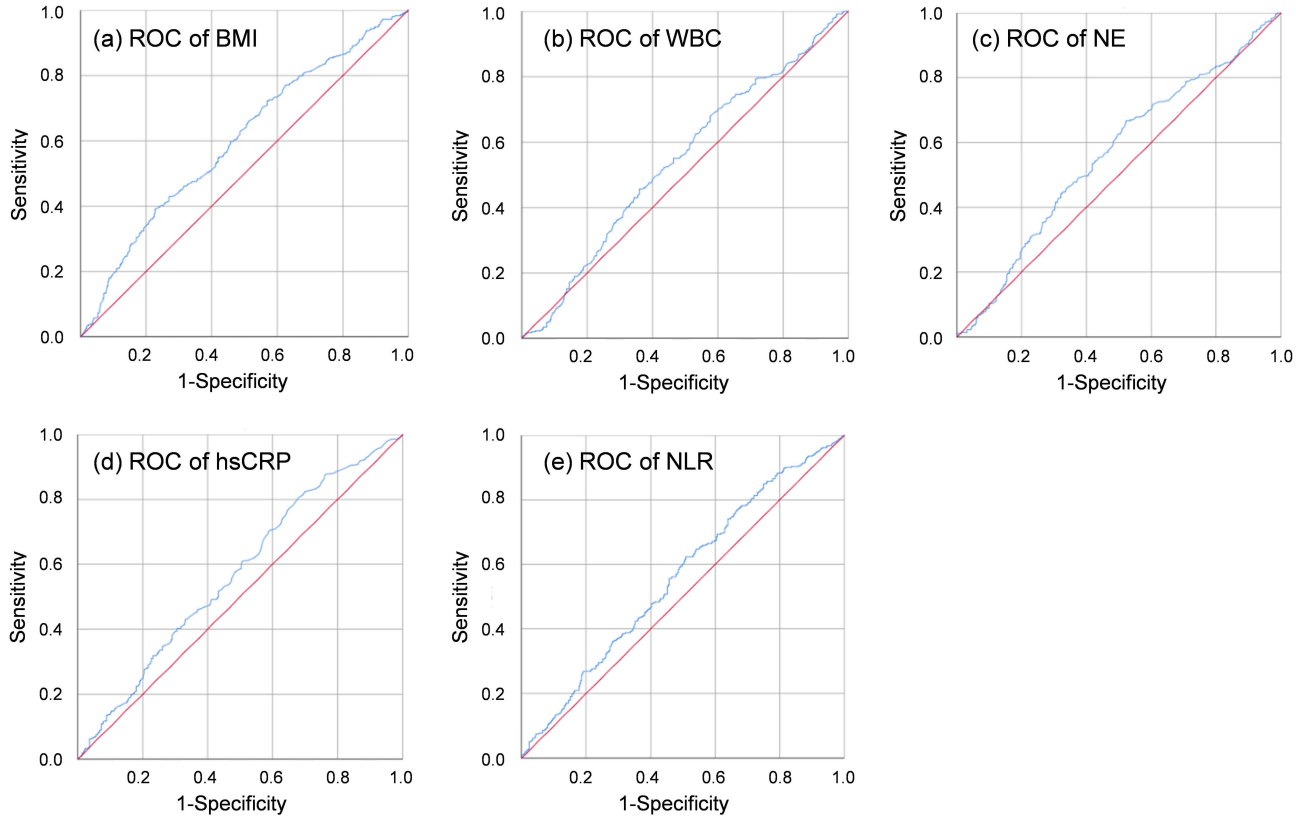

Figure 2 ROC curve of BMI (**a**) and WBC (**b**), NE (**c**), hsCRP (**d**), and NLR (**e**) in peripheral blood.

Table 7 Overweight and High Levels of Some Inflammatory Indicators are Putative-Risk Factors for Breast Cancer

	Optimal Cut-Off	AUC	Sensitivity (%)	Specificity (%)	*P* value	FDR
BMI (kg/m^2)	24.57	0.600	39	77	<0.001*	<0.001*
WBC (10^9/L)	4.95	0.544	68	42	0.040*	0.004*
NE (10^9/L)	2.96	0.560	67	48	0.005*	0.006*
hsCRP (mg/L)	0.34	0.569	81	32	0.001*	0.003*
NLR	1.85	0.560	62	49	0.005*	0.006*

Note: *P<0.05.

We then included statistically significant variables (WBC, >4.95×10^9/L; NE, >2.96×10^9/L; hsCRP, >0.34 mg/L; and NLR, >1.85) in multivariate logistic regression analysis and found that hsCRP was the only independent putative-risk factor for breast cancer (P<0.05, Table 8).

To determine which inflammatory indicator(s) are associated with the size of malignant breast tumors, we compared inflammatory indicators with the size of malignant breast tumors. The results showed that hsCRP was significantly associated with the size of malignant breast tumors (P<0.05, Table 9).

Table 8 Multivariate Logistic Regression Analysis of Inflammatory Indicators for Breast Cancer

Variable	B	SE	Wald χ^2	*P* value	FDR	OR	95% CI
WBC (>4.95×10^9/L)	0.113	0.217	0.270	0.603	0.603	1.119	0.732–1.711
NE (>2.96×10^9/L)	0.307	0.239	1.645	0.200	0.270	1.359	0.850–2.172
hsCRP (>0.34 mg/L)	0.541	0.173	9.732	0.002*	0.008*	1.718	1.223–2.413
NLR (>1.85)	0.226	0.177	1.628	0.202	0.270	1.254	0.886–1.776

Note: *P<0.05.

Table 9 Comparison of Inflammatory Indicators with the Size of Malignant Breast Tumors

	≤5 cm Median (25%-75%)	>5 cm Median (25%-75%)	Z score	*P* value	FDR
WBC (10^9/L)	5.50(4.62–6.55)	5.72(5.26–6.90)	−1.227	0.220	0.373
NE (10^9/L)	3.29(2.63–4.22)	4.01(3.02–4.50)	−1.638	0.102	0.272
LY (10^9/L)	1.64(1.33–1.94)	1.63(1.36–1.86)	−0.394	0.693	0.792
PLT (10^9/L)	219(186–258)	227(172–300)	−0.263	0.793	0.793
hsCRP (mg/L)	0.74(0.40–1.74)	1.99(0.46–5.40)	−2.054	0.040*	0.272
NLR	2.01(1.58–2.67)	2.17(1.92–2.99)	−1.791	0.073	0.272
PLR	133.74(106.08–162.76)	147.27(98.65–173.05)	−0.728	0.467	0.623
SII (10^9/L)	443.88(312.97–595.81)	456.21(343.69–710.24)	−1.192	0.233	0.373

Note: *P<0.05.

Discussion

Obese patients often suffer from chronic inflammation. In clinical tests, the easiest way to reflect the inflammatory state of patients is to detect WBC, NE, PLT, hsCRP, and other indicators in peripheral blood. WBC, NE, LY and PLT are all inflammatory cells from bone marrow that are involved in inflammation and immune responses. The NLR, PLR and SII calculated according to the basic inflammatory cell indicators also reflect the inflammatory status of the individual. CRP is considered to be a typical acute reactant and is a protein produced by the liver in response to various clinical conditions, such as infection, inflammation and trauma. This study showed that in overweight female patients with breast tumors, the inflammatory-related indicators in peripheral blood, such as WBC, NE, LY, PLT, hsCRP, NLR, and SII, were significantly higher than those in nonoverweight female patients with breast tumors, indicating that overweight patients with breast tumors had higher inflammatory indicators. Studies have shown that the plasma concentrations of inflammatory cytokines (such as TNF-α, PGE2, IL-6 and CRP) in obese patients are significantly increased,[42] and our results are consistent with these findings.

Chronic inflammation caused by obesity is an important cause of tumor development. Inflammatory factors can promote the formation of blood vessels and the proliferation of tumor cells, thereby promoting the occurrence and development of tumors.[38,39] Previous studies have shown that the above-mentioned inflammatory indicators are associated with the prognosis of tumors in the digestive system. Studies have shown that weight loss prevents the development of cancer and other obesity-related diseases and that dietary intervention significantly reduces the mortality of breast cancer.[43] The correlation between bariatric surgery and breast cancer risk reduction has been confirmed by controlled experimental studies.[44] In addition, metformin, thiazolidinediones, anti-inflammatory drugs and other weight-loss drugs also reduce the risk of breast cancer.[22,45] BMI is simply calculated according to a person's height and weight. A high BMI indicates high body fat. A longitudinal cohort study examining the relationship between BMI, cardiac risk score (CRS), and obesity-related proteins score (OPS) in postmenopausal women found that as BMI increases, CRS and OPS also increase. The higher the rate of BMI increase, the worse the trajectory of cardiac metabolism and breast cancer biomarker risks. This suggests that weight control to reduce cardiovascular metabolic risk factors may be beneficial for breast cancer prevention, particularly in postmenopausal women.[46] Another study found that among breast cancer patients aged <55 years, high BMI was associated with human epidermal growth factor receptor 2 (HER2) positivity and poorer progression-free survival. This indicates a significant correlation between BMI and breast cancer incidence among young breast cancer patients. Implementing strategies to control BMI in breast cancer patients may be beneficial in reducing recurrence and distant metastasis.[47]

Consistent with the above reports, in our study, we showed that overweight patients have a higher proportion of malignant breast tumors than nonoverweight patients. Importantly, our results show that BMI is an independent putative-risk factor for breast cancer. Therefore, BMI could be used as a simple predictor of breast cancer. Clinically, identifying BMI and inflammatory markers in the peripheral blood can help determine the outcome of patients in the preliminary stages. Encouraging individuals to lose weight is a possible way to delay the development of breast cancer.

Previous studies have shown that an increase in the NLR is related to poor prognosis in many tumors, and it can be used as a biomarker of tumor prognosis.[48–50] The specific mechanism of the relationship between a high NLR and the prognosis of cancer patients is still unclear. However, there are several possible reasons. First, the number of neutrophils and lymphocytes reflects the state of systemic inflammation. The inflammatory response has a protumor effect, helping the proliferation and survival of tumor cells and promoting angiogenesis and metastasis.[37] Second, neutrophils promote tumor progression by inhibiting the adaptive immune response in the tumor microenvironment. The increase in neutrophils has adverse effects on tumor patients.[51] Lymphocytes play an important role in tumor-related immunity, which inhibits the development of various tumors. A decrease in lymphocyte count indicates that the body is in a state of immunosuppression.[52,53] In addition, another study showed that PLR could be used as a predictor of breast cancer.[50] The NLR, PLR and SII are of great value in predicting the overall survival of gastric cancer.[54]

In this study, the levels of inflammatory indicators, including WBC, NE, hsCRP, and NLR, in breast cancer patients were significantly higher than those in non-cancer patients, suggesting that overweight patients were more likely to suffer from malignant breast tumors. The potential mechanisms underlying the possible link between hsCRP and cancer risk

include the following: 1) Tumor tissue can induce inflammation, thereby increasing serum hsCRP levels; 2) Tumor cells can produce various cytokines and chemokines, stimulating the production of hsCRP in the liver; 3) hsCRP is part of the host immune response to tumor cells; 4) hsCRP is a marker of chronic inflammation, which promotes carcinogenesis by creating an attractive environment; 5) hsCRP can serve as an internal exposure marker, reflecting the body's aging status.[55] Previous studies have revealed that elevated CRP levels were linked to an increased risk of breast cancer.[56–58] Consistently, our study revealed significantly elevated levels of hsCRP in cancer patients, with a notable correlation observed between hsCRP levels and the size of malignant breast tumors. Consequently, our cross-sectional study suggests that CRP may serve as a putative risk factor for malignant breast tumors.

Our study has some limitations. Firstly, it is unable to properly examine the relative risk factors because, as a cross-sectional study, the data are limited and subject to selection and memory bias. Secondly, although BMI is a standard for gauging overweight, it ignores the variation in weight across cancer patients. Instead of using BMI as a predictor of breast cancer risk, newly developed image processing software can determine the content of adipose tissues from conventional CT pictures. Further research is required because we did not follow up with the patient for an extended period of time and were unable to accurately determine the relationship between BMI, inflammatory markers, and the prognosis of breast cancer. Kaplan-Meier and other survival analyses may give better insights for our findings.

Conclusion

Our cross-sectional study explored the association of overweight and inflammatory indicators with breast cancer risk in Chinese patients. The levels of hsCRP were significantly elevated in cancer patients, and there was a significant correlation between the levels of hsCRP and the size of malignant breast tumors. Our data indicate that overweight and high levels of hsCRP may serve as putative risk factors for malignant breast tumors in Chinese women. Our work provides clinical evidence that BMI and hsCRP level are helpful in the supplementary evaluation of breast cancer risk. Based on the findings of previous studies, our research also suggests that controlling weight may reduce the incidence and progression of breast cancer to some extent in overweight patients. This study holds significance for the treatment and prognosis of breast cancer patients.

Ethical Statement

Patients were enrolled in the study after informed consent was obtained and following the approval and recommendations of the Ethics Review Board of The First Affiliated Hospital of Soochow University (2021 L.N.J. No.182). The guidelines outlined in the Declaration of Helsinki were followed.

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Disclosure

The authors report no conflicts of interest in this work.

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