Decreased Level of IgE is Associated with Breast Cancer and Allergic Diseases

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Background: The aim of this study was to explore the prevalence of type I allergic diseases in patients with breast cancer by carrying out a questionnaire survey and IgE detection in a healthy population and in patients with breast cancer.

Material/Method: There were 309 patients enrolled and they were further divided into the type I allergic disease group, the newly diagnosed breast cancer with type I allergic disease group, the re-visit breast cancer with type I allergic disease group, and the re-visit breast cancer without type I allergic disease group, as well as a healthy control group. Serum total IgE level was detected by immunoassay.

Results: The IgE value in the healthy population with type I allergic diseases (89.3±51.4 IU/ml) was significantly higher than in those without type I allergic diseases (45.6±65.1 IU/ml). There was no significant difference between IgE values in the re-visit breast cancer patients with type I allergic disease (25.1±65.1 IU/ml) and those without type I allergic disease (23.0±45.9 IU/ml). The area under the ROC curve was 0.618±0.04, sensitivity was 78%, specificity was 47.1%, Youden index was 0.251, and IgE threshold was 32.6 IU/ml.

Conclusions: The patients with newly diagnosed breast cancer were susceptible to type I allergic disease at about the same levels as in the healthy population. There was no correlation between breast cancer and type I allergic disease.

MeSH Keywords: **Breast • Immunization • Tumor Markers, Biological**

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Background

Breast cancer is the most common malignant tumor in women world-wide and more than 1.6 million Chinese women are diagnosed with breast cancer each year [1]. The etiology and pathogenesis of breast cancer are very complex. It is induced by many factors, including genetic factors, lifestyle, and environmental exposure, singly or in combination. Recent studies [2–4] have found that type I allergic reaction mediated by IgE is related to the development of malignant tumors. Studies [5,6] have shown that there is a significant negative correlation between IgE level and non-Hodgkin lymphoma, and other studies have shown that the metastasis and diffusion of non-Hodgkin lymphoma are negatively correlated with IgE level. However, there are few studies on the correlation between IgE and the occurrence of breast cancer. Many confounding factors can be filtered, and the correlation between allergic disease and breast cancer can be comprehensively reflected, if clinical diagnosis and IgE determination are combined in the correlation investigation.

By carrying out a questionnaire survey and IgE detection in a healthy population and in patients with breast cancer, we explored the prevalence of type I allergic diseases in patients with breast cancer, the relationship between breast cancer and IgE-mediated type I allergic diseases, the effects of breast cancer treatment on IgE level, and whether IgE can be used as a protective factor, hoping to provide a new perspective on the diagnosis and treatment of breast cancer.

Material and Methods

Epidemiological survey of allergic disease

Questionnaire design

We performed a questionnaire survey of allergic disease at the Allergic Reaction Department, Affiliated People's Hospital of Inner Mongolia Medical University (questionnaire of China National Natural Science Fund Project "Investigation of Airborne Pollen in Four Cities in Western Inner Mongolia" [81160371]) as revised for breast cancer diagnosis and treatment.

The definition of the disease in this study

Type I allergic diseases included hay asthma, allergic asthma, allergic rhinitis, eczema, urticaria, and other diseases, and did not include drug allergy, food allergic reaction, or personal care products allergic reaction mediated by IgG.

The newly diagnosed breast cancer patients had pathologically diagnosed invasive breast cancer and had not received comprehensive treatments (e.g., surgery, chemotherapy, radiotherapy, endocrine therapy, and targeted therapy).

Re-visit breast cancer patients were breast cancer patients who had received comprehensive breast cancer treatments (e.g., surgery, chemotherapy, radiotherapy, targeted therapy, and other treatment), including breast cancer patients undergoing endocrine therapy.

Survey methods in healthy populations

The "Allergic disease epidemiology investigation" was carried out by field questionnaire in women receiving routine physical examination at the Medical Examination Center, Shaanxi Provincial Tumor Hospital, from November 2013 to November 2014; subjects were screened and divided into the type I allergic patients group and the healthy people group.

Survey methods in newly diagnosed breast cancer patients

"Allergic disease epidemiology investigation" was carried out by field questionnaire or telephone follow-up in the female breast cancer patients who were admitted for the first time at the Breast Disease Diagnosis and Treatment Center, Shaanxi Provincial Tumor Hospital, from November 2013 to November 2014, and the patients were screened and divided into the first-time diagnosed breast cancer with type I allergic reaction group and the first-time diagnosed breast cancer without type I allergic reaction group.

Survey methods in re-visit breast cancer patients

All patients signed informed consent before enrolling in the study. The study was approved by the Ethics Committee of Shaanxi Provincial Tumor Hospital and Inner Mongolia Medical University. The "Allergic disease epidemiology investigation" was carried out by field questionnaire in the female breast cancer patients who re-visited the Outpatient Department of Shaanxi Provincial Tumor Hospital from November 2013 to November 2014, and the patients were screened and divided into the re-visit breast cancer with type I allergic reaction group and the re-visit breast cancer without type I allergic reaction group. Participants provided written informed consent and ethics board approval was granted by the hospital.

Screening for the experimental group

Based on the questionnaire survey, the following criteria for the selection were applied: (1) Patients pathologically diagnosed with invasive breast cancer; (2) Patients with breast cancer combined with other tumors had been excluded; (3) Patients with hypertension, coronary heart disease, diabetes, blood system diseases, tuberculosis, or hyperthyroidism disease had been excluded; (4) Female patients over 18 years of

age. The prevalence of type I allergic disease in first-time diagnosed and re-visit breast cancer patients were analyzed to screen out the experimental group: newly diagnosed breast cancer patients, re-visit breast cancer patients, patients with newly diagnosed breast cancer and type I allergic disease, and re-visit breast cancer patients with type I allergic disease.

Screening for the control group

Women who received regular physical examination at our hospital were enrolled into the healthy control group according to the following criteria: (1) No tumor lesion was found in physical examination; (2) No obvious breast disease was found by color ultrasound and molybdenum target examination; (3) Hypertension, coronary heart disease, diabetes, blood system diseases, tuberculosis, and hyperthyroidism disease had been excluded; (4) Over 18 years old. The prevalence of type I allergic disease was calculated and compared with that in breast cancer patients to screen for patients with simple type I allergic disease and healthy population without type I allergic disease.

Instruments and reagents

For determination of serum IgE we used immunoturbidimetry using an automatic biochemistry analyzer (Beckman Coulter, Inc., Palo Alto, CA, USA). We used pure water equipment (Beijing Shuangfeng Zhongbang Scientific Development Co., Ltd. Beijing, China) and a KDC-1042 centrifuge (USTC ZONKIA, Hefei, Anhui, China). For reagent, we used the IgE assay kit (Desai Diagnostic System Co., Ltd., Shanghai, China), batch number 07049/00000592.

Serum IgE detection

Enrolled subjects were from the control and experimental groups.

The healthy population included the healthy women with type I allergic reaction group and the healthy women without type I allergic reaction group. The newly diagnosed breast cancer group included the newly diagnosed breast cancer with type I allergic reaction group and the newly diagnosed breast cancer without type I allergic reaction group. The re-visit breast cancer group included the re-visit breast cancer with type I allergic reaction group and the re-visit breast cancer without type I allergic reaction group. There were about 100 subjects in each group. Fasting venous blood samples were collected in the 3 groups to detect the serum IgE level.

Methods and steps

From the subjects in each group, a 5-ml sample of fasting venous blood was collected in the morning to detect the serum IgE level.

The steps were as follows:

1. Five milliliter of venous blood sample was routinely collected.
2. Blood samples were kept at room temperature (20–25°C) ±1°C under coagulation for 1 h.
3. Centrifuged at 3000 rpm for 10 min.
4. After the supernatant was removed, samples were centrifuged again at 1300×g for 10 min.
5. The supernatant was collected in 3 quantitative tubes and stored at −40°C.

The reference values were as provided by the kit manufacturer: serum IgE value ≤100 IU/ml was negative, and IgE value >100 IU/ml was positive.

Statistical analysis

The data was statistically analyzed using SPSS 13.0 software (SPSS, Inc., Chicago, IL, USA). Quantitative data meeting the normal distribution requirements were statistically described by mean ± standard deviation (SD). Multi-group comparison was performed by variance analysis, and inter-group comparison was performed by student's t test. IgE values not meeting the normal distribution requirements were statistically described by mean ± quartile range (QR), and inter-group comparison was performed by nonparametric test. Inter-group comparisons of the calculation rate or composition ratio of categorical data were performed by chi square test. The data impacting the IgE value were analyzed with SPSS 22.0 (SPSS, Inc., Chicago, IL, USA). $P<0.05$ was statistically significant.

Results

The basic information on investigated population

Investigation for a healthy population

There were 800 questionnaires collected and 578 were qualified. There were 100 subjects randomly selected from the qualified population and divided into the healthy population with type I allergic reaction group and healthy population without type I allergic reaction group, and then the serum IgE level was tested.

Investigation for the newly diagnosed breast cancer patients

There were 150 questionnaires collected and 114 were qualified. Among those, there were 102 patients selected and divided into the newly diagnosed breast cancer with type I allergic reaction group and the newly diagnosed breast cancer without type I allergic reaction group, and the serum IgE level was tested.

Table 1. The qualification status of the three population groups under questionnaire survey (case (%)).

Group	Qualification of the population under survey		Total
	Unqualified	Qualified	
Patients in physical examination center	222 (27.8)	578 (72.2)	800
Patients in breast inpatient department	36 (24.0)	114 (76.0)	150
Patients in breast outpatient department	438 (29.2)	1062 (70.8)	1500
Total	696	1754	2450

Chi square test was performed for the comparison among the data of the three groups, χ^2=2.066, P=0.356.

Table 2. Allergic diseases in different populations (cases (%)).

Group	Allergic diseases						
	No disease	Type I allergic reaction	Drug	Food	Daily necessities	1 + multiple allergies	Non-1 + multiple allergies
Healthy control	416 (72.0)	94 (16.3)*	19 (3.3)*	7 (1.2)	13 (2.2)	26 (4.9)	3 (0.5)
Newly diagnosed breast cancer	86 (75.4)	16 (14.0)*	7 (6.1)*	2 (1.8)	3 (2.6)	0 (0.0)	0 (0.0)
Re-visit breast cancer	763 (71.8)	45 (4.2)	164 (15.4)	11 (1.0)	24 (2.3)	55 (5.2)	21 (2.0)

1 + multiple allergies refers to type I allergic reaction with other types of allergic reactions. Non-1 + multiple allergies refers to other types of allergic reactions except for type I allergic reaction. * As compared with re-visit breast cancer group, under chi square test, P<0.001, the difference was statistically significant.

Re-visit breast cancer patient investigation

There were 1500 questionnaires collected and 1062 were qualified. There were 45 (4.2%) cases of re-visit breast cancer with type I allergic reaction, but the serum IgE level could be tested in only 34 cases. There were 73 cases of re-visit breast cancer without type I allergic reaction randomly selected. The serum IgE test was performed in the 2 groups, including 107 cases.

Quality analysis for the population under questionnaire survey

Differences among the qualified rates of the population from the inpatient department, physical examination center, and outpatient department groups were not statistically significant (Table 1).

Basic description of the allergic diseases in different populations in the epidemiological survey

There were 1754 eligible patients enrolled in this study: 578 healthy persons, 114 patients with newly diagnosed breast cancer, and 1062 re-visit patients with breast cancer.

The prevalence of type I allergic disease in the healthy population was 16.3%, that in patients with newly diagnosed breast cancer was 14.0%, and the difference between the 2 groups was not statistically significant (chi square test, χ^2=0.354, P=0.552); however, both were higher than the 4.2% in the re-visit breast cancer patients, and the differences were statistically significant (Table 2, Figure 1). The prevalence of drug allergic reaction in the healthy population was 3.3%, that in patients with newly diagnosed breast cancer was 6.1%, and the difference between the 2 groups was not statistically significant (χ^2=2.232, P=0.173); however, both were lower than the 15.4% in re-visit breast cancer patients and the differences were statistically significant (Table 2, Figure 1). The ages of newly diagnosed breast cancer patients and re-visit patients were similar, but both were older than the healthy population and the differences were statistically significant (Table 3, Figure 1).

Variance analysis showed that the differences among the ages of the 3 population groups were statistically significant (F=136.145, P<0.001). The newly diagnosed breast cancer patients and the re-visit patients were older than the healthy population, but the difference between the 2 groups was not statistically significant.
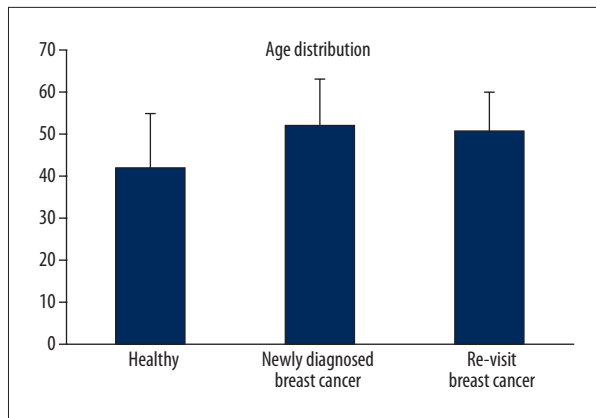
Figure 1. The age distribution in the populations.

Table 3. The basic information of populations in different ages.

Group	Case number	Age (years) (mean ±S.D.)
Healthy control	578	41.98±12.71
Newly diagnosed breast cancer	114	51.91±11.13*
Re-visit breast cancer	1062	50.76±9.261*

* The difference was statistically significant as compared with healthy population.

Table 4. The comparison of the IgE values of populations with and without type I allergic reaction (mean ±OR).

Group	Healthy population	Newly diagnosed breast cancer	Re-visit breast cancer
With type I allergic reaction	89.3±51.4	119.4±241.4	25.1±65.1
Without type I allergic reaction	45.6±65.1	33.1±46.8	23.0±45.9
Z	3.625	1.768	0.565
P	<0.001	0.077	0.565
IgE	59.4±73.1	36.9±49.5	
z	−2.904		
P	0.004		

Basic description of the IgE levels in different populations

We determined IgE values in 309 patients, including 108 with type I allergic reaction and 201 without type I allergic reaction. Among them there were 19 healthy subjects with type I allergic reaction (19.0%), 16 newly diagnosed breast cancer patients with type I allergic reaction (15.7%), and 73 re-visit breast cancer patients with type I allergic reaction (68.2%). As shown in Table 4, the IgE value of healthy subjects with type I allergic reaction (89.3±51.4 IU/ml) was significantly higher than in those without type I allergic reaction (45.6±65.1 IU/ml) (Figure 2) and the difference was statistically significant ($P<0.001$). The IgE value of newly diagnosed breast cancer patients with type I allergic reaction (119.4±241.4 IU/ml) was higher than in those without type I allergic reaction (33.1±46.8 IU/ml), but the difference was not statistically significant ($P=0.077$). The IgE value of re-visit breast cancer patients with type I allergic reaction (25.1±65.1 IU/ml) was similar to that without type I allergic reaction (23.0±45.9 IU/ml) but the difference was not statistically significant ($P=0.565$).
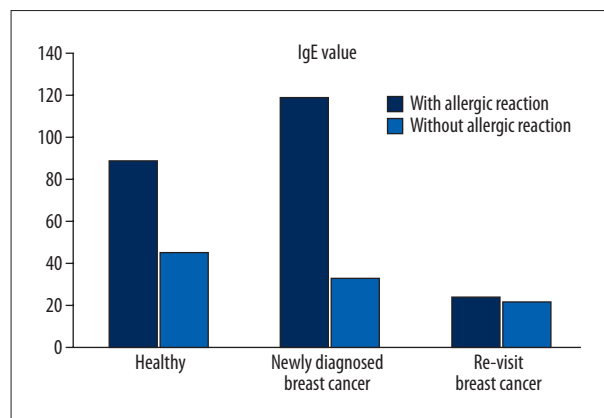

Figure 2. The IgE values of different populations with or without type I allergic reaction.

The relationship between newly diagnosed breast cancer and IgE-mediated type I allergic diseases

Randomly selected healthy population

There were 100 healthy subjects randomly selected based on the distribution of healthy persons and newly diagnosed breast cancer patients in the questionnaire survey. There were
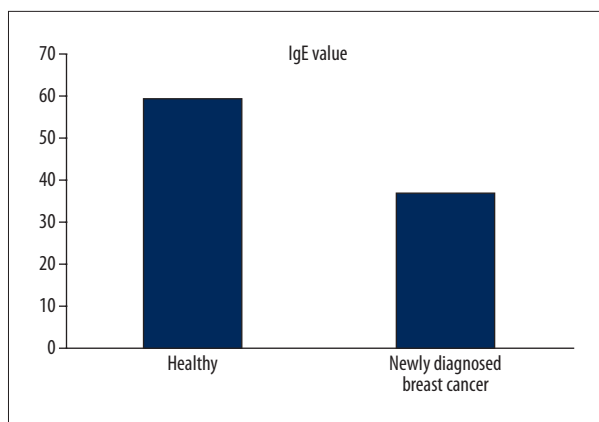
Figure 3. The IgE values in healthy population and newly diagnosed breast cancer patients.
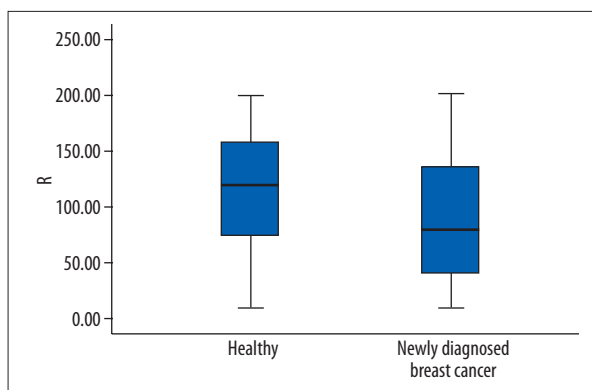

Figure 4. Rank transformation of the IgE values in the healthy population and newly diagnosed breast cancer patients.

Table 5. The comparison of the IgE values in newly diagnosed breast cancer patients and healthy population.

| Group | Positive IgE | | Negative IgE | |
	Negative (≤100)	Positive (>100)	Negative (≤100)	Positive (>100)
Health	12 (63.2)	7 (36.8)	63 (77.8)	18 (22.2)
Breast cancer	8 (50.0)	8 (50.0)	73 (84.9)	13 (15.1)
Total	20	15	136	31

19 with type I allergic reaction (19.0%) in the randomly selected healthy population, and 81 subjects did not have type I allergic reaction (81.0%). The prevalence of type I allergic reaction in the healthy population of the questionnaire survey was 16.3%; thus, the difference was not statistically significant.

Comparative serum analysis in newly diagnosed breast cancer patients and the healthy population

The comparative analysis of serum IgE in patients with newly diagnosed breast cancer and healthy population was done in 2 sections, with the comparison of IgE values and the comparison between negative and positive IgE results using IgE value of 100 IU/ml as the critical point.

The IgE value in the healthy population (59.4±73.1 IU/ml) was higher than that in newly diagnosed breast cancer patients (36.9±49.5 IU/ml) and the difference was statistically significant (Table 4, Figure 3).

Table 5 shows that there were 12 cases of negative IgE and 7 cases of positive IgE in the healthy population with type I allergic reaction. There were 8 cases of negative IgE and 8 cases of positive IgE in newly diagnosed breast cancer patients. The stratified chi square test showed $\chi^2=0.614$ and $P=0.200$. There were 63 cases of negative IgE and 18 cases of positive IgE in the healthy population without type I allergic reaction

and 73 cases of negative IgE and 13 cases of positive IgE in the newly diagnosed breast cancer patients. The stratified chi square test showed $\chi^2=0.614$ and $P=0.080$. There were 25 patients with positive IgE results in the total healthy population with a positive rate of 25.0%, and 21 patients with positive IgE results in the newly diagnosed breast cancer patients, with a positive rate of 20.9%. The overall stratified chi square test showed that the positive rates of IgE in the healthy population and the newly diagnosed breast cancer patients were similar ($\chi^2=0.559$, $P=0.101$). We found was no significant difference in the IgE-positive rate between the healthy population and the newly diagnosed breast cancer patients in the stratified comparison and overall comparison.

The factorial analysis of the impacts of population and allergic reaction on IgE value

The rank-transformed IgE values shown in Figure 4 were normally distributed. The influences of various factors on IgE value were analyzed by factorial analysis with 2 factors and 2 levels, taking age as covariates and population and type I allergic diseases as the primary effects. The results in Table 6 show that both population and type I allergic reaction influenced the IgE value, which was variable in different populations and in subjects with or without type I allergic reactions. Figures 5 and 6 show that there was no interaction between populations and type I allergic reaction. The IgE values were significantly higher

Table 6. Variance analysis of the IgE values of healthy population and type I allergic reaction.

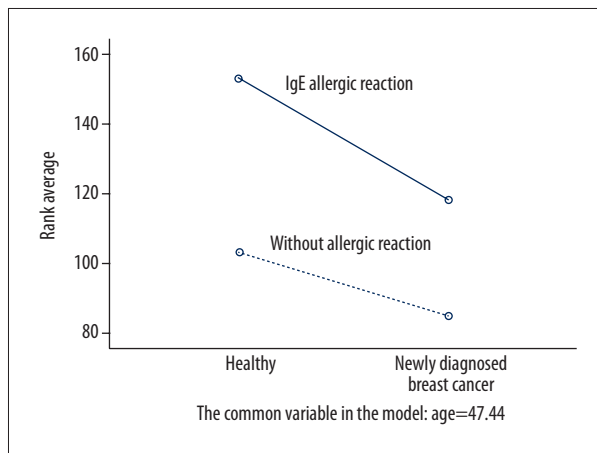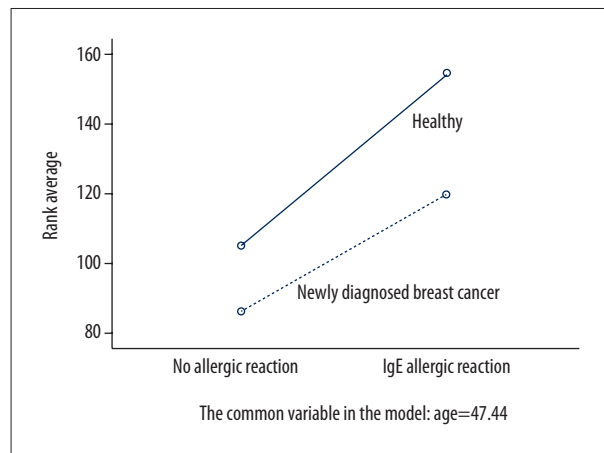| Source of variation	Freedom degree	SS	MS	F	P
Total variation	202	2767412.500			
Age	1	440.604	440.604	0.144	0.705
Newly diagnosed breast cancer	1	18000.180	18000.180	5.876	0.016
Type I allergic reaction	1	50242.820	50242.820	16.402	<0.001
Breast cancer* type I allergic reaction	1	1862.694	1862.694	1.723	0.436
Error	198	603462.838	3063.263		

Figure 5. Diagram of 2-factors interaction.

Figure 6. Diagram of 2-factors interaction.

in subjects with type I allergic disease, regardless of whether they were healthy people or breast cancer patients. Similarly, the IgE value of newly diagnosed breast cancer patients was significantly lower than that of the healthy population regardless of whether they had type I allergic disease.

Analysis for IgE critical point with breast cancer diagnostic value

A receiver operating characteristic (ROC) curve was obtained using the IgE value as the test variable, and the healthy population and newly diagnosed breast cancer population as the criterion standards. As shown in Figure 7, the area under the ROC curve was 0.618±0.04, the sensitivity was 78%, the specificity was 47.1%, the Youden index was 0.251, and the IgE critical point was 32.6 IU/ml. Table 7 shows that breast cancer was correlated with the IgE value. The IgE value was higher in healthy people, and the odds ratios (OR) values showed that the ratio of IgE value <32.6 in the healthy population was 46.8% of that in newly diagnosed breast cancer patients. The probability of IgE value >32.6 in the healthy population was 2.137 times that in newly diagnosed breast cancer patients. The
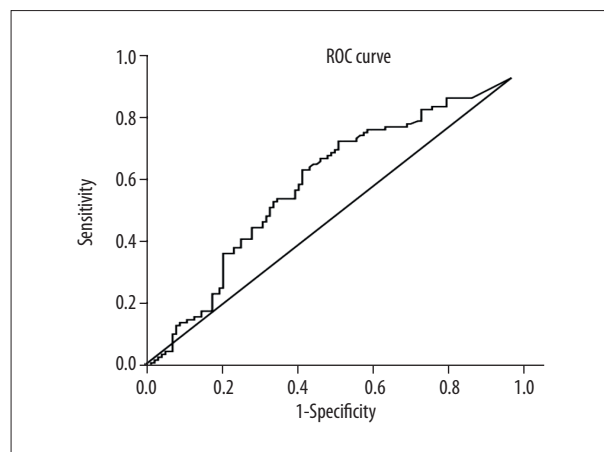

Figure 7. Diagram of 2-factors interaction.

95% confidence interval (CI) did not cover 1, suggesting that the difference was statistically significant. Therefore, breast cancer might be diagnosed using IgE=32.6 IU/ml as the critical point derived from the ROC curve (χ^2=14.002, P<0.001, statistically significant), suggesting that women with serum IgE value <32.6 IU/ml were susceptible to breast cancer (Table 8).

Table 7. The relationship between type I allergic disease and newly diagnosed breast cancer patients as well as re-visit breast cancer patients.

Group	Type I allergic reaction (cases (%))		Total
	With	Without	
Newly diagnosed breast cancer	16 (15.7)	86 (84.3)	102
Re-visit breast cancer	34 (31.8)	73 (68.2)	107
Total	50	159	209

Table 8. The comparison of the IgE values in newly diagnosed breast cancer patients and the healthy population.

Factor	IgE value (case (%))		χ^2 value	*P* value	*F* value	OR value 95% CI
	<32.6	>32.6				
Healthy	22 (22.0)	78 (78.0)	14.002	<0.001	0.468	0.306
Newly diagnosed breast cancer	48 (47.1)	54 (52.9)				0.713

Table 9. The comparison of the IgE values in newly diagnosed breast cancer patients and re-visit breast cancer patients without type I allergic reaction (mean ±OR).

Group	Case number	IgE	*Z*	*P*
Newly diagnosed breast cancer without type I allergic reaction group	86	33.1±46.8	−2.366	0.018
Re-visit breast cancer without type I allergic reaction group	73	23.0±45.9		
Newly diagnosed breast cancer with type I allergic reaction group	16	119.4±241.4	−1.994	0.046
Re-visit breast cancer with type I allergic reaction group	34	25.1±65.1		

Figure 8. The IgE values of newly diagnosed breast cancer without type I allergic reaction group and re-visit breast cancer without type I allergic reaction group.

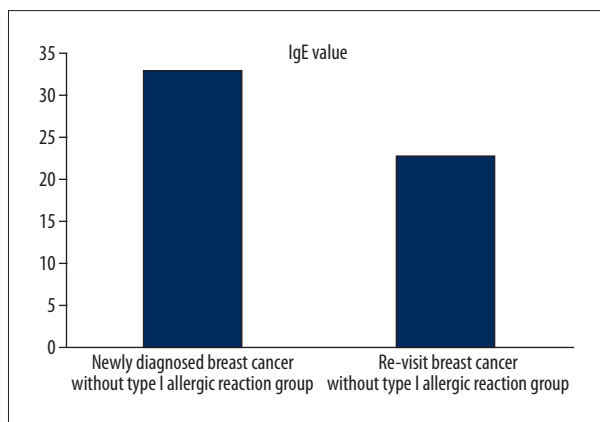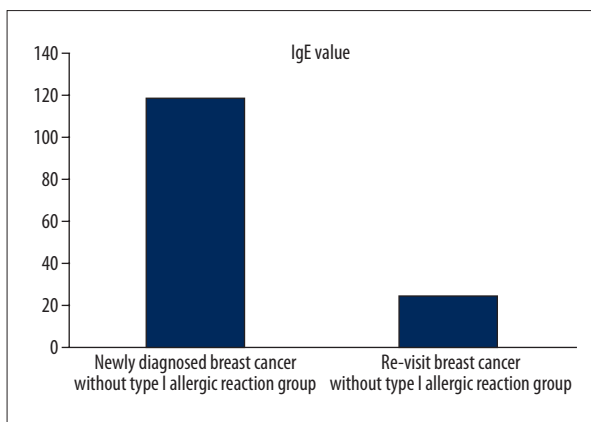**Figure 9.** The IgE values of newly diagnosed breast cancer with type I allergic reaction group and re-visit breast cancer with type I allergic reaction group.

Summary: The population with fasting venous serum IgE value <32.6 IU/ml was susceptible to breast cancer. IgE is a protective factor for breast cancer and has value in the diagnosis of breast cancer.

Effects of breast cancer treatment on IgE level

The general information of newly diagnosed breast cancer patients and re-visit breast cancer patients is shown in Table 7.

Table 10. Normal range of IgE in different age groups.

Age	95% upper limit (IU/ml)
Newborn	1.5
1 year old	15
1–5 years old	60
6–9 years old	90
10–15 years old	200
≥16 years old	100

The comparison of the IgE values in newly diagnosed breast cancer patients and re-visit breast cancer patients in the absence of type I allergic disease is shown in Table 9 and Figure 8.

The comparison of the IgE values in newly diagnosed breast cancer patients and re-visit breast cancer patients in the presence of type I allergic disease is shown in Figure 9.

Discussion

Petridou et al. [7] explored the roles of allergic reaction in breast cancer using biomarker IgE in a Greek population, and the results showed that the serum IgE level might be positively correlated with breast cancer (P=0.07). There was also a positive correlation between allergic history and serological evidence (P=0.06). However, the study did not show strongly positive relationships. The risk of breast cancer was slightly increased in women with a history of allergies. However, in type I allergic reaction and breast cancer-related studies, Hedderson et al. [8] found that breast cancer was reduced in women over 35 years old who had allergic history (OR=0.77, 95% CI=0.60–0.99). Wang et al. [9] investigated the relationship between allergic diseases, IgE, and the risks of prostate cancer, breast cancer, lung cancer, and colorectal cancer, showing that there was no statistically significant increase in the risk of breast cancer (OR=1.20, 95% CI=0.87–1.66) in IgE-positive patients. In a meta-analysis, Vojtechova et al. [10] also found there was no correlation between IgE and breast cancer.

The above studies showed that the relationship between IgE and breast cancer is still not clear. The contradictory results might be due to the influence of too many different allergic factors, which could interfere with the results. Therefore, we excluded the influences of season and region to avoid the bias, and carried out an epidemiological investigation for 1 year in an experimental group and control group in Shanxi province. In addition, the skin prick test and serum IgE detection are important criterion standards in the diagnosis of IgE-mediated

Table 11. The onset age of breast cancer.

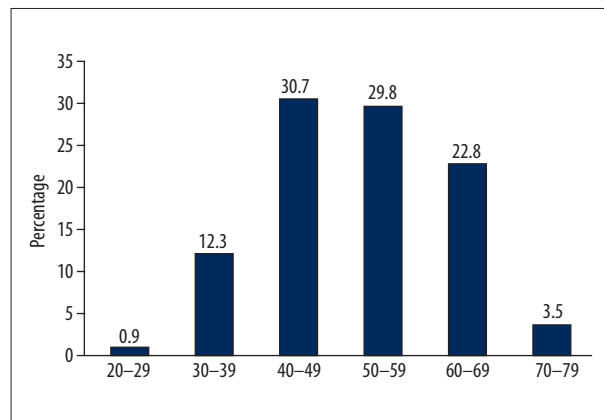| Age group	Number of subjects	Percentage
20–29	1	0.9
30–39	14	12.3
40–49	35	30.7
50–59	34	29.8
60–69	26	22.8
70–79	4	3.5

Figure 10. The percentage distribution of onset age in different groups.

allergic diseases (e.g., allergic rhinitis and asthma). After the treatment, the patients' immune systems change. In order to avoid such an influence on the skin prick test, we only selected serum IgE as the indicator and compared the differences in serum IgE among healthy people, simple allergic disease patients, newly diagnosed breast cancer patients, and re-visit breast cancer patients. The interferences of other diseases must be eliminated, including other tumors, hypertension, coronary heart disease, diabetes, blood system diseases, tuberculosis, and hyperthyroidism. Furthermore, the IgE value in the same individual was variable at different development stages (Table 10); therefore, women were enrolled in the control group based on the characteristics of breast cancer. Moreover, breast cancer can be divided into invasive and non-invasive cancer. We selected the invasive breast cancer of high incidence as the research subjects to exclude the interference of non-invasive cancers with low incidence.

Subjects in the experimental group and control group were strictly selected to perform the comparative analysis. The study found that the average age of newly diagnosed breast cancer patients was 51.91±11.13 years old, and the peak incidence between 40–49 years was 30.7% (Table 11, Figure 10), which is consistent with the disease occurrence in China. Rui [11],

Jianghui [12], and Xiangxiang et al. [13] analyzed the incidence of breast cancer in Henan, Hunan, Anhui, and other provinces of China, and the results showed that the incidence of breast cancer in China usually peaks at between 40 and 49 years old.

The prevalence of type I allergic disease in the healthy population was 16.3%, lower than the world average of 22%. This might be due to the exclusion of drug allergies, food allergies, and type I allergic reaction combined with other types of allergic reactions, or due to the regional factors of Shanxi province.

The interference of breast cancer treatment on the results was eliminated in order to understand the actual correlation between breast cancers and type I allergic disease. We merely analyzed the relationship between newly diagnosed breast cancers and type I allergic disease, which included 2 aspects: the epidemiological study and laboratory evidence. In the first aspect, the prevalence of type I allergic disease in the healthy population and newly diagnosed breast cancer patients were 16.3% and 14.0%, respectively, and the difference was not statistically significant. In the second aspect, the positive rate of IgE in newly diagnosed breast cancer and type I allergic disease was not statistically significant, according to the IgE value >100 IU/ml and the laboratory positive diagnosis indicator of type I allergic diseases, as suggested by the kit manufacturer. These 2 aspects jointly suggest that there was no correlation between breast cancer and I type allergic disease.

Serum IgE levels were significantly lower in breast cancer patients as compared with that in the healthy population. People with serum IgE values less than 32.6 IU/ml were susceptible to breast cancer (OR=0.468, 95% CI=0.306–0.713), suggesting that IgE is a protective factor for breast cancer and that IgE has a negative correlation with the occurrence of breast cancer. The underlying mechanisms are very complex and currently there is no consistent understanding. This might be due to the cell cancerization induced by abnormal gene regulation or viral gene integration [14,15]; the later could express certain proteins, the tumor antigens, which were not expressed in normal cells or were expressed at very low levels. The major histocompatibility complex is lost, or tumor-specific antigen with immunogenicity might be expressed, when the precancerous cells are transformed into cancer cells. People with high IgE levels or low IgE levels also have different levels of immune function, which might also affect the pathogenesis and treatment of cancer.

We found that the IgE level was reduced in newly diagnosed breast cancer patients regardless of whether there were type I allergic diseases, which might be due to the bone marrow suppression induced by breast cancer chemotherapy drugs. Wen et al. [16] analyzed the immune function indicators before and after neuroblastoma chemotherapy in children and concluded that IgG, IgM, IgE, and IgA decreased in children after intensive chemotherapy, suggesting that the intensive chemotherapy had an influence on humoral immunity. The incidence of drug allergy increased during the course of breast cancer hospitalization. In our study, the drug allergic reaction rate in re-visit breast cancer patients was 15.4%, which is higher than that in newly diagnosed breast cancer patients and the healthy population. The above results might be due to the drug treatment after the admission of patients with breast cancer. According to WHO statistics, the prevalence of drug allergic reactions among hospitalized patients is 10–20% [17].

Our study has certain limitations that should be considered in interpreting our results. (1) The patients themselves were not aware of the occurrence of the allergic diseases; therefore, some positive cases were missing. (2) The patients themselves were not aware of the occurrence of hypertension, coronary heart disease, diabetes, blood system diseases, tuberculosis, tumors, and hyperthyroidism disease; therefore, the confounding factors in the study subjects were not completely eliminated. (3) Clinical staff failed to identify the allergic diseases and there was no consultation with our allergic reaction department. (4) The sample size of the newly diagnosed breast cancer group was small, which might affect the accuracy of the results. (5) The incidence of allergic diseases was closely related with the seasons and regions; therefore, the accuracy of the results might be improved by extending the experimental period.

Conclusions

1. There was no correlation between breast cancer and type I allergic disease.
2. The patients with serum IgE values less than 32.6 IU/ml were susceptible to breast cancer (OR=0.468, 95% CI=0.306–0.713), which is valuable for the diagnosis of breast cancer.
3. The laboratory diagnostic criteria of type I allergic disease in the normal population was no longer suitable for re-visit breast cancer patients.

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