Research Article

Effects of Chinese Herbal Formula on Immune Function and Nutritional Status of Breast Cancer Patients

Min Liu

Department of Clinical Nutrition, Affiliated Hospital of Shandong University of TCM, Jinan 250011, China

Correspondence should be addressed to Min Liu; liumin@sdzydyy.org.cn

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Background. Chinese herbal formulas have certain effects on patients with breast cancer (BC). This article discussed the effect of Buqi Yangxue decoction on the immune function and nutritional status of BC patients and provided an evidence for traditional Chinese medicine (TCM) to improve the quality of life and curative effect of BC patients. Methods. 66 cases of BC patients were divided into control group (n = 33) and Chinese herbal formula group (n = 33). The control group was received with TE chemotherapy, and the Chinese herbal formula group was received with Buqi Yangxue decoction combined with TE chemotherapy. Nutritional status, immune function, TCM symptom quantitative score, and adverse reactions were compared between the two groups. Results. There was no difference in all indexes between the two groups before intervention. After 4 weeks, the nutritional indexes ALB, PA, TRF, and TP in Chinese herbal formula group were higher than those in control group, except Hgb. CD3+, CD4+, and CD4+/CD8+ in both groups were sharply higher than before treatment, while CD8+ was dramatically lower, and the changes in Chinese herbal formula group were more obvious than those in control group. In Chinese herbal formula group, the levels of IgG, IgA, and IgM were sharply increased compared with control group. The TCM syndrome scores in both groups were decreased significantly after treatment, especially in Chinese herbal formula group. In addition, nausea and vomiting, inappetence, liver function impairment, leukopenia, and thrombocytopenia occurred in both groups. There was no clear difference in the incidence of adverse reactions between Chinese herbal formula group and control group. Conclusion. Buqi Yangxue decoction can effectively improve the nutritional status and immune function of BC patients, which has important clinical significance for the later comprehensive treatment.

1. Introduction

Breast cancer (BC) is one of the most common malignant tumors that seriously endangers women’s health and life. In recent years, with environmental pollution, the change of people’s lifestyle, and the increase of competitive pressure, the incidence of BC is increasing year by year [1, 2]. The incidence of BC in western developed countries accounts for the first place of female malignant tumors [3]. The incidence of BC has increased significantly in China, and the onset age is gradually becoming younger [4]. BC has surpassed cervical cancer and become the most common malignant tumor in urban women. Sadly, BC is becoming younger and younger, which seriously endangers the physical, mental health, and life safety of young women.

The main treatment for BC is surgical resection and postoperative chemotherapy [5, 6]. The depression, damage of qi and blood, hematocoele, and fluid accumulation of postoperative BC patients affect the wound healing and body repair [7]. BC patients’ weak constitution, combined with the toxic damage of surgical chemoradiotherapy drugs, makes their vital qi more weak. The immune function of patients with BC is generally low [8]. Immune system plays a very important role in reducing postoperative complications and preventing and limiting the occurrence and development of tumors [9]. The postoperative immune function of patients with BC is low, which will increase the risk of infection and tumor recurrence. Therefore, it is very important to restore the patient’s immune function as soon as possible. However, due to the damage to the human immune system after treatment, as well as the depression of patients,
it will inevitably lead to insufficient nutritional intake of patients. Persistent nutritional deficiencies can further affect recovery and treatment [10].

In the comprehensive treatment of BC, Chinese herbal formulas play a positive role in increasing curative effect, enhancing physical fitness, improving life quality, and alleviating side effects [11, 12]. Surgery and chemotherapy are the methods of removing evil, which are easy to harm the patient’s vital qi, resulting in more deficiency of the patient’s vital qi. Malignant tumors belong to qi and blood deficiency syndrome, and massive blood loss caused by surgery will lead to aggravation of qi and blood deficiency [13]. Therefore, BC patients should be treated with Chinese herbal formula during the treatment to achieve the effect of nourishing and eliminating pathogenic factors. In recent years, the basic principle of TCM in treating BC is to replenish T qi and blood. Lee et al. found that Huanglian Wendan Tang improved the prognosis of BC patients [14]. Moreover, Yanghe decoction was found to improve the immune function of BC patients [15]. Buqi Yangxue decoction is a famous prescription for treating deficiency of qi and blood. In recent years, with the application of modern research technology, the pharmacological action of this decoction has been further studied. Studies have shown that Buqi Yangxue decoction can promote the treatment of renal anemia [16]. Furthermore, Buqi Yangxue decoction improved TCM clinical symptoms of patients with advanced colorectal cancer, reduced the side effects of chemotherapy, and provided patients with quality of life [17].

In this study, 66 patients with BC were treated with Buqi Yangxue decoction adjuvant therapy, in order to provide theoretical basis for the study of Chinese herbal formulas to improve the therapeutic effect of BC patients.

2. Materials and Methods

2.1. Clinical Data and Methods. A total of 66 patients with BC from December 2019 to January 2021 were selected as the study subjects. Patients were divided into the control group and Chinese herbal formula group by numerical randomization. There were no significant differences in age, weight, tumor site, TNM stage, and lymph node metastasis between the two groups (Table 1, P > 0.05). All patients were clearly diagnosed with BC by preoperative biopsy or intraoperative pathological section. This study was approved by the Hospital’s Ethics Committee. All patients were aware of the study and had signed informed consent.

2.2. Inclusion Criteria

(1) Diagnosed with breast cancer by cytology and histopathology
(2) No other malignant tumors
(3) The expected survival was greater than 6 months
(4) Those who agree to participate in the study and sign the informed consent

2.3. Exclusion Criteria

(1) Concurrent use of drugs affecting the results of this study
(2) Failure to follow the prescribed medication
(3) With heart, liver, kidney, and other serious diseases
(4) Mental disorders, unable to cooperate with evaluators

2.4. Interventions. The control group was treated with TE chemotherapy, and received routine nutritional intervention measures. Patients were given targeted dietary guidance according to the actual situation, chose light, digestible, and nutritious food, and avoided spicy stimulation and raw, cold, and greasy food.

The Chinese herbal formula group was treated with Buqi Yangxue decoction on the basis of the control group. The decoction was as follows: 15 g of Astragali Radix, 12 g of Codonopsis Radix, 10 g of Polygonati Rhizoma, 15 g of Rehmanniae Radix Praeparata, 10 g of Poria, 12 g of Radix Paeoniae Alba, 15 g of Angelica sinensis, 15 g of Chinese date, 6 g of licorice. These herbs were decocted to 300 ml in water and taken twice in the morning and evening once a day, and taken continuously for 4 weeks.

2.5. Nutritive Indexes. In both groups, fasting venous blood was taken in the morning. The levels of hemoglobin (HGb), serum albumin (ALB), prealbumin (PA), transferrin (TRF), and serum total protein (TP) were measured by an automatic biochemistry analyzer (Cobas c702, Roche, Switzerland).

2.6. Cellular Immune Function Detection. Fasting venous blood was collected to detect various immune function indexes. CD3+, CD4+, CD8+, and CD4+/CD8+ were measured by flow cytometry (BeckMan Coulter). Peripheral blood immunoglobulin (IgA, IgG, and IgM) concentration was detected by radioimmunoassay.

2.7. TCM Syndrome Score. TCM syndrome score of patients was evaluated according to the Guidelines for Clinical Research of TCM New Drugs. The main symptoms were
fatigue, self-care ability, nausea and vomiting, dizziness, loss of appetite, and insomnia. Symptoms were rated from 0 to 6 on a scale of severity. The score was 0 for no symptoms, 2 for mild symptoms, 4 for moderate symptoms, and 6 for severe symptoms. The total score was 0-36, with a lower score indicating a milder disease.

2.8. Adverse Reactions. The adverse reactions of BC patients in two groups during treatment were observed and recorded, including nausea and vomiting, loss of appetite, thrombocytopenia, leukopenia, and liver function damage.

2.9. Statistical Analysis. SPSS 24.0 was used to analyze and process the data. t test was used for measurement data analysis, and χ² test was used for counting data analysis. P < 0.05 indicated that the difference was statistically significant.

3. Results

3.1. Comparison of Nutritional Indexes between the Two Groups. There was no significant difference in nutritional indexes between the two groups before the intervention. After 4 weeks, the nutritional indexes ALB, TP, PA, and TRF in Chinese herbal formula group were superior to the control group, except HGB (Table 2). Our results indicated that Buqi Yangxue decoction can dramatically improve the nutritional status of BC patients.

3.2. Comparative Analysis of Immune Function between the Two Groups. After treatment, CD3+, CD4+, CD4+/CD8+ were significantly increased, and CD8+ was significantly decreased in Chinese herbal formula group and control group (Table 3). And the changes of T lymphocytes in Chinese herbal formula group were clearly higher than that of control group after treatment. There was no obvious difference in the levels of immune indexes (IgG, IgA, and IgM) in both groups before intervention (Table 4). After treatment, the levels of serum IgG, IgA, and IgM in Chinese herbal formula group were notably higher than those in control group. Therefore, the data indicated that Buqi Yangxue decoction might improve the immune function of BC patients.

3.3. Comparison of TCM Symptom Quantitative Score between the Two Groups. Before treatment, there was no difference in observation symptom quantitative score between the two groups. After 4 weeks of treatment, observation symptom quantitative evaluation scale score in Chinese herbal formula group was notably lower than that in control group (Table 5). Our results manifested that Buqi Yangxue decoction might be helpful to improve the clinical symptoms of BC patients.

3.4. Comparison of Adverse Reactions between the Two Groups. Adverse reactions were found to be occurred in both groups during treatment, including nausea and vomiting, inappetence, liver function impairment, leukopenia, and thrombocytopenia. Results of Table 6 showed that there was no clear difference in the incidence of adverse reactions between the Chinese herbal formula group and control group. Therefore, our results indicated that Buqi Yangxue decoction was safe for the treatment of BC.

4. Discussion

BC is a common malignant tumor in women, and its exact pathogenesis has not been clarified yet. TCM believes that deficiency of vital qi and deficiency of blood is the internal cause and root of BC [18]. “Vital qi” in TCM is the immune function of modern medicine. The basis of the occurrence of malignant tumors is the weakness of vital qi, which is manifested in the low immune function. In TCM, the method of “Fuzheng cultivation” is adopted, which is to improve the immune function of the body by tonifying the innate kidney essence and the acquired spleen and stomach [19]. In the process of disease progression, patients often have deficiency syndromes such as spleen and stomach weakness, deficiency of qi and blood, depletion of yang qi, kidney failure, and deficiency of essence. Therefore, the method of replenishing qi and nourishing blood should run through the treatment process of BC [20]. Researches have shown that Chinese medicine has played an important role in the treatment of BC. Chinese herbal formula can be used as a complementary therapy, combined with surgery, chemotherapy, or targeted therapy, to enhance the immune function of patients and reduce adverse reactions [21, 22].

In this study, on the basis of conventional treatment, Buqi Yangxue decoction was used. Astragali Radix [23] and Poria [24] can obviously enhance and regulate the immune function of the body. Codonopsis Radix can tonify and replenish the middle qi, and nourish the heart to tranquilize [25]. Angelica sinensis and Rehmanniae Radix Praeparata have the function of promoting blood circulation and replenishing blood [26]. Polygonati Rhi- zona can invigorate qi and nourish Yin [27]. Radix Paeo- niae Alba can nourish blood and liver [28]. All the above herbs can nourish and replenish blood, and play the role of replenishing both qi and blood. Combined with licorice and Chinese date can soothe the liver and regulate qi, harmonize the spleen and stomach, and nourish qi and yin [29, 30]. All herbs are used together to play the effect of regulating qi and relieving depression, nourishing blood, and supplementing qi.

Immunosuppressant factors will be secreted or produced during the occurrence and development of tumors, so the immune function of patients with advanced malignant tumors is mostly in a suppressed state, which is the “deficiency of vital qi” in TCM. When the body is lack of vital qi, it will lead to the decline of “zang fu” function over time, and the resistance to disease will also be reduced. The occurrence and development of diseases are closely related to the changes in the number, function, activity, and proportion of CD3+, CD4+, and CD8+ cells [31]. Measuring the changes of CD3+, CD4+, CD4+/CD8+ can directly reflect the immune function [32, 33]. CD3+ and CD4+ cells were significantly increased in Chinese herbal formula group, while CD8+ cell subsets were decreased, indicating that the cellular immune function of patients was improved. IgG, IgA, and IgM are important indexes of humoral immune response [34]. The
results of this study showed that Buqi Yangxue decoction notably increased the levels of IgG, IgA, and IgM, indicating that it can improve the immune function of BC patients. Malnutrition in BC patients affects not only the immune system but also the patient’s ability to tolerate treatment. Therefore, BC patients should strengthen nutrition during treatment to improve the therapeutic effect. Furthermore, Buqi Yangxue decoction was discovered to improve the TCM symptom. Ultimately, there was no significant difference in the incidence of adverse reactions.

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### Table 2: Comparison of nutritional indexes between two groups.

|                | HGb (g/L) | ALB (g/L) | TP (g/L) | PA (mg/L) | TRF (mg/L) |
|----------------|-----------|-----------|----------|-----------|------------|
| **Control group** |           |           |          |           |            |
| Before treatment | 110.48±12.62 | 35.37±6.24 | 50.16±7.34 | 254.84±24.17 | 954.16±154.23 |
| After treatment  | 120.23±18.50 | 40.71±4.14 | 57.31±6.68 | 270.63±18.55 | 2001.44±221.68 |
| **Chinese herbal formula group** |           |           |          |           |            |
| Before treatment | 110.24±5.47 | 36.62±4.50 | 49.67±7.45 | 262.47±25.39 | 975.51±183.17 |
| After treatment  | 122.67±6.59 | 43.27±6.09 | 65.25±6.03 | 293.41±20.65 | 2517.54±208.61 |
| \( t \)         | 3.517      | 5.347      | 11.064    | 2.368      | 151.471    |
| \( P \)         | <0.05      | <0.05      | <0.05     | <0.01      | <0.01      |

### Table 3: Comparison of lymphocyte subsets between two groups before and after treatment.

|                | CD3+ (%) | CD4+ (%) | CD8+ (%) | CD4+/CD8+ (%) |
|----------------|----------|----------|----------|---------------|
| **Chinese herbal formula group** |           |          |          |               |
| Before treatment | 53.34±7.05 | 31.27±5.40 | 36.21±4.24 | 0.86±0.22     |
| After treatment  | 66.12±5.68 | 40.22±3.34 | 31.24±5.37 | 1.29±0.39     |
| \( t \)         | 13.574    | 10.367    | 5.698     | 1.334         |
| \( P \)         | <0.01     | <0.01     | <0.01     | <0.01         |
| **Control group** |           |          |          |               |
| Before treatment | 53.15±9.17 | 31.47±6.25 | 36.93±5.08 | 0.85±0.11     |
| After treatment  | 56.73±6.46 | 35.04±6.21 | 35.82±3.63 | 0.98±0.27     |
| \( t \)         | 14.369    | 10.084    | 6.337     | 2.378         |
| \( P \)         | <0.05     | <0.01     | >0.05     | <0.05         |

### Table 4: Comparison of immunological indexes between two groups.

|                | IgG (g/l) | IgA (g/l) | IgM (g/l) |
|----------------|-----------|-----------|-----------|
| **Chinese herbal formula group** |           |          |           |
| Before treatment | 10.26±1.05 | 2.27±5.40 | 1.83±4.24 |
| After treatment  | 13.35±5.68 | 2.95±3.34 | 2.16±5.37 |
| \( t \)         | 0.444     | 0.286     | 0.559     |
| \( P \)         | <0.01     | <0.01     | <0.01     |
| **Control group**  |           |          |           |
| Before treatment | 10.37±9.17 | 2.35±6.25 | 1.79±5.08 |
| After treatment  | 11.50±6.46 | 2.33±6.21 | 2.09±3.63 |
| \( t \)         | 12.241    | 20.012    | 13.651    |
| \( P \)         | >0.05     | >0.05     | <0.05     |
between the two groups, suggesting that Buqi Yangxue decoction can be safely used for adjuvant treatment of BC.

To be sure, there are still some shortcomings in our research. For example, the number of experimental patients should be increased to ensure the accuracy of the experiment. The research method was simple and research indicators were few. Furthermore, the observation period was short, and the decoction for Buqi Yangxue decoction should be taken for a long time to verify its effect on BC. In addition, we should study the mechanism of Buqi Yangxue decoction in treating BC patients from the perspective of molecular biology.

5. Conclusion

To sum up, Buqi Yangxue decoction can improve the immune function, nutritional status, and TCM symptoms of BC patients, and with fewer adverse reactions. Our results may provide a new idea for the clinical treatment of BC with combination of Chinese and Western medicine.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The author declares no potential conflicts of interest with the respect to the research, authorship, and/or publication of this article.

References

[1] C. Xia, X. Dong, H. Li et al., “Cancer statistics in China and United States, 2022: profiles, trends, and determinants,” Chinese Medical Journal, vol. 135, no. 5, pp. 584-590, 2022.

[2] H. J. Youn and W. Han, “A review of the epidemiology of breast cancer in Asia: focus on risk factors,” Asian Pacific Journal of Cancer Prevention, vol. 21, no. 4, pp. 867-880, 2020.

[3] H. Sung, J. Ferlay, R. L. Siegel et al., “Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries,” CA: a Cancer Journal for Clinicians, vol. 71, no. 3, pp. 209-249, 2021.

[4] K. Wang, Y. Ren, H. Li et al., “Comparison of clinicopathological features and treatments between young (<40 years) and older (>40 years) female breast cancer patients in West China: a retrospective, epidemiological, multicenter, case only study,” PLoS One, vol. 11, no. 3, article e0152312, 2016.

[5] T. Fietz, H. Tesch, J. Rauh et al., “Palliative systemic therapy and overall survival of 1,395 patients with advanced breast cancer - results from the prospective German TMK cohort study,” Breast (Edinburgh, Scotland), vol. 34, pp. 122-130, 2017.

[6] N. Harbeck, “Neoadjuvant and adjuvant treatment of patients with HER2-positive early breast cancer,” Breast (Edinburgh, Scotland), vol. 62, pp. S12-S16, 2022.

[7] T. Shien and H. Iwata, “Adjuvant and neoadjuvant therapy for breast cancer,” Japanese Journal of Clinical Oncology, vol. 50, no. 3, pp. 225-229, 2020.

[8] J. Cho, M. Lee, S. Kim et al., “The effects of perioperative anesthesia and analgesia on immune function in patients undergoing breast cancer resection: a prospective randomized study,” International Journal of Medical Sciences, vol. 14, no. 10, pp. 970-976, 2017.

[9] L. Wang, D. Simons, X. Lu et al., “Breast cancer induces systemic immune changes on cytokine signaling in peripheral blood monocytes and lymphocytes,” eBioMedicine, vol. 52, p. 102631, 2020.

[10] A. Shastrti, J. Lombardo, S. C. Okere et al., “Personalized nutrition as a key contributor to improving radiation response in breast cancer,” International Journal of Molecular Sciences, vol. 23, no. 1, p. 175, 2022.

[11] V. Ho, H. Tan, W. Guo et al., “Efficacy and safety of Chinese herbal medicine on treatment of breast cancer: a meta-analysis of randomized controlled trials,” The American Journal of Chinese Medicine, vol. 49, no. 7, pp. 1557-1575, 2021.

[12] J. Hong, X. Chen, J. Huang et al., “Danggui Buxue decoction, a classical formula of traditional Chinese medicine, fails to prevent myelosuppression in breast cancer patients treated with adjuvant chemotherapy: a prospective study,” Integrative Cancer Therapies, vol. 16, no. 3, pp. 406-413, 2017.

[13] Z. Dang, X. Liu, X. Wang et al., “Comparative effectiveness and safety of traditional Chinese medicine supporting Qi and enriching blood for cancer related anemia in patients not receiving chemoradiotherapy: a meta-analysis and systematic
[14] Y. Lee, Y. H. Chen, Y. C. Huang, Y. F. Lee, and M. Y. Tsai, “Effectiveness of combined treatment with traditional Chinese medicine and western medicine on the prognosis of patients with breast cancer,” Journal of Alternative and Complementary Medicine (New York, NY), vol. 26, no. 9, pp. 835–842, 2020.

[15] X. Zhang, M. Hu, S. Li et al., “Clinical study on Yanghe decoction in improving neo-adjuvant chemotherapy efficacy and immune function of breast cancer patients,” Medicine, vol. 101, no. 10, article e29031, 2022.

[16] X. Niu, H. Zhang, Y. Liu, Z. Liu, C. Zhao, and T. Cai, “The intervention effect of Nourishing Qi and Nourishing Blood Decoction on the opportunity and target of renal anemia,” Heilongjiang Medicine and Pharmacy, vol. 39, no. 2, pp. 25–29, 2016.

[17] Y. Guo, The Clinical Study of Buqi Yangxue Decoction Combined with Chemotherapy in the Treatment of Advanced Colon Cancer with Qi and Blood Deficit, Shandong University of Traditional Chinese Medicine, China, 2020.

[18] L. Yang, Z. Wu, Z. Yang, S. Li, and C. Ouyang, “Exploring mechanism of key Chinese herbal medicine on breast cancer by data mining and network pharmacology methods,” Chinese Journal of Integrative Medicine, vol. 27, no. 12, pp. 919–926, 2021.

[19] H. Jiang, M. Li, K. Du et al., “Traditional Chinese Medicine for adjuvant treatment of breast cancer: Taohong Siwu Decoction,” Chinese Medicine, vol. 16, no. 1, p. 129, 2021.

[20] L. McPherson, S. Cochrane, and X. Zhu, “Current usage of traditional Chinese medicine in the management of breast cancer: a practitioner’s perspective,” Integrative Cancer Therapies, vol. 15, no. 3, pp. 335–342, 2016.

[21] C. Wu, Y. Tsai, J. Lin, S. Fu, and J. Lai, “Chinese herbal products and the reduction of risk of breast cancer among females with type 2 diabetes in Taiwan,” Medicine, vol. 97, no. 31, article e1600, 2018.

[22] B. Wang, R. Fei, Y. Yang et al., “The Shuganhuazheng formula in triple-negative breast cancer: a study based on network pharmacology and in vivo experiments,” Evidence-based Complementary and Alternative Medicine: Ecam, vol. 2020, article 8173147, 10 pages, 2020.

[23] Z. Chen, L. Liu, C. Gao et al., “Astragalus Radix (Huangqi): a promising edible immunomodulatory herbal medicine,” Journal of Ethnopharmacology, vol. 258, p. 112895, 2020.

[24] Y. Jiang and L. Fan, “Evaluation of anticancer activities of Poria cocos ethanol extract in breast cancer: in vivo and in vitro, identification and mechanism,” Journal of Ethnopharmacology, vol. 257, p. 112851, 2020.

[25] F. Luan, Y. Ji, L. Peng et al., “Extraction, purification, structural characteristics and biological properties of the polysaccharides from Codonopsis pilosula: a review,” Carbohydrate Polymers, vol. 261, p. 117863, 2021.

[26] P. Ji, Y. Wei, Y. Hua et al., “A novel approach using metabolomics coupled with hematological and biochemical parameters to explain the enriching-blood effect and mechanism of unprocessed Angelica sinensis and its 4 kinds of processed products,” Journal of Ethnopharmacology, vol. 211, pp. 101–116, 2018.

[27] R. Hong-Min, D. Ya-Ling, Z. Jin-Lian et al., “Research progress on processing history evolution, chemical components and pharmacological effects of Polygonati rhizoma,” Zhongguo Zhong Yao Za Zhi, vol. 45, no. 17, pp. 4163–4182, 2020.

[28] Y. Zhao, Y. Zhang, H. Kong et al., “Carbon dots from paeoniflorin: hepatoprotective effect,” International Journal of Nanomedicine, vol. 15, pp. 9049–9059, 2020.

[29] G. Pastorino, L. Cornara, S. Soares, F. Rodrigues, and M. B. P. Oliveira, “Liquorice (Glycyrrhiza glabra): a phytochemical and pharmacological review,” Phytotherapy Research, vol. 32, no. 12, pp. 2323–2339, 2018.

[30] Y. Lu, T. Bao, J. Mo, J. Ni, and W. Chen, “Research advances in bioactive components and health benefits of jujube (Ziziphus jujuba Mill.) fruit,” Journal of Zhejiang University Science B, vol. 22, no. 6, pp. 431–449, 2021.

[31] Z. Wu, Y. Zheng, J. Sheng et al., “CD3+CD4-CD8- (double-negative) T cells in inflammation, immune disorders and cancer,” Frontiers in Immunology, vol. 13, p. 816005, 2022.

[32] J. Stenström, I. Hedenfalk, and C. Hagerling, “Regulatory T lymphocyte infiltration in metastatic breast cancer—an independent prognostic factor that changes with tumor progression,” Breast Cancer Research, vol. 23, no. 1, p. 27, 2021.

[33] W. Wang, H. Xu, Z. Zhao, G. Zhang, and F. Lin, “Dynamic and significant changes of T-cell subgroups in breast cancer patients during surgery and chemotherapy,” International Immunopharmacology, vol. 65, pp. 279–283, 2018.

[34] S. Garaud, P. Zayakin, L. Buisseret et al., “Antigen specificity and clinical significance of IgG and IgA autoantibodies produced in situ by tumor-infiltrating B cells in breast cancer,” Frontiers in Immunology, vol. 9, p. 2660, 2018.