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Correlation between the Distribution of Traditional Chinese Medicine Syndromes and Molecular Types of Breast Cancer in Perichemotherapy Period

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Abstract

Objectives The objective of this study was to explore the correlation between the distribution of traditional Chinese medicine (TCM) syndromes and molecular types of breast cancer in the perichemotherapy period.

Methods A total of 325 cases with perichemotherapy breast cancer was classified according to syndrome differentiation in TCM , and $R \times C$ table χ^2 test was used to examine and analyze the relationship between TCM syndromes and molecular types of breast cancer in the perichemotherapy period.

Results (1) In the early stage of chemotherapy, there was no significant difference in the distribution of different TCM syndromes among molecular types, mainly liver depression syndrome and liver depression and phlegm coagulation syndrome ($p > 0.05$). (2) In the middle stage of chemotherapy, there were significant differences in the distribution of spleen deficiency and phlegm-dampness syndrome among HER-2 positive (HR positive), HER-2 positive (HR negative), and Luminal A type, Luminal B type (HER-2 negative), and triple-negative type ($p < 0.01$). (3) After chemotherapy, there were significant differences in the distribution of spleen and kidney yang deficiency syndrome and marrow sea insufficiency syndrome among HER-2 positive (HR negative), triple-negative type, and HER-2 positive (HR positive), Luminal A type, Luminal B type (HER-2 negative), and triple-negative type ($p < 0.01$).

Conclusion (1) In the middle stage of chemotherapy, HER-2 positive (HR positive) and HER-2 positive (HR negative) are more likely to show spleen deficiency and phlegm-dampness syndrome than other molecular types. (2) In the late stage of chemotherapy, the HER-2 positive (HR negative) and triple-negative type is more likely to show spleen-kidney yang deficiency syndrome than other molecular types, and the triple-negative type is more likely to show marrow sea insufficiency syndrome than other molecular types.

Keywords
- breast cancer
- perichemotherapy
- TCM syndromes
- molecular types

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Introduction

According to the latest cancer research data released by the International Agency for Research on Cancer of the World Health Organization, breast cancer ranks first in the number of new medical cases and fifth in the death rate,[1] which seriously endangers health. As the cornerstone of breast cancer treatment, chemotherapy plays an irreplaceable role, but its adverse effects also affect the quality of life and mental health of patients, and even affect the prognosis and long-term survival. Molecular types of breast cancer are an important factor that affects the chemotherapy plans. The intervention of Chinese medicine for the treatment of breast cancer in the peri-chemotherapy period can reduce adverse reactions and improve patients' quality of life.[2–5] There are reports in the literature that there is a certain correlation between traditional Chinese medicine (TCM) syndromes and molecular types in the consolidation phase of breast cancer,[6] but there is no report in the literature about whether TCM syndromes in the perichemotherapy period are related to molecular types. The study group observed 325 patients with breast cancer in the perichemotherapy period, analyzed the clinical data, and found that there was a correlation between TCM syndromes and molecular types in the perichemotherapy period of breast cancer. The results are reported below.

Data and Methods

Diagnostic Criteria

According to the *China Standards for Diagnosis and Treatment of Common Malignant Tumors* and the *China Anti-Cancer Association Guidelines and Standards for the Diagnosis and Treatment of Breast Cancer (2021 Edition)*,[7] all has pathological diagnosis basis.

Inclusion Criteria

Inclusion criteria were confirmed case of breast cancer by pathological examination; with the indication of chemotherapy, willingness to undergo preoperative neo-adjuvant chemotherapy or postoperative adjuvant chemotherapy, both kinds of chemotherapy are standard regimens recommended by Guidelines of Chinese Society of Clinical Oncology (CSCO) (2019 edition); no radiotherapy, chemotherapy or TCM treatment performed for malignant tumors before treatment; patients in good general condition, with a Carlisle score of >60 and tolerating chemotherapy; and patients with willingness to participate in this clinical investigation and having signed the informed consent form.

Exclusion Criteria

Exclusion criteria were patients who do not meet the inclusion criteria; patients with poor compliance; during chemotherapy period patients with medication of herbs with effects of promoting blood circulation and removing blood stasis, softening hardness and dissipating nodules, and having clear inhibitory effect on breast cancer in the usage instructions, or patients with medication of high-level evidence-based Chinese patent medicine; pregnant or lactating women; patients with diseases related to important organs such as severe damage to the heart, lung, and kidney; patients with mental diseases; patients changing other chemotherapy regimens due to the progression of the disease during chemotherapy; and patients with two or more primary malignancies.

General Data

A total of 325 patients with breast cancer hospitalized from January 2020 to September 2021 and met the inclusion criteria were selected, among which 89 were from Henan Cancer Hospital, 119 from The First Hospital Affiliated to Henan University of Chinese Medicine, 22 from Zhengzhou Central Hospital, 36 from the First Affiliated Hospital of Henan University of Science and Technology, 24 from People's Hospital of Linying County, and 35 from People's Hospital of Xihua County. The mean age of patients was 50.84 ± 9.801 years, of these, 324 were female and 1 was male; 138 cases of Luminal B type (HER-2 negative), 59 cases of HER-2 positive (HR positive), 56 cases of HER-2 positive (HR negative), 40 cases of triple-negative type, and 32 cases of Luminal A type were observed. The protocol was reviewed and approved by the Ethics Committee of the First Affiliated Hospital of Henan University of Chinese Medicine (Ethical No.: 2021HL-067).

Methods

Design of Traditional Chinese Medicine Syndrome Questionnaire

The questionnaire was formulated based on the *Expert Consensus on Traditional Chinese Medicine Syndrome Differentiation and Internal Treatment of Early Breast Cancer*,[8] *Consensus on Diagnosis and Treatment of Breast Cancer with Integrated Chinese and Western Medicine*,[9] *Guidelines for Chinese Medicine Diagnosis and Treatment of Malignant Tumors*,[10] *Guiding Principles for Clinical Research of New Chinese Medicinals*,[11] and clinical practice. After the preliminary completion of the questionnaire, the clinical presurvey was conducted, and experts were consulted for further improvement, forming 15 TCM syndromes (as specified in ►**Table 1**). A formal *Questionnaire on Syndromes of Patients with Breast Cancer in the Peri-chemotherapy Period* (hereinafter referred to as the Questionnaire) was formulated.

Filling and Judgement of Questionnaire

Patients' syndrome data were collected by on-site investigation combined with off-site investigation (telephone follow-up). Complete information was collected, and questionnaires were filled in the early period of chemotherapy, middle period of chemotherapy and late period of chemotherapy, respectively.

For the judgment of syndromes, it is required to be recognized by two deputy chief physicians or above with oncology research background and TCM specialty.

Criteria for Western Medicine Molecular Types

Molecular types of breast cancer are based on *CSCO Breast Cancer (2019 Edition)*,[12] which is divided into the following 5

Table 1 TCM syndrome differentiation criteria

TCM syndromes	Primary symptoms	Secondary symptoms
Liver-depression syndrome	Mental depression, irritability, chest and hypochondriac pain, or distending pain in breast	Chest tightness, bitter taste in the mouth, frequent sighing, light tongue, thin and white coating, taut pulse
Spleen qi deficiency syndrome	Poor appetite and abdominal distension, nausea, fatigue, loose stools	Weariness and unwillingness to speak, dizziness, sallow complexion, weak defecation, pale tongue, fatty tongue or tongue with teeth marks in the margin, thin and white coating, thin and forceless pulse
Qi and blood deficiency syndrome	Weariness and unwillingness to speak, low voice and shortness of breath, dizziness, insomnia and forgetfulness	Pale or sallow complexion, spontaneous sweating, pale lips, eyelids and nails, light scanty menstruation, delayed menstruation or amenorrhea, pale tongue, thin and white coating, thin and forceless pulse
Qi and yin deficiency syndrome	Weariness and unwillingness to speak, low voice and shortness of breath, dry mouth and throat, dysphoria and insomnia	Spontaneous sweating, tidal fever and flushed cheeks, red tongue with scanty body fluid and fur, thin and forceless pulse
Liver-depression and phlegm-coagulation syndrome	Hard breast lump (necessary), mental depression, irritability, chest and hypochondriac pain or distending pain in breast	Chest tightness, bitter taste in the mouth, frequent sighing, light tongue, thin and white coating, taut pulse
Intermingled phlegm and blood stasis syndrome	Hard breast lump hard (necessary), stabbing pain of the breast, dark menstrual color, or with blood clots	Irregular menstruation, dysmenorrhea, blue and swollen or dark blood stasis of sublingual vessels, purple and dark tongue with greasy fur, uneven pulse or taut and slippery pulse
Syndrome of thoroughfare vessel and conception vessel dysfunction	Hard breast lump (necessary), premenstrual breast distension and pain, dysmenorrhea, soreness and softness of waist and knees, irregular menstruation, tidal fever and night sweating	Dark complexion, chloasma, tinnitus, infertility after marriage, history of multiple miscarriages (>3 times), light tongue with thin coating, taut and thin pulse
Liver-depression and spleen-deficiency syndrome	Mental depression or irritability, nausea, poor appetite and abdominal distension, loose stools	Flatulence or pain in the stomach or lower ribs, frequent sighing, borborygmus and flatus, immediate diarrhea after abdominal pain and pain relieved after diarrhea, white or greasy tongue coating, taut or thin pulse
Spleen deficiency and phlegm-dampness syndrome	Chest tightness, poor appetite and abdominal distension, nausea and vomiting, fatigue and lethargy, loose stools	Thirst without desire for drinking, heavy sensation of the head and body, swollen, heavy and distending sensation of the upper limbs, pale and fatty tongue with white and greasy coating, slow and soft pulse
Spleen and stomach yang deficiency syndrome	Poor appetite and abdominal distension, nausea and vomiting, abdominal coldness and pain and preference for warmth and pressure, loose stools	Weariness and unwillingness to speak, cold body and limbs, pale tongue with white and moist coating, deep, retarded and forceless pulse
Spleen and kidney yang deficiency syndrome	Chest fullness and tightness, poor appetite, cold body and limbs, alopecia	Pale complexion, fatigue, abdominal distension, soreness and weakness of waist and knees, dizziness, frequent urination, edema of face and limbs, loose stools, pale tongue with teeth marks in the margins, white and slippery coating, thin, weak or deep, retarded and forceless pulse
Liver and kidney yin deficiency syndrome	Irritability, alopecia, dysphoria in the chest, palms and soles, numbness of limbs, weakness of both feet	Soreness and weakness of waist and knees, dizziness, tinnitus, insomnia, amnesia, fatigue, emaciation, night sweating, red tongue with scanty coating, thin and rapid pulse
Heart-kidney imbalance syndrome	Palpitations, vexation and insomnia, dizziness, tinnitus, soreness and weakness of waist and knees	Dry mouth and throat, dysphoria in the chest, palms and soles, constipation and dark urine, red tongue with scanty fur, thin and rapid pulse

(*Continued*)

Table 1 (*Continued*)

TCM syndromes	Primary symptoms	Secondary symptoms
Qi deficiency and blood stasis syndrome	Fatigue, dark or lusterless nails, stabbing pain with fixed location	Weariness and unwillingness to speak, dark complexion, numbness of limbs, dark purple tongue or with ecchymosis, uneven pulse
marrow sea insufficiency syndrome	Forgetfulness, poor memory, dizziness, tinnitus	Dull expression, thought slowness, drowsiness in daytime and insomnia in night, light red and enlarged tongue with thin and white coating, deep, taut and forceless pulse or taut, thin and tight pulse

Notes: For each of the above syndromes, at least 3 primary symptoms and 0 secondary symptom should be involved; or 2 primary symptoms and 2 secondary symptoms should be involved; or 1 primary symptom and 3 secondary symptoms should be involved; the necessary symptoms are required before diagnosis.

types: Luminal A type, Luminal B type (HER-2 negative), HER-2 positive (HR positive), HER-2 positive (HR negative), and triple-negative type.

Statistical Methods

SPSS 26.0 statistical software was used for statistical analysis. χ^2 test was used for the comparison of counting data, and $p < 0.05$ was considered as statistically significant difference.

Results

Distribution of Traditional Chinese Medicine Syndromes of 325 Patients with Breast Cancer in the Perichemotherapy Period

In the early stage of chemotherapy, the frequency of TCM syndromes from high to low was 172 cases (52.92%) of liver depression syndrome, 61 cases (18.77%) of liver depression and phlegm coagulation syndrome, 26 cases (8.00%) of qi and yin deficiency syndrome, 24 cases (7.38%) of qi and blood deficiency syndrome, 21 cases (6.46%) of syndrome of thoroughfare vessel and conception vessel dysfunction, and 21 cases (6.46%) of intermingled phlegm and blood stasis syndrome.

In the middle stage of chemotherapy, TCM syndromes were mainly liver depression and spleen deficiency syndrome + qi deficiency and blood stasis syndrome, spleen deficiency and phlegm-dampness syndrome + qi deficiency and blood stasis syndrome. Accurate statistical analysis of each single syndrome was made, and the frequency after integration of the same syndrome from high to low was 227 cases (65.04%) of liver depression and spleen deficiency syndrome, 57 cases (16.33%) of spleen qi deficiency syndrome, 38 cases (10.89%) of qi deficiency and blood stasis syndrome, and 27 cases (7.74%) of spleen deficiency and phlegm-dampness syndrome.

In the late stage of chemotherapy, the main TCM syndromes were marrow sea insufficiency syndrome + qi deficiency and blood stasis syndrome, and spleen and stomach yang deficiency syndrome + qi deficiency and blood stasis syndrome. Accurate statistical analysis of each single syndrome was made and the frequency after integration of the same syndrome from high to low was 120 cases (28.78%) of liver and kidney yin deficiency syndrome, 111 cases (26.62%) of qi deficiency and blood stasis syndrome, 59 cases (14.15%) of spleen and kidney yang deficiency syndrome, 44 cases (10.55%) of marrow sea insufficiency syndrome, 35 cases (8.39%) of spleen qi deficiency syndrome, 23 cases (5.52%) of spleen and stomach yang deficiency syndrome, 13 cases (3.12%) of heart-kidney imbalance syndrome, and 12 cases (2.88%) of spleen deficiency and phlegm dampness syndrome.

Correlation between Traditional Chinese Medicine Syndromes and Molecular Types in Patients with Breast Cancer in the Early Stage of Chemotherapy

In the early stage of chemotherapy, there were mainly liver depression syndrome, liver depression and phlegm coagulation syndrome, qi and yin deficiency syndrome, qi and blood deficiency syndrome, syndrome of thoroughfare vessel and conception vessel dysfunction, and intermingled phlegm and blood stasis syndrome. There is no significant difference in the distribution of each syndrome among HER-2 positive (HR positive), HER-2 positive (HR negative), Luminal A type, Luminal B type (HER-2 negative), and triple-negative type ($p > 0.05$), as specified in ►**Table 2**.

Correlation between Traditional Chinese Medicine Syndromes and Molecular Types in Breast Cancer Patients in the Middle Stage of Chemotherapy

In the middle stage of chemotherapy, there were mainly liver depression and spleen deficiency syndrome, spleen qi deficiency syndrome, qi deficiency and blood stasis syndrome, and spleen deficiency and phlegm-dampness syndrome. There were significant differences in the distribution of spleen deficiency and phlegm-dampness syndrome among HER-2 positive (HR positive), HER-2 positive (HR negative), Luminal A type, Luminal B type (HER-2 negative), and triple-negative type ($p < 0.01$). HER-2 positive (HR positive) and HER-2 positive (HR negative) were more likely to show spleen deficiency and phlegm-dampness syndrome than Luminal A type, Luminal B type (HER-2 negative), and triple-negative type, as specified in ►**Table 3**.

Table 2 TCM syndromes and molecular types in the early stage of chemotherapy

Type		HER-2 positive (HR positive)	HER-2 positive (HR negative)	Luminal A type	Luminal B type (HER-2 negative)	Triple-negative type	χ^2	*p*
	n	59	56	32	138	40	18.551	0.551
Syndrome of thoroughfare vessel and conception vessel dysfunction	21	5a	4a	2a	9a	1a		
	Proportion (%)	8.47	7.14	6.25	6.52	2.5		
Liver-depression and phlegm-coagulation syndrome	61	15a	14a	4a	21a	7a		
	Proportion (%)	25.42	25	12.50	15.22	17.5		
Liver-depression syndrome	172	28a	24a	19a	81a	20a		
	Proportion (%)	47.46	42.86	59.38	58.70	50		
Qi and blood deficiency syndrome	24	2a	5a	3a	10a	4a		
	Proportion (%)	3.39	8.93	9.38	7.25	10		
Qi and yin deficiency syndrome	26	3a	4a	4a	9a	6a		
	Proportion (%)	5.08	7.14	12.5	6.52	15		
Intermingled phlegm-blood stasis syndrome	21	6a	5a	0a	8a	2a		
	Proportion (%)	10.17	8.93	0	5.80	5		

Abbreviation: TCM, traditional Chinese medicine.
Note: If the letters marked are the same, it indicates that there is no difference between the corresponding two sets of data, while if the letters marked are different, it indicates that the difference is statistically significant.

Correlation between Traditional Chinese Medicine Syndromes and Molecular Types in Breast Cancer Patients in the Late Stage of Chemotherapy

In the late stage of chemotherapy, there were mainly liver and kidney yin deficiency syndrome, qi deficiency and blood stasis syndrome, spleen and kidney yang deficiency syndrome, marrow sea insufficiency syndrome, spleen qi deficiency syndrome, spleen-stomach yang deficiency syndrome, heart-kidney imbalance syndrome, and spleen deficiency and phlegm-dampness syndrome. There were significant differences in the distribution of spleen and kidney yang deficiency syndrome and marrow sea insufficiency syndrome among HER-2 positive (HR positive), HER-2 positive (HR negative), Luminal A type, Luminal B type (HER-2 negative), and triple-negative type ($p < 0.01$). HER-2 positive (HR negative) and triple-negative type was more likely to show spleen and kidney yang deficiency syndrome than HER-2 positive (HR positive), Luminal A type, and Luminal B type (HER-2 negative). Triple-negative type was more likely to show marrow sea insufficiency syndrome than other molecular types, as specified in ►**Table 4**.

Discussion

The research group have been long engaged in the study of TCM syndromes of breast cancer in recent years. Through clinical practice, it is found that there is a certain correlation between syndromes and molecular types, especially in the perichemotherapy period. The research group believe that the pathogenetic process in the perichemotherapy period is from qi depression to qi deficiency, yang deficiency, and finally yin impairment. Chemotherapy first impairs the spleen and stomach. The spleen governs rise of the clear and the stomach governs descent of the turbid. If the spleen fails to raise the clear and the stomach fails to descend the turbid and the spleen becomes too weak to transport, phlegm and dampness will generate, and body fluid distribution becomes abnormal. The stomach fails to descend, and this causes upward flowing of qi. And thus, spleen deficiency and phlegm dampness syndrome will occur marked by primary symptoms of poor appetite, abdominal distension, and loose stools. Then, with the gradual progress of chemotherapy, the chemotherapeutic drugs accumulate in the body

Table 3 TCM syndromes and molecular types in the middle stage of chemotherapy

Type		HER-2 positive (HR positive)	HER-2 positive (HR negative)	Luminal A type	Luminal B type (HER-2 negative)	Triple-negative type	χ^2	*p*
	n	63	60	34	147	45	67.942	0.000
Liver depression and spleen deficiency syndrome	227	30a	28a	22a, b	110b	37b		
	Proportion (%)	47.62	46.67	64.71	74.83	82.22		
Spleen qi deficiency syndrome	57	10a	15a	7a	22a	3a		
	Proportion (%)	15.87	25	20.59	14.97	6.67		
Spleen deficiency and phlegm-dampness syndrome	27	14a	13a	0b	0b	0b		
	Proportion (%)	22.22	21.67	0	0	0		
Qi deficiency and blood stasis syndrome	38	9a	4a	5a	15a	5a		
	Proportion (%)	14.29	6.67	14.71	10.20	11.11		

Abbreviation: TCM, traditional Chinese medicine.
Note: If the letters marked are the same, it indicates that there is no difference between the corresponding two sets of data, while if the letters marked are different, it indicates that the difference is statistically significant.

and cause low spirits, which further develops from the spleen qi deficiency syndrome to the impairment of the spleen and stomach yang. Internal stagnation of yang qi cannot be channeled, and yin cannot be controlled, which results in relatively excess yin qi and depleted yang qi.[13] Long-term spleen and stomach yang deficiency involves the kidney and consumes yang qi in the kidney, and thus the spleen and kidney yang deficiency syndrome occurs and it is marked by the primary symptoms of poor appetite, cold body and limbs, and alopecia. Yin and yang interact with each other, and long-term kidney yang deficiency involve kidney. The brain is the "marrow sea" and depends on the nourishment of kidney yin essence to give full play of its physiological function of "housing original spirit." If kidney yin essence is insufficient and the marrow sea is malnourished, dizziness, memory loss and other symptoms related to marrow sea insufficiency are prone to occur.

In this study, 325 patients with breast cancer in the perichemotherapy period were observed. The results showed that there was no significant difference in the distribution of TCM syndromes in the early stage of chemotherapy among HER-2 positive (HR positive), HER-2 positive (HR negative), Luminal A type, Luminal B type (HER-2 negative), and triple-negative type. The molecular types were mainly liver depression syndrome (pertaining to qi stagnation). In the middle stage of chemotherapy, there were significant differences in the distribution of spleen deficiency and phlegm-dampness syndrome among HER-2 positive (HR positive), HER-2 positive (HR negative), Luminal A type, Luminal B type (HER-2 negative), and triple-negative type. HER-2 positive (HR positive) and HER-2 positive (HR negative) were more likely to show spleen deficiency and phlegm-dampness syndrome (pertaining to qi deficiency) than Luminal A type, Luminal B type (HER-2 negative), and triple-negative type. In the late stage of chemotherapy, there were significant differences in the distribution of spleen and kidney yang deficiency syndrome and marrow sea insufficiency syndrome among HER-2 positive (HR positive), HER-2 positive (HR negative), Luminal A type, Luminal B type (HER-2 negative), and triple-negative type. HER-2 positive (HR negative) and triple-negative type was more likely to show spleen and kidney yang deficiency syndrome (pertaining to yang deficiency) than HER-2 positive (HR positive), Luminal A type, and Luminal B type (HER-2 negative). Triple-negative type was more likely to show marrow sea insufficiency syndrome (pertaining to yin deficiency). The results were consistent with the long-term clinical observation of the research group.

According to the HER-2 status and the expression levels of ER, PR, and ki-67 in immunohistochemistry, the molecular types of breast cancer in current breast cancer CSCO guidelines[12] are divided into HER-2 positive (HR negative), HER-2 positive (HR positive), and triple-negative type, Luminal A type and Luminal B type (HER-2 negative), and these five types are clinically recognized. Zeng[14] explored the correlation between the molecular types of breast cancer and different TCM staging syndromes, and the results showed that after two rounds of chemotherapy, the triple-negative type mainly manifests as spleen and kidney deficiency syndrome, and the HER-2 amplified type mainly manifests

Table 4 TCM syndromes and molecular types in the late stage of chemotherapy

Type		HER-2 positive (HR positive)	HER-2 positive (HR negative)	Luminal A type	Luminal B type (HER-2 negative)	Triple-negative type	χ^2	*p*
	n	78	76	37	167	59	422.599	0.000
Liver and kidney yin deficiency syndrome	120	22a	2b	16a, c	80c	0b		
	Proportion (%)	28.21	2.63	43.24	47.90	0		
Spleen qi deficiency syndrome	35	3a, b, c	1c	8d	23b, d	0a, c		
	Proportion (%)	3.85	1.32	21.62	13.77	0		
Spleen and kidney yang deficiency syndrome	59	6a	36b	0a	2a	15b		
	Proportion (%)	7.69	47.37	0	1.20	25.42		
Spleen and stomach yang deficiency syndrome	23	7a, b	11b	1a, b	3a	1a, b		
	Proportion (%)	8.97	14.47	2.70	1.80	1.69		
Spleen deficiency and phlegm-dampness syndrome	12	10a	0b	0a, b	2b	0b		
	Proportion (%)	12.82	0	0	1.20	0		
Qi deficiency and blood stasis syndrome	111	28a	15a	12a	47a	9a		
	Proportion (%)	35.90	19.74	32.43	28.14	15.25		
Marrow sea insufficiency syndrome	44	0a	0a	0a	10a	34b		
	Proportion (%)	0	0	0	5.99	57.63		
Heart-kidney imbalance syndrome	13	2a, b	11b	0a, b	0a	0a		
	Proportion (%)	2.56	14.47	0	0	0		

Abbreviation: TCM, traditional Chinese medicine.
Note: If the letters marked are the same, it indicates that there is no difference between the corresponding two sets of data, while if the letters marked are different, it indicates that the difference is statistically significant.

as liver and kidney deficiency syndrome. Zhang[15] discussed the correlation between breast cancer-related gene expression and TCM syndromes after breast cancer surgery, and the results showed that HER-2 over-expression and triple-negative type accounted for a larger proportion in the spleen and kidney yang deficiency syndrome. These results are similar to the results of this study.

Conclusion

In the middle stage of chemotherapy, HER-2 positive (HR positive) and HER-2 positive (HR negative) are more likely to show spleen deficiency and phlegm-dampness syndrome than other molecular types. In the late stage of chemotherapy, the HER-2 positive (HR negative) and triple-negative type is more likely to show spleen-kidney yang deficiency syndrome than other molecular types, and the triple-negative type is more likely to show marrow sea insufficiency syndrome than other molecular types. However, this project needs further in-depth study due to limited study time and sample size.

Authors' Contribution
B.M. was responsible for conceptualization, data curation, formal analysis, investigation, and writing—original draft. X.C. was responsible for writing—original draft, data curation, funding acquisition, project administration, supervision, and writing—review and editing. Q.L. was

responsible for data curation, formal analysis, investigation, and writing—review and editing. H.Z. was responsible for data curation, formal analysis, and investigation. B. W. was responsible for data curation, formal analysis, investigation, data curation, investigation, and writing—original draft. L.X. was responsible for data curation, formal analysis, investigation, and writing—original draft.

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Conflict of Interest
The authors declare no conflict of interest.

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