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Original Article

Effects of Yipi Huayu decoction on tumor markers, immune function, and adverse reactions during chemotherapy in gastric cancer patients: a retrospective propensity score-matched study

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Abstract: Objective: To analyze the effects of Yianpi Huayu Decoction on tumor markers, immune function and adverse reactions during chemotherapy in patients with gastric cancer. Method: The clinical data of 154 patients with progressive gastric cancer who attended Baoji Maternal and Child Health Hospital (Daijiawan Branch) from January 2020 to March 2022 were retrospectively analyzed. The patients were divided into an observation group (61 cases) and a control group (93 cases) according to the treatment method and were matched using propensity score matching (PSM). The control group was given SOX neoadjuvant chemotherapy regimen (oxaliplatin + tiglio), and the observation group was given spleen-strengthening and blood-stasis-reducing tonics as adjuvant treatment on the basis of the treatment given to the control group. Clinical efficacy in the two groups was observed, as well as Carbohydrate Antigen 19-9 (CA19-9), Carbohydrate Antigen 72-4 (CA72-4), and Carcinoembryonic Antigen (CEA) levels, immune function (IgA, IgM, and IgG), Karnofsky Performance Scale (KPS), and occurrence of adverse reactions. Results: After matching, there was no significant difference in the total clinical efficiency between the two groups ($P > 0.05$). After matching, there were no differences in CA19-9, CA72-4, and CEA levels between the observation group and the control group before or after treatment ($P > 0.05$). After matching, the IgA, IgM, and IgG levels in the observation group were significantly better than those in the control group after treatment ($P < 0.05$). The incidence of leukopenia ($P = 0.011$) and diarrhea ($P = 0.011$) during treatment was higher in the control group than in the observation group after matching. The KPS score of the observation group was higher than that of the control group after matching ($P < 0.05$). After matching, Cox regression analysis found that the treatment regimen ($P < 0.001$, HR = 2.527), TNM staging ($P = 0.001$, HR = 0.471), local recurrence ($P = 0.001$, HR = 2.147), and pretreatment CEA ($P = 0.011$, HR = 1.131) were independent prognostic factors affecting patients' 2-year survival. Conclusion: While the spleen-enhancing and blood-stasis-removing herbal formula combined with the SOX chemotherapy regimen did not improve therapeutic outcomes in gastric cancer patients, it did enhance immune function, reduce adverse reactions, and improve quality of life.

Keywords: Spleen-strengthening and blood-stasis-removing Jianpi Huayu decoction, gastric cancer, chemotherapy, tumor marker, immune function

Introduction

Cancer ranks as the second leading cause of death globally, surpassed only by cardiovascular diseases, with its incidence continually escalating [1]. According to 2018 data from the National Cancer Center of China, lung cancer presents the highest incidence and mortality rates in the country, paralleling those in developed nations [2]. Additionally, cancers of the digestive tract, particularly gastric cancer, impose a significant health burden on Chinese residents, with notably high incidence and mortality rates in urban areas [3]. According to 2015 statistics, China witnessed approximately 4,292,000 new cases of malignant tumors, predominantly lung and stomach cancers [4]. The elevated prevalence of gastric cancer is

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attributed to factors such as unhealthy lifestyle and dietary habits, alongside infections like Helicobacter pylori [5]. Despite advancements in surgical methods and chemotherapy, the prognosis for patients with intermediate- and late-stage gastric cancer remains dismal, exhibiting five-year survival rates between 5% and 15%. In contrast, early-stage gastric cancer survival rates in Japan and South Korea are approximately 70%, starkly higher than China's rate of less than 20% [6]. Ongoing research into gastric cancer-related genes and the potential synergies between molecularly targeted drugs and chemotherapy holds promise for improving outcomes in patients suffering from advanced stages of this malignancy.

Surgery for advanced gastric cancer primarily serves a palliative purpose, and the frequent occurrence of postoperative recurrence or metastasis significantly undermines treatment efficacy [7]. Due to the resistance of gastric adenocarcinoma cells to radiotherapy, chemotherapy has emerged as the preferred treatment method. Commonly administered chemotherapeutic agents include oxaliplatin, cisplatin, fluorouracil (5-FU), capecitabine, S-1, and paclitaxel analogs [8, 9]. Research indicates that dual-agent chemotherapy regimens, such as SOX (S-1 plus oxaliplatin) and CS (cisplatin plus S-1), are both practical and well-tolerated. These two-agent combinations generally induce fewer side effects and are more acceptable to patients compared to three-agent regimens [10]. However, both single-agent and multi-agent chemotherapy regimens invariably cause adverse effects, including diminished immune function, myelosuppression, gastrointestinal disturbances, and peripheral neuropathy. These side effects are often intolerable for patients or significantly degrade their quality of life, consequently impacting treatment compliance [11]. Thus, the balance between treatment effectiveness and quality of life remains a critical challenge in the management of gastric cancer.

Recent studies have demonstrated that Chinese medicine can potentiate the efficacy of chemotherapy, counteract multidrug resistance, and mitigate chemotherapy's adverse effects [12, 13]. A specific spleen-strengthening and blood-stasis-removing soup, Jianpi Huayu decoction, comprised of Rhizoma Pinelliae Preparatum, Dandelion, Codonopsis Root, and Magnolia Bark, has shown capabilities in clearing heat, detoxifying, enhancing the spleen, promoting blood circulation, and alleviating heat and dampness. Notably, it has also been reported to bolster immune function [14].

However, there remains a lack of empirical evidence on whether Jianpi Huayu decoction can reduce the incidence of adverse reactions and enhance immune function in gastric cancer patients undergoing the SOX chemotherapy regimen. The primary objective of this study was to examine the effects of this decoction on tumor markers, immune function, and adverse effects in gastric cancer patients during chemotherapy, as well as to investigate the prognostic factors contributing to the two-year survival rates in patients. This research aims to provide valuable insights for optimizing clinical treatment strategies.

Methods and data

Sample size calculation

We assessed the number of patients based on the incidence of adverse reactions in patients, which was found to be 5%-20% in previous literature [13, 14]. Assuming that we expected the incidence of leukopenia to be 5% and 20% in the observation and control groups [14], respectively, with a significance level (α) of 0.05 and a statistical efficacy (β) of 0.80, the sample size was calculated using the following formula:

$$n = \frac{\left(Z_{\alpha/2}\sqrt{2P(1-P)} + Z_{\beta}\sqrt{P_1(1-P_1)+P_2(1-P_2)}\right)^2}{\left(P_1-P_2\right)^2}.$$

The critical values of the standard normal distribution were obtained using standard statistical tables. With a significance level of 0.05, the critical value (Zα/2) is 1.96, and with a statistical power of 0.80, the critical value (Zβ) is 0.84. Substituting these values into the formula gives a final minimum of 75 samples per group. The specific sample data was determined according to the actual clinical collection quantity.

Clinical data

Clinical data of gastric cancer patients who attended Maternal and Child Health Hospital (Daijiawan Branch) from January 2020 to March 2022 were retrospectively analyzed. The study was conducted with the approval of the

Medical Ethics Committee of Baoji Maternal and Child Health Hospital (Daijiawan Branch). Inclusion criteria: Patients with gastric cancer diagnosed by cytology or pathology and clinically staged as stage III to IV [15]; Patients who were older than 18 years old at the time of first treatment; Patients who received initial chemotherapy with Tegio or capecitabine in combination with oxaliplatin; Patients with an expected survival of more than three months; Patients without abnormalities in the blood and liver, or renal systems. Exclusion Criteria: Patients with presence of a primary malignancy other than gastric cancer; Patients with comorbidities with severe cardiopulmonary or other systemic diseases; Patients who failed to complete at least two cycles of chemotherapy; Patients who had received prior chemotherapy (not their initial treatment).

Propensity matching

This study used a propensity score matching (PSM) approach to reduce selection bias due to non-randomized assignment in observational studies [16]. PSM involves calculating the likelihood (propensity score) of each participant receiving a particular treatment, thereby facilitating the matching of patients in the treatment and control groups based on these scores [16]. This approach ensures that the two groups are similar on key baseline variables, thereby increasing the reliability of the comparison results. In addition, we set a PSM threshold of 0.02, i.e., two patients were considered successfully matched only if their propensity scores differed within 0.02.

Treatment plan

Patients in the control group received intravenous chemotherapy consisting of oxaliplatin injection (50 mg, Yangzijiang Pharmaceutical Group Co., Ltd., State Drug License H200941-58) diluted in dextrose (500 ml; 25 g, Foshan Haolang Pharmaceutical Co., Ltd., State Drug License H20013100). This regimen was administered once every three weeks. Additionally, during the first 14 days of each treatment cycle, patients orally took Tegio capsules (Yangzijiang Pharmaceutical Group Co., Ltd., State Drug Permit H20243202) containing Tegafur 20 mg, Gemcitabine 5.8 mg, and Potassium diazepam 19.6 mg. The recommended dosage was 40-60 mg twice daily. A full course of chemotherapy was completed every three weeks, and treatment was immediately discontinued upon the occurrence of any adverse reactions. The treatment was continued for two months.

In addition to the control group's regimen, patients in the observation group received an adjunctive traditional Chinese medicine treatment called Jianpi Huayu decoction. The herbal formula for this mixture included: Rhizoma Pinelliae Preparatum, 10 g; Dandelion, 15 g; Chicken's Gizzard-Membrane-Membrane, 5 g; Curcuma Rhizome, 10 g; Codonopsis Root, 15 g; Magnolia Bark, 10 g; Atractylodes Rhizome, 10 g; Trichosanthes Seed, 15 g; Nardostachys Root, 10 g; Rhubarb, 3 g; Hawthorn Berry, 15 g; Perilla Stem, 10 g; and Gecko, 5 g. These herbs were decocted in 1000 ml of water, which were then condensed to 300 ml. The resulting decoction was consumed twice daily, in the morning and evening, over a two-month period.

Patient grouping

According to the inclusion-exclusion criteria, a total of 154 cases were identified and included. The patients were divided into an observation group (61 cases) and a control group (93 cases) according to the treatment method. Subsequently, we leveled the samples using the PSM method with 61 patients in each of the two groups.

Data collection

Data was systematically gathered through various sources including outpatient review records, electronic medical records, and the in-hospital follow-up system.

1. Baseline information and pathological information included age, gender, TNM stage, histological typing, locoregional recurrence, site of the tumor, clinical efficacy, incidence of adverse events and Karnofsky Performance Scale (KPS) [17].

2. Tumor markers included Carbohydrate Antigen 19-9 (CA19-9), Carbohydrate Antigen 72-4 (CA72-4), and Carcinoembryonic Antigen (CEA). These markers were detected using a fully automated immunoassay analyzer (CLIA 500, Shandong Laibao Bio-technology Co.).

3. Immune markers included Immunoglobulin A (IgA), Immunoglobulin G (IgG), and Immuno-

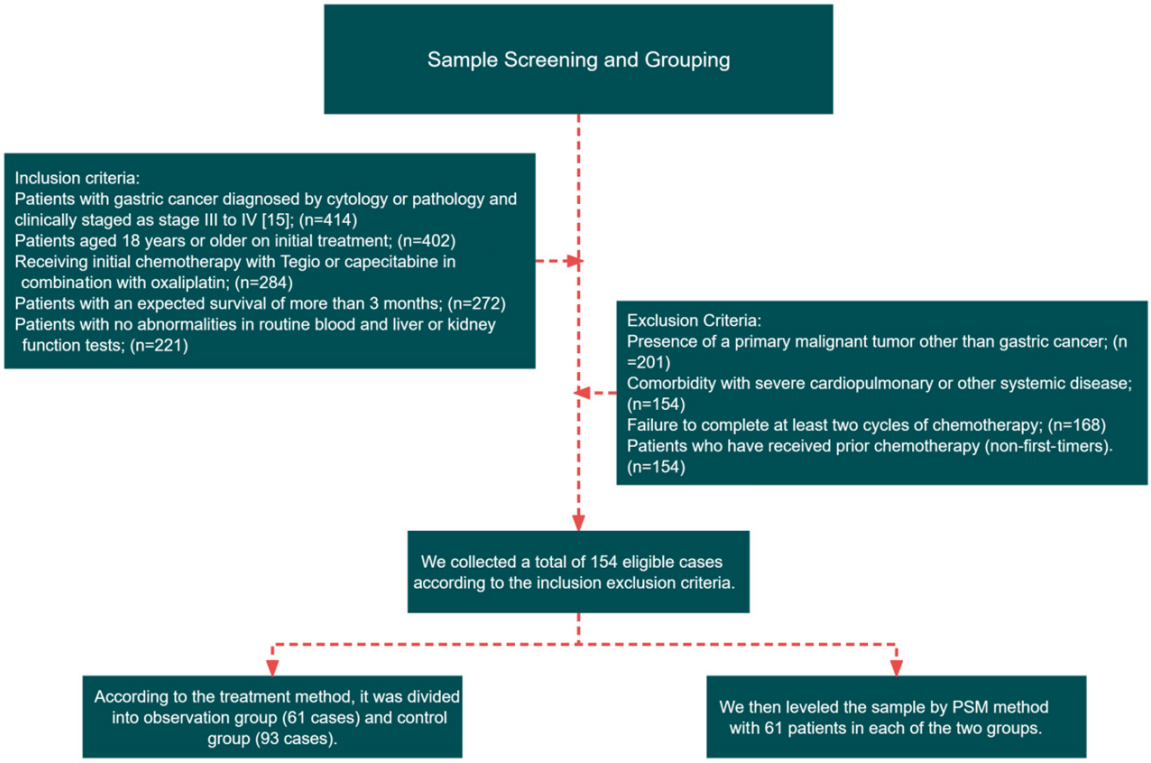

Figure 1. Sample screening flowchart.

globulin M (IgM). These were detected by a specific protein analyzer (IMMAGE 800, Beckman).

Note: Tests were performed before and two months after treatment.

Follow up

The patients were followed up for two years. Data collection during follow-up was conducted through a combination of telephone calls and clinic records. The frequency of telephone follow-up was every four months.

Outcome measurement

Main results: The clinical treatment effectiveness of patients [18] was compared between the two groups. The changes in tumor markers, and immunoglobulin before and after treatment were compared between two groups [19].

Secondary results: The differences in patients' baseline information and the incidence of adverse reactions were compared between the two groups. Besides, the differences in KPS scores before and after treatment was compared [20]. The factors affecting patients' 2-year survival was analyzed using Cox regression [21] (**Figure 1**).

Statistical analysis

SPSS 26.0 software was used to process the data. K-S test was used to analyze the normal distribution of the data. Normally distributed data were expressed as mean ± standard deviation (mean ± sd); independent sample t-test was used for comparison between groups, and paired t-test was used for comparison within groups. Non-normal distribution data were expressed as quartiles P50 [P25, P75], and rank sum test was used. Count data were expressed as a rate (%), and comparisons were made using the χ^2 test; GraphPad Prism 9 was used to visualize the data. Cox regression was used to analyze the independent prognostic factors affecting patients' 2-year survival, and K-M curves were plotted to demonstrate the differences between prognostic factors. The nearest neighbor matching method was used (Caliper = 0.02), and the matching ratio between the two groups was set to 1:1.

Table 1. Comparison of baseline data between two groups of patients

Factor	Before matching		*P* value	After matching		*P* value
	Observation group (n = 61)	Control group (n = 93)		Observation group (n = 61)	Control group (n = 61)	
Age						
≥ 65 year	39	54	0.531	39	41	0.703
< 65 year	22	39		22	20	
Gender						
Male	35	51	0.096	35	34	0.855
Female	26	42		26	27	
TNM staging						
III	35	58	0.383	35	38	0.580
IV	26	35		26	23	
Histological classification						
Medium/low differentiation	46	65	0.557	46	50	0.377
Well-differentiated	15	28		15	11	
Local recurrence						
Yes	34	47	0.400	34	33	0.856
No	27	46		27	28	
Tumor site						
Corpora ventriculi	33	45	0.481	33	30	0.587
Other	28	48		28	31	

Note: TNM staging, Tumor Node Metastasis staging.

Table 2. Clinical efficacy assessment

Groups	CR	PR	SD	PD	Overall effectiveness rate
Observation group before matching (n = 61)	5	32	15	9	37 (60.66%)
Control group before matching (n = 93)	9	42	26	16	51 (54.84%)
x^2-value		0.792			0.509
P-value		0.852			0.475
Observation group after matching (n = 61)	5	32	15	9	37 (60.66%)
Control group after matching (n = 61)	4	30	16	11	34 (55.74%)
x^2-value		0.407			0.303
P-value		0.938			0.581

Notes: CR, Complete Response; PR, Partial Response; SD, Stable Disease; PD, Progressive Disease.

Statistical differences were indicated when P < 0.05.

Results

Comparison of baseline information

Upon analysis, the baseline characteristics of patients in both groups, such as age, gender, TNM stage, histological typing, locoregional recurrence, and tumor site, showed no significant differences before and after propensity score matching (PSM). This indicates effective matching, ensuring comparability between the groups (all P > 0.05, **Table 1**).

Clinical efficacy assessment

In both the pre- and post-matching cohorts, the comparison of clinical efficacy between the two groups of patients revealed no statistical differences in the overall clinical effectiveness and total effective rate between the two groups before and after matching (all P > 0.05, **Table 2**).

Tumor marker levels

In the before matching cohorts, the comparison of the tumor markers revealed no significant difference in pre-treatment CA19-9, CA72-

4, and CEA levels between the two groups (P > 0.05, **Figure 2**). After the treatment, these marker all decreased in both groups. However, CA19-9 was higher in patients of the control group than in patients of the observation group after treatment (P = 0.026, **Figure 2**). In the after matching cohorts, no statistical differences were observed between the two groups before and after the treatment.

Immunoglobulin levels

In both the pre- and post-matching cohorts, there were no statistical difference in IgA, IgG, and IgM levels between the two groups before treatment (all P > 0.05, **Figure 3**); and these levels increased in both groups after the treatment (all P < 0.01, **Figure 3**). Besides, these levels were significantly higher in the observation group as compared to those in the control group (all P < 0.01, **Figure 3**).

Adverse reactions

Adverse reactions were counted in both groups. Before matching, it was found that the incidence of leukopenia (P = 0.038), malignant vomiting (P = 0.021), and diarrhea (P = 0.007) was higher in the control group than in the observation group (**Table 3**). After matching, it was found that the incidence of leukopenia (P = 0.011) and diarrhea (P = 0.011) was higher in the control group than in the observation group (**Table 3**). However, the incidence of vomiting was not statistically different between the two groups (P = 0.060).

Quality of life assessment

In both the pre- and post-matching cohorts, the comparison of KPS scores revealed that there was no statistical difference in pre-treatment KPS scores between the two groups (all P > 0.05, **Table 4**). After the treatment, the KPS scores in both groups increased significantly (all P < 0.001, **Table 4**). Besides, the KPS score in the observation group was higher than those in the control group after treatment both before and after matching (all P < 0.001, **Table 4**).

Cox regression for 2-year patient survival analysis

Cox regression was used to analyze the risk factors affecting patients' 2-year survival. In before matching cohorts, the results revealed that regimen (P < 0.001, HR = 2.456), TNM staging (P < 0.001, HR = 0.500), local recurrence (P < 0.001, HR = 2.046), and pre-treatment CEA (P < 0.001, HR = 1.153) were the independent prognostic factors affecting patients' 2-year survival (**Figure 4A**, **4B**). While after matching cohorts, the treatment regimen (P < 0.001, HR = 2.527), TNM stage (P = 0.001, HR = 0.471), local recurrence (P = 0.001, HR = 2.147), and pretreatment CEA (P = 0.011, HR = 1.131) were also found to be the independent prognostic factors affecting patients' two-year survival (**Figure 5A**, **5B**). Lastly, the K-M survival curves of patients stratified by the four prognostic factors in both pre- and post-matching cohorts were plotted, demonstrating a significantly higher survival rate in those with combined treatment, stage III, without recurrence and lower CEA levels compared with their counterparts (**Figure 6A**, **6B**).

Discussion

D2 radical surgery is widely recognized as the standard surgical intervention for resectable gastric cancer. Although surgical techniques have improved, patients who undergo surgery still face a high risk of recurrence and metastasis, with a modest five-year survival rate of approximately 20% [22]. In recent years, despite enhancements in surgical methods and the introduction of new pharmacological treatments, a uniform standard for chemotherapy protocols in the management of middle and advanced stages of gastric cancer is still lacking. Integrating new pharmacological agents and molecular-targeted therapies offers a promising direction for future treatments [23]. Nonetheless, applying both chemotherapeutic single-agent and multi-agent medicines presents a considerable challenge, as these treatments target both tumor cells and immune cells, thereby impairing the patient's immune function. Additionally, chemotherapy is associated with a range of systemic toxic side effects, including neurological, gastrointestinal, and cardiac complications, diminishing the overall effectiveness of the treatment [24]. This underscores the need for continuous refinement of therapeutic strategies to enhance efficacy while minimizing adverse outcomes in the treatment of gastric cancer.

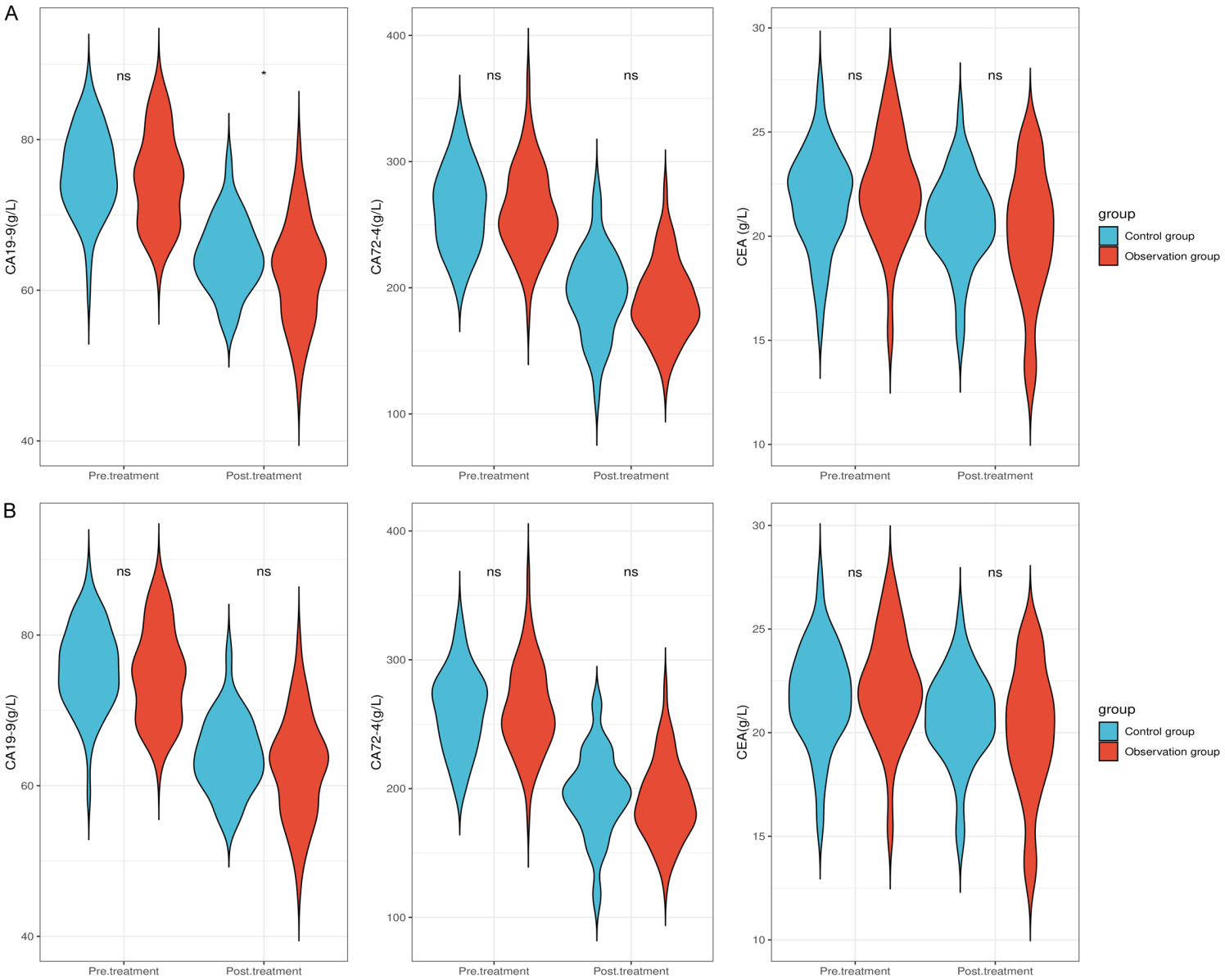

Figure 2. Comparison of changes in tumor markers before and after treatment. A. Changes in tumor markers in before matching cohorts. B. Changes in tumor markers in after matching cohorts. Notes: CA19-9, Carbohydrate Antigen 19-9; CA72-4, Carbohydrate Antigen 72-4; CEA, Carcinoembryonic Antigen. nsP > 0.05, *P < 0.05.

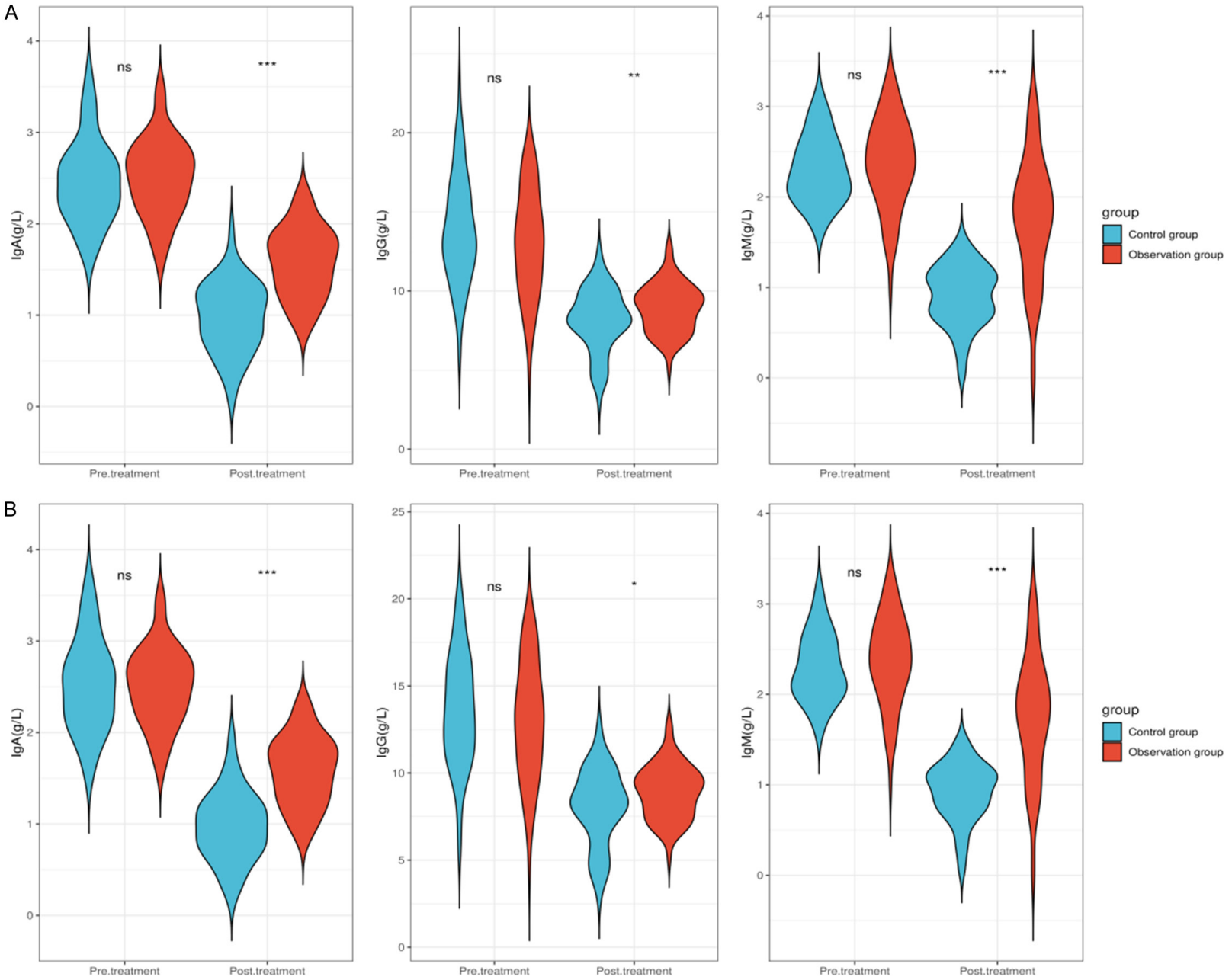
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Figure 3. Comparison of changes in immunoglobulin before and after treatment. A. Changes in immunoglobulin in before matching cohorts. B. Changes in immunoglobulin in after matching cohorts. Notes: IgA, Immunoglobulin A; IgG, Immunoglobulin G; IgM, Immunoglobulin M. nsP > 0.05, *P < 0.05, **P < 0.01, ***P < 0.001.

Table 3. Statistics of adverse reaction

Adverse reactions	Observation group before matching (n = 61)	Control group before matching (n = 93)	*P*-value	Observation group after matching (n = 61)	Control group after matching (n = 61)	*P*-value
Leucopenia	4	17	0.038	4	14	0.011
Nausea and vomiting	7	25	0.021	7	15	0.060
Elevated transaminases	5	10	0.601	5	5	1.000
Elevated blood creatinine	7	13	0.651	7	13	0.142
Diarrhea	6	26	0.007	6	17	0.011
Hand-to-foot syndrome	11	27	0.121	11	17	0.196

Table 4. Changes in patients' KPS scores

Group	KPS score	
	Pre-treatment	Post-treatment
Control group before matching (n = 93)	60.00 [50.00, 60.00]	70.00 [60.00, 80.00]
Observation group before matching (n = 61)	60.00 [60.00, 60.00]	80.00 [70.00, 90.00]
Statistic	-0.735	-5.222
*p*_value	0.425	< 0.001
Control group after matching (n = 61)	60.00 [50.00, 70.00]	70.00 [60.00, 80.00]
Observation group after matching (n = 61)	60.00 [60.00, 60.00]	80.00 [70.00, 90.00]
Statistic	-0.131	-4.496
*p*_value	0.891	< 0.001

Note: KPS, Karnofsky Performance Scale.

In the framework of traditional Chinese medicine (TCM), gastric cancer is primarily attributed to a deficiency in spleen qi, which is considered the root cause of the illness, while blood stasis and cancerous toxins are seen as symptomatic manifestations [25]. Gastric cancer primarily impacts the stomach, leading to an accumulation of cancerous toxins, which in turn damages the spleen and stomach functions, disrupting digestion and nutrient absorption. This disruption adversely affects the generation of qi and blood. As the disease progresses, the body's positive qi becomes insufficient, exacerbating the loss of qi and blood. Treatment strategies, therefore, focus on supporting the beneficial qi and dispelling the harmful influences, nourishing qi, and replenishing blood [26]. This study highlights that combining the SOX chemotherapy regimen with a Yianpi Huayu Decoction can significantly improve the immune function of patients, reduce the incidence of adverse reactions, and enhance overall quality of life. In this formula, Rhizoma Pinelliae Preparatum drys dampness and transforms phlegm, reduces nausea, and prevents vomiting; Chicken's Gizzard-Membrane can strengthen the spleen and aid digestion; Codonopsis Root enhances qi and nourish the spleen and lungs; Magnolia Bark has the properties of drying dampness and reducing phlegm; Atractylodes macrocephala has spleen-strengthening and dampness-eliminating effects; Nardostachys Root invigorates the spleen and alleviate span; and Hawthorn Berry promotes digestion and invigorates blood circulation [27, 28]. These herbs collectively bolster the spleen and stomach, regulate qi and blood, and improve immune responses, thus mitigating adverse effects in patients undergoing treatment for gastric cancer.

Modern pharmacological research has elucidated the beneficial effects of several TCM extracts in cancer therapy. For instance,

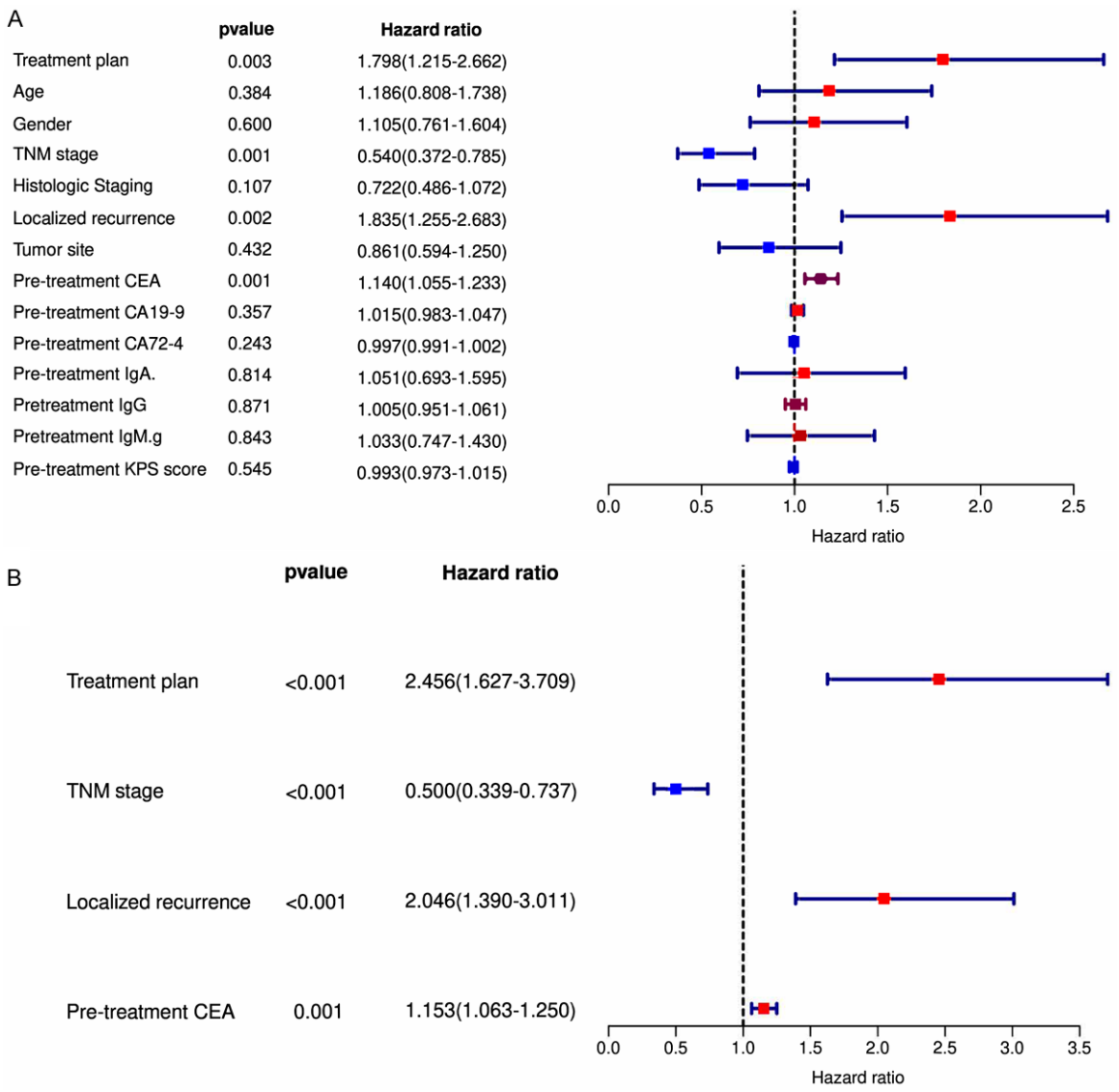

Figure 4. Cox regression analysis of risk factors for patient's two-year survival before PSM matching. A, B. Cox regression analysis of risk factors for 2-year survival in patients before matching. Notes: TNM staging, Tumor Node Metastasis staging; CA19-9, Carbohydrate Antigen 19-9; CA72-4, Carbohydrate Antigen 72-4; CEA, Carcinoembryonic Antigen; IgA, Immunoglobulin A; IgG, Immunoglobulin G; IgM, Immunoglobulin M; KPS, Karnofsky Performance Scale.

extracts of Pinellia Tuber, recognized for their anti-inflammatory and dampness-drying properties, have been shown to inhibit the growth of cervical tumors and enhance anti-tumor immunity by promoting a Th1 response in CD4+ T-cells [29]. Additionally, the polysaccharide components found in Codonopsis Root are noted for boosting liver metabolism and antioxidant capacity, which in turn supports enhanced immune function by reducing organ damage [30]. Furthermore, huperzine components from Huperzia serrata have been found to improve T-cell subset functionality and cellular immunity, significantly boosting immune responses [31]. Atractylodes macrocephala also plays a role in enhancing T-cell function and cellular immunity; at the same time, its anticancer effects include promoting cell cycle arrest and reducing the proliferation of gastric cancer cells through apoptosis in both cell and xenograft models [32]. Notably, despite these promising attributes, additional Jianpi Huayu decoction didn't bring significant improvements in clinical outcomes or tumor markers. The pri-

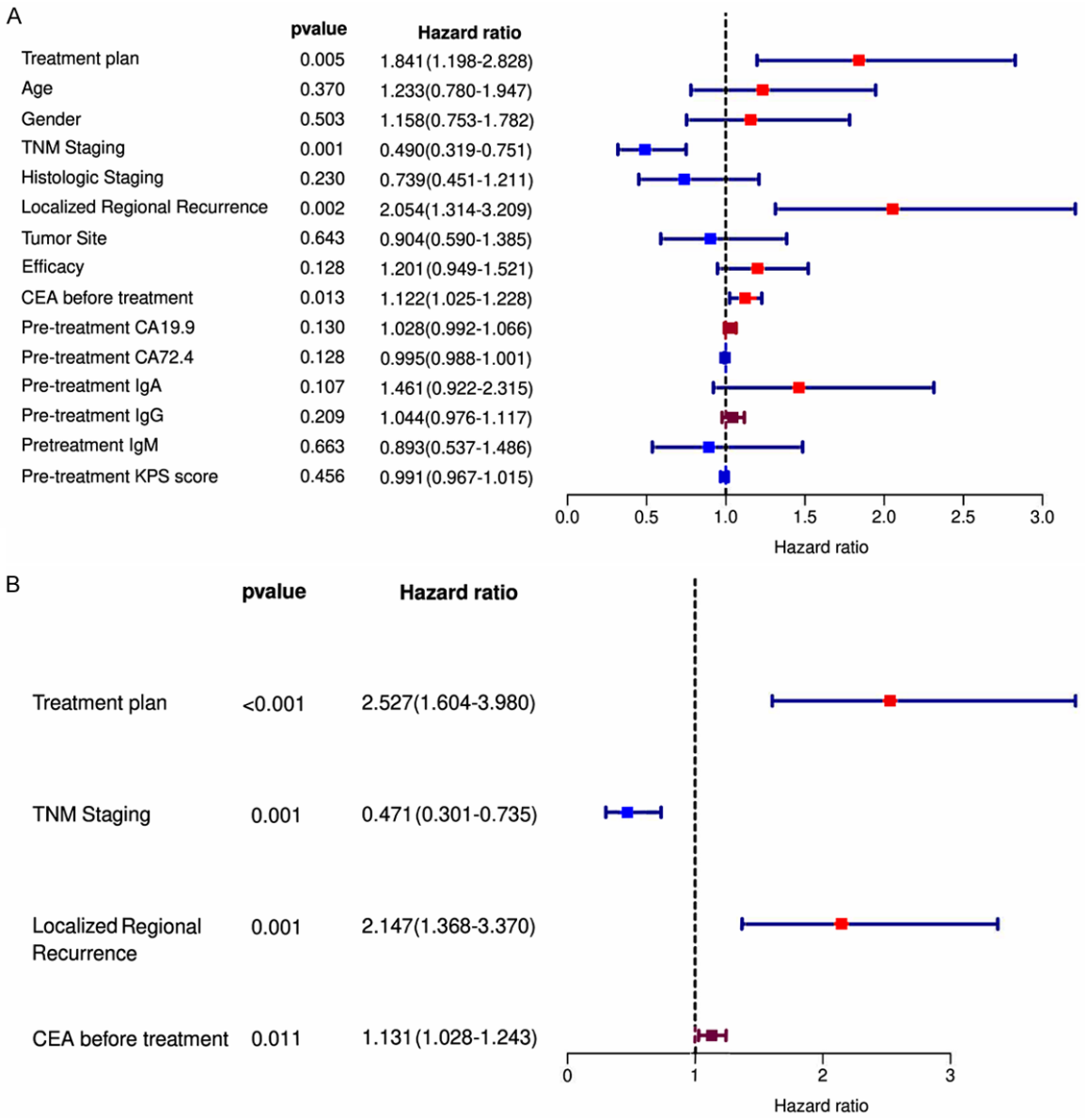

Figure 5. Cox regression analysis of risk factors for patient's two-year survival after PSM matching. A, B. Cox regression analysis of risk factors for patient survival at 2 years after patient matching. Notes: TNM staging, Tumor Node Metastasis staging; CA19-9, Carbohydrate Antigen 19-9; CA72-4, Carbohydrate Antigen 72-4; CEA, Carcinoembryonic Antigen; IgA, Immunoglobulin A; IgG, Immunoglobulin G; IgM, Immunoglobulin M; KPS, Karnofsky Performance Scale.

mary benefit of this formula seems to focus on enhancing overall health, such as improving immune functions and patient physique, rather than directly targeting tumor cells [33]. This discrepancy may be due to tumor markers, which reflect tumor load and activity, do not immediately respond to treatments as clinical symptoms do. The impacts of herbal medicines on these markers may manifest slowly or subtly, complicating the achievement of statistically significant results in short-term studies. Empirical evidence, including studies by Kim et al. [34] and Wang et al. [35], supports the efficacy of TCM in conjunction with chemotherapy. These studies highlight significant improvements in the quality of life for gastric cancer patients, with notable reductions in the incidence of leukopenia, malignant vomiting, and diarrhea when treated with TCM herbs. Similarly, Wang et al. found that Injectable

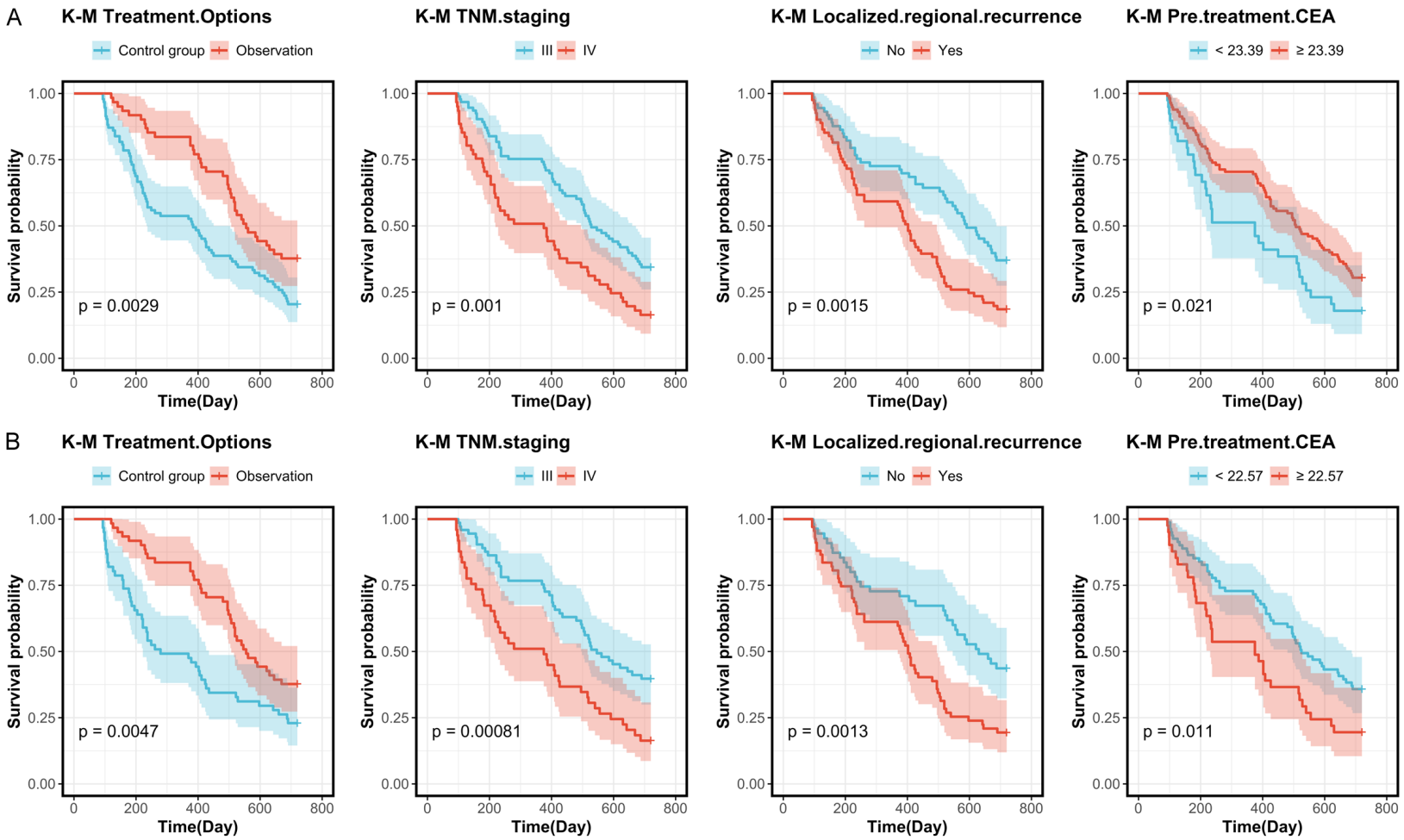

Figure 6. Survival curves of patients stratified by the four prognostic factors. A. Survival curves of patients before matching. B. Survival curves of patients after matching. Notes: TNM staging, Tumor Node Metastasis staging; CEA, Carcinoembryonic Antigen.

Lentinan, when used alongside chemotherapy, not only enhanced immune function but also effectively controlled the incidence of leukopenia and gastrointestinal reactions in gastric cancer patients [35]. In conclusion, while TCM supplements show promising results in enhancing immune function and mitigating adverse reactions during chemotherapy, more extensive clinical trials are needed to confirm their therapeutic efficacy in a broader patient population.

Propensity score matching (PSM) is a statistical approach primarily employed in observational studies to minimize selection bias when estimating treatment effects. It simulates the conditions of a randomized controlled trial, thereby equalizing the observed covariates between two groups to enable fairer and more valid comparisons [36]. Our study analyzed prognostic factors influencing 2-year survival outcomes for gastric cancer patients. Findings before and after employing PSM indicated that the treatment regimen, TNM stage, local recurrence, and pre-treatment CEA levels were independent prognostic factors affecting 2-year survival rates. The combination of the SOX chemotherapy regimen with the TCM formula, Jianpi Huayu decoction, leverages the direct antitumor effects of chemotherapy and enhances patients' overall physical condition and immune function through TCM modifications, thereby potentially increasing survival rates [37]. TNM staging, which reflects tumor size, extent, and metastatic spread, is crucial for prognosis determination [38]. Local recurrence indicates resistance to initial treatments, often signaling a higher risk of further recurrence and poorer survival outcomes [39]. Additionally, elevated pre-treatment CEA levels may suggest a more considerable tumor burden and more extensive disease spread, which can negatively impact treatment efficacy [40]. These insights underscore the critical importance of early diagnosis, the careful selection of treatment regimens, and meticulous monitoring of disease progression. Such measures are essential to implement the most effective therapeutic strategies and enhance the survival prospects of patients with gastric cancer.

Our study preliminary explored the effectiveness of the SOX regimen combined with Jianpi Huayu decoction in treating gastric cancer. However, there are some limitations. First, the limited sample size may affect the generalizability and statistical efficacy of the results, and future studies should expand the sample size to improve the extrapolation and reliability of the study. Second, the lack of randomization methods may introduce selection bias and affect the accuracy of the results; therefore, future studies should use randomized controlled trial designs to enhance the validity of causal inferences. In addition, our focus was primarily on short-term treatment effects, with insufficient assessment of long-term survival and disease recurrence. Extended follow-up periods are essential to fully assess the durability and potential delayed effects of the treatment regimens. With these improvements, more comprehensive and reliable evidence can be provided for the clinical management of gastric cancer.

Jianpi Huayu decoction combined with SOX neoadjuvant chemotherapy regimen may not enhance the direct therapeutic effects on gastric cancer, but can improve the immune function, reduce adverse effects, and enhance quality of life of gastric cancer patients.

Disclosure of conflict of interest

None.

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