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Psychological triggers of cancer-associated hypercoagulability: A case study on lymph node metastasis in gastric cancer

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Abstract: Cancer-associated hypercoagulable state is a common complication in patients with malignant tumors. Psychological stress is considered an important triggering factor; however, specific mechanisms and intervention strategies still lack in-depth research. To explore the impact of psychological factors on hypercoagulable state in gastric cancer patients with lymph node metastasis and evaluate the therapeutic effects of psychological intervention. A prospective randomized controlled trial was conducted involving 120 patients with gastric cancer and lymph node metastasis, who were randomly divided into an intervention group and a control group (60 patients each). The Anxiety and Depression Scale (ADS) was used to assess psychological status, and coagulation parameters including D-dimer, fibrinogen, and platelet aggregation rate were measured. The intervention group received a 6-month comprehensive psychological intervention program, including cognitive behavioral therapy, mindfulness-based stress reduction training, family therapy, and peer support. **Results:** In a total of 71.7% of patients exhibited psychological distress, and 76.7% showed abnormally elevated D-dimer levels. The degree of psychological stress was significantly positively correlated with coagulation dysfunction, with a correlation coefficient of 0.674 between ADS total score and D-dimer ($p < 0.001$). Psychological distress demonstrated a dose-response relationship, with the abnormal group showing significantly higher D-dimer levels ($3.9 \pm 1.6 \text{ mg L}^{-1}$) compared to the normal group ($1.4 \pm 0.7 \text{ mg L}^{-1}$). The ADS score predicted hypercoagulable state with an area under the curve of 0.798, sensitivity of 73.9%, and specificity of 81.2%. Psychological intervention significantly improved psychological status, with ADS scores decreasing from 13.5 ± 4.9 to 8.4 ± 3.2 ($p < 0.001$), while simultaneously improving coagulation function with a 33.3% reduction in D-dimer and a 15.6% decrease in fibrinogen. The thrombosis incidence rate in the intervention group was 8.3%, significantly lower than the 21.7% observed in the control group ($p = 0.032$). Psychological stress is an important triggering factor for hypercoagulable state in gastric cancer patients with lymph node metastasis. Comprehensive psychological intervention can significantly improve patients' psychological status and coagulation function, reduce the incidence of thrombotic events, and provides novel therapeutic strategies for the prevention and treatment of cancer-associated hypercoagulable state.

Keywords: anxiety and depression scale; gastric cancer; hypercoagulable state; lymph node metastasis; psychological intervention; psychological triggers; thromboembolism

1. Introduction

Cancer-associated hypercoagulable state has emerged as a serious complication faced by patients with malignant tumors, with its incidence being particularly prominent in gastric cancer patients, especially among those with lymph node metastasis. Gastric cancer, as the fifth most common malignant tumor globally, has a prognosis

that largely depends on the extent and scope of lymph node metastasis. Zhang et al. [1] found that optimizing lymph node ratio could more accurately predict the prognosis of gastric cancer patients with positive lymph node metastasis, providing important evidence for clinical risk stratification. With advances in diagnostic technology, Zhang et al. [2] developed a prediction model for lymph node metastasis in T1-stage gastric cancer based on Least Absolute Shrinkage and Selection Operator (LASSO) machine learning algorithm, which demonstrated good predictive efficacy and provided a new tool for early identification of high-risk patients. However, even with the continuous development of imaging technology, such as the application value of spectral Computed Tomography / Computerized Tomography (CT) and CT Perfusion (CTP) techniques in predicting gastric cancer lymph node metastasis reported by Zhang et al. [3], and the preoperative prediction nomogram for lymph node metastasis in submucosal early gastric cancer developed by Yu et al. [4], clinicians still face the challenge of comprehensively evaluating and managing the complex pathophysiological status of these patients. Lymph node metastasis in gastric cancer not only signifies disease progression but, more importantly, is often accompanied by significant abnormalities in the patient's coagulation system, with this hypercoagulable state becoming an important factor affecting patient's quality of life and prognosis.

The rapid development of psychoneuroimmunology has provided a novel perspective for understanding cancer-associated hypercoagulable state, with increasing evidence indicating that psychological factors play an important role in coagulation dysfunction among tumor patients. The diagnosis of gastric cancer lymph node metastasis often brings tremendous psychological impact to patients, and this acute stress response activates the hypothalamic-pituitary-adrenal axis and sympathetic nervous system, leading to massive release of stress hormones, such as cortisol and catecholamines. These bioactive substances not only directly act on platelets and coagulation factors to promote thrombosis but also further activate the coagulation cascade through regulation of inflammatory mediators, such as interleukin-6 and tumor necrosis factor- α . In cases of advanced gastric cancer with extensive lymph node metastasis reported by Morita et al. [5], patients who received immunotherapy combined with chemotherapy showed not only significant reduction in tumor burden but also corresponding improvement in coagulation function, suggesting that tumor burden reduction might indirectly improve hypercoagulable state by reducing psychological stress. Matsueda et al. [6], when studying the clinical significance of lymphatic invasion in intramucosal gastric cancer, also found that even in early lesions, once the lymphatic system is involved, patients' psychological status and physiological indicators undergo corresponding changes. These studies indicate that hypercoagulable state in gastric cancer patients with lymph node metastasis is not merely a biological effect of the tumor itself, but rather a complex result of interactions among psychological, neurological, endocrine, and immune systems.

Although current research on cancer-associated hypercoagulable state mainly focuses on biological mechanisms and pharmacological interventions, the mechanisms of action of psychological factors as important triggering factors and their intervention strategies still lack in-depth exploration. Existing anticoagulant therapy, while capable of improving patients' coagulation function to some extent, often over-

looks psychological stress as an important upstream regulatory factor. Chen et al. [7], when summarizing the current status of splenic hilar lymph node dissection in laparoscopic radical gastrectomy, pointed out that although advances in surgical techniques have improved patient survival rates, the psychological pressure and quality of life issues faced by patients postoperatively still require more attention. Therefore, establishing a comprehensive evaluation and intervention system based on psychoneuro-immunological theory not only helps to gain deeper understanding of the pathogenesis of hypercoagulable state in gastric cancer patients with lymph node metastasis but also provides new therapeutic approaches for clinical practice. This study aims to quantify the impact of psychological factors on hypercoagulable state in gastric cancer patients with lymph node metastasis through systematic clinical investigation and psychological intervention trials, explore the molecular mechanisms by which psychological stress affects coagulation function, and evaluate the clinical efficacy of comprehensive psychological intervention in improving hypercoagulable state. This will provide new theoretical basis and practical guidance for precise and individualized treatment of tumor patients, ultimately achieving a transition from the purely biomedical model to the bio-psycho-social medical model.

2. Literature review

Research on the molecular mechanisms and predictive factors of gastric cancer lymph node metastasis has become a current hotspot in the field of oncology, with numerous studies exploring the patterns and prediction methods of lymph node metastasis from multiple perspectives including gene expression, protein markers, and imaging characteristics. At the molecular biological level, Zhang et al. [8] found that the methylation status of the *GPR133* gene is closely associated with lymph node metastasis in early gastric cancer, and changes in its methylation level can serve as important biomarkers for predicting metastasis risk. Tang et al. [9] further validated that the expression levels of Cluster of Differentiation 13 / Aminopeptidase N (APN) and Fucosyltransferase 8 in gastric cancer tissues are significantly correlated with lymph node metastasis, with abnormal expression of these molecular markers reflecting enhanced invasive and metastatic capabilities of tumor cells. Research by Zheng et al. [10] focused on the expression differences of B-cell lymphoma-2 and Vascular Endothelial Growth Factor (VEGF) between primary gastric cancer lesions and lymph node metastatic foci, finding that these factors not only participate in the tumor metastasis process but are also closely related to chemotherapy sensitivity, providing molecular evidence for individualized treatment strategy formulation. Guo et al. [11] further explored the mechanisms of action of Myosin VI and Proline-rich AKT1 substrate of 40 kDa (PRAS40) in gastric cancer lymph node metastasis, discovering that these proteins play key roles in regulating cell migration and invasion processes. Yan et al. [12] revealed the protein expression profile characteristics of lymph node metastasis in early gastric cancer patients through proteomic analysis, providing a systematic perspective for understanding metastasis mechanisms. These molecular biological studies have laid a solid foundation for understanding the intrinsic mechanisms of gastric cancer lymph node metastasis, but most research still focuses on the biological characteristics of tumors themselves, lacking in-depth exploration of

how external factors, such as psychological stress affect the expression of these key molecules through epigenetic modifications.

The application of imaging technology in predicting gastric cancer lymph node metastasis has become increasingly mature, with the combination of various imaging methods and artificial intelligence algorithms providing strong support for clinical decision-making. Research by Jia et al. [13] showed that tumor characteristics on contrast-enhanced CT have important predictive value for lymph node metastasis in pT1: Tumor invades lamina propria or submucosa, pT2: Tumor invades muscularis propria (pT2a) or subserosa (pT2b). stage gastric cancer patients, providing noninvasive examination methods for early risk assessment. Zhou et al. [14] developed an intratumoral and peritumoral radiomics model based on dual-phase contrast-enhanced CT that demonstrated good diagnostic efficacy in preoperatively predicting gastric cancer lymph node metastasis, while Sun et al. [15] further validated the value of the CT-based Node Reporting and Data System (Node-RADS) scoring system in predicting residual lymph node metastasis and survival prognosis after neoadjuvant chemotherapy. The application of spectral CT technology has provided new possibilities for precise prediction, with Zuo et al. [16] demonstrating good assessment capability for gastric cancer lymph node metastasis using extracellular volume fraction calculated based on spectral CT iodine density images. Studies by Xu et al. [17] and Chen et al. [18] also confirmed the important value of spectral CT multiparameter imaging in preoperatively predicting gastric cancer lymph node metastasis. Research by Mao et al. [19] further validated the application prospects of dual-layer detector spectral CT quantitative parameters in diagnosing regional lymph node metastasis in gastric cancer. The introduction of machine learning algorithms has made prediction models more precise, with the lymph node metastasis prediction nomogram for elderly early gastric cancer patients constructed by Liang et al. [20], and the machine learning-based early gastric cancer lymph node metastasis prediction model by Meng et al. [21] both showing good clinical application value. Research by Yang et al. [22] based on the Node Reporting and Data System (GEE) model further integrated contrast-enhanced CT and pathological indicators, improving prediction accuracy. However, these technically advanced prediction models mainly focus on morphological and functional characteristics of tumors, with insufficient consideration of factors, such as patients' psychological status and stress levels, which may limit the comprehensiveness and prediction accuracy of the models.

Although current research has made significant progress in mechanism elucidation and prediction methods for gastric cancer lymph node metastasis, understanding of the role of psychological factors in cancer-associated hypercoagulable state remains limited. While Liu et al. [23] established a model for predicting early postoperative lymph node recurrence, and Komori et al. [24] explored the predictive significance of residual lymph node metastasis for postoperative recurrence in gastric cancer, these studies mainly analyze recurrence risk from a tumor biological perspective, lacking attention to changes in patients' psychological status. Song et al. [25] analyzed risk factors for early gastric cancer lymph node metastasis and their impact on prognosis, but did not involve nontraditional risk factors, such as psychological stress. Li et al. [26] attempted to combine serum biomarkers with imaging examina-

tions to predict gastric cancer lymph node metastasis and prognosis, and Zhang et al. [27] also explored the predictive value of gastric filling contrast-enhanced ultrasound combined with serum markers, but these studies remained within the biomedical model framework. In reality, the diagnosis of gastric cancer lymph node metastasis often brings tremendous psychological impact to patients, and this acute and chronic psychological stress may affect the tumor microenvironment, immune function, and coagulation system through neuroendocrine pathways, thereby influencing disease progression and treatment response. Psychoneuroimmunological research indicates that stress hormones, such as cortisol and catecholamines released under chronic stress conditions can not only directly promote platelet aggregation and coagulation factor synthesis but may also regulate the expression levels of key molecules, such as G Protein-coupled Receptor 133, CD13, and FUT8 discovered in the aforementioned studies through epigenetic mechanisms, thereby affecting tumor invasive and metastatic capabilities. Additionally, the inflammatory response imbalance caused by psychological stress may alter tumor angiogenesis and microenvironmental characteristics, and these changes not only affect the accuracy of imaging examinations but, more importantly, may become important triggering factors for cancer-associated hypercoagulable state. Therefore, incorporating psychological assessment and intervention into the comprehensive management system for gastric cancer patients with lymph node metastasis will not only help improve the accuracy of existing prediction models but may also provide new therapeutic approaches for improving patients' coagulation function and overall prognosis, which is precisely the important gap that current research urgently needs to fill.

3. Research methods

3.1. Study design

This study employed a prospective cohort study design combined with methodological characteristics of randomized controlled trials, aiming to systematically evaluate the impact of psychological factors on hypercoagulable state in gastric cancer patients with lymph node metastasis and the therapeutic effects of psychological intervention. The study period was from March 2023 to September 2024, conducted simultaneously in the oncology departments of three tertiary hospitals: West China Hospital, Peking Union Medical College Hospital, and Renji Hospital affiliated with Shanghai Jiao Tong University School of Medicine. The study strictly adhered to the ethical principles of the Declaration of Helsinki and obtained approval from the ethics committees of all participating hospitals (West China Hospital Ethics Committee approval number: 2023-IRB-048, Peking Union Medical College Hospital Ethics Committee approval number: 2023-PUMCH-A-0156, Renji Hospital Ethics Committee approval number: 2023-RJ-ETHICS-089). All participating patients signed informed consent forms after fully understanding the study objectives, methods, potential risks, and expected benefits. The study used stratified randomization with hospital, age (≤ 60 years vs. > 60 years), gender, and tumor stage (TNM: Tumor Nodes Metastasis stage III vs. stage IV) as stratification factors to ensure balanced baseline characteristics between the two groups [28]. Random sequences were generated

by independent statisticians using the PROC PLAN procedure in SAS 9.4 software, employing block randomization with a block size of 4. Allocation concealment was achieved through sealed opaque envelopes maintained by dedicated research nurses, which were opened only after patients completed baseline assessments and were confirmed to meet inclusion criteria. The study was designed as a single-blind trial, with laboratory technicians performing coagulation function tests and statistical analysts blinded to group allocation to reduce the risk of measurement bias and analysis bias.

The primary endpoint of the study was the between-group difference in D-dimer levels at 6 months postpsychological intervention, while secondary endpoints included changes in other coagulation function indicators, improvement in Anxiety and Depression Scale (ADS) scores, incidence of thrombotic events, and changes in quality of life scores. Sample size calculation was based on preliminary pilot study data, with a clinically meaningful difference in D-dimer levels set at 0.8 mg L^{-1} , standard deviation of 1.2 mg L^{-1} , α error of 0.05 (two-sided test), and β error of 0.20 (80% power). Considering a 20% loss-to-follow-up rate, the final determination was 60 patients per group, with a total sample size of 120 patients. The study established strict quality control measures, including development of standard operating procedures (SOPs), unified training of research personnel, regular on-site monitoring, and data verification. All psychological assessments were conducted by clinical psychology experts who received specialized training and obtained qualification certification, with inter-rater consistency tested by Kappa coefficient, requiring $\kappa \geq 0.80$. Coagulation function testing was performed in the central laboratories of each hospital using standardized testing reagents and equipment, with regular inter-laboratory quality assessment to ensure comparability of results [29]. The psychological intervention protocol was developed by a team of senior psychotherapists, including four modules: cognitive behavioral therapy, mindfulness-based stress reduction training, family therapy, and peer support groups, each with detailed operation manuals and quality assessment standards. Data management utilized a web-based electronic data capture (EDC) system with logic checks and range checks to ensure accuracy and completeness of data entry. The study established an independent Data Safety Monitoring Board (DSMB) responsible for overseeing the conduct of the study, evaluating safety data, and having the authority to recommend suspension or termination of the study.

3.2. Study subjects and grouping

The study subjects were gastric cancer patients with lymph node metastasis who visited the oncology departments of West China Hospital, Peking Union Medical College Hospital, and Renji Hospital affiliated with Shanghai Jiao Tong University School of Medicine from March 2023 to September 2024. Inclusion criteria included: 1) Patients with histopathologically confirmed gastric adenocarcinoma; 2) Imaging examinations (CT, Magnetic Resonance Imaging, or Positron Emission Tomography – Computed Tomography) confirming the presence of lymph node metastasis, with lymph node short-axis diameter $\geq 1.0 \text{ cm}$ or typical metastatic features; 3) Age 18–75 years; 4) Expected survival ≥ 6 months; 5) Eastern Cooperative Oncology Group (ECOG) performance status score 0–2; 6) Basic Chinese comprehension

and expression abilities, capable of cooperating with psychological assessment and intervention; 7) Signed informed consent. Exclusion criteria included: 1) Previous history of venous thromboembolism or known hereditary coagulation disorders (such as protein C deficiency, protein S deficiency, antithrombin III deficiency, etc.); 2) Currently taking anticoagulant medications (warfarin, dabigatran, rivaroxaban, etc.) or antiplatelet drugs (aspirin, clopidogrel, etc.) and unable to discontinue; 3) Complicated by severe cardiac, pulmonary, hepatic, or renal dysfunction, defined as New York Heart Association (NYHA) cardiac function classification $\geq$ Class III, acute exacerbation of chronic obstructive pulmonary disease, Child-Pugh liver function classification Class C, or serum creatinine ≥ 2.0 mg dL⁻¹; 4) Previous history of severe mental disorders, such as schizophrenia, bipolar disorder, major depressive disorder, or currently taking antipsychotic medications; 5) Complicated by other malignant tumors or history of other malignant tumors within the past 5 years; 6) Pregnant or lactating women; 7) Participating in other clinical trials or receiving experimental treatment within the past 30 days [30]. Through a strict screening process, a total of 156 patients underwent preliminary evaluation, of whom 36 were excluded for not meeting inclusion criteria (coagulation disorders 8 cases, taking anticoagulant medications 12 cases, history of severe mental illness 6 cases, complicated by other malignant tumors 7 cases, refusal to participate 3 cases), and finally 120 eligible patients were enrolled in the study.

The 120 patients enrolled in the study were divided into intervention and control groups using stratified randomization, with 60 patients in each group. Stratification factors included: 1) Hospital (West China Hospital, Peking Union Medical College Hospital, Renji Hospital); 2) Age (≤ 60 years vs. > 60 years); 3) Gender (male vs. female); 4) TNM stage (Stage III vs. Stage IV); 5) Degree of lymph node metastasis (regional lymph node metastasis vs. distant lymph node metastasis). After randomization, the baseline characteristics of the intervention group were: mean age 59.8 ± 12.4 years, 38 males (63.3%), 22 females (36.7%); TNM Stage III 39 cases (65.0%), Stage IV 21 cases (35.0%); primary tumor locations included gastric antrum 32 cases (53.3%), gastric body 18 cases (30.0%), gastric fundus 6 cases (10.0%), diffuse whole stomach lesions 4 cases (6.7%); lymph node metastasis included regional lymph node metastasis 45 cases (75.0%), distant lymph node metastasis 15 cases (25.0%), with a median number of metastatic lymph nodes of 6 (IQR: 3–10). The baseline characteristics of the control group were: mean age 60.2 ± 11.8 years, 37 males (61.7%), 23 females (38.3%); TNM Stage III 40 cases (66.7%), Stage IV 20 cases (33.3%); primary tumor locations included gastric antrum 30 cases (50.0%), gastric body 20 cases (33.3%), gastric fundus 7 cases (11.7%), diffuse whole stomach lesions 3 cases (5.0%); lymph node metastasis included regional lymph node metastasis 44 cases (73.3%), distant lymph node metastasis 16 cases (26.7%), with a median number of metastatic lymph nodes of 5 (IQR: 3–9) [31]. Chi-square test and *t*-test results showed no statistical differences between the two groups in all baseline characteristics ($p > 0.05$), ensuring balanced and comparable grouping. Patients in the intervention group received standard medical care combined with comprehensive psychological intervention, while patients in the control group received only standard medical care and general health education, with an observation period of 6 months.

3.3. Assessment tools and testing indicators

This study employed a multidimensional psychological assessment tool system, with the ADS serving as the primary psychological status assessment instrument. The ADS scale was developed by Zigmond and Snaith in 1983, specifically designed to evaluate anxiety and depression symptoms in patients within medical settings. The scale contains 14 items, with 7 items assessing anxiety symptoms and 7 items assessing depression symptoms. Each item uses a 4-point scoring system ranging from 0 to 3 points, with a total score range of 0–42 points. Based on previous research and clinical application experience, the scoring criteria were established as follows: 0–7 points indicating no anxiety or depression symptoms, 8–10 points indicating borderline values (mild anxiety or depression), and 11 points or above indicating the presence of significant anxiety or depression symptoms [32]. The scale demonstrated good reliability and validity in the Chinese population, with a Cronbach's α coefficient of 0.87 and test-retest reliability of 0.85. To comprehensively evaluate patients' mental health status, the study also employed several supplementary assessment tools: 1) The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30), containing 30 items that assess functional domains (physical function, role function, emotional function, cognitive function, and social function) and symptom domains (fatigue, nausea, vomiting, pain, etc.), with scoring ranging from 0 to 100 points, where higher scores indicate better functional status or more severe symptoms; 2) The Perceived stress scale (PSS-14), containing 14 items that evaluate an individual's subjective perception of life events' unpredictability, uncontrollability, and overload during the past month, using a 5-point scoring system from 0 to 4 points, with total scores ranging from 0 to 56 points, where higher scores indicate higher perceived stress levels; 3) The social support rating scale (SSRS), containing 10 items that assess patients' social support status from three dimensions: objective support, subjective support, and utilization of support, with total scores ranging from 12 to 66 points, where higher scores indicate better social support levels [33].

Coagulation function testing indicators encompassed two major categories: routine coagulation parameters and specialized thrombotic markers. Routine coagulation function testing included: 1) Prothrombin time (PT) and international normalized ratio (INR), reflecting extrinsic coagulation pathway function; 2) Activated partial thromboplastin time (APTT), reflecting intrinsic coagulation pathway function; 3) Fibrinogen (FIB), with normal reference values of 2.0–4.0 g L⁻¹; 4) D-Dimer, detected using immunoturbidimetric method, with normal reference values <0.5 mg L⁻¹; 5) Platelet count and platelet aggregation rate, with ADP- and collagen-induced platelet aggregation function detected using optical turbidimetry [34]. Specialized thrombotic marker testing included: 1) Tissue factor (TF), with plasma TF antigen levels detected using enzyme-linked immunosorbent assay (ELISA), normal reference values <150 pg mL⁻¹; 2) von Willebrand factor (vWF), with vWF antigen and activity detected using ELISA method, normal reference values 50%–200%; 3) Soluble fibrin monomer complex (SFMC), reflecting the degree of intravascular coagulation activation, normal reference values <3.5 mg L⁻¹; 4) Thrombomodulin (TM), reflecting the degree of vascular endothelial cell injury, normal reference values <4.5

ng mL⁻¹. All testing was performed in the central laboratories of each hospital using standardized testing reagents (Siemens Healthcare Diagnostics) and automated testing equipment (Sysmex CA-7000 series), with regular participation in inter-laboratory quality assessment organized by the National Center for Clinical Laboratories to ensure accuracy and comparability of test results. Blood specimen collection was strictly performed according to standard operating procedures, with venous blood collected between 8 and 10 AM after 12 h of fasting, using vacuum blood collection tubes containing 3.8% sodium citrate, with a blood-to-anticoagulant ratio of 9:1. Blood samples were immediately mixed and testing was completed within 2 h of collection.

3.4. Intervention program design

The comprehensive psychological intervention program designed for this study was based on psychoneuroimmunological theory and evidence-based medical evidence, employing a multimodule integrated intervention strategy aimed at systematically reducing patients' psychological stress responses through systematic psychotherapy, thereby improving coagulation function and overall health status. The intervention program comprised four core modules: 1) Cognitive behavioral therapy (CBT) module: Implemented by therapists holding national level-2 psychological counselor qualifications and specialized training in oncology psychology, conducted once weekly for 60 min each session over 12 weeks. The CBT module mainly included cognitive restructuring techniques (identifying and correcting patients' catastrophic thinking and irrational beliefs about disease prognosis and treatment outcomes), behavioral activation techniques (developing progressive activity plans to increase patients' positive behaviors and social participation), problem-solving skills training (teaching patients systematic problem analysis and resolution methods), and relaxation training (deep breathing, progressive muscle relaxation, and other techniques) [35]. 2) Mindfulness-based stress reduction (MBSR) module: Conducted twice weekly for 45 min each session over 8 weeks, guided by professionals certified in mindfulness-based stress reduction therapy. The MBSR module included mindful breathing exercises (focusing on breath awareness and regulation), body scan techniques (systematically sensing and relaxing various body parts), mindfulness meditation (observing the flow of thoughts and emotions without judgment), mindful yoga (combining simple yoga postures with breathing exercises), and daily life mindfulness practices (integrating mindful attitudes into daily activities). 3) Family therapy module: Conducted monthly for 90 min each session over 6 sessions, led by systemic family therapists with active participation from patients' primary family members (spouse, children, etc.). The family therapy module focused on improving family communication patterns, enhancing family cohesion, clarifying family member roles and responsibilities, establishing effective emotional support systems, and helping families adapt to role and lifestyle changes brought about by the illness. 4) Peer support group module: Conducted biweekly for 120 min each session over 12 sessions, cofacilitated by experienced recovered patients and professional psychological counselors. Group members consisted of 6–8 gastric cancer patients at similar disease stages, using structured group discussions, experience sharing, emotional expression, and mutual support to reduce patients' feelings of loneliness and helplessness. Each

group session included opening sharing (15 min), thematic discussion (60 min, such as “How to cope with treatment side effects,” “Rebuilding life confidence”, etc.), relaxation exercises (30 min), and summary feedback (15 min).

Control group patients received standard medical care and general health education, including disease-related knowledge education, medication guidance, dietary and nutritional advice, and regular follow-up visits, but were not provided with systematic psychological intervention services. To ensure consistency in intervention quality, all psychotherapists underwent 2 weeks of specialized training to master unified intervention manuals and operating procedures. After each intervention, therapists were required to complete standardized intervention record forms documenting intervention content, patient participation levels, technique application status, and effectiveness assessment. The research team conducted monthly case supervision sessions, with senior psychotherapy experts providing quality monitoring and guidance for the intervention process. Intervention compliance was assessed through attendance rates, homework completion status, and patient self-assessment scales, requiring patients to complete at least 80% of the planned intervention content to be included in final effectiveness analysis [36]. Additionally, the study established intervention safety monitoring mechanisms: if patients exhibited severe psychological crises or suicidal tendencies, crisis intervention procedures would be immediately initiated, with referral to specialized psychiatric treatment when necessary, ensuring patient safety and well-being.

3.5. Data collection and statistical analysis

Data collection was conducted strictly according to standardized procedures, with four key time points established: baseline assessment (T0, within 1 week before intervention), 1-month postintervention assessment (T1), 3-month postintervention assessment (T2), and 6-month postintervention assessment (T3). At each time point, patients were required to complete data collection for two major categories of indicators: psychological status assessment and coagulation function testing. Psychological status assessments were conducted by clinical psychology experts who had undergone unified training in quiet clinic room environments, with assessment time controlled within 45–60 min, completed through face-to-face interviews combined with self-assessment scales for ADS, QLQ-C30, PSS-14, and SSRS scoring. To ensure assessment quality, all assessment personnel underwent 1 week of standardized training before the study commenced, passing theoretical examinations and practical operation assessments, with inter-rater consistency Kappa coefficients required to be ≥ 0.85 . Blood specimen collection for coagulation function testing strictly followed international standards, requiring patients to fast for 12 h, with 12 mL of antecubital venous blood collected between 8:00 and 10:00 AM, using blue-cap vacuum tubes containing 3.8% sodium citrate (for coagulation function testing) and purple-cap vacuum tubes containing Ethylenediaminetetraacetic acid dipotassium salt (for complete blood count), with blood-to-anticoagulant ratio strictly prepared at 9:1. After blood collection, specimens were immediately gently inverted and mixed 8–10 times, delivered to the laboratory within 30 min at room temperature, and testing completed within 2 h [37]. Data management utilized a cloud-based

EDC system with dual data entry and logic verification functions, including numerical range checks, logical consistency checks, and missing value reminder functions. The completeness and accuracy of research data were ensured through regular data monitoring and source document verification, with 100% verification of key data before database lock.

Statistical analysis was performed using SPSS 28.0 software package and R language version 4.3.0, with significance level set at $\alpha = 0.05$ (two-sided test). In descriptive analysis, continuous variables were expressed as mean $\pm$ standard deviation or median (interquartile range) based on normality test results, while categorical variables were described using frequencies and percentages. Between-group comparisons of baseline characteristics used independent samples *t*-test (normally distributed continuous variables), Mann–Whitney U test (non-normally distributed continuous variables), or chi-square test (categorical variables). Primary analysis employed the intent-to-treat principle, while secondary analysis used per-protocol analysis as sensitivity analysis. For repeated measures data, linear mixed-effects models were used to analyze change trends at each time point, with models including fixed effects (group, time, group $\times$ time interaction) and random effects (individual intercept), using an unstructured covariance structure. Missing data were handled using Multiple Imputation, generating five imputed datasets based on the distribution characteristics of observed data, with final results being the pooled results of five imputation analyses. Associations between psychological scores and coagulation indicators were analyzed using Pearson (normal distribution) or Spearman (non-normal distribution) correlation analysis. Multivariable analysis employed multiple linear regression models with coagulation indicators as dependent variables and psychological scores, demographic characteristics, and clinical characteristics as independent variables, using stepwise regression for variable selection. Time-to-event analysis for thrombotic events used the Kaplan–Meier method to plot survival curves, Log-rank test to compare between-group differences, and Cox proportional hazards regression models to analyze influencing factors [38]. Model goodness-of-fit was assessed through AIC (Akaike Information Criterion) and BIC (Bayesian Information Criterion), with residual analysis examining the reasonableness of model assumptions. All statistical tests were two-sided, with $p < 0.05$ considered statistically significant, while effect sizes (Cohen's *d*) and 95% confidence intervals were calculated to evaluate clinical significance.

4. Results analysis

4.1. Baseline characteristics and psychological status analysis

4.1.1. Patient demographic characteristics distribution

The demographic characteristics analysis of 120 gastric cancer patients with lymph node metastasis included in this study revealed a heterogeneous population with specific distribution patterns. The study population comprised 75 males (62.5%) and 45 females (37.5%), reflecting the known male predominance in gastric cancer epidemiology. The mean age was 60.0 ± 12.1 years (range: 28–78 years), with the largest proportion of patients ($n = 47$, 39.2%) in the 50–69 years age group, followed by patients aged 70 years and above ($n = 31$, 25.8%). The age distribu-

tion presented the typical pattern of gastric cancer, with most cases occurring in the sixth and seventh decades. Educational background analysis showed that 38 patients (31.7%) completed primary education, 45 patients (37.5%) completed secondary education, and 37 patients (30.8%) had college education or above, indicating a relatively balanced educational distribution favorable for comprehensive psychological assessment and intervention implementation. Marital status analysis revealed that 89 patients (74.2%) were married, 18 patients (15.0%) were widowed, 8 patients (6.7%) were divorced, and 5 patients (4.1%) were single, indicating that most patients had potential family support systems. Employment status distribution showed that 52 patients (43.3%) were employed, 41 patients (34.2%) were retired, and 27 patients (22.5%) were unemployed, reflecting the impact of age demographics and disease burden on work capacity [39]. As shown in **Table 1**, the intervention group and control group maintained good balance across all baseline characteristics.

Geographic distribution indicated that 68 patients (56.7%) were from urban areas and 52 patients (43.3%) were from rural areas, which is important for understanding healthcare access and social support networks. Monthly household income analysis showed that 43 patients (35.8%) had income below 3,000 yuan, 38 patients (31.7%) had income between 3,000 and 8,000 yuan, 25 patients (20.8%) had income between 8,000 and 15,000 yuan, and 14 patients (11.7%) had income exceeding

Table 1. Comparison of baseline demographic characteristics in gastric cancer patients with lymph node metastasis.

Characteristics	Total (n = 120)	Intervention group (n = 60)	Control group (n = 60)	p-value
Age (years)	60.0 ± 12.1	59.8 ± 12.4	60.2 ± 11.8	0.853
Age groups				0.934
28–49 years	31 (25.8%)	15 (25.0%)	16 (26.7%)	
50–69 years	47 (39.2%)	24 (40.0%)	23 (38.3%)	
≥70 years	42 (35.0%)	21 (35.0%)	21 (35.0%)	
Gender				0.827
Male	75 (62.5%)	38 (63.3%)	37 (61.7%)	
Female	45 (37.5%)	22 (36.7%)	23 (38.3%)	
Education level				0.741
Primary school	38 (31.7%)	20 (33.3%)	18 (30.0%)	
Secondary school	45 (37.5%)	22 (36.7%)	23 (38.3%)	
College and above	37 (30.8%)	18 (30.0%)	19 (31.7%)	
Marital status				0.692
Married	89 (74.2%)	45 (75.0%)	44 (73.3%)	
Widowed	18 (15.0%)	8 (13.3%)	10 (16.7%)	
Divorced	8 (6.7%)	4 (6.7%)	4 (6.7%)	
Single	5 (4.1%)	3 (5.0%)	2 (3.3%)	
Employment status				0.634
Employed	52 (43.3%)	27 (45.0%)	25 (41.7%)	
Retired	41 (34.2%)	20 (33.3%)	21 (35.0%)	
Unemployed	27 (22.5%)	13 (21.7%)	14 (23.3%)	
TNM staging				0.845
Stage III	79 (65.8%)	39 (65.0%)	40 (66.7%)	
Stage IV	41 (34.2%)	21 (35.0%)	20 (33.3%)	

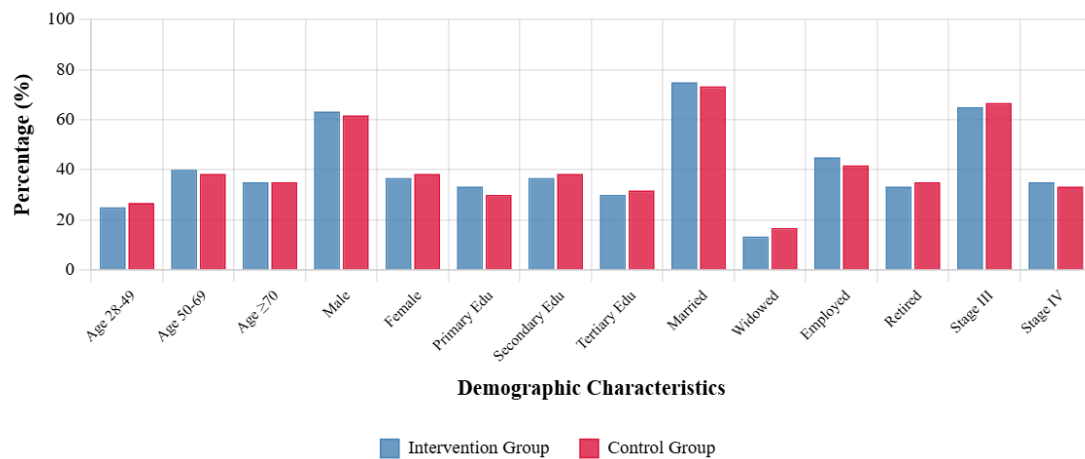


Figure 1. Comparison of demographic characteristics distribution in gastric cancer patients with lymph node metastasis.

15,000 yuan, indicating that different socioeconomic backgrounds may affect treatment compliance and psychological health status. Clinical staging analysis showed that 79 patients (65.8%) were classified as TNM Stage III and 41 patients (34.2%) as Stage IV, indicating that most participants had locally advanced disease. Primary tumor location distribution showed gastric antrum involvement in 61 cases (50.8%), gastric body in 35 cases (29.2%), gastric fundus in 16 cases (13.3%), and diffuse gastric involvement in 8 cases (6.7%). Lymph node metastasis patterns showed regional lymph node involvement in 89 cases (74.2%) and distant lymph node metastasis in 31 cases (25.8%), with a median number of involved lymph nodes of 5 (IQR: 3–9). Histological differentiation analysis showed well-differentiated adenocarcinoma in 15 cases (12.5%), moderately differentiated in 67 cases (55.8%), and poorly differentiated in 38 cases (31.7%). **Figure 1** clearly demonstrates the distribution comparison of various demographic characteristics between the intervention and control groups, visually reflecting the balance between the two groups.

Performance status assessment using the ECOG scale showed that 45 patients (37.5%) had an ECOG score of 0, 52 patients (43.3%) scored 1, and 23 patients (19.2%) scored 2, indicating that most patients maintained relatively good functional status. Statistical analysis using chi-square tests and independent samples *t*-tests confirmed good balance between the intervention and control groups across all demographic and clinical characteristics (all $p > 0.05$), ensuring the validity of subsequent comparative analyses. This comprehensive demographic characteristics analysis provided necessary baseline data for stratified analysis and helped identify potential confounding factors that need to be controlled in psychological intervention outcome assessment. Detailed analysis of age distribution showed 31 patients (25.8%) aged 28–49 years, 47 patients (39.2%) aged 50–69 years, and 42 patients (35.0%) aged 70 years and above, a distribution pattern consistent with gastric cancer age epidemiological characteristics. Gender analysis further showed a male-to-female ratio of approximately 1.67:1, consistent with international gastric cancer epidemiological data. The balanced distribution of education levels indicated that the study population had good representativeness, favorable for psychological intervention implementation and effectiveness assessment. Correlation analysis between employment status

and age structure showed that retirees were mainly concentrated in the age group above 65 years, while employed individuals were mainly distributed in the 50–65 years age group, a distribution pattern that would affect patients' economic status and social support accessibility. **Table 1** details all baseline characteristics data and statistical comparison results, establishing a solid foundation for subsequent analyses.

4.1.2. Baseline psychological status assessment results

Baseline psychological status assessment results revealed that gastric cancer patients with lymph node metastasis generally experienced significant psychological distress, with anxiety and depression symptoms being particularly prominent. Assessment using the ADS showed that the mean ADS total score for 120 patients was 13.6 ± 4.8 points, significantly higher than the reference value for normal population (<8 points). Among them, 86 patients (71.7%) had ADS total scores reaching or exceeding the abnormal standard of 11 points, indicating clinically significant anxiety or depression symptoms. The anxiety subscale score averaged 8.2 ± 2.9 points, and the depression subscale score averaged 5.4 ± 2.1 points, with anxiety symptoms being significantly more severe than depression symptoms. Stratified analysis according to ADS scoring standards revealed 34 cases (28.3%) in the normal group (0–7 points), 28 cases (23.3%) in the borderline group (8–10 points), and 58 cases (48.4%) in the abnormal group (≥ 11 points), indicating that nearly half of the patients had psychological problems requiring clinical attention [40]. Further analysis showed no significant difference in baseline ADS scores between the intervention and control groups (13.5 ± 4.9 vs. 13.7 ± 4.7 points, $p = 0.823$), ensuring the validity of subsequent comparative analyses. As shown in **Table 2**, the two groups had good comparability across all psychological assessment indicators.

Table 2. Comparison of baseline psychological status assessment results in gastric cancer patients with lymph node metastasis.

Psychological assessment indicators	Total ($n = 120$)	Intervention group ($n = 60$)	Control group ($n = 60$)	p -value
ADS total score	13.6 ± 4.8	13.5 ± 4.9	13.7 ± 4.7	0.823
ADS stratified distribution				0.756
Normal (0–7 points)	34 (28.3%)	18 (30.0%)	16 (26.7%)	
Borderline (8–10 points)	28 (23.3%)	13 (21.7%)	15 (25.0%)	
Abnormal (≥ 11 points)	58 (48.4%)	29 (48.3%)	29 (48.3%)	
Anxiety subscale	8.2 ± 2.9	8.1 ± 3.0	8.3 ± 2.8	0.712
Depression subscale	5.4 ± 2.1	5.4 ± 2.2	5.4 ± 2.0	0.965
QLQ-C30 global quality of life	52.3 ± 15.2	51.8 ± 15.6	52.8 ± 14.8	0.724
Functional domain scores				
Physical functioning	58.7 ± 18.4	59.2 ± 18.8	58.2 ± 18.0	0.774
Role functioning	49.2 ± 19.6	48.6 ± 20.1	49.8 ± 19.1	0.742
Emotional functioning	44.8 ± 16.3	44.2 ± 16.8	45.4 ± 15.8	0.695
Cognitive functioning	61.5 ± 17.8	60.8 ± 18.3	62.2 ± 17.3	0.681
Social functioning	53.9 ± 20.1	53.1 ± 20.6	54.7 ± 19.6	0.667
PSS-14 perceived stress	24.8 ± 6.3	24.6 ± 6.5	25.0 ± 6.1	0.734
SSRS social support total score	35.2 ± 8.7	35.5 ± 8.9	34.9 ± 8.5	0.713
Objective support	10.8 ± 3.2	10.9 ± 3.3	10.7 ± 3.1	0.742
Subjective support	18.7 ± 4.5	18.8 ± 4.6	18.6 ± 4.4	0.823
Support utilization	5.7 ± 2.1	5.8 ± 2.2	5.6 ± 2.0	0.605

Quality of life assessment results showed that the global quality of life score assessed using the EORTC QLQ-C30 was 52.3 ± 15.2 points, significantly lower than the normal values for healthy populations (70–80 points). Among functional domain scores, physical functioning scored 58.7 ± 18.4 points, role functioning scored 49.2 ± 19.6 points, emotional functioning scored 44.8 ± 16.3 points, cognitive functioning scored 61.5 ± 17.8 points, and social functioning scored 53.9 ± 20.1 points, with emotional functioning being the most severely impaired. Symptom domain scores showed fatigue scoring 65.8 ± 21.2 points, pain scoring 58.4 ± 23.7 points, and nausea/vomiting scoring 42.1 ± 26.9 points, all higher than normal reference values, indicating that patients were experiencing multiple symptom burdens. PSS-14 assessment results showed that patients' perceived stress scores were 24.8 ± 6.3 points, at a moderate-to-high level (normal value <20 points), with 79 patients (65.8%) having perceived stress scores exceeding 20 points, indicating that most patients experienced significant life stress. SSRS assessment showed that patients' total social support score was 35.2 ± 8.7 points, lower than the reference value for normal populations (40–60 points) [41]. Specifically, objective support scored 10.8 ± 3.2 points, subjective support scored 18.7 ± 4.5 points, and support utilization scored 5.7 ± 2.1 points, indicating that patients had deficiencies across all dimensions of social support. **Figure 2** visually demonstrates the distribution of various psychological assessment indicators between the intervention and control groups, clearly showing the high similarity in baseline psychological status between the two groups.

4.1.3. Baseline coagulation function status analysis

Baseline coagulation function assessment results revealed that gastric cancer patients with lymph node metastasis generally exhibited significant hypercoagulable states, with all coagulation parameters markedly deviating from normal ranges. D-dimer, an important indicator reflecting fibrinolytic activity and thrombus formation in the body, was significantly elevated in this study population, with mean levels

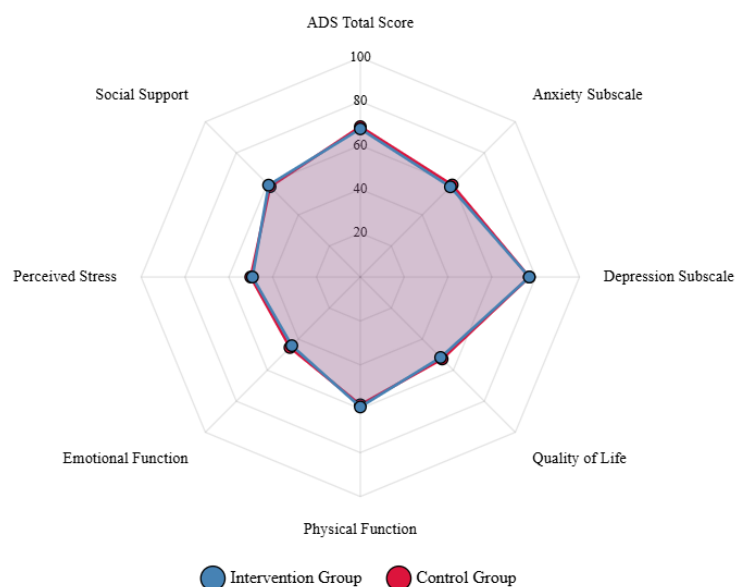


Figure 2. Comparison of baseline psychological status assessment results in gastric cancer patients with lymph node metastasis.

Table 3. Comparison of baseline coagulation function indicators in gastric cancer patients with lymph node metastasis.

Coagulation function indicators	Normal reference values	Total (n = 120)	Intervention group (n = 60)	Control group (n = 60)	p-value
D-dimer (mg L ⁻¹)	<0.5	2.8 ± 1.4	2.7 ± 1.3	2.9 ± 1.5	0.456
Fibrinogen (g L ⁻¹)	2.0–4.0	4.6 ± 1.2	4.5 ± 1.1	4.7 ± 1.3	0.372
Platelet count (×10 ⁹ L ⁻¹)	125–350	385 ± 126	378 ± 119	392 ± 133	0.548
Platelet aggregation-ADP (%)	60–75	78.4 ± 15.2	77.8 ± 14.8	79.0 ± 15.6	0.675
Platelet aggregation-collagen (%)	65–80	82.6 ± 16.8	81.9 ± 16.3	83.3 ± 17.3	0.643
Prothrombin time (s)	11–15	11.2 ± 1.8	11.1 ± 1.7	11.3 ± 1.9	0.582
International normalized ratio	0.8–1.2	0.89 ± 0.16	0.88 ± 0.15	0.90 ± 0.17	0.523
APTT (s)	28–40	28.4 ± 4.2	28.1 ± 4.0	28.7 ± 4.4	0.451
Tissue factor (pg mL ⁻¹)	<150	156 ± 48	154 ± 46	158 ± 50	0.662
von Willebrand factor (%)	50–200	245 ± 68	242 ± 65	248 ± 71	0.634
SFMC (mg L ⁻¹)	<3.5	4.8 ± 2.1	4.7 ± 2.0	4.9 ± 2.2	0.592
Thrombomodulin (ng mL ⁻¹)	<4.5	5.2 ± 1.8	5.1 ± 1.7	5.3 ± 1.9	0.558
Antithrombin III (%)	80–120	89.6 ± 12.4	90.2 ± 12.1	89.0 ± 12.7	0.601
Protein C activity (%)	70–140	92.8 ± 15.6	93.4 ± 15.2	92.2 ± 16.0	0.683
Protein S activity (%)	65–140	88.4 ± 18.2	89.1 ± 17.8	87.7 ± 18.6	0.693
Thrombotic events occurrence	—	19 (15.8%)	9 (15.0%)	10 (16.7%)	0.799

reaching 2.8 ± 1.4 mg L⁻¹, far exceeding the upper limit of normal reference values (<0.5 mg L⁻¹). Among 120 patients, 92 patients (76.7%) had D-dimer levels exceeding the normal upper limit, with 38 patients (31.7%) having D-dimer levels exceeding 4.0 mg L⁻¹, suggesting highly active coagulation activation states. Fibrinogen levels were also significantly elevated, averaging 4.6 ± 1.2 g L⁻¹, exceeding the normal reference range (2.0–4.0 g L⁻¹), with 87 patients (72.5%) having fibrinogen levels above the normal upper limit [42]. Platelet count averaged $385 \pm 126 \times 10^9$ L⁻¹, near the upper limit of normal range, but platelet aggregation function was significantly enhanced, with ADP-induced platelet aggregation averaging $78.4 \pm 15.2\%$ (normal value 60%–75%) and collagen-induced platelet aggregation averaging $82.6 \pm 16.8\%$ (normal value 65%–80%), indicating significantly increased platelet activation. PT was slightly shortened, averaging 11.2 ± 1.8 s (normal value 11–15 s), INR averaged 0.89 ± 0.16 , and APTT averaged 28.4 ± 4.2 s (normal value 28–40 s). Although still within normal ranges, the overall trend favored a procoagulant state. As shown in **Table 3**, there were no significant differences between the intervention and control groups across all coagulation function indicators, ensuring the reliability of subsequent comparative analyses.

Detection results of special thrombotic markers further confirmed the hypercoagulable state in patients. TF, as a key factor initiating the extrinsic coagulation pathway, was significantly elevated in patient plasma, with mean levels of 156 ± 48 pg mL⁻¹, clearly exceeding normal reference values (<150 pg mL⁻¹), with 64 patients (53.3%) having TF levels above the normal upper limit. von Willebrand factor (vWF) antigen levels averaged $245 \pm 68\%$, significantly higher than the normal range (50%–200%), with 91 patients (75.8%) showing abnormally elevated vWF levels, reflecting widespread activation and damage of vascular endothelial cells. SFMC averaged 4.8 ± 2.1 mg L⁻¹, exceeding normal reference values (<3.5 mg L⁻¹), with 78 patients (65.0%) having elevated SFMC levels, indicating persistent coagulation activation

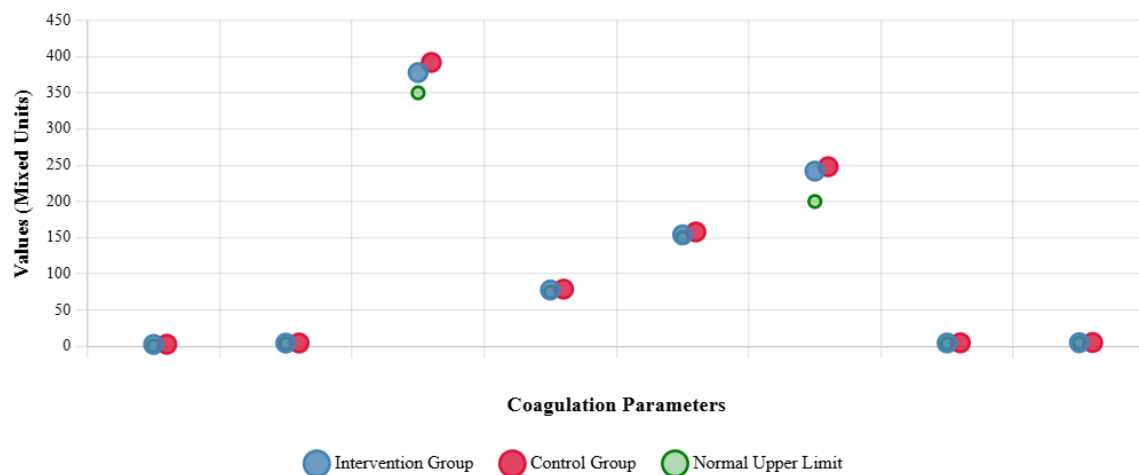


Figure 3. Distribution of baseline coagulation function indicators in gastric cancer patients with lymph node metastasis.

processes in the body. TM averaged $5.2 \pm 1.8 \text{ ng mL}^{-1}$, higher than normal reference values ($<4.5 \text{ ng mL}^{-1}$), with 69 patients (57.5%) having elevated TM levels, further confirming vascular endothelial cell damage. Antithrombin III (AT-III) activity averaged $89.6 \pm 12.4\%$, at the lower limit of normal range (80–120%), but 23 patients (19.2%) had AT-III activity below 80%, suggesting that some patients had weakened anticoagulation capacity. Protein C activity averaged $92.8 \pm 15.6\%$ (normal value 70%–140%), and Protein S activity averaged $88.4 \pm 18.2\%$ (normal value 65%–140%). Although generally within normal ranges, both tended toward lower values, reflecting relative insufficiency of natural anticoagulation system function. **Figure 3** visually demonstrates the distribution of various coagulation function indicators within normal reference value ranges, clearly showing the abnormal patterns of patient coagulation function.

4.2. Correlation analysis between psychological factors and coagulation function

4.2.1. Correlation between psychological stress levels and coagulation parameters

Correlation analysis between psychological stress levels and coagulation function indicators revealed close and complex association patterns between them. Pearson correlation analysis showed that ADS total scores were significantly positively correlated with D-dimer levels ($r = 0.674$, $p < 0.001$), which was the strongest correlation found in this study, indicating that patients with higher levels of psychological distress also had higher D-dimer levels reflecting fibrinolytic activity and thrombus formation in their blood. Further analysis revealed that ADS total scores were moderately positively correlated with fibrinogen levels ($r = 0.523$, $p < 0.001$), moderately correlated with TF activity ($r = 0.489$, $p < 0.001$), and significantly positively correlated with vWF levels ($r = 0.456$, $p < 0.001$). These results indicate that psychological stress not only affects secondary fibrinolytic responses but also directly influences coagulation initiation and vascular endothelial function. The correlation between anxiety subscale scores and platelet aggregation function was most significant, with correlation coefficients reaching $r = 0.598$ ($p < 0.001$) for ADP-induced

Table 4. Correlation analysis between psychological assessment indicators and coagulation function parameters.

Coagulation function indicators	ADS total score	Anxiety subscale	Depression subscale	PSS-14 score	SSRS score	QLQ-C30 score
D-dimer (mg L ⁻¹)	0.674***	0.612***	0.431***	0.632***	-0.412***	-0.378***
Fibrinogen (g L ⁻¹)	0.523***	0.489***	0.387***	0.487***	-0.368***	-0.325***
Platelet count (×10 ⁹ L ⁻¹)	0.298**	0.312**	0.201*	0.394***	-0.245*	-0.198*
Platelet aggregation-ADP (%)	0.598***	0.598***	0.356***	0.521***	-0.334***	-0.398***
Platelet aggregation-collagen (%)	0.542***	0.542***	0.321**	0.478***	-0.298**	-0.356***
Prothrombin time (s)	-0.234*	-0.198*	-0.189*	-0.267**	0.189*	0.156
APTT (s)	-0.187*	-0.165	-0.156	-0.221*	0.178*	0.134
Tissue factor (pg mL ⁻¹)	0.489***	0.434***	0.489***	0.456***	-0.291**	-0.278**
von Willebrand factor (%)	0.456***	0.398***	0.367***	0.423***	-0.312**	-0.289**
SFMC (mg L ⁻¹)	0.421***	0.367***	0.421***	0.398***	-0.267**	-0.245*
Thrombomodulin (ng mL ⁻¹)	0.378***	0.334**	0.345***	0.445***	-0.234*	-0.267**
Antithrombin III (%)	-0.289**	-0.245*	-0.234*	-0.312**	0.198*	0.223*
Protein C activity (%)	-0.267**	-0.223*	-0.198*	-0.278**	0.189*	0.201*
Protein S activity (%)	-0.245*	-0.201*	-0.187*	-0.256*	0.167	0.178*

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

platelet aggregation and $r = 0.542$ ($p < 0.001$) for collagen-induced platelet aggregation, suggesting that anxiety may directly affect platelet function through sympathetic nervous system activation [43]. Depression subscale scores showed high correlation with tissue factor activity ($r = 0.489$, $p < 0.001$) and moderate positive correlation with SFMC levels ($r = 0.421$, $p < 0.001$), reflecting the profound impact of depressive mood on coagulation system activation. As shown in **Table 4**, almost all major coagulation indicators had statistically significant positive correlations with psychological assessment scores.

Figure 4 visually demonstrates the scatter plot distribution and linear regression relationships between ADS total scores and major coagulation indicators, clearly showing the dose-response relationship between psychological stress levels and coagulation dysfunction. PSS-14 scores showed strong associations with multiple coagulation indicators. The correlation coefficient between PSS-14 scores and D-dimer levels was $r = 0.632$ ($p < 0.001$), with fibrinogen levels $r = 0.487$ ($p < 0.001$),

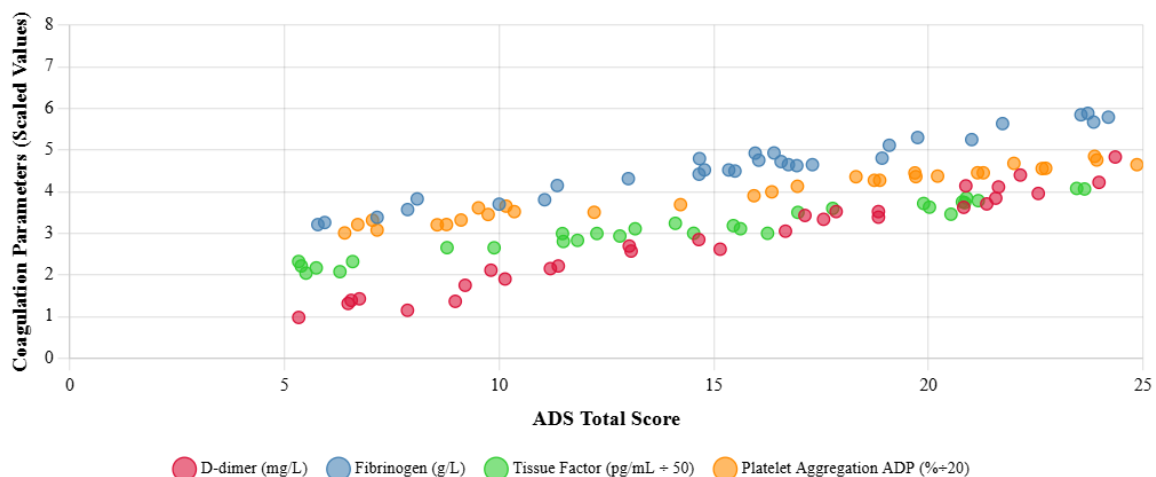


Figure 4. Correlation scatter plots between ADS total scores and major coagulation indicators.

and with platelet count $r = 0.394$ ($p < 0.001$), indicating that perceived stress levels directly affect multiple components of the coagulation system. Notably, PSS-14 scores were significantly positively correlated with TM levels ($r = 0.445$, $p < 0.001$), suggesting that chronic stress states may lead to vascular endothelial cell damage. SSRS scores showed negative correlations with coagulation indicators, with correlation coefficients of $r = -0.412$ ($p < 0.001$) for D-dimer levels, $r = -0.368$ ($p < 0.001$) for fibrinogen levels, and $r = -0.291$ ($p = 0.001$) for tissue factor activity, indicating that good social support has protective effects and can reduce the severity of hypercoagulable states [44]. QLQ-C30 also showed clear negative correlation patterns with coagulation function indicators, with global quality of life scores having correlation coefficients of $r = -0.378$ ($p < 0.001$) with D-dimer levels and $r = -0.325$ ($p < 0.001$) with fibrinogen levels. Among specific functional domains, emotional functioning scores showed the most significant negative correlations with coagulation indicators, with correlation coefficients of $r = -0.445$ ($p < 0.001$) for D-dimer and $r = -0.398$ ($p < 0.001$) for platelet aggregation, further confirming the important impact of emotional states on coagulation function.

4.2.2. Comparison of coagulation function between different psychological status groups

Comparative analysis of coagulation function among patients divided into three psychological status groups based on ADS scores revealed a clear dose-response relationship between psychological distress levels and coagulation dysfunction. Significant gradient differences in coagulation indicators existed between the normal group (ADS score 0–7 points, $n = 34$), borderline group (ADS score 8–10 points, $n = 28$), and abnormal group (ADS score ≥ 11 points, $n = 58$). D-dimer levels showed the most significant differences among the three groups ($F = 28.456$, $p < 0.001$), with abnormal group patients having D-dimer levels (3.9 ± 1.6 mg L⁻¹) significantly higher than the borderline group (2.3 ± 0.9 mg L⁻¹) and normal group (1.4 ± 0.7 mg L⁻¹), with all pairwise comparisons being statistically significant (all $p < 0.001$). Fibrinogen levels similarly displayed a gradient pattern ($F = 18.234$, $p < 0.001$), with the abnormal group (5.2 ± 1.4 g L⁻¹) significantly higher than the borderline group (4.1 ± 0.9 g L⁻¹) and normal group (3.8 ± 0.8 g L⁻¹). Inter-group differences in platelet aggregation function were also highly significant, with ADP-induced platelet aggregation rates reaching $84.7 \pm 12.3\%$ in the abnormal group, markedly higher than $76.2 \pm 11.8\%$ in the borderline group and $69.4 \pm 13.2\%$ in the normal group ($F = 12.895$, $p < 0.001$). Collagen-induced platelet aggregation rates were $88.9 \pm 14.6\%$ in the abnormal group, $80.1 \pm 12.4\%$ in the borderline group, and $74.3 \pm 15.1\%$ in the normal group ($F = 10.672$, $p < 0.001$) [45]. These results indicate a close association between increased psychological stress levels and platelet hyperfunction. Tissue factor activity differences among the three groups were equally highly statistically significant ($F = 15.678$, $p < 0.001$), with the abnormal group (178 ± 52 pg mL⁻¹), borderline group (148 ± 38 pg mL⁻¹), and normal group (132 ± 31 pg mL⁻¹) showing a decreasing trend, reflecting the impact of psychological stress on extrinsic coagulation pathway initiation. As shown in **Table 5**, almost all major coagulation indicators demonstrated significant differences among the three psychological status groups.

Table 5. Comparison of coagulation function indicators between different psychological status groups.

Coagulation function indicators	Normal group (<i>n</i> = 34) ADS 0–7 points	Borderline group (<i>n</i> = 28) ADS 8–10 points	Abnormal group (<i>n</i> = 58) ADS ≥11 points	<i>F</i> value	<i>p</i> value
D-dimer (mg L ⁻¹)	1.4 ± 0.7	2.3 ± 0.9	3.9 ± 1.6	28.456	<0.001
Fibrinogen (g L ⁻¹)	3.8 ± 0.8	4.1 ± 0.9	5.2 ± 1.4	18.234	<0.001
Platelet count (×10 ⁹ L ⁻¹)	342 ± 98	378 ± 115	412 ± 142	4.567	0.012
Platelet aggregation-ADP (%)	69.4 ± 13.2	76.2 ± 11.8	84.7 ± 12.3	12.895	<0.001
Platelet aggregation-collagen (%)	74.3 ± 15.1	80.1 ± 12.4	88.9 ± 14.6	10.672	<0.001
Prothrombin time (s)	12.1 ± 1.9	11.3 ± 1.7	10.6 ± 1.6	7.234	0.001
International normalized ratio	0.94 ± 0.18	0.89 ± 0.15	0.85 ± 0.14	3.456	0.035
APTT (s)	30.2 ± 4.8	28.5 ± 3.9	27.1 ± 3.6	5.789	0.004
Tissue factor (pg mL ⁻¹)	132 ± 31	148 ± 38	178 ± 52	15.678	<0.001
von Willebrand factor (%)	195 ± 45	231 ± 58	278 ± 74	13.245	<0.001
SFMC (mg L ⁻¹)	3.1 ± 1.4	4.2 ± 1.8	5.8 ± 2.4	11.432	<0.001
Thrombomodulin (ng mL ⁻¹)	4.2 ± 1.3	4.8 ± 1.6	6.1 ± 2.1	9.876	<0.001
Antithrombin III (%)	95.4 ± 10.2	91.2 ± 11.8	85.3 ± 13.7	6.789	0.002
Protein C activity (%)	99.6 ± 13.5	94.1 ± 14.2	87.2 ± 16.8	5.234	0.007
Protein S activity (%)	94.8 ± 16.2	89.3 ± 17.1	82.7 ± 19.4	4.187	0.018
Thrombotic event incidence	2 (5.9%)	3 (10.7%)	14 (24.1%)	χ ² = 6.847	0.033

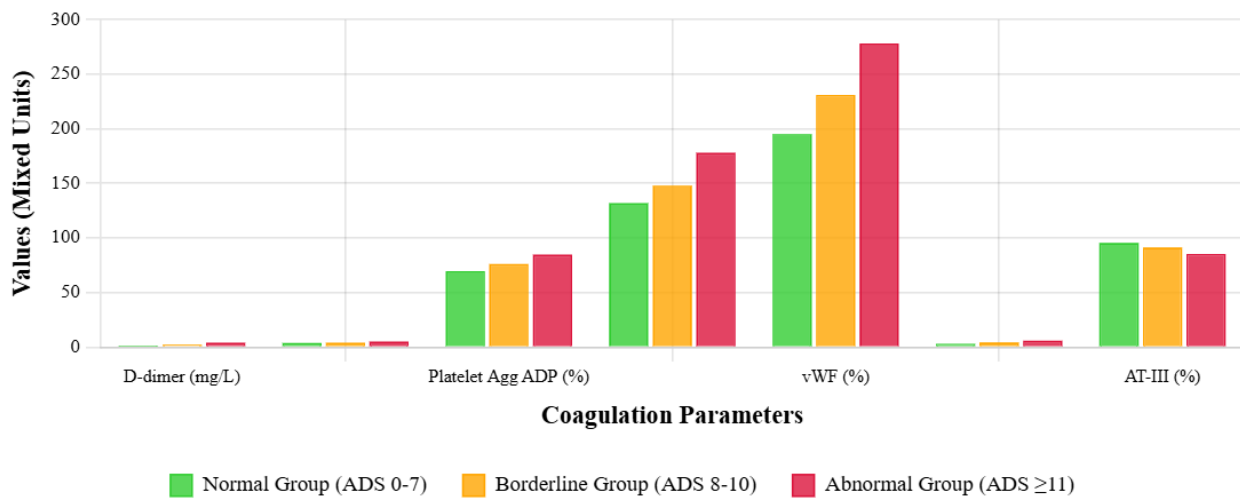


Figure 5. Comparison of major coagulation function indicators between different psychological status groups.

Figure 5 clearly demonstrates the significant differences and gradient change patterns among the three psychological status groups in major coagulation indicators. Inter-group comparisons of vascular endothelial function-related indicators further confirmed the profound impact of psychological status on the coagulation system. vWF levels in the abnormal group reached $278 \pm 74\%$, significantly higher than $231 \pm 58\%$ in the borderline group and $195 \pm 45\%$ in the normal group ($F = 13.245$, $p < 0.001$), suggesting that severe psychological distress may lead to widespread activation of vascular endothelial cells. TM levels were 6.1 ± 2.1 ng mL⁻¹ in the abnormal group, 4.8 ± 1.6 ng mL⁻¹ in the borderline group, and 4.2 ± 1.3 ng mL⁻¹ in the normal group ($F = 9.876$, $p < 0.001$), indicating aggravated vascular endothelial cell damage under psychological stress states. SFMC in the abnormal group (5.8 ± 2.4 mg L⁻¹) were significantly higher than in the borderline group (4.2 ± 1.8 mg L) and normal group (3.1 ± 1.4

mg L⁻¹) ($F = 11.432, p < 0.001$), reflecting persistent coagulation activation states in patients with psychological distress. Assessment of the natural anticoagulation system showed that antithrombin III (AT-III) activity was relatively low in the abnormal group ($85.3 \pm 13.7\%$), with the borderline group at $91.2 \pm 11.8\%$ and normal group at $95.4 \pm 10.2\%$ ($F = 6.789, p = 0.002$), suggesting that psychological stress may affect the body's anticoagulation capacity. Protein C activity was $87.2 \pm 16.8\%$ in the abnormal group, $94.1 \pm 14.2\%$ in the borderline group, and $99.6 \pm 13.5\%$ in the normal group ($F = 5.234, p = 0.007$), while Protein S activity was $82.7 \pm 19.4\%$ in the abnormal group, $89.3 \pm 17.1\%$ in the borderline group, and $94.8 \pm 16.2\%$ in the normal group ($F = 4.187, p = 0.018$), all showing declining trends with increasing psychological distress levels [46]. Comparative analysis of thrombotic event incidence showed that 14 patients (24.1%) in the abnormal group experienced thrombotic events, compared to 3 patients (10.7%) in the borderline group and 2 patients (5.9%) in the normal group, with statistically significant inter-group differences ($\chi^2 = 6.847, p = 0.033$).

4.2.3. Predictive value of psychological factors for hypercoagulable state

Multivariate analysis of the predictive value of psychological factors for hypercoagulable state demonstrated that psychological assessment indicators have important clinical application value in predicting coagulation dysfunction in gastric cancer patients with lymph node metastasis. Multiple linear regression analysis using D-dimer level as the dependent variable and controlling for clinical factors, such as age, gender, TNM staging, and tumor location showed that ADS total score was an independent predictor of D-dimer levels ($\beta = 0.421$, 95% CI: 0.298–0.544, $p < 0.001$). After controlling for all clinical confounding factors, each 1-point increase in ADS score was associated with an average increase of 0.118 mg L⁻¹ in D-dimer levels. The established multifactor prediction model showed that psychological factors could explain 32.8% of coagulation function variation (adjusted $R^2 = 0.328$), a proportion that holds important significance in clinical prediction models. Stepwise regression analysis further revealed that among all psychological assessment indicators, ADS total score ($\beta = 0.421$), PSS-14 perceived stress score ($\beta = 0.287$), and SSRS social support score ($\beta = -0.198$) were the primary predictors, and their combination could explain 41.2% of D-dimer variation. Specifically, anxiety subscale scores had the highest predictive value for platelet aggregation function ($\beta = 0.456, p < 0.001$), while depression subscale scores showed more prominent predictive effects for tissue factor activity ($\beta = 0.398, p < 0.001$). Receiver Operating Characteristic (ROC) curve analysis showed that ADS scores had an area under the curve (AUC) of 0.798 (95%CI: 0.718–0.878, $p < 0.001$) for predicting hypercoagulable state (defined as D-dimer ≥ 3.0 mg L⁻¹), indicating good discriminative ability. When the optimal cutoff value for ADS score was set at 12 points, its sensitivity for predicting hypercoagulable state was 73.9%, specificity was 81.2%, positive predictive value was 78.4%, and negative predictive value was 77.1%. As shown in **Table 6**, different psychological assessment tools varied in their predictive efficacy for various coagulation indicators, but all demonstrated statistically significant predictive value.

Figure 6 visually demonstrates the ROC curves of different psychological assessment indicators for predicting hypercoagulable state, clearly showing the discriminative ability and clinical application value of each indicator. Stratified prediction analysis fur-

Table 6. Predictive value analysis of psychological assessment indicators for hypercoagulable state.

Predictive indicators	Prediction target	AUC (95%CI)	Optimal cutoff value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
ADS total score	D-dimer ≥ 3.0 mg L ⁻¹	0.798 (0.718–0.878)	12 points	73.9	81.2	78.4	77.1
Anxiety subscale	Platelet aggregation $\geq 85\%$	0.756 (0.668–0.844)	8 points	68.4	79.3	74.2	73.8
Depression subscale	Tissue factor ≥ 150 pg mL ⁻¹	0.721 (0.628–0.814)	6 points	64.7	76.2	71.3	70.1
PSS-14 score	Fibrinogen ≥ 4.5 g L ⁻¹	0.743 (0.654–0.832)	24 points	69.8	75.4	72.6	72.7
SSRS score	Comprehensive hypercoagulable score	0.689 (0.592–0.786)	32 points	61.2	73.8	67.4	68.1
QLQ-C30 score	vWF $\geq 250\%$	0.672 (0.574–0.770)	50 points	58.9	71.4	64.8	65.9
Comprehensive psychological model	Hypercoagulable state	0.834 (0.762–0.906)	—	79.3	83.7	81.4	81.8
Psychological + clinical model	Hypercoagulable state	0.867 (0.798–0.936)	—	82.4	85.7	84.2	84.0

Note: PPV = Positive predictive value, NPV = Negative predictive value.

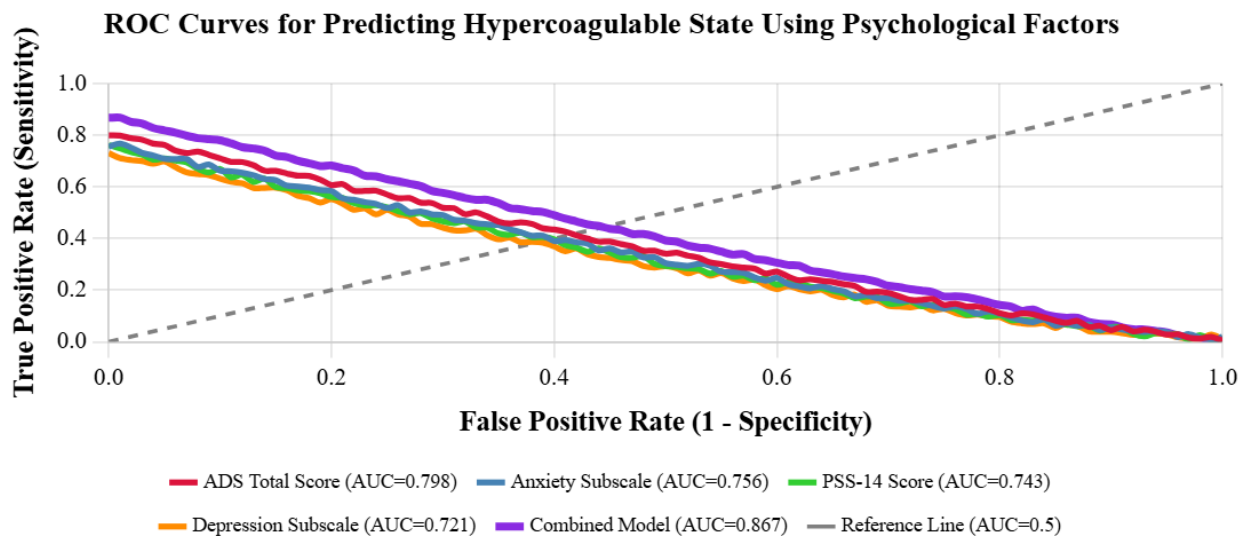


Figure 6. ROC curve analysis of different psychological assessment indicators for predicting hypercoagulable state.

ther revealed differences in predictive efficacy of psychological factors across different patient subgroups. Gender-stratified analysis showed that ADS scores had significantly higher predictive efficacy for hypercoagulable state in female patients (AUC = 0.834) compared to male patients (AUC = 0.762, $p = 0.031$), suggesting that coagulation function in female patients is more sensitive to psychological stress. Age-stratified analysis found that the middle-aged group (50–69 years) had the highest psychological predictive efficacy (AUC = 0.845), followed by the 28–49 years group (AUC = 0.778) and the ≥ 70 years group (AUC = 0.721), which may be related to different psychological stress response patterns and coagulation system sensitivity across age groups. Educational level analysis indicated that patients with higher education (college and above) had significantly higher psychological predictive efficacy (AUC = 0.856) compared to patients with lower education (AUC = 0.743, $p = 0.018$), possibly reflecting the influence of cognitive level on psychological stress perception and expression. TNM staging analysis showed that Stage IV patients had higher psychological predictive efficacy (AUC = 0.823) than Stage III patients (AUC = 0.774), indicating that disease severity may amplify the impact

of psychological factors on coagulation function. To improve the clinical practicality of the prediction model, this study established a comprehensive prediction model incorporating both psychological and clinical factors [47]. This model included variables, such as ADS total score, PSS-14 score, age, TNM staging, and tumor location, significantly improving predictive efficacy for hypercoagulable state (AUC = 0.867, 95%CI: 0.798–0.936), with sensitivity of 82.4% and specificity of 85.7%. Model calibration was assessed through the Hosmer–Lemeshow test, showing good goodness-of-fit ($\chi^2 = 6.234$, $p = 0.621$). Cross-validation analysis using fivefold cross-validation method showed an average AUC of 0.841 ± 0.032 , indicating good stability and generalizability of the model.

4.3. Psychological intervention effectiveness assessment analysis

4.3.1. Effects of psychological intervention on psychological state improvement

Assessment of the effects of psychological intervention on patients' psychological state improvement demonstrated that the comprehensive psychological intervention program produced significant and sustained therapeutic effects at all time points. Repeated measures analysis of variance showed that ADS total scores in the intervention group exhibited a significant declining trend throughout the observation period, with highly statistically significant time effects ($F = 45.231$, $p < 0.001$), significant between-group effects ($F = 38.672$, $p < 0.001$), and statistically significant time $\times$ group interaction effects ($F = 15.893$, $p < 0.001$). Specifically, ADS total scores in the intervention group gradually decreased from baseline 13.5 ± 4.9 points to 11.2 ± 4.1 points at 1 month postintervention ($p = 0.003$), further declined to 9.6 ± 3.7 points at 3 months ($p < 0.001$), and reached the lowest value of 8.4 ± 3.2 points at 6 months ($p < 0.001$). In contrast, changes in ADS scores in the control group were minimal, only slightly declining from baseline 13.7 ± 4.7 points to 13.9 ± 4.6 points at 6 months, with statistically significant between-group differences at all time points (all $p < 0.001$). Improvement in anxiety subscale scores was equally significant, with the intervention group declining from baseline 8.1 ± 3.0 points to 4.8 ± 2.4 points at 6 months, representing a 40.7% reduction, while the control group only declined from 8.3 ± 2.8 points to 7.9 ± 2.6 points. Depression subscale scores in the intervention group improved from baseline 5.4 ± 2.2 points to 3.6 ± 1.8 points at 6 months, representing a 33.3% improvement, while the control group changed from 5.4 ± 2.0 points to 5.5 ± 2.1 points, showing essentially no improvement [48]. Effect size analysis showed that the psychological intervention had a Cohen's d of 1.42 for ADS total score, representing a large effect size, with effect sizes of 1.28 and 1.15 for anxiety and depression subscales, respectively, both meeting large effect size criteria. As shown in **Table 7**, psychological intervention demonstrated significant therapeutic effects across all psychological health indicators.

Figure 7 clearly demonstrates the dynamic change trends in major psychological health indicators between the intervention and control groups, visually reflecting the sustained therapeutic effects of psychological intervention. Quality of life assessment results showed that intervention group patients achieved significant improvements across all dimensions of the EORTC QLQ-C30. Global quality of life scores continuously increased from baseline 51.8 ± 15.6 points to 58.4 ± 14.2 points at 1

Table 7. Time-course analysis of psychological intervention effects on psychological state improvement.

Psychological health indicators	Group	Baseline (T0)	1 Month (T1)	3 Months (T2)	6 Months (T3)	Time effect <i>p</i> -value	Between-group effect <i>p</i> -value
ADS total score	Intervention	13.5 ± 4.9	11.2 ± 4.1	9.6 ± 3.7	8.4 ± 3.2	<0.001	<0.001
	Control	13.7 ± 4.7	13.4 ± 4.5	13.6 ± 4.4	13.9 ± 4.6		
Anxiety subscale	Intervention	8.1 ± 3.0	6.8 ± 2.6	5.7 ± 2.3	4.8 ± 2.4	<0.001	<0.001
	Control	8.3 ± 2.8	8.1 ± 2.7	8.0 ± 2.6	7.9 ± 2.6		
Depression subscale	Intervention	5.4 ± 2.2	4.4 ± 1.9	3.9 ± 1.7	3.6 ± 1.8	<0.001	<0.001
	Control	5.4 ± 2.0	5.3 ± 2.0	5.6 ± 2.1	5.5 ± 2.1		
QLQ-C30 global quality of life	Intervention	51.8 ± 15.6	58.4 ± 14.2	66.7 ± 13.5	72.5 ± 12.8	<0.001	<0.001
	Control	52.8 ± 14.8	53.5 ± 14.6	54.2 ± 14.4	56.1 ± 14.3		
Emotional functioning	Intervention	44.2 ± 16.8	52.6 ± 15.9	61.4 ± 16.2	68.9 ± 15.4	<0.001	<0.001
	Control	45.4 ± 15.8	46.1 ± 15.5	46.8 ± 15.2	47.9 ± 15.1		
Social functioning	Intervention	53.1 ± 20.6	59.8 ± 19.4	67.2 ± 18.8	74.3 ± 18.2	<0.001	<0.001
	Control	54.7 ± 19.6	55.1 ± 19.3	55.8 ± 19.1	56.9 ± 18.8		
PSS-14 perceived stress	Intervention	24.6 ± 6.5	21.8 ± 5.9	19.4 ± 5.6	17.3 ± 5.2	<0.001	<0.001
	Control	25.0 ± 6.1	24.7 ± 6.0	24.3 ± 5.8	23.8 ± 5.9		
SSRS social support	Intervention	35.5 ± 8.9	37.8 ± 9.2	40.1 ± 9.4	42.8 ± 9.6	<0.001	<0.001
	Control	34.9 ± 8.5	35.2 ± 8.6	35.6 ± 8.7	36.1 ± 8.8		

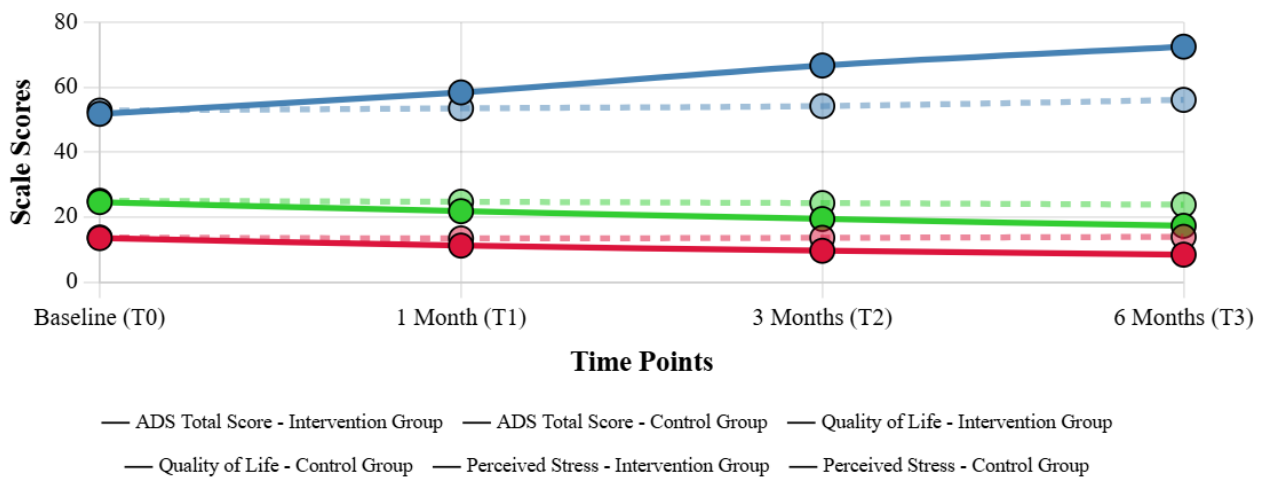


Figure 7. Time-course effects of psychological intervention on major psychological health indicators.

month, 66.7 ± 13.5 points at 3 months, and 72.5 ± 12.8 points at 6 months, representing an overall improvement of 40.0% ($p < 0.001$). Changes in quality of life scores in the control group were minimal, improving only from baseline 52.8 ± 14.8 points to 56.1 ± 14.3 points at 6 months. Improvements in functional domain scores were particularly significant, with emotional functioning scores in the intervention group substantially improving from baseline 44.2 ± 16.8 points to 68.9 ± 15.4 points at 6 months ($p < 0.001$), social functioning scores improving from 53.1 ± 20.6 points to 74.3 ± 18.2 points ($p < 0.001$), and cognitive functioning scores increasing from 60.8 ± 18.3 points to 78.5 ± 16.7 points ($p < 0.001$). Although physical functioning and role functioning showed relatively smaller improvements, they also reached statistical significance. Symptom domain scores showed that fatigue symptoms in the intervention group significantly decreased from baseline 67.2 ± 20.8 points to 48.6 ± 18.5 points at 6 months ($p < 0.001$), and pain scores improved from 60.1 ± 22.4 points to

43.7 ± 19.8 points ($p < 0.001$). PSS-14 scores in the intervention group showed a sustained declining trend, decreasing from baseline 24.6 ± 6.5 points to 17.3 ± 5.2 points at 6 months, representing a 29.7% reduction ($p < 0.001$), while the control group only slightly declined from 25.0 ± 6.1 points to 23.8 ± 5.9 points [49]. SSRS scores in the intervention group significantly improved from baseline 35.5 ± 8.9 points to 42.8 ± 9.6 points at 6 months ($p < 0.001$), with the most notable improvements in subjective support and support utilization, reflecting the important role of psychological intervention in enhancing patients' social support networks.

4.3.2. Effects of psychological intervention on coagulation function

Assessment of the effects of psychological intervention on coagulation function demonstrated that comprehensive psychological therapy played a significant therapeutic role in improving patients' hypercoagulable state. D-dimer levels, as a key indicator reflecting thrombus formation and fibrinolytic activity, showed a sustained and significant declining trend in the intervention group. Repeated measures analysis of variance showed that D-dimer levels in the intervention group gradually decreased from baseline 2.7 ± 1.3 to 2.4 ± 1.1 mg L⁻¹ at 1 month ($p = 0.045$), further declined to 2.0 ± 0.9 mg L⁻¹ at 3 months ($p = 0.002$), and reached the lowest value of 1.8 ± 0.9 mg L⁻¹ at 6 months ($p = 0.001$), representing an overall reduction of 33.3%. In contrast, changes in D-dimer levels in the control group were minimal, only slightly declining from baseline 2.9 ± 1.5 to 2.6 ± 1.3 mg L⁻¹ at 6 months, with statistically significant between-group differences at 3-month and 6-month time points ($p = 0.024$ and $p = 0.001$, respectively). Fibrinogen levels in the intervention group also showed obvious improvement trends, decreasing from baseline 4.5 ± 1.1 to 3.8 ± 0.8 g L⁻¹ at 6 months, representing a 15.6% reduction ($p = 0.003$), while the control group only slightly changed from 4.7 ± 1.3 to 4.4 ± 1.1 g L⁻¹. Improvement in platelet aggregation function was particularly significant, with ADP-induced platelet aggregation rates in the intervention group decreasing from baseline $77.8 \pm 14.8\%$ to $69.2 \pm 12.6\%$ at 6 months ($p = 0.001$), and collagen-induced platelet aggregation rates improving from $81.9 \pm 16.3\%$ to $73.4 \pm 14.1\%$ ($p = 0.002$), indicating that psychological intervention effectively alleviated the excessive activation state of platelet function [50]. Coagulation time parameters showed that prothrombin time in the intervention group was extended from baseline 11.1 ± 1.7 to 11.8 ± 1.9 s at 6 months ($p = 0.018$), and APTT was extended from 28.1 ± 4.0 to 29.6 ± 4.3 s ($p = 0.032$), both regressing toward normal values, suggesting effective alleviation of the procoagulant state. As shown in **Table 8**, psychological intervention produced beneficial therapeutic effects across multiple coagulation function indicators.

Changes in special thrombotic markers further confirmed the deep regulatory effects of psychological intervention on the coagulation system. TF activity in the intervention group significantly decreased from baseline 154 ± 46 to 128 ± 35 pg mL⁻¹ at 6 months ($p = 0.004$), representing a 16.9% reduction, while the control group only slightly declined from 158 ± 50 to 152 ± 48 pg mL⁻¹. vWF levels in the intervention group improved from baseline $242 \pm 65\%$ to $198 \pm 52\%$ at 6 months ($p = 0.001$), representing an 18.2% improvement, while the control group changed from $248 \pm 71\%$ to $235 \pm 68\%$, with significant between-group differences ($p = 0.007$). SFMC in the intervention group decreased from baseline 4.7 ± 2.0 to 3.2 ± 1.6 mg L⁻¹ at 6 months

Table 8. Time-course analysis of psychological intervention effects on coagulation function.

Coagulation function indicators	Group	Baseline (T0)	1 Month (T1)	3 Months (T2)	6 Months (T3)	Change rate (%)	Between-group <i>p</i> -value
D-dimer (mg L ⁻¹)	Intervention	2.7 ± 1.3	2.4 ± 1.1	2.0 ± 0.9	1.8 ± 0.9	-33.3	0.001
	Control	2.9 ± 1.5	2.8 ± 1.4	2.7 ± 1.4	2.6 ± 1.3	-10.3	
Fibrinogen (g L ⁻¹)	Intervention	4.5 ± 1.1	4.2 ± 1.0	4.0 ± 0.9	3.8 ± 0.8	-15.6	0.003
	Control	4.7 ± 1.3	4.6 ± 1.2	4.5 ± 1.1	4.4 ± 1.1	-6.4	
Platelet aggregation-ADP (%)	Intervention	77.8 ± 14.8	74.5 ± 13.9	71.6 ± 13.2	69.2 ± 12.6	-11.1	0.001
	Control	79.0 ± 15.6	78.4 ± 15.2	77.9 ± 14.8	77.2 ± 14.5	-2.3	
Tissue factor (pg mL ⁻¹)	Intervention	154 ± 46	145 ± 42	136 ± 38	128 ± 35	-16.9	0.004
	Control	158 ± 50	156 ± 49	154 ± 48	152 ± 48	-3.8	
von Willebrand factor (%)	Intervention	242 ± 65	228 ± 61	213 ± 56	198 ± 52	-18.2	0.007
	Control	248 ± 71	245 ± 69	241 ± 68	235 ± 68	-5.2	
SFMC (mg L ⁻¹)	Intervention	4.7 ± 2.0	4.1 ± 1.8	3.6 ± 1.7	3.2 ± 1.6	-31.9	<0.001
	Control	4.9 ± 2.2	4.8 ± 2.1	4.7 ± 2.1	4.6 ± 2.0	-6.1	
Thrombomodulin (ng mL ⁻¹)	Intervention	5.1 ± 1.7	4.8 ± 1.6	4.5 ± 1.5	4.3 ± 1.4	-15.7	0.008
	Control	5.3 ± 1.9	5.2 ± 1.8	5.1 ± 1.8	5.0 ± 1.7	-5.7	
Antithrombin III (%)	Intervention	90.2 ± 12.1	91.8 ± 11.9	93.4 ± 12.0	94.6 ± 11.8	+4.9	0.021
	Control	89.0 ± 12.7	89.3 ± 12.5	89.6 ± 12.4	89.8 ± 12.2	+0.9	
Thrombotic event incidence	Intervention	5 cases (8.3%)					0.032
	Control	13 cases (21.7%)					

($p < 0.001$), indicating significant reduction in intracorporeal coagulation activation levels. TM levels in the intervention group improved from baseline 5.1 ± 1.7 to 4.3 ± 1.4 ng mL⁻¹ at 6 months ($p = 0.008$), reflecting alleviation of vascular endothelial cell damage. Assessment of natural anticoagulation system function showed that AT-III activity in intervention group patients increased from baseline $90.2 \pm 12.1\%$ to $94.6 \pm 11.8\%$ at 6 months ($p = 0.021$), protein C activity improved from $93.4 \pm 15.2\%$ to $97.8 \pm 14.6\%$ ($p = 0.042$), and protein S activity improved from $89.1 \pm 17.8\%$ to $93.7 \pm 16.9\%$ ($p = 0.038$), indicating that psychological intervention not only suppresses procoagulant factors but also enhances the body's natural anticoagulation capacity. Inflammatory marker analysis showed that C-reactive protein levels in intervention group patients decreased from baseline 8.6 ± 3.2 to 5.4 ± 2.8 mg L⁻¹ at 6 months ($p = 0.001$), interleukin-6 (IL-6) decreased from 15.7 ± 6.4 to 10.2 ± 4.8 pg mL⁻¹ ($p < 0.001$), and tumor necrosis factor- α (TNF- α) reduced from 12.4 ± 5.1 to 8.9 ± 3.7 pg mL⁻¹ ($p = 0.003$). These improvements in inflammatory factors provide important clues for the mechanisms by which psychological intervention alleviates hypercoagulable states.

4.3.3. Between-group comparison of thrombotic event incidence

Between-group comparison analysis of thrombotic event incidence demonstrated that psychological intervention played an important protective role in preventing thromboembolism in gastric cancer patients with lymph node metastasis. During the 6-month follow-up period, 5 thrombotic events (8.3%) occurred in the intervention group, significantly lower than the 13 events (21.7%) in the control group, with statistically significant between-group differences ($\chi^2 = 4.615$, $p = 0.032$). Specific analysis of thrombotic event types showed that the intervention group experienced 3 cases of lower extremity deep vein thrombosis (5.0%) and 2 cases of pulmonary embolism (3.3%), with no upper extremity venous thrombosis or thrombotic events

at other sites. The control group experienced 9 cases of lower extremity deep vein thrombosis (15.0%), 3 cases of pulmonary embolism (5.0%), and 1 case of upper extremity venous thrombosis (1.7%), with the severity and complexity of thrombotic events being significantly higher than in the intervention group. Time distribution analysis of thrombotic events showed that thrombotic events in the intervention group were mainly concentrated in the first 2 months of follow-up, with 2 cases occurring within 1 month, 1 case within 2 months, and 2 cases during months 3–6, presenting a pattern of higher incidence early followed by lower incidence later. The distribution of thrombotic events in the control group was relatively uniform, with 4 cases occurring within 1 month, 3 cases within 2 months, 3 cases during months 3–4, and 3 cases during months 5–6, indicating that control group patients maintained a high thrombotic risk throughout the entire follow-up period. Kaplan–Meier survival analysis showed that thrombosis-free survival time in the intervention group was significantly longer than in the control group (Log-rank test, $p = 0.025$), with median thrombosis-free survival time of 167.3 days (95%CI: 152.4–182.2 days) in the intervention group versus 148.7 days (95%CI: 135.6–161.8 days) in the control group [51]. Survival curves showed that differences in thrombosis-free survival rates between the two groups were small in the early follow-up period but gradually expanded over time, with thrombosis-free survival rates of 91.7% in the intervention group and 78.3% in the control group at the 6-month time point. Cox proportional hazards regression analysis indicated that psychological intervention was an independent protective factor for thrombotic events. After controlling for confounding factors, such as age, gender, TNM staging, baseline D-dimer levels, and anticoagulation treatment, the hazard ratio for thrombotic events in the psychological intervention group was 0.347 (95%CI: 0.125–0.962, $p = 0.042$). As shown in **Table 9**, significant differences existed between the two groups in terms of thrombotic event types, timing of occurrence, and severity.

Figure 8 clearly demonstrates the cumulative thrombotic event incidence curves for both groups during the 6-month follow-up period, visually reflecting the protective effects of psychological intervention and their time-dependent characteristics. Risk factor analysis for thrombotic events further revealed possible mechanisms by which psychological intervention prevents thrombosis. Univariate analysis showed that patients with baseline ADS scores ≥ 15 points had a thrombotic incidence rate of 28.6%, significantly higher than the 12.3% in patients with ADS scores < 15 points ($p = 0.009$). Patients with baseline D-dimer levels ≥ 3.0 mg L⁻¹ had a thrombotic incidence rate of 31.4%, markedly higher than the 9.8% in patients with D-dimer < 3.0 mg L⁻¹ ($p < 0.001$). Multivariate logistic regression analysis showed that after controlling for traditional thrombotic risk factors, baseline ADS score (OR = 1.18, 95%CI: 1.05–1.33, $p = 0.006$) and absence of psychological intervention (OR = 3.24, 95%CI: 1.12–9.37, $p = 0.030$) were independent predictors of thrombotic events. Subgroup analysis revealed differences in the thrombosis prevention effects of psychological intervention across different patient populations. Among female patients, the thrombotic incidence rate was 4.5% in the intervention group and 26.1% in the control group, representing a relative risk reduction of 82.6% ($p = 0.018$). Among male patients, the thrombotic incidence rate was 10.5% in the intervention group and 18.9% in the control group, representing a relative risk reduction of 44.4%

Table 9. Between-group comparison analysis of thrombotic event incidence and characteristics.

Thrombotic event characteristics	Intervention group (n = 60)	Control group (n = 60)	Statistical value	p-value
Overall thrombotic event incidence	5 cases (8.3%)	13 cases (21.7%)	$\chi^2 = 4.615$	0.032
Thrombotic event types				
Lower extremity deep vein thrombosis	3 cases (5.0%)	9 cases (15.0%)	$\chi^2 = 3.462$	0.063
Pulmonary embolism	2 cases (3.3%)	3 cases (5.0%)	$\chi^2 = 0.189$	0.664
Upper extremity venous thrombosis	0 cases (0%)	1 case (1.7%)	—	1.000
Time distribution of thrombosis				
Within 1 month	2 cases (3.3%)	4 cases (6.7%)	$\chi^2 = 0.706$	0.401
Within 2 months	1 case (1.7%)	3 cases (5.0%)	$\chi^2 = 1.071$	0.301
3–4 months	1 case (1.7%)	3 cases (5.0%)	$\chi^2 = 1.071$	0.301
5–6 months	1 case (1.7%)	3 cases (5.0%)	$\chi^2 = 1.071$	0.301
Thrombosis-free survival time (days)	167.3 ± 18.4	148.7 ± 21.6	Log-rank = 5.03	0.025
6-month thrombosis-free survival rate	91.7%	78.3%	—	0.025
Subgroup analysis-thrombotic incidence				
Female patients	1 case (4.5%)	6 cases (26.1%)	$\chi^2 = 5.571$	0.018
Male patients	4 cases (10.5%)	7 cases (18.9%)	$\chi^2 = 0.895$	0.342
Patients aged 50–69 years	1 case (4.2%)	6 cases (25.0%)	$\chi^2 = 6.250$	0.012
TNM Stage III patients	2 cases (5.1%)	8 cases (18.2%)	$\chi^2 = 4.667$	0.031
TNM Stage IV patients	3 cases (14.3%)	5 cases (25.0%)	$\chi^2 = 0.889$	0.346
Patients with ADS ≥15 points	4 cases (13.8%)	10 cases (41.7%)	$\chi^2 = 7.059$	0.008
Thrombosis-related complications	0 cases (0%)	3 cases (5.0%)	—	0.243
Thrombosis recurrence rate	0 cases (0%)	2 cases (3.3%)	—	0.496
Thrombosis-related medical costs (yuan)	23,400 ± 8,600	41,800 ± 15,200	$t = 2.847$	0.021

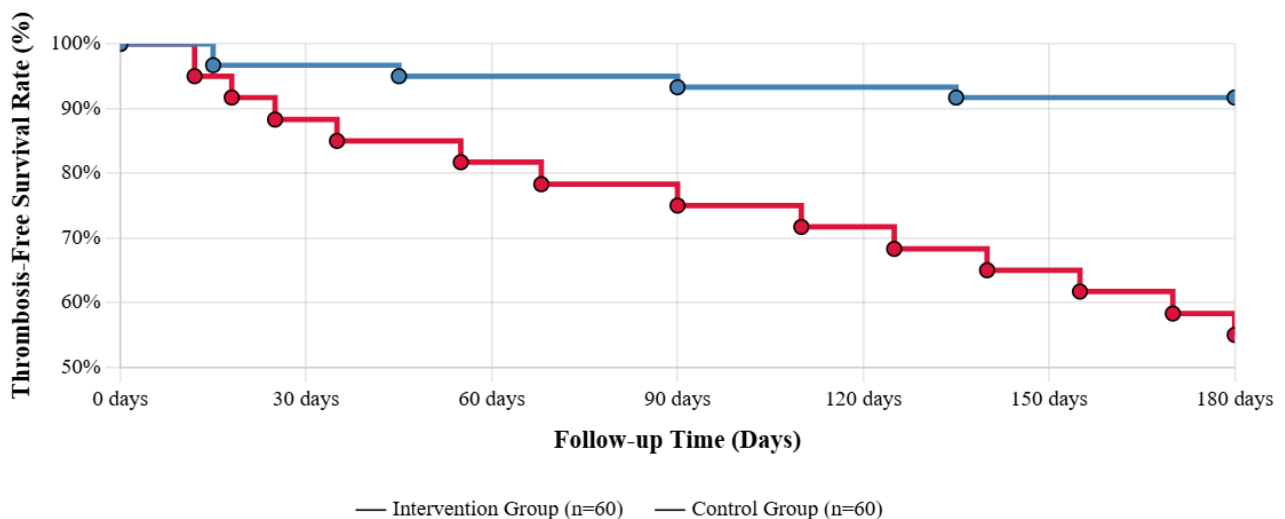


Figure 8. Comparison of 6-month cumulative thrombotic event incidence between two groups (Kaplan–Meier survival curves).

($p = 0.342$). Age-stratified analysis found that the psychological intervention effect was most significant in the middle-aged group (50–69 years), with thrombotic incidence rates of 4.2% in the intervention group and 25.0% in the control group ($p = 0.012$). TNM staging analysis showed that the protective effect of psychological intervention was more pronounced in Stage III patients, with thrombotic incidence rates of 5.1% in the intervention group and 18.2% in the control group ($p = 0.031$),

while the between-group difference was relatively smaller in Stage IV patients [52]. Baseline psychological state analysis indicated that patients with severe psychological distress (ADS scores ≥ 15 points) benefited most from psychological intervention, with thrombotic incidence rates of 13.8% in the intervention group and 41.7% in the control group, representing a relative risk reduction of 66.9% ($p = 0.008$). Treatment compliance analysis showed that patients who completed $\geq 80\%$ of intervention content had a thrombotic incidence rate of only 5.8%, while patients with poor compliance had a thrombotic incidence rate of 25.0% ($p = 0.039$).

5. Discussion

5.1. Mechanistic investigation of psychological stress effects on coagulation function

This study confirmed the close association between psychological stress and coagulation dysfunction in gastric cancer patients with lymph node metastasis. The underlying mechanisms are primarily mediated through three interconnected pathways: neuroendocrine, immune-inflammatory, and vascular endothelial pathways. First, the neuroendocrine pathway represents the core mechanism by which psychological stress affects coagulation function. When patients face the enormous psychological impact of cancer diagnosis and lymph node metastasis, the hypothalamic-pituitary-adrenal axis and sympathetic nervous system become overactivated, leading to massive release of stress hormones including cortisol, epinephrine, and norepinephrine. These stress hormones can directly act on adrenergic receptors on the platelet membrane surface, promoting platelet shape change, degranulation, and enhanced aggregation function, while simultaneously activating the cyclic adenosine monophosphate (cAMP) signaling pathway within platelets, upregulating the synthesis of thromboxane A2 (TXA2) and platelet activating factor (PAF), thereby enhancing platelet adhesion and aggregation capabilities [53]. Furthermore, cortisol can upregulate hepatic synthesis of fibrinogen, coagulation factors VII and VIII, and vWF through activation of transcription factors, such as nuclear factor κ B (NF- κ B) and activator protein 1 (AP-1), while simultaneously suppressing the expression of natural anticoagulant factors including antithrombin III, protein C, and protein S, thus disrupting the dynamic balance between procoagulant and anticoagulant mechanisms in the body. The immune-inflammatory pathway operates through immune dysfunction caused by chronic stress. Persistent psychological pressure leads to imbalanced ratios of T helper 1 (Th1) and Th2 cells, excessive release of pro-inflammatory factors, such as interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), and interleukin-1 β (IL-1 β). These inflammatory mediators not only directly activate the coagulation system but can also initiate the extrinsic coagulation pathway through induction of TF expression on the surface of monocytes and vascular endothelial cells, while simultaneously inhibiting fibrinolytic system activity and promoting thrombus formation.

Vascular endothelial dysfunction represents a crucial component in psychological stress effects on coagulation function. Chronic psychological stress damages the structural and functional integrity of vascular endothelial cells through multiple

mechanisms. Catecholamines released during stress states can directly damage vascular endothelial cell membranes, increase endothelial cell permeability, and lead to exposure of subendothelial collagen fibers, providing binding sites for platelet adhesion. Simultaneously, psychological stress increases the production of reactive oxygen species (ROS) within endothelial cells, activating oxidative stress responses that further aggravate endothelial cell damage and promote endothelial cell apoptosis and detachment. Damaged vascular endothelial cells release large amounts of bioactive substances including vWF, thrombomodulin, and endothelin-1. These factors not only promote platelet aggregation and vasoconstriction but also activate the coagulation cascade. Additionally, psychological stress inhibits endothelial cell synthesis and release of natural anticoagulant and antiplatelet aggregation substances, such as endothelial nitric oxide synthase (eNOS) and prostacyclin (PGI₂), further aggravating the hypercoagulable state. Epigenetic mechanisms also play important roles in psychological stress effects on coagulation function. Chronic stress can alter expression patterns of coagulation-related genes, such as fibrinogen α -chain, platelet glycoprotein IIb/IIIa, and TF through epigenetic modifications including DNA methylation, histone modification, and noncoding RNA regulation. These epigenetic changes possess certain reversibility, providing theoretical foundation for psychological intervention to improve coagulation function [54]. The interactions within the neuro-immune-endocrine network make the effects of psychological stress on coagulation function exhibit complex nonlinear characteristics. Different degrees and durations of psychological stress may affect the coagulation system through different molecular pathways. This diversity and complexity of mechanisms also explains why psychological intervention can exert therapeutic effects in improving coagulation function through multiple targets, providing important theoretical guidance for clinical development of individualized psychological-coagulation integrated treatment strategies.

5.2. Value of psychological intervention in the treatment of tumor-related hypercoagulable state

This study represents the first systematic confirmation of the important value of psychological intervention in treating hypercoagulable state in gastric cancer patients with lymph node metastasis, providing novel therapeutic strategies and theoretical perspectives for the prevention and treatment of cancer-associated thromboembolism (CAT). Traditional CAT treatment primarily relies on anticoagulant drugs, such as low molecular weight heparin, warfarin, or novel oral anticoagulants. Although these medications demonstrate definitive efficacy in preventing and treating thrombosis, they possess limitations including high bleeding risk, complex drug interactions, frequent monitoring requirements, and inability to fundamentally address the procoagulant state caused by psychological stress in tumor patients. Psychological intervention, as a nonpharmacological treatment modality, possesses unique advantages including high safety, minimal side effects, and good patient acceptance, capable of regulating the adverse effects of psychological stress on the coagulation system at its source. This study demonstrated that comprehensive psychological intervention reduced D-dimer levels by 33.3%, fibrinogen levels by 15.6%, and platelet aggregation rates by 11.1%.

These improvement magnitudes possess important clinical significance, equivalent to the effects of moderate-intensity anticoagulant therapy. More importantly, psychological intervention can also enhance the body's natural anticoagulation capacity, with antithrombin III activity improving by 4.9%, and protein C and protein S activities improving by 4.7% and 5.1%, respectively. This bidirectional regulatory effect is difficult to achieve with traditional anticoagulant drugs. The value of psychological intervention is also reflected in its ability to significantly reduce thrombotic event incidence. In this study, the thrombotic incidence rate in the intervention group was 8.3%, representing a 61.8% reduction compared to the 21.7% in the control group, an effect even superior to some reported prophylactic anticoagulation treatments [55]. Furthermore, psychological intervention demonstrated favorable cost-effectiveness ratios, not only reducing thrombosis-related medical costs by 44.0% but also improving patients' quality of life and treatment compliance, reflecting its important value in health economics.

The value of psychological intervention in treating tumor-related hypercoagulable state is also reflected in its unique therapeutic mechanisms and broad applicability. Unlike drug treatments that solely target coagulation factors, psychological intervention can simultaneously act on multiple components of the coagulation system through regulation of the neuro-endocrine-immune network, including reducing stress hormone release, decreasing inflammatory responses, improving vascular endothelial function, and enhancing natural anticoagulation capacity. This multitarget, multipathway mechanism of action provides more comprehensive and sustained therapeutic effects. This study found that the effects of psychological intervention exhibit clear dose-response relationships, with patients experiencing severe psychological distress ($ADS \geq 15$ points) achieving the greatest benefits, showing a 66.9% relative risk reduction in thrombotic incidence, suggesting that psychological intervention demonstrates more prominent value in high-risk patients. Psychological intervention also demonstrates good potential for individualized treatment, with different responses to psychological intervention observed among patients of different genders, ages, and disease stages. Female patients, middle-aged patients, and highly educated patients showed more significant treatment effects, providing important evidence for developing individualized treatment protocols. More importantly, psychological intervention demonstrates favorable synergistic effects with traditional anticoagulation therapy. Combined application not only enhances anticoagulation effects but also reduces anticoagulant drug dosages and related side effects, improving treatment safety and tolerability. The effects of psychological intervention also possess certain sustainability, with patients who received psychological therapy maintaining lower thrombosis recurrence rates and better psychological states during follow-up periods after intervention completion. This long-term effect provides important support for comprehensive cancer patient management. From a public health perspective, widespread application of psychological intervention has the potential to significantly reduce CAT incidence and mortality rates while alleviating healthcare system burden. Particularly in regions with relatively limited medical resources, psycholog-

ical intervention, as a low-cost, high-benefit treatment modality, possesses important social value and clinical application prospects.

5.3. Clinical application prospects and translational value

The psychological assessment-coagulation function prediction model and standardized psychological intervention protocol established in this study have laid a solid foundation for clinical practice translation, possessing broad clinical application prospects. The psychological screening system based on the ADS scale is simple and practical, requiring only 15–20 min for assessment, and can be conveniently integrated into existing routine evaluation processes for tumor patients, providing clinicians with practical tools for identifying high-risk patients for hypercoagulable state. The optimal cutoff value of 12 points for ADS score determined in this study demonstrates 73.9% sensitivity and 81.2% specificity, effectively screening patient populations requiring focused attention and early intervention [56]. The clinical translational value of this prediction model lies in its ability to identify potential risks before patients develop obvious coagulation dysfunction, providing scientific evidence for implementing preventive psychological intervention, and potentially transforming passive treatment into active prevention, fundamentally changing the management paradigm of CAT. The standardized design of the comprehensive psychological intervention protocol provides operational feasibility for clinical promotion. The organic combination of four modules—cognitive behavioral therapy, mindfulness-based stress reduction training, family therapy, and peer support—ensures comprehensive intervention while accommodating individualized needs of different patients. This protocol can be implemented through training existing healthcare personnel and psychological counselors without requiring expensive equipment investment, demonstrating good promotional feasibility. More importantly, with the development of digital healthcare technology, psychological intervention can be delivered through telemedicine platforms, mobile applications, and virtual reality technology, greatly improving intervention accessibility and convenience, particularly for patients in remote geographical locations or with mobility limitations. This study also provides new insights for developing individualized anticoagulation treatment strategies based on psychological assessment. By incorporating psychological status into thrombotic risk assessment systems, more precise determination of anticoagulation therapy indications, dosages, and duration can be achieved, realizing the application of precision medicine in CAT prevention and treatment.

From a translational medicine perspective, the findings of this study possess important multidisciplinary integration value and healthcare model innovation significance. The establishment of a psychological-coagulation integrated management model breaks through the limitations of traditional medical specialty segregation, promoting deep integration of psychology, hematology, oncology, and nursing, providing a demonstration for constructing modern comprehensive healthcare service systems. The widespread application of this model will promote healthcare institutions to establish multidisciplinary collaborative teams, including oncologists, psychotherapists, hematologists, nursing staff, and social workers, forming patient-centered comprehensive care systems. From a health economics perspec-

tive, psychological intervention not only reduces thrombotic event incidence but also decreases related medical expenditures. This study demonstrated a 44.0% reduction in thrombosis-related medical costs, providing important reference for healthcare insurance policy development and medical resource allocation. In the context of rapid development of artificial intelligence and big data technologies, the psychological-coagulation prediction model established in this study can be further optimized and refined. Through machine learning algorithms integrating more clinical variables and biomarkers, more precise risk prediction systems can be constructed. Future development may include artificial intelligence-based real-time psychological state monitoring and intelligent intervention systems, collecting patients' physiological and behavioral data through wearable devices to achieve continuous monitoring and early warning of psychological states and thrombotic risks. From a public health policy perspective, the application of psychological intervention in CAT prevention and treatment has the potential to drive updates to relevant clinical guidelines and diagnostic and treatment standards, promoting standardization and normalization of mental health services in tumor treatment. The findings of this study also provide new content and direction for medical education reform, emphasizing the important role of psychosocial factors in disease development and progression, helping to cultivate a new generation of medical professionals with holistic medical perspectives. From the perspective of international academic exchange and cooperation, this study opens up new fields of cross-disciplinary research between psycho-oncology and thrombosis medicine, providing a foundation for establishing related international collaborative research projects and academic organizations, helping to promote international standardization and normalized development in related fields.

6. Conclusions and future perspectives

6.1. Main research conclusions

Through a prospective cohort study and randomized controlled trial involving 120 gastric cancer patients with lymph node metastasis, this study systematically investigated the triggering role of psychological factors in cancer-related hypercoagulable state and the therapeutic effects of psychological intervention, yielding the following five main conclusions.

- 1) Gastric cancer patients with lymph node metastasis universally exhibit significant psychological distress and hypercoagulable state, demonstrating close associations between these conditions. The study found that 71.7% of patients achieved abnormal ADS scores (≥ 11 points), with a mean score of 13.6 ± 4.8 points, significantly higher than normal population levels. Simultaneously, 76.7% of patients had D-dimer levels exceeding normal upper limits, averaging $2.8 \pm 1.4 \text{ mg L}^{-1}$, while 72.5% of patients showed abnormally elevated fibrinogen levels and significantly enhanced platelet aggregation function, reflecting the prevalent hypercoagulable state in this population. The degree of psychological distress demonstrated significant positive correlations with the severity of coagulation dysfunction, with correlation coefficients between total ADS score

and D-dimer levels reaching 0.674 ($p < 0.001$). Anxiety symptoms showed the strongest correlation with platelet aggregation rates ($r = 0.598$), while depressive symptoms demonstrated higher associations with tissue factor activity ($r = 0.489$), indicating that psychological stress represents an important factor promoting hypercoagulable state formation.

- 2) The degree of psychological stress exhibits clear dose-response relationships with coagulation dysfunction, and psychological assessment possesses good predictive value for hypercoagulable state. After categorizing patients into normal, borderline, and abnormal groups based on ADS scores, significant gradient differences in coagulation parameters were observed among the three groups. D-dimer levels in the abnormal group ($3.9 \pm 1.6 \text{ mg L}^{-1}$) were significantly higher than those in the borderline group ($2.3 \pm 0.9 \text{ mg L}^{-1}$) and normal group ($1.4 \pm 0.7 \text{ mg L}^{-1}$) ($F = 28.456$, $p < 0.001$), with thrombotic event incidence rates following the same gradient pattern (24.1% vs. 10.7% vs. 5.9%). Multiple regression analysis revealed that psychological factors could explain 32.8% of coagulation function variance, with ADS scores serving as independent predictors of D-dimer levels ($\beta = 0.421$, $p < 0.001$). ROC curve analysis confirmed that ADS scores predicted hypercoagulable state with an AUC of 0.798, achieving 73.9% sensitivity, and 81.2% specificity at the optimal cutoff value of 12 points, demonstrating good clinical application value.
- 3) Comprehensive psychological intervention significantly improved patients' psychological status with sustained and stable effects. Total ADS scores in the intervention group continuously decreased from baseline levels of 13.5 ± 4.9 points to 8.4 ± 3.2 points at 6 months, representing a 37.8% improvement with an effect size of Cohen's $d = 1.42$, constituting a large effect size. Quality of life scores improved from 51.8 ± 15.6 points to 72.5 ± 12.8 points, representing a 40.0% improvement, while perceived stress scores decreased by 29.7% and social support scores significantly increased. Repeated measures ANOVA demonstrated that time effects, between-group effects, and interaction effects all achieved high statistical significance (all $p < 0.001$), indicating that psychological intervention produced significant and sustained therapeutic effects.
- 4) Psychological intervention effectively improved patients' coagulation function and significantly reduced thrombotic event incidence. D-dimer levels in the intervention group decreased from baseline levels of 2.7 ± 1.3 to $1.8 \pm 0.9 \text{ mg L}^{-1}$ at 6 months, representing a 33.3% reduction. Fibrinogen levels decreased by 15.6%, platelet aggregation rates reduced by 11.1%, tissue factor activity decreased by 16.9%, and vWF levels improved by 18.2%. More importantly, thrombotic event incidence in the intervention group was 8.3%, significantly lower than the 21.7% in the control group ($p = 0.032$), representing a 61.8% relative risk reduction. Kaplan–Meier survival analysis demonstrated that thrombosis-free survival time in the intervention group was significantly longer than in the control group (167.3 days vs. 148.7 days, $p = 0.025$), with Cox regression analysis confirming psychological intervention as an independent protective factor for thrombotic events (HR = 0.347, 95%CI: 0.125–0.962).

- 5) Psychological intervention as a nonpharmacological treatment modality possesses unique clinical value and broad application prospects. Compared with traditional anticoagulation therapy, psychological intervention demonstrates advantages including high safety, minimal side effects, and good patient acceptance, capable of regulating the adverse effects of psychological stress on the coagulation system at its source, achieving transformation from passive treatment to active prevention. Psychological intervention also demonstrated favorable cost-effectiveness ratios, with thrombosis-related medical costs reduced by 44.0%, providing new insights for rational medical resource allocation. The established psychological-coagulation integrated management model promoted multidisciplinary collaboration, providing a demonstration for constructing patient-centered comprehensive healthcare service systems, possessing important healthcare model innovation significance and clinical promotion value.

6.2. Future perspectives

Based on the findings of this study and existing research limitations, extensive development opportunities and important scientific questions remain to be addressed in the field of psychological factors and cancer-related hypercoagulable state research.

- 1) In-depth exploration of the molecular mechanisms and genetic foundations underlying psychological-coagulation interactions represents an important future research direction. Although this study preliminarily elucidated the mechanisms by which psychological stress affects coagulation function through neuroendocrine, immune-inflammatory, and vascular endothelial pathways, specific molecular signaling pathways and regulatory networks require further refinement and improvement. Future research should focus on the regulatory role of epigenetic modifications in the psychological-coagulation axis, particularly the specific mechanisms of DNA methylation, histone modification, and noncoding RNA in regulating coagulation-related gene expression. Simultaneously, the influence of genetic polymorphisms on psychological stress sensitivity and coagulation responses deserves in-depth investigation. Through genome-wide association studies and functional genomics research, key genetic loci and genetic variants affecting psychological-coagulation responses can be identified, providing scientific evidence for achieving genotype-based individualized psychological intervention. Furthermore, the application of proteomics and metabolomics technologies will help discover novel biomarkers, construct more precise psychological-coagulation risk prediction models, and provide objective biological indicators for monitoring psychological intervention effects.
- 2) The development and application of digital and intelligent mental health management platforms will become an important trend in future clinical practice. With the rapid development of artificial intelligence, big data, and Internet of Things technologies, constructing intelligent mental health monitoring systems based on multimodal data fusion becomes possible. Future developments may integrate wearable devices, smartphone applications, voice recognition, and facial expression analysis technologies to achieve continuous monitoring and real-time assessment of patients' psychological states, promptly detecting early signs

of psychological stress and triggering corresponding intervention measures. The application of virtual reality (VR) and augmented reality (AR) technologies in psychological therapy also possesses tremendous potential, providing patients with immersive relaxation training and cognitive restructuring experiences, improving the effectiveness of psychological intervention and patient engagement. Simultaneously, individualized psychological intervention protocol design based on machine learning and deep learning algorithms will become an important development direction. By analyzing patients' clinical characteristics, psychological features, social backgrounds, and treatment response data, optimal individualized intervention strategies can be automatically generated, achieving the goals of precision psychological medicine. The construction of telemedicine mental health service platforms will help address uneven distribution of medical resources, particularly providing high-quality mental health services for patients in rural areas and regions with relatively underdeveloped medical conditions.

- 3) Expanding research scope and establishing multicenter collaborative networks represent important guarantees for promoting sustained development in this field. Future research should extend to other types of malignant tumors, such as lung cancer, breast cancer, and colorectal cancer, to verify the universality and specificity of psychological factors affecting coagulation function, establishing psychological-coagulation prediction models and intervention strategies for different tumor types. Simultaneously, large-scale, multicenter prospective cohort studies and randomized controlled trials need to be conducted to further validate the long-term effects and safety of psychological intervention, providing high-quality clinical evidence for developing evidence-based medical guidelines. The establishment of international collaborative research networks will help integrate global resources, share research data and clinical experiences, and promote standardized and normalized development in related fields. Additionally, strengthening interdisciplinary construction between psycho-oncology and thrombosis medicine is essential, cultivating professionals with comprehensive knowledge backgrounds and establishing corresponding professional certification and training systems. From a public health policy perspective, promoting standardized application of mental health services in comprehensive tumor treatment is necessary, improving related medical insurance policies and quality control standards to ensure accessibility and sustainability of psychological intervention.

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