Postprint of an Association Study Between Quantified Blood Stasis Syndrome and Clinical Features of Primary Sjögren's Syndrome

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Date: 2025-06-26T17:52:01+00:00

Abstract

Background: Blood stasis syndrome is an important concurrent syndrome of primary Sjögren's syndrome (pSS), yet research on its quantitative characteristics and clinical associations remains insufficient.

Objective: To investigate the quantitative characteristics of blood stasis syndrome in pSS patients and its association with glandular secretory function, imaging features, serological indicators, and risk of systemic involvement.

Methods: This prospective cohort study enrolled 171 patients with suspected pSS who were diagnosed and treated at Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine from July 2022 to January 2024. According to the 2016 American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) classification criteria, patients were divided into the pSS group (n=130) and non-pSS group (n=41). General data including gender, age, clinical manifestations, comorbid autoimmune diseases, other medical history, and medication history were collected. Clinical indicators included: unstimulated salivary flow rate, xerostomia Visual Analogue Scale (VAS) score, salivary gland ultrasonography (SGUS), and labial gland biopsy results. Laboratory indicators included: antinuclear antibody (ANA), anti-Sjögren's syndrome A (SSA)/Ro antibody, IgG, erythrocyte sedimentation rate (ESR), rheumatoid factor, C3/C4, and systemic involvement status. The International Guidelines for the Diagnosis of Blood Stasis Syndrome were used to calculate the blood stasis syndrome score. Differences in general data, clinical indicators, and blood stasis syndrome scores between the two groups were compared. Pearson or Spearman correlation analysis was used to analyze the correlation between blood stasis scores and various clinical indicators. The distribution of high-frequency blood stasis syndrome scores was analyzed.

Results: The pSS group exhibited higher positive rate of blood stasis syndrome, blood stasis syndrome score, xerostomia VAS score, total bilateral SGUS grading, positive rate of labial gland biopsy, positive rate of anti-SSA/Ro antibody, ANA titer, ESR, and IgG level compared with the non-pSS group ($P<0.05$). The unstimulated salivary flow rate in the pSS group was lower than that in the non-pSS group, with statistically significant difference ($P<0.05$). Correlation analysis revealed that in the pSS group, the blood stasis score was positively correlated with xerostomia VAS score ($r=0.520$, $P<0.05$) and total bilateral SGUS grading ($rs=0.492$, $P<0.05$), and negatively correlated with unstimulated salivary flow rate ($r=-0.491$, $P<0.05$). The systemic involvement rate in the moderate-to-severe blood stasis group was higher than that in the mild group ($P<0.05$). Analysis of high-frequency blood stasis items showed that dark purple tongue/sublingual vessel stasis, fixed pain, limb numbness/joint deformity, and pathological mass had relatively high positive rates in blood stasis syndrome differentiation for pSS patients. In salivary gland ultrasonography grading, the blood stasis score in the parotid and submandibular gland grade 3 group was higher than that in lower grading groups, with statistically significant difference ($P<0.05$).

Conclusion: Blood stasis syndrome is widely prevalent in pSS patients, and its severity is closely associated with glandular dysfunction, SGUS imaging abnormalities, and risk of systemic involvement. SGUS can serve as an objective assessment tool for blood stasis syndrome, providing evidence for the Traditional Chinese Medicine theory of "blood stasis causing dryness" and offering theoretical basis and clinical reference for personalized diagnosis and treatment of pSS.

Full Text

Clinical Feature Correlation Analysis of Primary Sjögren's Syndrome Based on Quantitative Assessment of Blood Stasis Syndrome

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Abstract

Background
Blood stasis syndrome represents a significant concurrent condition in primary Sjögren's syndrome (pSS), yet its quantitative characteristics and clinical correlations remain insufficiently explored.

Objective
To investigate the quantitative features of blood stasis syndrome in pSS patients and examine its associations with glandular secretory function, imaging characteristics, serological indicators, and systemic involvement risk.

Methods
This prospective cohort study enrolled 171 patients with suspected pSS treated at Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine, between July 2022 and January 2024. Based on the 2016 ACR/EULAR classification criteria, patients were divided into a pSS group (130 cases) and a non-pSS group (41 cases). General data including gender, age, clinical manifestations, comorbid autoimmune diseases, medical history, and medication history were collected. Clinical indicators comprised unstimulated salivary flow rate, dry mouth visual analog scale (VAS) score, salivary gland ultrasound (SGUS), and labial gland biopsy results. Laboratory indicators included antinuclear antibodies (ANA), anti-SSA/Ro antibodies, IgG, erythrocyte sedimentation rate (ESR), rheumatoid factor, C3/C4, and systemic involvement status. Blood stasis syndrome scores were calculated using the *International Diagnostic Guidelines for Blood Stasis Syndrome*. Intergroup differences in general data, clinical indicators, and blood stasis syndrome scores were compared. Pearson or Spearman correlation analyses were employed to evaluate relationships between blood stasis scores and clinical parameters. The distribution of high-frequency blood stasis syndrome scores was also analyzed.

Results
The pSS group exhibited significantly higher rates of positive blood stasis syndrome, blood stasis syndrome scores, dry mouth VAS scores, bilateral SGUS total grades, positive labial gland biopsy rates, anti-SSA/Ro antibody positivity, ANA titers, ESR, and IgG levels compared to the non-pSS group ($P<0.05$), while unstimulated salivary flow rate was significantly lower ($P<0.05$). Correlation analysis revealed that blood stasis scores in the pSS group were positively correlated with dry mouth VAS scores ($r=0.520$, $P<0.05$) and bilateral SGUS total grades ($rs=0.492$, $P<0.05$), and negatively correlated with unstimulated salivary flow rate ($r=-0.491$, $P<0.05$). The rate of systemic involvement was higher in the moderate-to-severe blood stasis group than in the mild group ($P<0.05$). High-frequency blood stasis item analysis showed that purple-dark tongue/sublingual venous engorgement, fixed pain, limb numbness/joint deformity, and pathological masses had high positive rates in pSS patients. Regarding SGUS grading, blood stasis scores in both parotid and submandibular

gland grade 3 groups were significantly higher than those in lower-grade groups ($P<0.05$).

Conclusion
Blood stasis syndrome is prevalent among pSS patients, and its severity is closely associated with glandular dysfunction, SGUS imaging abnormalities, and systemic involvement risk. SGUS can serve as an objective assessment tool for blood stasis syndrome, supporting the Traditional Chinese Medicine theory of "blood stasis leading to dryness," and providing a theoretical basis and clinical reference for personalized diagnosis and treatment of pSS.

Keywords
Primary Sjögren's syndrome; Blood stasis syndrome; Dryness impediment; Salivary gland ultrasound; Prospective cohort study

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1. Introduction

Primary Sjögren's syndrome (pSS) is a common autoimmune disease characterized by abnormal lymphocyte activation, predominantly affecting women over 50 years old with a prevalence of 0.33%-0.77% in Chinese populations. Salivary and lacrimal glands are the primary target organs, with 98% of patients experiencing dry mouth and/or dry eyes. At least 70% of pSS patients suffer from systemic symptoms affecting the skin, hematological system, nervous system, and lungs. The risk of lymphoma in pSS patients is 8.7-44 times higher than in normal individuals, significantly impacting quality of life and prognosis. Current treatment for Sjögren's syndrome remains challenging, focusing primarily on symptom relief, immune dysregulation control, and disease progression delay, with limited efficacy in reversing glandular secretory function.

In Traditional Chinese Medicine (TCM), pSS belongs to the categories of "dryness impediment" or "dryness syndrome," with traditional theory attributing yin deficiency as the fundamental pathogenesis. However, clinical practice reveals limited efficacy of yin-nourishing approaches alone. The "blood stasis leading to dryness" theory has gained increasing attention, with multiple systematic reviews identifying blood stasis syndrome as a core concurrent condition, occurring at frequencies of 17.0%-30.2%, second only to yin deficiency syndrome, and significantly correlating with disease activity. The *Jin Gui Yao Lue* (Essential Prescriptions from the Golden Cabinet) first documented that "when patients have chest fullness, withered lips, cyanotic tongue, dry mouth with thirst but only desire to rinse without swallowing…this indicates blood stasis," suggesting that blood stasis obstruction and fluid distribution failure constitute key pathogenic mechanisms in dryness impediment formation. Modern research has also identified microcirculatory disturbances and hypercoagulable states as microscopic manifestations of blood stasis in pSS patients. However, previous studies have been limited to qualitative analyses, lacking internationally standardized quantitative tools for blood stasis syndrome, and the dynamic

relationship between blood stasis and glandular damage with immune dysregulation remains unclear.

Salivary gland ultrasound (SGUS) has demonstrated important value in pSS clinical diagnosis and management due to its non-invasive nature and high repeatability. Studies have shown that SGUS can objectively reflect salivary gland inflammatory infiltration and fibrosis by detecting structural destruction features such as hypoechoic areas and heterogeneous hyperplasia, and has been incorporated as a key imaging tool for pSS disease assessment. These microscopic structural changes in glands may have intrinsic associations with the TCM concept of "collateral vessel obstruction" as a microscopic manifestation. However, existing research has focused primarily on correlation analysis, and whether SGUS can serve as an objective marker for blood stasis syndrome differentiation, as well as the quantitative relationship between its grading and glandular functional damage with immune dysregulation, remains to be systematically validated.

This study introduces the quantitative standards from the *International Diagnostic Guidelines for Blood Stasis Syndrome*, combined with SGUS imaging technology, glandular secretory function testing, and immunological indicators, to multi-dimensionally analyze the dynamic associations between blood stasis syndrome and pSS clinical features. We aim to explore the quantitative relationship between blood stasis severity and glandular structural destruction with immune dysregulation, and the value of SGUS grading in TCM micro-differentiation, thereby clarifying the quantitative characteristics and distribution patterns of blood stasis syndrome in pSS and providing modern scientific evidence for the "blood stasis leading to dryness" theory.

2. Methods

2.1 Study Subjects

We prospectively enrolled 171 patients with suspected pSS who visited the Department of Rheumatology and Immunology at Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine, between July 2022 and January 2024. Based on the 2016 ACR/EULAR classification criteria, patients were divided into a pSS group (130 cases) and a non-pSS group (41 cases). The study was approved by the Ethics Committee of Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine (Approval No.: 2023-039), and all patients provided informed consent.

2.1.1 Inclusion Criteria

(1) Presence of at least one chief complaint: daily persistent dry eyes/gritty sensation for $ $3 months, or requiring artificial tears $ $3 times/day; daily persistent dry mouth for $ $3 months requiring repeated water intake to assist swallowing. (2) Age 18-75 years, regardless of gender. (3)

Complete clinical data (including labial gland biopsy, SGUS, unstimulated salivary flow rate, immunological indicators). (4) Voluntary participation with signed informed consent.

2.1.2 Exclusion Criteria

(1) Exclusion of the following conditions through clinical assessment: history of head or neck radiotherapy; active hepatitis B, hepatitis C, or HIV infection; sarcoidosis; amyloidosis; graft-versus-host disease; IgG4-related disease; diabetes. (2) Cases where salivary glands could not be adequately visualized for ultrasound scoring. (3) Patients with incomplete relevant clinical data. (4) Interval between labial gland biopsy and salivary gland ultrasound exceeding 3 months. (5) Patients with malignant tumors. (6) Patients with acute suppurative parotitis, salivary gland tumors, or other salivary gland lesions. (7) Patients with definitive vascular lesions such as coronary heart disease, cerebral infarction, or arterial occlusion. (8) Patients using antiplatelet/anticoagulant drugs (e.g., aspirin, clopidogrel), immunosuppressants, or glucocorticoids within 3 months. (9) Patients with other rheumatic diseases such as rheumatoid arthritis or systemic lupus erythematosus. (10) Patients with severe cardiac, cerebral, or renal diseases. (11) Patients with psychiatric disorders, cognitive dysfunction, or those deemed unsuitable for participation by investigators.

2.2 Measurements

2.2.1 General Data General information including gender, age, clinical manifestations, comorbid autoimmune diseases, medical history, and medication history was extracted from the Weining electronic medical record system of Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine.

2.2.2 Salivary Gland Secretory Function Indicators (1) Unstimulated Whole Salivary Flow Rate (UWSFR) Collection
Subjects were tested between 14:00-17:00 daily. After fasting and avoiding water for 1 hour and resting for 15 minutes, subjects collected oral saliva naturally into a graduated tube while tilting their head down for 15 minutes. The average flow rate was calculated (mL/min). The normal value was defined as $ $1.5 mL/15 min; <1.5 mL/15 min indicated reduced salivary secretory function.

(2) Visual Analogue Scale (VAS) for Dry Mouth
A 0-10 point horizontal scale was used, with patients marking subjective dry mouth severity based on the past week (0: no dry mouth; 10: intolerable dry mouth; $ $4 indicated significant dry mouth).

2.2.3 Imaging Indicators All patients underwent bilateral parotid and submandibular gland ultrasound evaluation by experienced chief ultrasound physicians using a Logiq-E20 color Doppler ultrasound device with probe frequency

8.0-13.0 MHz. Subjects assumed a comfortable supine position without a pillow, fully exposing the cheek and anterior neck regions. The head was turned to the contralateral side when scanning one salivary gland, and slightly extended backward for submandibular gland visualization. Long and short axes of bilateral glands were observed. Two-dimensional ultrasound assessed gland size and internal echogenicity. Optimal images were obtained by adjusting ultrasound parameters and saved to record parotid/submandibular gland grading, parenchymal echo mass size, and presence of abnormal lymph nodes. Physicians were blinded to patient general information, clinical diagnosis, and laboratory results. In cases of inconsistent SGUS grading, a third physician was consulted for final grading. The maximum grade sum for unilateral parotid and submandibular glands was recorded as the unilateral SGUS total grade; the sum of bilateral parotid and submandibular gland grades was recorded as the bilateral SGUS total grade.

SGUS lesion grading followed the OMERACT (Outcome Measures in Rheumatology Clinical Trials) working group grading system: Grade 0: normal; Grade 1: mild heterogeneity; Grade 2: moderate heterogeneity with focal hypoechoic areas; Grade 3: diffuse hypoechoic changes.

2.2.4 Laboratory Examination Indicators (1) Antinuclear Antibodies (ANA)
Detected by indirect immunofluorescence, with titers $ $1:80 considered positive.

(2) Anti-SSA/Ro60 and Anti-SSA/Ro52 Antibodies
Detected by enzyme-linked immunosorbent assay to identify specific antibodies against SSA/Ro antigens.

(3) Immunoglobulin G (IgG)
Measured by immunoturbidimetry, with reference range 7.51-15.60 g/L.

(4) Erythrocyte Sedimentation Rate (ESR)
Measured by the Westergren method after 1 hour of vertical tube standing. Reference range: $ $15 mm/h for males, $ $20 mm/h for females.

(5) Rheumatoid Factor (RF)
Measured by immunoturbidimetry, with <20.0 U/mL defined as negative.

(6) Complement C3/C4
Measured by immunoturbidimetry, with reference ranges: C3 0.9-1.8 g/L, C4 0.1-0.4 g/L.

2.2.5 Pathological Examination Labial Salivary Gland Biopsy (LSGB) was performed under local anesthesia by excising 4 mm^2 of labial gland tissue from the inner lower lip. After formalin fixation and HE staining, lymphocytic infiltration was assessed and focus score calculated as: Focus score = number of lymphocytic foci / glandular tissue area (4 mm^2) × 4. A focus score

$ 1focus/4mm^{2}$ was considered positive, indicating significant lymphocytic infiltration.

2.2.6 Blood Stasis Score Based on the *International Diagnostic Guidelines for Blood Stasis Syndrome* issued by the Professional Committee of Blood Stasis Syndrome, Chinese Association of Integrative Medicine in 2022, a scoring scale was developed comprising 16 items (8 major and 8 minor criteria). Major criteria were assigned 2 points each, minor criteria 1 point each, with a total score $ $2 defined as presence of blood stasis syndrome.

2.3 Statistical Methods

Statistical analysis was performed using SPSS 26.0 software. Normally distributed continuous data were expressed as ($\bar{x}\pm s$) and compared between groups using independent samples t-test. Non-normally distributed continuous data were expressed as M(P_{25}, P_{75}) and compared using Mann-Whitney U test. Categorical data were expressed as frequencies and compared using ^{2} test or Fisher's exact test. Pearson and Spearman correlation analyses were used to examine relationships between parotid gland ultrasound grading and blood stasis scores. Bonferroni correction was applied for multiple comparisons to adjust significance levels. $P<0.05$ was considered statistically significant.

3. Results

3.1 Comparison of Baseline Data Between pSS and Non-pSS Groups

A total of 171 patients with suspected pSS were enrolled, including 12 males (7.02%) and 159 females (92.98%), with a mean age of 52.2$±$13.2 years. The pSS group comprised 130 cases (76.03%) and the non-pSS group 41 cases (23.95%). No significant differences were observed between groups in gender, age, C3, C4, hypocomplementemia positivity, or rheumatoid factor positivity ($P>0.05$). The pSS group showed significantly higher rates of blood stasis syndrome positivity, blood stasis syndrome scores, dry mouth VAS scores, UWSFR abnormality, parotid gland ultrasound grades, submandibular gland ultrasound grades, unilateral SGUS total grades, bilateral SGUS total grades, labial gland biopsy positivity, lymphocytic infiltration foci numbers, anti-SSA/Ro antibody positivity, ANA titers, ESR, IgG, and hypergammaglobulinemia compared to the non-pSS group ($P<0.05$). UWSFR was significantly lower in the pSS group ($P<0.05$). Detailed data are presented in Table 1 .

3.2 Comparison of Clinical Indicators Among pSS Subgroups with Different Blood Stasis Scores

Among the 130 pSS patients, blood stasis severity was categorized by tertiles: mild blood stasis subgroup (26 cases, 20%) with scores 2-4, moderate blood stasis subgroup (56 cases, 43.08%) with scores 5-8, and severe blood stasis subgroup (48 cases, 36.92%) with scores $ $9. Significant differences were found among

the three subgroups in dry mouth VAS scores, UWSFR, ANA titers, ESR, IgG, and systemic involvement (P<0.05). No significant differences were observed in anti-SSA/Ro antibody positivity, C3/C4 levels, or RF positivity (P>0.05). The severe blood stasis subgroup showed significantly higher dry mouth VAS scores, ANA titers, ESR, C4, IgG levels, and systemic involvement rates compared to mild and moderate subgroups (P<0.05), while UWSFR was significantly lower (P<0.05). Detailed data are presented in Table 2 .

3.3 Comparison of Blood Stasis Syndrome Scores Among pSS Patients with Different SGUS Grades

Significant differences in blood stasis syndrome scores were observed among patients with different parotid gland ultrasound grades (P<0.05), with grade 3 patients showing significantly higher scores than grade 1 and grade 2 patients (P<0.05). Similarly, significant differences were found among different submandibular gland ultrasound grades (P<0.05), with grade 3 patients exhibiting significantly higher blood stasis scores than grade 2 patients (P<0.05). Detailed data are presented in Table 3 .

3.4 Correlation Between Blood Stasis Scores and Clinical Indicators in the pSS Group

In the pSS group, blood stasis scores showed positive correlations with dry mouth VAS scores (r=0.520, P=0.000), ANA titers (rs=0.227, P=0.013), ESR (r=0.269, P=0.002), IgG (r=0.240, P=0.006), parotid gland ultrasound grades (rs=0.348, P=0.000), submandibular gland ultrasound grades (rs=0.325, P=0.000), and bilateral SGUS total grades (rs=0.492, P=0.000), and a negative correlation with UWSFR (r=-0.491, P=0.000).

3.5 Analysis of High-Frequency Blood Stasis Items

In the pSS group, 93 patients (71.54%) exhibited positive tongue manifestations (purple-dark tongue or sublingual venous engorgement), 96 (73.85%) had fixed pain, 105 (80.77%) showed limb numbness or joint deformity, and all 130 patients (100%) had pathological masses, including 130 (100%) with SGUS abnormalities, 94 (72.3%) with thyroid nodules, and 46 (35.4%) with parotid enlargement. The distribution of blood stasis items in the non-pSS group and other criteria are detailed in Table 4 .

4. Discussion

Primary Sjögren's syndrome is a chronic autoimmune disease characterized by exocrine gland involvement, with typical symptoms including dry mouth and dry eyes. In TCM theory, pSS is classified under "dryness impediment," where "dryness" constitutes the primary pathological basis, and nourishing yin and moistening dryness represent the fundamental treatment principle. With advancing modern research, the classical discourse from *Jin Gui Yao Lue* regard-

ing “blood stasis causing dryness” has been re-examined. Increasing evidence demonstrates that blood stasis plays a crucial role in pSS pathogenesis. However, the specific characteristics of blood stasis syndrome in pSS and its relationship with clinical indicators lack systematic evaluation. This study constructed a “macro-syndrome-micro-indicator-disease assessment” tripartite analysis model to systematically investigate the distribution patterns of blood stasis syndrome in pSS patients and its correlations with salivary gland function, immunological markers, and systemic involvement, providing theoretical foundations and clinical guidance for integrated Chinese-Western medicine treatment of pSS.

This study is the first to introduce the quantitative standards from the *International Diagnostic Guidelines for Blood Stasis Syndrome* into pSS research, revealing that pSS patients had significantly higher blood stasis syndrome positivity rates and scores compared to the non-pSS group. This indicates that blood stasis syndrome is both prevalent and more severe in pSS patients. Contrary to traditional views, blood stasis manifestations are not limited to advanced-stage pSS patients but are universally present at initial diagnosis, corroborating the pathological mechanism from *Su Wen* (Basic Questions) that “when qi and blood are disharmonious, all diseases arise from transformation,” and suggesting that blood stasis is both a pathological product and an initiating factor.

High-frequency blood stasis items in the pSS group included purple-dark tongue or sublingual venous engorgement, fixed pain, limb numbness or joint deformity, and presence of pathological masses. These blood stasis characteristics align closely with the “dryness-stasis intermingling pattern” differentiation points in the *Guidelines for Diagnosis and Treatment of Sjögren’s Syndrome with Integrated Pattern and Disease*. Pathological masses encompassed hypoechoic salivary gland areas, parotid swelling, thyroid nodules, and breast nodules. This study found a strong correlation between SGUS grading and blood stasis scores, expanding the traditional concept of “concretions and conglomerations” to include specialized ultrasound imaging features. All pSS patients in this cohort had SGUS grades $ $1, suggesting that morphological changes such as heterogeneous glandular echogenicity and hypoechoic areas can serve as objective evidence for micro-differentiation. This finding resonates with the “micro-concretions” theory—capturing salivary gland structural abnormalities through modern imaging technology supplements the “stasis-obstructed collaterals” manifestations inaccessible through traditional four-examination methods. pSS patients with high SGUS grades should receive particular attention to blood stasis-resolving and collateral-dredging therapy. Chen Zijia et al. found that pSS patients with stasis-toxin patterns exhibited more significant SGUS abnormalities, corroborating the clinical value of micro-differentiation. Lu Dongqing et al. demonstrated that salivary gland ultrasound can assist in evaluating the efficacy of Chinese medicine treatment for primary Sjögren’s syndrome.

This study confirmed the critical phenomenon of “stasis transforming into toxin.” Blood stasis scores positively correlated with immunological indicators including ANA titers, ESR, and IgG, suggesting that chronic stasis can lead to “en-

dogenous toxin formation," resulting in microvascular changes such as immune complex deposition and vascular inflammation, consistent with the TCM pathological manifestation of "toxin accumulating in collaterals." pSS patients typically exhibit abnormalities in humoral and cellular immunity, including excessive pro-inflammatory cytokine secretion and reduced anti-inflammatory factor expression. Elevated C-reactive protein and accelerated ESR can be accompanied by abnormal blood viscosity, vascular endothelial damage, vasculitis, and microcirculatory disturbances.

Regarding salivary gland function, our previous research demonstrated that blood stasis syndrome is closely associated with salivary gland pathological changes. Animal experiments showed that blood stasis-resolving and collateral-dredging therapy not only improved glandular function but also effectively inhibited inflammatory cell infiltration and ameliorated salivary gland damage. The pathological mechanism of "blood stasis causing dryness" received multidimensional validation in this study. Based on the classical description of "desire to rinse with water but not to swallow," the study found that pSS patients had significantly greater glandular functional impairment than the non-pSS group. Moreover, the correlation between glandular dysfunction and blood stasis was stronger in the pSS group, with blood stasis scores showing significant positive correlation with dry mouth VAS scores. This provides modern interpretation for Tang Rongchuan's "blood thirst" theory: stasis obstructing qi mechanism leads to impaired fluid distribution, which may underlie the pathological basis of abnormal stimulated salivary flow rate and partially explains the superior efficacy of stasis-resolving methods in improving subjective dry mouth.

Further analysis of the correlation between blood stasis severity and systemic involvement revealed that moderate-to-severe blood stasis significantly increased systemic involvement risk, corroborating the *Blood Syndromes Treatise* statement that "stasis accumulating in viscera forms concretions," an aspect insufficiently explored in previous research. Therefore, we recommend incorporating blood stasis scores into prognostic assessment systems, emphasizing early application of detoxification methods for patients with moderate or higher blood stasis. Zhao Yonglu et al., through data mining of Chinese medicine treatment for pSS over the past two decades, concluded that besides nourishing yin and moistening dryness, activating blood and resolving stasis combined with heat-clearing and detoxification should be routinely employed, consistent with our findings.

This study has several limitations: (1) As a single-center study, the sample may have regional bias affecting generalizability. (2) Blood stasis diagnosis involves subjectivity; although the *International Diagnostic Guidelines* were adopted, some syndrome assessments still rely on clinical observation, necessitating integration with more objective indicators (e.g., hemodynamic parameters) to improve diagnostic precision in future research. (3) Systemic involvement requires clearer definition, as different organ involvements may carry different weights for blood stasis scores, warranting further differentiation in future studies.

In summary, this study reveals the characteristics of blood stasis syndrome in pSS patients, demonstrating that blood stasis permeates the entire disease course as an important pathogenic factor and pathological product. Blood stasis severity closely correlates with glandular dysfunction, abnormal clinical indicators, high SGUS grades, and poor prognostic markers, providing objective evidence for blood stasis differentiation in pSS and a theoretical foundation for treating pSS "from stasis." Future multi-center, large-sample studies should be conducted to provide evidence-based medicine support for precise and effective integrated Chinese-Western medicine treatment of primary Sjögren's syndrome.

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Author Contributions: SHI Zhonghao participated in study design, patient recruitment, data analysis, and manuscript writing; CHEN Yueying participated in patient recruitment and manuscript revision; DONG Xiaoyan performed all salivary gland ultrasound examinations; HOU Jiaqi conducted data verification; XUE Luan supervised the project and was responsible for manuscript revision. All authors reviewed and approved the final manuscript.

Funding: National Natural Science Foundation of China General Project (82374318); National Natural Science Foundation of China Youth Project (82104719).

Conflict of Interest: The authors declare no conflict of interest.

Citation: SHI Z H, CHEN Y Y, DONG X Y, et al. Clinical feature correlation analysis of primary sjögren's syndrome based on quantitative assessment of blood stasis syndrome[J]. Chinese General Practice, 2025. DOI: 10.12114/j.issn.1007-9572.2025.0096. [Epub ahead of print]

Editorial Office: Chinese General Practice.