Clinical Study on the Evolution Patterns of Syndromes and Syndrome Elements during the High-Risk HPV Infectious Cervicitis-to-Cancer Transformation Process: Postprint

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Abstract

Background High-risk human papillomavirus (HPV) infectious cervicitis is a major causative factor for cervical cancer and has become a significant public health issue in China. Traditional Chinese medicine (TCM) syndrome differentiation and treatment are of great significance in preventing, delaying, or even blocking the further progression of high-risk HPV infection; however, current research is limited, lacking standardized syndrome determination and standardized treatment protocols. Objective To explore the distribution and evolution patterns of TCM syndromes and syndrome elements during the transformation process from high-risk HPV infectious cervicitis to cervical intraepithelial neoplasia (CIN) and cervical cancer (CC). Methods A retrospective collection was conducted of 288 patients with high-risk HPV infectious cervicitis, 146 patients with cervical intraepithelial neoplasia, and 322 patients with cervical cancer, all confirmed by pathological biopsy and hospitalized at Shanxi Provincial Academy of Traditional Chinese Medicine from January 2023 to June 2024. EpiData 3.1 was used to establish a database to record general patient information, auxiliary examination results, and TCM four diagnostic information. Principal component analysis was employed to extract common factors, with cumulative variance contribution rate $ $70% or eigenvalue $ $1 selected as common factors after comprehensive consideration of cumulative variance contribution rate and eigenvalues. Factor rotation was performed using the Kaiser standardized varimax method, and K-means clustering was used for cluster analysis. Results Using four diagnostic information with frequency $ $20% as factor analysis items, 17 items of TCM four diagnostic information were obtained for the malignant transformation from high-risk HPV infectious cervicitis to cancer, including 13 symptom information items, 2 tongue appearance information items,

and 2 pulse information items. Comparisons of symptoms, tongue appearance, and pulse among patients with high-risk HPV infectious cervicitis, CIN, and CC showed statistically significant differences (P<0.001). Principal component and factor cluster analysis results revealed that TCM syndromes in patients with high-risk HPV infectious cervicitis, CIN, and CC were classified into six types: spleen-kidney yang deficiency syndrome, qi stagnation and blood stasis syndrome, spleen deficiency with dampness excess syndrome, damp-heat pouring downward syndrome, dampness toxin accumulation syndrome, and yin deficiency with dampness syndrome. The syndrome distribution in patients with high-risk HPV infectious cervicitis was dominated by damp-heat pouring downward syndrome (28.47%), with excess syndromes (47.57%) significantly higher than deficiency syndromes (22.57%) (P<0.001). Syndrome element distribution was dominated by dampness (71.18%) and heat (28.47%). Disease location was primarily in the uterus (77.43%), followed by the liver (57.33%). In CIN patients, syndrome distribution was dominated by damp-heat pouring downward syndrome (24.65%), with no statistically significant difference between excess syndromes (36.98%) and deficiency syndromes (32.19%) (P=0.486). Syndrome element distribution was dominated by dampness (69.18%) and heat (24.65%). Disease location was primarily in the uterus (67.81%), followed by the liver (60.27%). In CC patients, syndrome distribution was mainly dominated by spleen deficiency with dampness excess syndrome (25.16%), with deficiency syndromes (43.48%) significantly higher than excess syndromes (22.67%) (P<0.001). Syndrome element distribution was dominated by dampness (69.88%) and qi deficiency (25.16%). Disease location was primarily in the uterus (56.52%), followed by the spleen (55.59%). Comparisons of TCM syndromes, syndrome elements, and disease locations among patients with high-risk HPV infectious cervicitis, CIN, and CC all showed statistically significant differences (P<0.001). Conclusion During the malignant transformation process from high-risk HPV infectious cervicitis to cancer, the disease location is primarily in the uterus, associated with the liver in the early stage, and often involving the spleen and kidney in the later stage. With disease progression, the evolution patterns of syndromes and syndrome elements generally manifest as "intermingled deficiency and excess, transitioning from excess to deficiency, with dampness pathogen persisting throughout."

Full Text

Preamble

Clinical Study on the Evolution of Syndrome and Syndrome Elements in the Transformation Process from High-Risk HPV Infectious Cervicitis to Cancer

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Abstract

Background: High-risk human papillomavirus (HPV) infectious cervicitis is the primary cause of cervical cancer and has become a major public health concern in China. Traditional Chinese Medicine (TCM) syndrome differentiation and treatment hold significant potential for preventing, delaying, or even blocking the progression of high-risk HPV infection. However, current research remains limited, with a lack of standardized syndrome determination and treatment protocols.

Objective: To investigate the distribution and evolution patterns of TCM syndromes and syndrome elements during the transformation from high-risk HPV infectious cervicitis to cervical intraepithelial neoplasia (CIN) and cervical cancer (CC).

Methods: We retrospectively collected data from 756 patients hospitalized at Shanxi Provincial Institute of Traditional Chinese Medicine between January 2023 and June 2024, including 288 cases of high-risk HPV infectious cervicitis, 146 cases of CIN, and 322 cases of CC, all confirmed by pathological biopsy. A database was established using EpiData 3.1 to record general patient information, auxiliary examination results, and TCM four-diagnostic information. Principal component analysis was employed to extract common factors, with selection criteria of cumulative variance contribution rate $ $70% or eigenvalue $ $1. The Kaiser-standardized varimax method was used for factor rotation, and K-means clustering was performed for classification.

Results: Seventeen TCM diagnostic items with frequency $ $20% were selected for factor analysis, comprising 13 symptom items, 2 tongue appearance items, and 2 pulse items. Significant differences were observed in symptoms, tongue appearance, and pulse characteristics among cervicitis, CIN, and CC patients ($P<0.001$). Principal component and factor cluster analysis identified six TCM syndrome patterns: spleen-kidney yang deficiency, qi stagnation and blood stasis, spleen deficiency with dampness excess, damp-heat pouring downward, damp-toxin accumulation, and yin deficiency with dampness. In cervicitis patients, damp-heat pouring downward syndrome predominated (28.47%), with excess syndromes (47.57%) significantly outnumbering deficiency syndromes (22.57%) ($P<0.001$). Syndrome elements were primarily dampness (71.18%) and heat (28.47%), with disease location mainly in the uterus (77.43%), followed by

the liver (57.33%). In CIN patients, damp-heat pouring downward syndrome was also most common (24.66%), with no significant difference between excess (36.98%) and deficiency syndromes (32.19%) (P=0.486). Syndrome elements were mainly dampness (69.18%) and heat (24.65%), with disease location primarily in the uterus (67.81%), followed by the liver (60.27%). In CC patients, spleen deficiency with dampness excess syndrome predominated (25.16%), with deficiency syndromes (43.48%) significantly exceeding excess syndromes (22.67%) (P<0.001). Syndrome elements were primarily dampness (69.88%), qi deficiency (25.16%), and yin deficiency (22.05%), with disease location mainly in the uterus (56.52%), followed by the spleen (55.59%). Statistically significant differences existed among the three groups in TCM syndromes, syndrome elements, and disease locations (P<0.001).

Conclusion: During the malignant transformation from high-risk HPV infectious cervicitis to cancer, the primary disease location is the uterus, associated with the liver in early stages and commonly involving the spleen and kidneys in later stages. As the disease progresses, the evolution of syndromes and syndrome elements demonstrates the characteristics of "mixed deficiency and excess, transformation from excess to deficiency, with dampness persisting throughout."

Keywords: cervicitis; HPV; inflammation-cancer transformation; syndrome elements; evolutionary pattern; factor analysis; cluster analysis

Introduction

Cervical cancer (CC) is one of the most common gynecological malignancies, ranking fourth in incidence among female cancers worldwide [1]. According to Global Cancer Statistics 2022 [2], there were over 660,000 new CC cases and approximately 350,000 deaths globally in 2022, with China' s incidence still increasing [3]. Persistent infection with high-risk human papillomavirus (HR-HPV) types such as HPV16/18/26 represents the primary cause of CC [4]. Additionally, chronic recurrent gynecological inflammation and prolonged disease courses constitute important risk factors for CC development [5]. HPV infection and cervicitis influence each other mutually: HPV infection increases cervicitis incidence [6], while chronic cervicitis causes vaginal flora imbalance and suppresses local immune function, thereby increasing HPV infection risk [7]. Thus, high-risk HPV infection and cervical inflammation interact synergistically to induce CC development. Due to chronic, repeated inflammatory infiltration, early stages typically manifest as cervical intraepithelial neoplasia (CIN), representing precancerous lesions. The evolution pathway from high-risk HPV infectious cervicitis to CC– "inflammation → CIN → cancer" –is termed the "inflammation-cancer chain" [8]. Therefore, identifying critical nodes in the inflammation-cancer transformation and early intervention for high-risk HPV infectious cervicitis are essential for CC prevention and treatment.

As a traditional medicine, TCM can exert precise intervention and effective

control under the guidance of holistic concepts and syndrome differentiation theory, playing a significant role in delaying, blocking, or even reversing malignant transformation to reduce CC incidence [9]. However, due to the complex multidimensionality of syndromes and subjective diagnostic limitations, current standards, guidelines, and consensus opinions lack unified diagnostic criteria for different disease stages, limiting clinical reproducibility and international recognition. This study employs principal component analysis, factor analysis, and cluster analysis to conduct a cross-sectional investigation of syndrome, syndrome element, and disease location evolution patterns across large clinical samples during the cervicitis-cancer transformation process, aiming to provide references for objective TCM syndrome identification and standardized clinical treatment.

Methods

1.1 Study Subjects

We retrospectively selected 756 patients meeting inclusion criteria who were hospitalized at Shanxi Provincial Institute of Traditional Chinese Medicine between January 2023 and June 2024. Inclusion criteria were: (1) sexually active women aged 18-75 years; (2) high-risk HPV infection confirmed by HPV DNA testing; (3) no surgery, radiotherapy, chemotherapy, or molecular targeted therapy within the previous three months; (4) complete and accurate TCM four-diagnostic information enabling syndrome differentiation; (5) expected survival >6 months with Karnofsky Performance Status score $ $70. Exclusion criteria included: (1) co-infection with other viruses or bacteria; (2) other primary tumors besides cervical cancer and its metastases; (3) pregnancy or lactation; (4) severe internal medical diseases or infectious diseases; (5) psychiatric disorders or inability to accurately describe subjective symptoms; (6) incomplete clinical data or poor compliance. This study was approved by the Medical Ethics Committee of Shanxi Provincial Institute of Traditional Chinese Medicine (Approval No.: 2024KY-07036).

1.2 Diagnostic Criteria

1.2.1 Western Medicine Diagnostic Criteria: HPV infection and cervicitis diagnosis followed the *Guidelines for Comprehensive Prevention and Control of Cervical Cancer (2nd Edition)* [10]. CIN and CC diagnosis followed the *Guidelines for Diagnosis and Treatment of Cervical Cancer (4th Edition)* [11], with cervical biopsy pathology as the final diagnostic basis.

1.2.2 TCM Syndrome and Syndrome Element Criteria: Syndrome types were standardized according to the National Standard of the People' s Republic of China *Clinical Terminology of Traditional Chinese Medicine: Syndromes* [12] and the *Chinese Medicine Terms* published by the National Committee for Terms in Sciences and Technologies [13], supplemented by the *Syndrome Element Differentiation* [14]. The specific method involved selecting factor loading

coefficient 0.3 as the threshold for factor composition, obtaining the connotation and coefficients of common factors. Based on each common factor' s variable composition and loading coefficients, syndrome elements of disease nature and location were determined according to *Syndrome Element Differentiation* [14]. Factor scores calculated by regression method were used as variables for K-means cluster analysis. Three senior clinical experts in integrated traditional and Western medicine performed syndrome differentiation to summarize major TCM syndrome types and elements, with names standardized according to *Clinical Terminology of Traditional Chinese Medicine: Syndromes* [12] and *Chinese Medicine Terms* [13].

1.3 Data Collection Methods and Quality Control

Based on inclusion and exclusion criteria, five senior physicians from our department developed an information collection form for TCM syndromes in high-risk HPV infectious cervicitis-cancer transformation. The form included patient demographics, disease course, previous infection history, marital history, family history (HPV infection and cervical cancer), sexual history, education level, and 65 TCM syndrome factors (including symptoms, tongue appearance, pulse). Positive and negative syndrome factors were scored as 1 and 0, respectively. All data collection was completed by clinicians trained in standard operating procedures (SOP). Data were independently entered into Epidata 3.1 software by two operators using separate computers. Quality control was performed by a third person conducting consistency checks to ensure accurate and reliable raw data.

1.4 Sample Size Estimation

According to Kendall' s sample size estimation method [15], the sample size should be 5-10 times the number of questionnaire items. Considering other uncontrollable factors, a 20% bias sample size was added. With 65 questionnaire items, the required sample size was estimated at 390-780 cases; 756 cases were actually collected.

1.5 Statistical Methods

Epidata 3.1 software was used to establish the information database, collecting all items from the TCM syndrome information collection form, including symptoms, tongue appearance, and pulse. SPSS 27.0 statistical software was used for data analysis. Count data were expressed as constituent ratios, with intergroup comparisons using ^{2} tests. Diagnostic information with frequency $ $20% was selected for descriptive statistics. Principal component and factor analyses were performed when Kaiser-Meyer-Olkin (KMO) value >0.5 and Bartlett' s test P<0.01. The maximum variance method was used, with common factors selected based on cumulative variance contribution rate $ $70% or eigenvalue $ $1. K-means clustering was employed for cluster analysis, with syndrome

and syndrome element frequencies calculated. Two-sided tests were used, with P<0.05 considered statistically significant.

Results

2.1 Comparison of General Data

A total of 756 patients were included: 288 cases of high-risk HPV infectious cervicitis (38.1%), 146 cases of CIN (19.3%), and 322 cases of CC (42.6%). No significant differences were found among the three groups in sexual history or education level (P>0.05). However, significant differences existed in age, disease course, previous infection history, marital history, family history of HPV infection, and family history of cervical cancer (P<0.05) .

2.2 Comparison of Four-Diagnostic Information Distribution

Diagnostic items with frequency $ $20% were selected for factor analysis, yielding 17 TCM diagnostic items for high-risk HPV infectious cervicitis-cancer transformation, including 13 symptom items, 2 tongue appearance items, and 2 pulse items. Chi-square tests of these 17 diagnostic factors revealed significant differences in symptoms, tongue appearance, and pulse among cervicitis, CIN, and CC patients (P<0.05) .

2.3 Principal Component, Factor, and Cluster Analysis

Preliminary principal component and factor analyses using SPSS 27.0 showed: for high-risk HPV infectious cervicitis, 7 principal components with eigenvalue >1 (F1-F7) and cumulative contribution rate of 77.76%; for CIN, 8 principal components (F1-F8) with cumulative contribution rate of 71.16%; for CC, 8 principal components (F1-F8) with cumulative contribution rate of 69.09%. KMO and Bartlett' s test results were: cervicitis group KMO=0.905, P<0.001; CIN group KMO=0.74, P<0.001; CC group KMO=0.8, P<0.001. After varimax rotation, convergence was achieved after 19 iterations for cervicitis, 10 for CIN, and 12 for CC. A factor loading coefficient of 0.3 was selected as the threshold, yielding common factor connotations and loadings. K-means cluster analysis was performed with cluster numbers set at 5-8, with results showing the most reasonable syndrome mean distribution when the cluster number was 6 (P<0.05 for all groups).

By consulting the "Syndrome Differentiation Scale" in Professor Zhu Wenfeng' s *Syndrome Element Differentiation* [14] and combining common factor connotations with coefficients, symptoms in each common factor were evaluated. Combined with TCM disease nature, disease location syndrome elements, and expert opinions, high-risk HPV infectious cervicitis, CIN, and CC patients' TCM syndromes were summarized into six types: spleen-kidney yang deficiency, qi stagnation and blood stasis, spleen deficiency with dampness excess, damp-heat

pouring downward, damp-toxin accumulation, and yin deficiency with dampness . Symptom and syndrome element analysis results are shown in .

2.4 Distribution of Syndromes, Syndrome Elements, and Disease Locations

Analysis of syndromes, syndrome elements, and disease locations revealed: In high-risk HPV infectious cervicitis patients, damp-heat pouring downward syndrome (28.47%) and damp-toxin accumulation syndrome (19.10%) predominated, with excess syndromes (47.57%) significantly exceeding deficiency syndromes (22.57%) (^{2}=25.663, P<0.001). Syndrome elements were primarily dampness (71.18%) and heat (28.47%), with disease location mainly in the uterus (77.43%), followed by the liver (57.33%). In CIN patients, damp-heat pouring downward syndrome (24.66%) and yin deficiency with dampness syndrome (18.49%) were most common, with no significant difference between excess (36.98%) and deficiency syndromes (32.19%) (^{2}=0.485, P=0.486). Syndrome elements were mainly dampness (69.18%) and heat (24.65%), with disease location primarily in the uterus (67.81%), followed by the liver (60.27%). In CC patients, spleen deficiency with dampness excess syndrome (25.16%) and yin deficiency with dampness syndrome (22.05%) predominated, with deficiency syndromes (43.48%) significantly exceeding excess syndromes (22.67%) (^{2}=21.075, P<0.001). Syndrome elements were primarily dampness (69.88%), qi deficiency (25.16%), and yin deficiency (22.05%), with disease location mainly in the uterus (56.52%), followed by the spleen (55.59%). Statistically significant differences existed among the three groups in TCM syndromes, syndrome elements, and disease locations (P<0.001) .

Discussion

Cervical cancer has become the fourth most threatening cancer to women' s health worldwide. Persistent high-risk HPV infection is the main cause of cervical lesions progressing to CIN and even CC. The pathogenesis involves activation of cervical endometrial and epithelial cells releasing chemokines, growth factors, and cyclooxygenase (COX), leading to rapid cell proliferation and differentiation. Meanwhile, the inflammatory microenvironment generates free radicals that damage DNA molecules, inducing cellular mutation and malignant transformation, and promoting HPV-induced inflammation-to-cancer conversion [16]. Due to nonspecific early symptoms, CC easily progresses and metastasizes, posing severe threats to women' s physical and mental health and becoming a major public health issue in China [17]. However, modern medicine lacks effective anti-HPV drugs, employing watchful waiting for high-risk HPV infection patients [18]. When CIN occurs, cervical conization with standardized follow-up is recommended, with no effective interventions for residual, recurrent, or progressive CIN lesions [19]. TCM, guided by holistic concepts and syndrome differentiation theory, can provide precise intervention and effective control. Timely TCM treatment during inflammatory infection or CIN stages can pre-

vent or even reverse the inflammation-cancer progression, thereby reducing CC incidence [20].

Principal component analysis and cluster analysis can automatically classify main components from sample data, and combined with TCM theory, select representative indicators to simplify syndrome criteria more objectively [21]. This study' s cluster analysis of the high-risk HPV infectious cervicitis-cancer transformation process revealed that as the disease progresses, the proportion of excess syndromes like damp-heat pouring downward and damp-toxin accumulation gradually decreases, while mixed deficiency-excess and deficiency syndromes such as spleen deficiency with dampness excess, yin deficiency with dampness, and spleen-kidney yang deficiency gradually increase. This indicates an evolution trend of "mixed deficiency and excess, transforming from excess to deficiency" during the transformation process. From the syndrome element perspective, the pattern evolves from dampness and heat predominance in the inflammatory stage, to dampness, heat, and yin deficiency in the CIN stage, and finally to dampness, qi deficiency, and yin deficiency in the cancer stage. Syndrome elements similarly follow the evolution trend of "mixed deficiency and excess, transforming from excess to deficiency," consistent with syndrome analysis results. Furthermore, "dampness" persists as an important pathological factor throughout the cervicitis-cancer transformation. Yang Mengping et al. [22] proposed that the pathogenesis of HR-HPV infection inflammation-cancer transformation involves dampness-heat accumulation and latent toxin onset, generating toxic cancer, and considered "dampness" as an important condition promoting cervicitis-cancer transformation. This aligns with our findings. Additionally, our results show that the fundamental disease location in high-risk HPV infectious cervicitis-cancer transformation is the uterus, associated with the liver in early stages and involving the spleen and kidneys in later stages.

In TCM theory, cervical lesions belong to the "leukorrhea disease" category, primarily caused by dampness pouring downward. Dampness is both an external "six excess" pathogenic factor and an internal "five endogenous" factor. Dampness tends to descend, easily attacking yin locations and damaging the lower body. As stated in *Suwen · Taiyin Yangming Lun*: "When dampness causes disease, the lower body is affected first," and in *Lingshu · Bai Bing Shi Sheng Pian*: "When clear dampness attacks deficiency, disease originates from below." Prolonged dampness stagnation easily transforms into heat and damages yin. The inflammatory microenvironment caused by persistent HR-HPV infection resembles TCM dampness-heat pathogenic factors [20]. Dampness and heat interact and transform into each other. Anatomically, the female reproductive tract opening is located between the urethral and anal openings, making it vulnerable to various pathogens. The vagina' s unique temperature and humidity also provide an environment for pathogen proliferation. Therefore, high-risk HPV cervicitis commonly presents as damp-heat pouring downward syndrome, consistent with our findings. Dampness most easily traps the spleen, causing spleen deficiency and impaired middle-jiao pivot function, making the spleen and stomach the pathological center of dampness-heat. As Zhang Xugu stated:

"Dampness-heat evils attract each other. Although dampness-heat evils initially invade externally, they ultimately affect the spleen and stomach." "When blood is unsmooth, it becomes water." Further dampness-heat progression can obstruct qi and blood circulation, generating pathological products like phlegm and stasis. The combination of "phlegm, dampness, heat, and stasis" constitutes toxin, and excessive heat toxin corroding blood vessels can transform into cancer [20]. Based on our team' s previous research, we propose that "dampness-heat invading the spleen" is the fundamental pathogenesis of cervical "inflammation-cancer transformation." "Spleen deficiency" constitutes the internal condition for disease onset, while dampness-heat provides the soil for inflammation-cancer transformation, characterized by root deficiency and branch excess with mixed deficiency-excess.

High-risk HPV infectious cervicitis-cancer transformation is a complex process involving multiple pathological stages and dynamic evolution. This study' s summary of TCM syndrome elements and evolution patterns provides guidance for treating different disease stages and population characteristics, leveraging TCM' s holistic concept and individualized treatment advantages. Our findings show that in the cervicitis stage, the pathological characteristics mainly involve struggle between healthy qi and pathogenic factors with excess predominance. The core syndromes are damp-heat pouring downward and damp-toxin accumulation. Treatment should focus on clearing heat, resolving dampness, and detoxifying, supplemented by regulating qi, activating blood, and resolving stasis [23]. Jiang Yuanyuan et al. [24] treated dampness-heat accumulation-type cervicitis with HPV infection using self-designed Qingre Tiaoxue Decoction, demonstrating superior efficacy in improving TCM syndromes, increasing HPV clearance rates, and reducing adverse reactions. Pang Siyu et al. [25] observed that Zaoshi Jiedu Powder significantly improved clinical symptoms, accelerated HR-HPV clearance, and repaired cervical erosion-like changes in chronic cervicitis patients with HR-HPV infection. When the disease progresses to CIN, the pathological characteristics involve mixed deficiency-excess, with core syndromes of damp-heat pouring downward and yin deficiency with dampness. As toxin removal is essential for healthy qi recovery, the critical inflammation-cancer transformation stage requires addressing both root and branch, focusing on strengthening the spleen, resolving dampness, and stopping leukorrhea while supplementing anti-cancer heat-clearing methods [26]. Wang Yongmei et al. [27] found that Jiawei Ermiao Granules combined with recombinant human interferon $ $2b vaginal effervescent capsules could block CIN progression to CC, with a clinical total effective rate of 91.33% in the study group, significantly higher than the control group. Our previous research found that treating CIN with the main formula combined with the herb pair Hedyotis diffusa-Scutellaria barbata to clear heat, counteract cancer, and detoxify [28], plus insect medicines like centipede, wasp nest, and scorpion to unblock collaterals and disperse nodules, showed significant efficacy in reversing inflammation-cancer transformation. When the disease progresses to the CC stage, pathological characteristics mainly involve spleen deficiency with dampness excess and deficiency predominance. The core

syndrome is spleen deficiency with dampness excess, with yin deficiency with dampness and spleen-kidney yang deficiency also commonly observed. Treatment should focus on nourishing blood, tonifying the liver, strengthening the spleen, and benefiting kidneys to restore qi-blood-yin-yang balance in the tumor microenvironment. Concurrent treatment according to different pathogenesis, such as activating blood, resolving phlegm, expelling stasis, and detoxifying, can prevent recurrence and metastasis while delaying disease progression. Chen Min et al. [29] confirmed that Bushen Yiqi Huoxue Formula can act on the cervicitis-cancer transformation process through TNF, AGE-RAGE, TLR, and other signaling pathways to block further development.

This study has several limitations: (1) As a retrospective study, recall bias and other confounding factors may exist; (2) Due to geographical limitations, samples were from a single hospital, which may not represent the syndrome and syndrome element distribution characteristics of all high-risk HPV cervicitis populations at different stages; (3) No relevant animal experiments were conducted for validation. Future research should conduct large-sample, multicenter, prospective studies, combined with biobanks, multi-omics, bioinformatics, and big data technologies to further validate findings and contribute to understanding high-risk HPV infectious cervicitis-cancer transformation patterns and promoting precision syndrome-based medicine.

In summary, during high-risk HPV infectious cervicitis-cancer transformation, the disease location is primarily the uterus, associated with the liver in early stages and commonly involving the spleen and kidneys in later stages. As the disease progresses, syndrome and syndrome element evolution demonstrates the characteristics of "mixed deficiency and excess, transforming from excess to deficiency, with dampness persisting throughout." Through data mining and statistical analysis, this study summarizes TCM syndrome and syndrome element evolution patterns at different stages of high-risk HPV infectious cervicitis-cancer transformation, providing evidence for clinical syndrome element determination and standardized TCM treatment.

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Note: Figure translations are in progress. See original paper for figures.