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ORIGINAL RESEARCH

The Relationship between Systemic Expression Levels of Immune Cells and Tumor Markers and High-Risk HPV Infection in Patients with Cervical Cancer, Cervical Intraepithelial Neoplasia, and Chronic Cervicitis, and its Clinical Significance

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Objective: To analyze the relationship and clinical significance between systemic expression levels of immune cells and tumor markers and high-risk human papillomavirus (HPV) infection in patients with cervical cancer, cervical intraepithelial neoplasia, and chronic cervicitis.

Methods: A retrospective analysis was conducted on the clinical data of 69 patients with cervical cancer infected with HPV (Group A), 78 patients with CIN (Group B), and 52 patients with chronic cervicitis (Group C) treated at Hebei Central Hospital of petroleum gynecology from April 2021 to April 2023. Peripheral blood immune cells (CD4+/CD8+, CD56+, Treg) and serum tumor markers (CA125, SCC-Ag, TSGF, Cyfra211) were compared. Correlations with HPV-DNA levels, lymph node metastasis, and survival were analyzed.

Results: Group A had lower CD4+/CD8+ and CD56+ levels but higher Treg and tumor marker levels vs Groups B/C ($P<0.05$). Group B showed similar trends vs Group C ($P<0.05$). In Group A, Treg and tumor markers positively correlated with HPV-DNA levels ($r=0.552$–0.613), while CD4+/CD8+ and CD56+ negatively correlated ($r=-0.482$/-0.467, $P<0.05$). Patients with lymph node metastasis or mortality exhibited worse immune/tumor marker profiles than controls ($P<0.05$).

Conclusion: Compared with patients with CIN and chronic cervicitis associated with high-risk HPV infection, cervical cancer patients exhibit decreased systemic immune function and increased circulating tumor marker expression. These findings are closely associated with HPV-DNA levels. Systemic detection of these markers may provide valuable guidance for the early prevention, diagnosis, and prognosis assessment of cervical cancer in patients with high-risk HPV infection.

Keywords: cervical cancer, cervical intraepithelial neoplasia, chronic cervicitis, immune cells, tumor markers, high-risk HPV infection, relationship, clinical significance

Introduction

Cervical cancer is one of the most common malignancies among women worldwide, with persistently high incidence and mortality rates, particularly in developing countries.[1] Data[2] indicate that approximately 600,000 new cases of cervical cancer and 340,000 cervical cancer-related deaths occurred globally in 2020, posing a severe threat to women's health and lives. Although the development of cervical cancer is a multifactorial and cumulative process, previous studies[3,4] have clearly established that high-risk human papillomavirus (HPV) infection is the primary causative factor. High-risk HPV plays a pivotal role in the onset, progression, and prognosis of cervical cancer by integrating into the host genome and promoting the continuous expression of viral oncogenes (E6, E7), which suppress the functions of tumor suppressor

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genes p53 and Rb and induce uncontrolled cell proliferation.[5,6] While most women can clear HPV through their immune systems, some individuals experience persistent infection due to immune dysfunction or alterations in the immune microenvironment, potentially leading to CIN or even cervical cancer.[6] Therefore, exploring the role of immune cells in high-risk HPV infection, particularly their systemic changes across different stages of cervical disease, is essential for understanding the pathogenesis of cervical cancer and optimizing prevention strategies.

In recent years, advancements in tumor immunology have provided new perspectives on the mechanisms underlying cervical cancer. Studies[7–9] have demonstrated that changes in the proportions and functions of immune cells, such as CD4+/CD8+ T cells, natural killer cells (CD56+), and regulatory T cells (Treg), both locally within the tumor microenvironment and systemically in peripheral blood, may directly influence tumor development and progression. For instance, Brito[7] reported that a decreased CD4+/CD8+ ratio in peripheral blood correlates with advanced cervical cancer stages, while Gutierrez-Silerio[8] identified impaired cytotoxic activity of circulating CD56+ NK cells in HPV-positive patients. Additionally, Rocha Martins[9] highlighted the role of elevated systemic Treg levels in suppressing antitumor immunity and promoting HPV persistence. However, most existing studies have focused on local immune alterations, and the specific systemic changes of these immune cells in high-risk HPV-associated cervical diseases remain limited, especially the dynamic variations across chronic cervicitis, CIN, and cervical cancer stages.

In addition to immune cells, circulating tumor markers play a crucial role in the diagnosis and prognosis of cervical cancer and related diseases. These markers not only reflect tumor burden and biological characteristics but are also potentially linked to high-risk HPV infection.[10] However, research on the differences in systemic tumor marker expression levels among patients with various cervical diseases and their relationship with HPV infection is insufficient. Specifically, the clinical relevance of combining peripheral immune cell profiles (eg, CD4+/CD8+, CD56+, Treg) with serum tumor markers (eg, CA125, SCC-Ag) for disease staging and prognosis remains underexplored. This study retrospectively analyzed clinical data from patients with cervical cancer, CIN, and chronic cervicitis associated with high-risk HPV infection, focusing on the systemic expression levels of immune cells (assessed in peripheral blood) and tumor markers (measured in serum) and their relationship with high-risk HPV-DNA loads. Furthermore, this study examined differences in systemic immune cell and tumor marker levels between high-risk HPV-infected cervical cancer patients with and without lymph node metastasis, as well as between deceased and surviving patients. Through these investigations, this study aims to provide scientific evidence for the early diagnosis, personalized treatment, and prognosis management of cervical cancer and related diseases and to offer new insights into the systemic immune mechanisms of high-risk HPV infection and the clinical significance of circulating tumor markers.

Materials and Methods

General Information

A retrospective analysis was conducted on clinical data from 69 cervical cancer patients with HPV infection (Group A), 78 patients with cervical intraepithelial neoplasia (Group B), and 52 patients with chronic cervicitis (Group C) treated in Hebei Central Hospital of petroleum gynecology from April 2021 to April 2023. Inclusion Criteria: (1) All participants were confirmed to have cervical cancer, cervical intraepithelial neoplasia, or chronic cervicitis through histopathological examination, with clear staging or grading.[11,12] (2) High-risk HPV infection was confirmed through HPV genotyping tests.[13] (3) Complete medical records, laboratory results, and imaging reports were available for all patients. (4) No patients had undergone surgery, radiotherapy, chemotherapy, or immunomodulatory therapy prior to inclusion or during the follow-up period. (5) All patients and their families were informed about the study and signed informed consent forms.

Exclusion Criteria: (1) Patients with a history of malignant tumors in other parts of the body or with active malignant tumors. (2) Patients with autoimmune diseases, chronic inflammatory diseases, or those receiving immunosuppressive therapy. (3) Patients with severe functional impairment of vital organs, including the heart, liver, and kidneys. (4) Pregnant or lactating patients due to the potential impact of their physiological state on immunity and tumor marker levels. (5) Patients with incomplete medical records or test data, or those unable to adhere to regular follow-ups. (6) Patients recently treated with antiviral drugs or medications affecting immune function and tumor marker expression. (7) Patients with a history of psychiatric disorders and/or cognitive dysfunction.

Participant Characteristics: Group A: Ages 24–63 years, mean age (43.51 ± 7.12) years; clinical staging: stage I (11 cases), stage II (27 cases), stage III (19 cases), stage IV (12 cases); lymph node metastasis present (27 cases) or absent (42 cases). Group B: Ages 25–65 years, mean age (42.79 ± 6.85) years; pathological grading: grade I (21 cases), grade II (25 cases), grade III (32 cases). Group C: Ages 23–67 years, mean age (43.08 ± 7.31) years. The age comparison among the three groups ($P > 0.05$) was not statistically significant, demonstrating comparability. This study was approved by the Medical Ethics Committee of Hebei Central Hospital of petroleum gynecology (Approval No. FK-24-JB0017) and adhered to the ethical standards outlined in the Declaration of Helsinki. Informed consent was obtained from all study participants.

Detection Methods

Immune Cell Level Detection

(1) Sample Collection and Processing: ① Sample Collection: Morning fasting venous blood samples (5 mL) were collected from each patient using non-anticoagulant vacuum tubes. ② Sample Processing: Peripheral blood mononuclear cells (PBMC) were isolated via Ficoll density gradient centrifugation to obtain clean single-cell suspensions. ③ Storage: Isolated cell suspensions were immediately used for testing or stored at −80°C for delayed testing to maintain cell viability. (2) Flow Cytometry Detection: ① Antibody Labeling: Flow cytometry antibody kits containing fluorescently labeled monoclonal antibodies specific for CD4+, CD8+, CD56+, and Treg were used. ② Staining Procedure: Cells were counted at 1×10^6 cells/tube and distributed into flow cytometry tubes. Appropriate amounts of antibody mixtures were added, gently mixed, and incubated in the dark for 30 minutes at 4°C. Cells were washed twice with PBS to remove unbound antibodies and resuspended in 200 μL PBS. ③ Instrument and Analysis: BD FACSCalibur flow cytometer was used for detection, and FlowJo software was utilized to analyze the proportions of CD4+/CD8+, CD56+, and Treg.

Tumor Marker Expression Level Detection

(1) Sample Collection and Processing: ① Sample Collection: A single baseline blood sample (5 mL) was collected from each patient at enrollment. Morning fasting venous blood samples were drawn into EDTA-anticoagulant tubes. ② Sample Processing: Samples were centrifuged at 3000 rpm for 10 minutes to separate serum, which was immediately tested or stored at −20°C for subsequent analysis. (2) Enzyme-Linked Immunosorbent Assay (ELISA): ① Reagents and Consumables: ELISA kits for CA125, SCC-Ag, TSGF, and Cyfra211 were used according to the manufacturer's instructions. Specific steps: ELISA plates were prepared, and standards, samples, and blank controls (50 μL per well) were added. Enzyme-linked conjugates (50 μL) were added, gently mixed, and incubated at 37°C for 30 minutes. Plates were washed five times using an automatic or manual washer. Substrate solution (100 μL) was added to each well and reacted in the dark for 15 minutes, followed by the addition of 50 μL stop solution to terminate the reaction. OD values were measured at 450 nm using a microplate reader. ② Result Calculation: Concentrations of CA125, SCC-Ag, TSGF, and Cyfra211 were calculated using a standard curve, and the serum tumor marker concentrations for each patient were recorded.

Follow-Up

All patients were followed for one year. Follow-up methods included telephone and home visits, with endpoints being patient deaths from any cause.

Observation Indicators

(1) Differences in immune cell and tumor marker levels among the three groups were observed. (2) The relationship between HPV levels and immune cells and tumor markers in high-risk HPV cervical cancer patients was analyzed. (3) Differences in immune cell and tumor marker expression levels between high-risk HPV-infected cervical cancer patients with and without lymph node metastasis were observed. (4) Differences in immune cell and tumor marker expression levels between deceased and surviving cervical cancer patients were observed.

Statistical Analysis

GraphPad Prism 8 was used for graphing, and SPSS 22.0 was used for data analysis. Measurement data were expressed as mean ± standard deviation (SD). Independent sample *t*-tests were used for two-group comparisons, and ANOVA was used for

multi-group comparisons. The relationship between HPV levels and immune cells and tumor markers in high-risk HPV cervical cancer patients was analyzed using Spearman correlation. A P-value < 0.05 was considered statistically significant.

Results

Comparison of Immune Cell and Tumor Marker Levels Among the Three Groups

All indicators showed significant differences among the three groups (P < 0.05). Group A had significantly lower CD4+/CD8+ (1.18 ± 0.25 vs 1.42 ± 0.22* and 1.58 ± 0.19*#) and CD56+ (12.35 ± 3.28% vs 15.67 ± 3.10%* and 18.04 ± 2.97%*#) levels, and higher Treg (8.92 ± 1.85% vs 6.41 ± 1.74%* and 4.87 ± 1.56%*#) and tumor markers compared to Groups B and C (P < 0.05). Similar trends were observed in Group B vs Group C (Table 1). Notably, these systemic immune and tumor marker profiles consistently worsened with disease progression (chronic cervicitis → CIN → cervical cancer).

Correlation between HPV Levels and Immune Cells and Tumor Markers in High-Risk HPV Cervical Cancer Patients

In Group A, peripheral blood Treg levels and serum tumor markers (CA125, SCC-Ag, TSGF, Cyfra211) showed strong positive correlations with HPV-DNA levels (r = 0.552–0.613, P < 0.05), whereas CD4+/CD8+ and CD56+ levels were inversely correlated (r = −0.482 and −0.467, P < 0.05). These correlations suggest a dose-dependent relationship between HPV viral load and systemic immune suppression/tumor burden.

Comparison of Immune Cell and Tumor Marker Levels in High-Risk HPV Cervical Cancer Patients with and without Lymph Node Metastasis

Patients with lymph node metastasis exhibited more pronounced immune dysfunction (CD4+/CD8+: 0.88 ± 0.12 vs 1.15 ± 0.14; CD56+: 11.65 ± 2.84% vs 16.23 ± 3.12%) and elevated tumor markers (eg, CA125: 52.83 ± 10.22 U/mL vs 37.43 ± 8.91 U/mL) compared to those without metastasis (P < 0.05) (Table 2). These findings highlight the association between systemic immune dysregulation and metastatic progression.

Comparison of Immune Cell and Tumor Marker Levels between Deceased and Surviving Cervical Cancer Patients

After a 1-year follow-up, deceased patients (n=22) demonstrated severely compromised immune profiles (CD4+/CD8+: 0.84 ± 0.11 vs 1.18 ± 0.15; Treg: 12.17 ± 1.64% vs 7.96 ± 1.32%) and markedly higher tumor marker levels (eg, TSGF: 90.72 ± 14.36 μg/mL vs 63.25 ± 11.18 μg/mL) compared to survivors (n=47) (P < 0.05) (Table 3). These systemic indicators strongly predicted poor survival outcomes.

Table 1 Comparison of Immune Cell and Tumor Marker Levels Among the Three Groups ($\bar{x} \pm s$)

Immune Cells	Group A (n=69)	Group B (n=78)	Group C (n=52)	*F*	*P*
CD4+/CD8+	1.18±0.25	1.42±0.22*	1.58±0.19*#	49.553	<0.001
CD56+ (%)	12.35±3.28	15.67±3.10*	18.04±2.97*#	50.817	<0.001
Treg (%)	8.92±1.85	6.41±1.74*	4.87±1.56*#	85.458	<0.001
Tumor Markers	–	–	–	–	–
CA125 (U/mL)	42.36±8.74	27.89±6.35*	15.27±5.63*#	218.822	<0.001
SCC-Ag (ng/mL)	3.84±0.91	2.12±0.68*	1.34±0.49*#	192.688	<0.001
TSGF (μg/mL)	72.18±10.64	56.29±8.57*	43.78±7.92*#	145.413	<0.001
Cyfra211 (ng/mL)	4.52±0.94	2.86±0.72*	1.98±0.63*#	168.408	<0.001

Notes: Data are presented as mean ± SD; Compared with Group A, *P < 0.05; compared with Group B, #P < 0.05.

Table 2 Comparison of Immune Cell and Tumor Marker Levels in High-Risk HPV Cervical Cancer Patients With and Without Lymph Node Metastasis ($\bar{x} \pm s$)

Immune Cells	Group A (n=69)		t	P
	With Metastasis (n=27)	Without Metastasis (n=42)		
CD4+/CD8+	0.88±0.12	1.15±0.14	8.254	<0.001
CD56+ (%)	11.65±2.84	16.23±3.12	6.159	<0.001
Treg (%)	11.32±1.57	8.22±1.43	8.457	<0.001
Tumor Markers	–	–	–	–
CA125 (U/mL)	52.83±10.22	37.43±8.91	6.613	<0.001
SCC-Ag (ng/mL)	3.56±0.87	2.12±0.65	7.855	<0.001
TSGF (μg/mL)	85.42 ±12.63	66.34±10.85	6.683	<0.001
Cyfra211 (ng/mL)	6.15±1.23	4.82±1.10	4.679	<0.001

Note: Data are presented as mean ± SD.

Table 3 Comparison of Immune Cell and Tumor Marker Levels Between Deceased and Surviving Cervical Cancer Patients ($\bar{x} \pm s$)

Immune Cells	Group A (n=69)		t	P
	Deceased (n=22)	Surviving (n=47)		
CD4+/CD8+	0.84±0.11	1.18±0.15	9.488	<0.001
CD56+ (%)	10.92±2.53	16.85±3.07	7.884	<0.001
Treg (%)	12.17±1.64	7.96±1.32	11.412	<0.001
Tumor Markers	–	–	–	–
CA125 (U/mL)	58.43±11.85	35.67±9.54	8.537	<0.001
SCC-Ag (ng/mL)	3.78±0.91	2.05±0.68	8.816	<0.001
TSGF (μg/mL)	90.72±14.36	63.25±11.18	8.669	<0.001
Cyfra211 (ng/mL)	6.45±1.35	4.52±1.08	6.378	<0.001

Discussion

Cellular immunity occupies a central role in the immune defense system, with CD4+ helper T cells, CD8+ cytotoxic T cells, and CD56+ natural killer cells collectively forming a critical barrier against viral infections and tumor cell proliferation.[14,15] However, high-risk HPV infection evades immune surveillance and weakens antitumor immune responses through various mechanisms. Importantly, our study focused on systemic immune alterations by analyzing peripheral blood immune cell profiles, which reflect the body's global immune status rather than localized tumor microenvironment changes. For instance, the HPV viral proteins E6 and E7 not only disrupt host cell cycle regulation but also inhibit antigen presentation and interfere with the activation of effector T cells, further promoting immunosuppression.[16] The observed systemic decline in CD4+/CD8+ and CD56+ levels (peripheral blood) in cervical cancer patients suggests that HPV-induced immune dysfunction extends beyond the local tumor site, potentially compromising host-wide antiviral and antitumor defenses.

Moreover, excessive activation of circulating Tregs is considered a key factor in immunosuppression induced by high-risk HPV infection, creating a systemic immune microenvironment conducive to tumor proliferation and metastasis.[17] The results of this study indicate that cervical cancer patients (Group A) exhibited significantly lower peripheral CD4+/CD8+ ratios and CD56+ NK cell frequencies compared to patients with cervical intraepithelial neoplasia (Group B) and chronic cervicitis (Group C), whereas systemic Treg cell levels were higher in Group A. This systemic immune imbalance (reduced cytotoxic T/NK activity and elevated immunosuppressive Tregs) contrasts with prior reports focusing on local tumor-infiltrating lymphocytes,[18,19] highlighting the need to evaluate both tissue-specific and systemic immune alterations in HPV-related diseases. The reduced CD4+/CD8+ ratio reflects weakened

immune surveillance, potentially due to HPV's interference with antigen presentation and T cell activation, resulting in dysfunctional helper and cytotoxic T cells.[20] The decrease in CD56+ natural killer cells indicates that HPV infection may suppress innate immune pathways, impairing the body's ability to eliminate infected cells and early cancerous cells. The significant increase in Treg cells suggests that HPV infection may enhance the activity of immunosuppressive cells, suppressing effector immune responses[21] and thus creating conditions favorable for tumor cell survival and proliferation.

The development and progression of cervical cancer are closely related not only to immune system dysfunction but also to abnormal systemic expression of circulating tumor markers, which represent important biological characteristics of the disease. These markers not only indicate the presence of tumors but also reflect their invasiveness, growth activity, and metastatic potential, playing a crucial role in staging, therapeutic efficacy evaluation, and prognostic prediction.[22,23] Notably, our measurement of serum tumor markers (eg, CA125, SCC-Ag) provides a non-invasive approach to assess tumor burden, complementing tissue-based diagnostic methods. CA125 and SCC-Ag are common tumor markers in cervical cancer, with elevated serum levels often associated with tumor invasiveness and metastasis. CA125, a carbohydrate antigen, may be upregulated in the tumor microenvironment due to enhanced glycosylation, enabling tumor cells to evade immune surveillance.[24] SCC-Ag, a specific marker of squamous cell carcinoma, is elevated potentially due to apoptosis inhibition and antigen presentation dysfunction, promoting tumor survival and dissemination.[25] Additionally, TSGF and Cyfra211, as newer tumor markers, primarily reflect tumor cell proliferation and structural dynamics. TSGF supports tumor survival by promoting angiogenesis and regulating cytokine networks, with its increased expression possibly resulting from adaptive changes in the tumor microenvironment.[26] Elevated Cyfra211 levels often indicate remodeling of tumor cell cytoskeletal structures and weakened intercellular connections, processes that may be associated with epithelial-mesenchymal transition (EMT) initiation and increased metastatic potential.[27] Recent studies confirm that high-risk HPV infection plays a central role in driving changes in these tumor markers. The E6 and E7 gene products of high-risk HPV interfere with host p53 and Rb pathways, inhibiting cell cycle regulation and DNA repair. Additionally, they may influence the metabolism and distribution of tumor markers by upregulating related enzymes. For example, HPV infection may increase CA125 levels by inducing glycosylase activity,[28] while inhibiting protease degradation mechanisms,[29] resulting in more pronounced serum accumulation of SCC-Ag and Cyfra211. TSGF expression may be influenced by interactions between HPV viral proteins and host signaling pathways, further enhancing the energy and nutrient demands of tumor cells. This study demonstrates significantly higher levels of CA125, SCC-Ag, TSGF, and Cyfra211 in cervical cancer patients compared to those with cervical intraepithelial neoplasia and chronic cervicitis, with these markers showing significant positive correlations with HPV-DNA load. This finding not only further verifies the crucial role of HPV infection in cervical cancer development but also provides theoretical support for the combined application of tumor markers in diagnosing and prognosticating high-risk HPV-related diseases.

Furthermore, this study analyzed lymph node metastasis and prognosis in cervical cancer patients with high-risk HPV infection. Results showed that cervical cancer patients with lymph node metastasis had lower CD4+/CD8+ and CD56+ levels but higher levels of Treg, CA125, SCC-Ag, TSGF, and Cyfra211 compared to patients without lymph node metastasis. This finding, consistent with Chen et al,[30] suggests that immune system dysfunction may be a key mechanism underlying disease exacerbation in patients with lymph node metastasis. Lymph node metastasis not only marks increased tumor invasiveness but may also be accompanied by more severe immunosuppression and higher tumor biological activity, factors that collectively drive rapid disease progression. Follow-up observations further revealed the potential application value of these immunological and molecular markers in prognostic evaluation. Results showed that deceased cervical cancer patients had lower CD4+/CD8+ and CD56+ levels but higher levels of Treg, CA125, SCC-Ag, TSGF, and Cyfra211 compared to survivors. These findings indicate that further immune dysfunction and sustained tumor marker abnormalities may be major contributors to poor outcomes. The marked decline in immune markers among deceased patients may reflect a comprehensive imbalance in antitumor immunity, while elevated tumor markers suggest increased tumor burden and activity. These findings have important clinical implications. On one hand, the synergistic effects of lymph node metastasis and immunosuppression, along with their impact on tumor behavior, provide new insights into critical nodes of cervical cancer progression. On the other hand, monitoring dynamic changes in immune function and tumor markers during follow-up offers a reliable basis for disease evaluation and optimization of treatment decisions.

Despite the significant insights revealed by this study on the role of high-risk HPV infection in cervical disease, some limitations remain. First, as a single-center retrospective analysis with a limited sample size, the generalizability of the findings may be affected. Second, the lack of long-term longitudinal studies and molecular mechanism experiments precludes a comprehensive elucidation of the specific mechanisms by which HPV infection induces immunosuppression and tumor marker elevation. Third, while our systemic approach (peripheral blood/serum analysis) offers clinical practicality, it may not fully capture immune and molecular changes within the cervical tumor microenvironment. Future studies should integrate both local (tissue) and systemic (blood) markers to comprehensively evaluate HPV-associated pathogenesis. And expand sample sizes, incorporate multicenter data, and explore the role of high-risk HPV infection in cervical cancer through prospective and mechanistic studies. Such efforts aim to provide more reliable theoretical evidence and practical guidance for early diagnosis, precise treatment, and individualized prognostic management of the disease. Additionally, targeted interventions addressing the immune microenvironment, especially those that inhibit Treg cell activity or enhance CD8+ T cell and natural killer cell functions, should be explored to improve the immune status and therapeutic outcomes of patients with high-risk HPV-related cervical cancer.

Conclusion

In conclusion, high-risk HPV infection induces systemic immune dysfunction (evidenced by reduced peripheral CD4+/CD8+ and CD56+ levels, elevated Tregs) and aberrant circulating tumor marker expression (eg, serum CA125, SCC-Ag) in cervical cancer. These systemic alterations play critical roles in disease progression and prognosis. Peripheral blood-based monitoring of immune cells and serum tumor markers offers a non-invasive approach for early diagnosis, metastasis risk assessment, and survival prediction in HPV-associated cervical diseases. Furthermore, targeting systemic immunosuppression (eg, enhancing CD8+/NK activity or inhibiting Tregs) may represent a promising therapeutic strategy. Future studies should integrate local (tissue) and systemic (blood) biomarkers to comprehensively elucidate HPV-driven oncogenesis.

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Disclosure

The authors report no conflicts of interest in this work.

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