

ORIGINAL RESEARCH

Analysis of the value of transvaginal color Doppler ultrasound parameters combined with systemic immune-inflammation index in predicting the risk of lymph node metastasis in cervical cancer

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Abstract

Background: The study aimed to explore the predictive value of transvaginal color Doppler ultrasound parameters combined with the systemic immune-inflammation index (SII) in assessing the risk of lymph node metastasis in cervical cancer. **Methods:** A total of 172 patients diagnosed with cervical cancer from January 2016 to January 2024 were enrolled, and divided into a lymph node metastasis group (56 cases) and a non-lymph node metastasis group (116 cases) based on biopsy results as the gold standard. Clinical data, transvaginal color Doppler ultrasound parameters, and SII were compared between the two groups. Variables showing significantly different values were selected to construct a logistic model, and the diagnostic performance was analyzed using the receiver operating characteristic (ROC) curve. **Results:** Logistic regression analysis identified Lymph Node Short-axis Diameter (SAD), tumor length-to-short-axis diameter ratio (LS) <2, peak systolic velocity (PSV), and SII as the independent risk factors for lymph node metastasis in cervical cancer patients. The transvaginal ultrasound pulsatility index (PI) and resistance index (RI) were protective factors. The predictive model incorporating SAD, LS, PSV, PI, RI, and SII achieved an area under the ROC curve (AUC) of 0.946, with a Youden index of 0.762, and sensitivity and specificity of 85.70% and 95.00%, respectively. **Conclusions:** The risk prediction model integrating transvaginal color Doppler ultrasound parameters and SII demonstrates high predictive value for cervical cancer lymph node metastasis, suggesting a valuable clinical application potential.

Keywords

Transvaginal color Doppler ultrasound; Systemic immune-inflammation index; Cervical cancer; Lymph node metastasis; Risk prediction

1. Introduction

Cervical cancer remains one of the common malignancies among women, consistently maintaining high incidence and mortality rates globally, posing a severe threat to women's lives and health [1, 2]. The clinical symptoms of early-stage cervical cancer are not evident, and once the disease progresses to the advanced stage, the treatment outcomes are often poor [3]. Therefore, early diagnosis of cervical cancer and assessment of its lymph node metastasis risk are crucial for formulating effective treatment plans and improving patient survival rates [4, 5]. Recent advances in imaging technology and immunological research have introduced novel detection methods, such as transvaginal color Doppler ultrasound (TVS) and the systemic immune-inflammation index (SII), in the diagnosis and prognostic assessment of cervical cancer [6]. In addition to TVS, non-invasive imaging techniques,

such as Fluorodeoxyglucose Positron Emission Tomography-Computed Tomography (FDG PET-CT), have high sensitivity in the diagnosis of lymph node metastasis. However, their high cost and radiation exposure risk limit their routine application. On one hand, TVS, as a non-invasive examination method, offers high resolution, clear visualization, and ease of operation [7]. It enables accurate assessment of tumor size, morphology, blood flow signals, and other parameters, thereby providing an important basis for the diagnosis of cervical cancer [8]. The SII, on the other hand, assesses inflammatory changes in the body based on neutrophil, lymphocyte, and platelet counts in peripheral blood. It has been shown to correlate with the prognosis of various tumors, reflecting the immune status and inflammatory response of the body [9]. Both the TVS parameters [10] and the SII [11] have been indicated to have a certain value in predicting the risk of lymph node metastasis in cervical cancer. However, systematic research and reports

on the combined application of these two methods and their specific value in predicting the risk of lymph node metastasis in cervical cancer are lacking.

Therefore, this study aimed to address the gap by analyzing clinical data from cervical cancer patients to explore the predictive utility of combining TVS parameters with the SII in assessing the risk of lymph node metastasis in cervical cancer. The findings may provide new ideas and methods for the early diagnosis and treatment planning in cervical cancer.

2. Materials and methods

2.1 General information

This was a retrospective study conducted among cervical cancer patients treated in our hospital from January 2016 to January 2024. Inclusion criteria were: ① aged 18 to 75 years; ② pathologically diagnosed with cervical cancer, consistent with the diagnostic criteria of the British Gynaecological Cancer Society (BGCS) [12]; ③ no history of preoperative radiotherapy, chemotherapy, or other interventional treatments; ④ underwent transvaginal color Doppler ultrasound examination; and ⑤ having complete medical records. Exclusion criteria were: ① coexistence of other malignancies; ② presence of severe heart, liver, or renal dysfunction; and ③ history of infectious diseases or autoimmune diseases. A total of 172 patients meeting the above criteria were enrolled. These patients were divided into lymph node metastasis group (56 cases) and non-lymph node metastasis group (116 cases) based on the presence or absence of lymph node metastasis.

2.2 Methods

2.2.1 Transvaginal color Doppler ultrasound examination

All patients underwent preoperative transvaginal color Doppler ultrasound examination. Before the examination, patients were asked to empty their bladder and take the lithotomy position to ensure clear visualization of pelvic structures. Examination was conducted using a Esaote Mylab Twice EHD color Doppler ultrasound diagnostic apparatus (Mylab Twice EHD, Esaote S.p.A., Esaote, Florence, Italy) equipped with a high-frequency (6–10 MHz) vaginal probe. The data is sourced from archived reports/images of preoperative routine transvaginal ultrasound examinations of patients, which were retrospectively reviewed by two doctors in a double-blind manner. The cervix and its surrounding tissues were observed in detail, and the tumor size, morphology, boundary clarity, internal echo characteristics, and the presence of liquefaction necrosis or calcification were recorded. Appropriate blood flow sensitivity and filters were adjusted to focus on observing the blood flow distribution patterns (such as dotted, strip, or reticular) and signal intensity within and around the tumor. The pulse Doppler mode was activated at the location with the most prominent blood flow signal to measure the following hemodynamic parameters: peak systolic velocity (PSV, cm/s); pulsatility index (PI): (peak velocity—minimum velocity)/mean velocity; and resistance index (RI): (peak

velocity—minimum velocity)/peak velocity.

2.2.2 Calculation of systemic immune-inflammation index (SII)

We obtained the patients' SII through the case system. The calculation method of SII was as follows: For each patient, 2 mL of peripheral venous blood was collected in the morning after an overnight fasting. The blood samples were analyzed within one week before surgery in a routine hematology laboratory of our hospital using a XP-100 hematology analyzer (SYSMEX CORPORATION, XP-100, Kobe, Japan) to obtain the patient's neutrophil count ($\times 10^9/L$), lymphocyte count ($\times 10^9/L$), and platelet count ($\times 10^9/L$). The SII was calculated using the following formula: $SII = (\text{peripheral platelet count} \times \text{absolute neutrophil count}) / \text{absolute lymphocyte count}$.

2.2.3 Lymph node metastasis assessment

We obtained the lymph node metastasis status of patients through the case system. The diagnosis of lymph node metastasis was as follows: During surgery, the operating surgeon performed sampling biopsies of suspicious lymph nodes. Indocyanine Green (ICG) and other lymph node mapping techniques were not used, and the status of lymph nodes was judged mainly by palpation combined with frozen pathological biopsy. Suspicious lymph nodes, based on intraoperative palpation and gross morphological features (*e.g.*, enlarged size, firm texture, or irregular surface), were either fully or partially resected and immediately sent to the pathology department for rapid frozen section analysis and routine paraffin section examination. Hematoxylin-eosin (HE) staining and immunohistochemical analysis was used to confirm the presence of tumor cell metastasis in the lymph nodes. The intraoperative rapid pathological results were used to guide intraoperative adjustments to the surgical approach, while postoperative routine pathological results served as the definitive diagnostic reference.

2.3 Statistical methods

Statistical analysis was performed using SPSS 26.0 software (IBM SPSS Statistics, Armonk, NY, USA). Continuous data were expressed as mean $\pm$ standard deviation ($\bar{x} \pm s$), and compared using the *t*-test. Categorical variables were expressed as percentages (%) and compared using the χ^2 test. Logistic regression models were used to analyze the relationship between transvaginal color Doppler ultrasound parameters (such as tumor size, blood flow resistance index, *etc.*) and the SII with the risk of lymph node metastasis in cervical cancer. The predictive efficacy of each parameter was calculated, and Receiver Operating Characteristic (ROC) curves were plotted to determine the sensitivity and specificity of the combined prediction model. A *p*-value < 0.05 was considered statistically significant.

3. Results

3.1 Comparison of clinical data between the two groups

Compared with patients in the non-lymph node metastasis group, lymph node metastasis group had a higher proportion of positive vascular infiltration, indistinct tumor margins, presence of Lymph Node Short-axis Diameter (SAD), tumor size >4 cm, and a tumor length-to-width ratio ≤ 2 ($p < 0.05$). Additionally, patients in the lymph node metastasis group exhibited higher PSV and SII values ($p < 0.05$) and lower PI and RI values ($p < 0.05$). No significant differences were observed in other tested clinical parameters ($p > 0.05$). Detailed results are presented in Table 1.

3.2 Multivariable analysis of risk factors for lymph node metastasis in cervical cancer

With group assignment as the dependent variable (lymph node metastasis group assigned as 1 and non-lymph node metastasis group assigned as 0), statistically significant variables between the two groups were used as independent variables. The PSV, PI, RI, and SII indices were analyzed as continuous variables. Categorical variables were coded as follows: positive vascular infiltration = 1, negative = 0; clear tumor margins = 1, indistinct = 2; SAD >10 mm = 1, ≤ 10 mm = 2; tumor size ≤ 4 cm = 1, >4 cm = 2; and a tumor length-to-width ratio ≤ 2 = 1, >2 = 2. Logistic regression analysis indicated that transvaginal ultrasonography-detected SAD, tumor length-to-short-axis diameter ratio (LS), blood flow parameter PSV, and SII were independent risk factors for lymph node metastasis in cervical cancer patients. Conversely, blood flow parameters, PI and RI from transvaginal ultrasonography were protective factors. The detailed logistic regression results are presented in Table 2.

3.3 Construction and validation of a risk prediction model for lymph node metastasis in cervical cancer

A risk prediction model for lymph node metastasis in cervical cancer was constructed based on SAD, LS, PSV, PI, RI, and SII. The probability (P) of lymph node metastasis in cervical cancer was calculated as follows: $P = 1.810\text{SAD} + 2.069\text{LS} + 0.145\text{PSV} - 19.130\text{PI} - 18.157\text{RI} + 0.009\text{SII} - 2.300$. Variance expansion factor (VIF) was used to evaluate the multicollinearity of variables. The results showed that VIF of all indicators was less than 2, suggesting no significant collinearity ($p > 0.05$). ROC analysis revealed the Area Under the Curve (AUC) of the risk prediction model for lymph node metastasis in cervical cancer to be 0.946, with a Youden index of 0.762, and sensitivity and specificity of 85.70% and 95.00%, respectively. Detailed statistical results are presented in Table 3, and the ROC curve is shown in Fig. 1.

4. Discussion

Lymph node metastasis is a critical pathway in the progression of cervical cancer, and its incidence is closely related to disease stage and treatment regimen [13, 14]. Studies have shown that the incidence of lymph node metastasis in cervical cancer

patients, especially those in stages IIB, III, and IV, is 9%, 13–30%, and 50%, respectively [15]. The presence of lymph node metastasis not only shortens patient survival, but also increases the challenges of treatment. Therefore, assessing the risk of lymph node metastasis in cervical cancer is of great clinical significance. Previous studies have identified several potential predictors of lymph node metastasis in cervical cancer patients, including squamous cell carcinoma antigen (SCCA), maximum normalized standardized uptake value (nSUVmax) of lymph nodes, PET/CT evidence of uterine body invasion, and PET/CT-derived tumor size [16]. Other studies have also shown that lymphovascular invasion (LVI), depth of invasion (DI), tumor size (TS), and squamous cell carcinoma (SCC) antigen levels are independent risk factors for lung cancer [17]. At the genetic level, somatic *single nucleotide variant (SNV)/Indel* mutation in *E1A Binding Protein P300 (EP300)* and *F-Box And WD Repeat Domain Containing 7 (FBXW7)*, as well as *Signature 3 (SBS3)* homologous recombination-mediated DNA repair defects, are most frequent in lymph node-positive patients. *Tumor mutational burden (TMB)* and *Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Alpha (PIK3CA)* mutations have also been proposed as biomarkers for lymph node metastasis [18]. This study demonstrates that the combination of transvaginal color Doppler ultrasonography parameters and the SII has significant value in predicting the risk of lymph node metastasis in cervical cancer. Compared with many previously reported predictors, this combined approach is non-invasive, free from radiation exposure, relatively convenient and inexpensive, making it highly suitable for clinical application.

Transvaginal color Doppler ultrasonography is an important tool in gynecological examinations due to its non-invasive, real-time, and high-resolution capabilities [19]. Studies have shown that extracting radiomic features from transvaginal ultrasound images and incorporating them into an XGBoost model-based nomogram, combined with clinical features and radiomics, can significantly improve the prediction of lymph node metastasis in endometrial cancer [20]. This technique allows in-depth pelvic observation of organ structures using high-frequency probes, providing detailed information on the uterus, ovaries, and other pelvic tissues, and is widely used in lesion screening, tumor property assessment, and preoperative planning [21]. A meta-analysis by Borges *et al.* [22] indicated that transvaginal ultrasonography has broad diagnostic value for preoperative lymph node metastasis in gynecological cancers, with a specificity of 98% (95% CI, 93–99%). Their results showed that patients in the lymph node metastasis group had significantly different multiple pathological and ultrasound characteristics compared with patients in the no lymph node metastasis group. Specifically, the lymph node metastasis group had a higher incidence of vascular invasion, blurred tumor boundaries, SAD, tumor sizes >4 cm and a tumor length-to-width ratio ≤ 2 compared with those in non-metastasis group ($p < 0.05$). Additionally, ultrasound blood flow parameters revealed that the PSV in the lymph node metastasis group was significantly higher than in the non-metastasis group ($p < 0.05$), while PI and RI were significantly lower in the same group ($p < 0.05$). Notably, when used as standalone predictors (Table 3), PI and RI exhib-

TABLE 1. Comparison of general information between the two groups.

Parameter	Lymph node metastasis group (n = 56)	Non-lymph node metastasis group (n = 116)	<i>t</i> -test/ χ^2	<i>p</i> -value
Age (yr, $\bar{x} \pm s$)	46.09 $\pm$ 10.52	47.35 $\pm$ 11.50	0.692	0.490
BMI (kg/m ² , $\bar{x} \pm s$)	24.85 $\pm$ 2.98	25.28 $\pm$ 2.89	0.908	0.365
Number of pregnancies, n (%)				
<2	4 (7.14)	12 (10.34)	0.459	0.498
≥ 2	52 (92.86)	104 (89.66)		
Menopause or not, n (%)				
Yes	21 (37.50)	46 (39.66)	0.074	0.786
No	35 (62.50)	70 (60.34)		
History of diabetes, n (%)				
Yes	11 (19.64)	20 (17.24)	0.147	0.701
No	45 (80.36)	96 (82.76)		
History of hypertension, n (%)				
Yes	17 (30.36)	40 (34.48)	0.290	0.590
No	39 (69.64)	76 (65.52)		
Drinking history, n (%)				
Yes	3 (5.36)	7 (6.03)	0.032	0.859
No	53 (94.64)	109 (93.97)		
Smoking history, n (%)				
Yes	3 (5.36)	9 (7.76)	0.336	0.562
No	53 (94.64)	107 (92.24)		
Pathological type, n (%)				
Squamous cell carcinoma	52 (92.86)	104 (89.66)	0.459	0.498
Non squamous cell carcinoma	4 (7.14)	12 (10.34)		
Vascular invasion, n (%)				
Positive	34 (60.71)	47 (40.52)	6.183	0.013
Negative	22 (39.29)	69 (59.48)		
Tumor boundary, n (%)				
Clear	19 (33.93)	58 (50.00)	3.945	0.047
Vague	37 (66.07)	58 (50.00)		
SAD, n (%)				
>10 mm	34 (60.71)	50 (43.10)	4.688	0.030
≤ 10 mm	22 (39.29)	66 (56.90)		
Tumor size, n (%)				
≤ 4 cm	30 (53.57)	85 (73.28)	3.882	0.049
>4 cm	26 (46.43)	31 (26.72)		
HPV infection, n (%)				
Yes	6 (10.71)	20 (17.24)	1.254	0.263
No	50 (89.29)	96 (82.76)		
Long diameter/short diameter ratio, n (%)				
≤ 2	40 (71.43)	36 (31.03)	24.988	<0.001
>2	16 (28.57)	80 (68.97)		
PSV (cm/s, $\bar{x} \pm s$)	19.54 $\pm$ 5.74	16.34 $\pm$ 4.76	3.851	<0.001
PI ($\bar{x} \pm s$)	0.25 $\pm$ 0.06	0.31 $\pm$ 0.08	6.161	<0.001
RI ($\bar{x} \pm s$)	0.22 $\pm$ 0.06	0.28 $\pm$ 0.08	5.839	<0.001
SII ($\bar{x} \pm s$)	572.06 $\pm$ 161.53	424.38 $\pm$ 155.92	5.753	<0.001

SII: systemic immune-inflammation index; PSV: peak systolic velocity; PI: pulsatility index; RI: resistance index; BMI: body mass index; SAD: Short-axis Diameter; HPV: human papilloma virus.

TABLE 2. Logistic regression analysis of risk factors for lymph node metastasis in cervical cancer.

Variable	B	Standard Error	Wald	<i>p</i>	OR	95% CI lower limit	95% CI upper limit
Vascular Invasion	0.938	0.563	2.774	0.096	2.555	0.847	7.705
Tumor Boundary	0.666	0.597	1.247	0.264	1.947	0.605	6.267
SAD	1.839	0.639	8.274	0.004	6.288	1.797	22.007
Tumor Size	0.746	0.585	1.627	0.202	2.108	0.670	6.633
LS	2.219	0.609	13.291	<0.001	9.199	2.790	30.33
PSV	0.141	0.059	5.728	0.017	1.151	1.026	1.292
PI	-20.013	4.720	17.978	<0.001	0.112	0.000	0.211
RI	-17.91	4.711	14.455	<0.001	0.023	0.000	0.036
SII	0.009	0.002	16.551	<0.001	1.009	1.005	1.014

SII: systemic immune-inflammation index; PSV: peak systolic velocity; PI: pulsatility index; RI: resistance index; SAD: Short-axis Diameter; LS: length-to-short-axis diameter ratio; CI: confidence interval; OR: odds ratio; B: Regression Coefficient.

TABLE 3. Diagnostic value of the risk prediction model for lymph node metastasis in cervical cancer.

Variable	Cut-off	AUC (95% CI)	SE	<i>p</i>	Sensitivity	Specificity	Youden index
SAD	0.500	0.588 (0.497–0.679)	0.046	0.062	0.607	0.569	0.176
LS	1.500	0.702 (0.618–0.786)	0.043	<0.001	0.714	0.690	0.404
PSV	19.355	0.643 (0.553–0.734)	0.046	0.002	0.536	0.724	0.260
PI	0.348	0.743 (0.670–0.816)	0.037	<0.001	1.000	0.431	0.431
RI	0.300	0.718 (0.642–0.794)	0.039	<0.001	1.000	0.440	0.440
SII	668.465	0.730 (0.651–0.809)	0.040	<0.001	0.375	0.991	0.366
Combined	0.421	0.946 (0.911–0.982)	0.018	<0.001	0.857	0.950	0.762

SII: systemic immune-inflammation index; PSV: peak systolic velocity; PI: pulsatility index; RI: resistance index; SAD: Short-axis Diameter; LS: length-to-short-axis diameter ratio; CI: confidence interval; AUC: Area Under the Curve; SE: standard error.

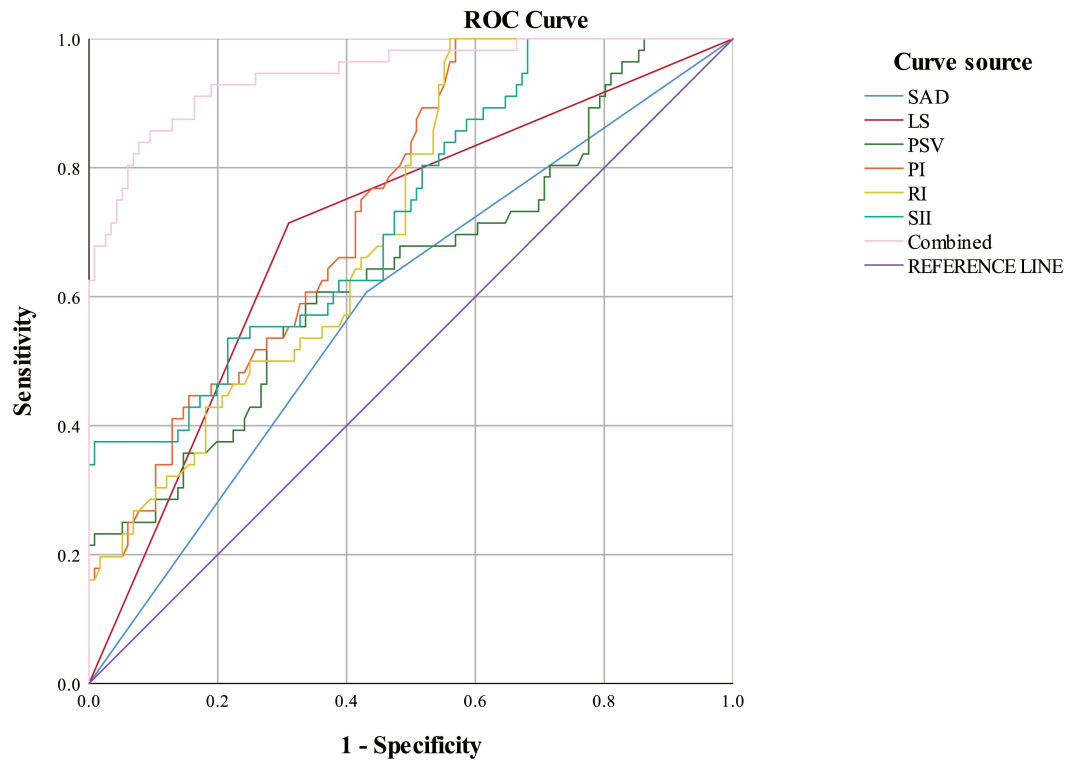


FIGURE 1. ROC curve of cervical cancer lymph node metastasis risk prediction model. ROC: receiver operating characteristic; SAD: Short-axis Diameter; LS: length-to-short-axis diameter ratio; PSV: peak systolic velocity; PI: pulsatility index; RI: resistance index; SII: systemic immune-inflammation index.

ited 100% sensitivity but low specificity (43.1% and 44.0%, respectively), indicating their limited utility for independent diagnosis due to high false-positive rates. This aligns with their role as protective factors, but highlights the need for integration into a multi-parameter model to balance sensitivity and specificity. The associations found in this study between lymph node metastasis and tumor hemodynamic characteristics are consistent with the conclusions of previous studies, showing that increased tumor angiogenesis is associated with reduced PI and RI, while elevated PSV reflects the high-velocity neovascularization [23]. Furthermore, morphological characteristics, such as a tumor length-to-width ratio ≤ 2 and blurred tumor boundaries, are also considered indicators of enhanced tumor aggressiveness, further supporting the conclusions of this study. SII has been widely used to assess local immune responses and systemic inflammatory states in recent years. In gynecological examinations, SII exhibits unique advantages as a non-invasive, easily accessible, and low-cost biomarker [24]. The results of this study indicate that patients in the lymph node metastasis group had significantly higher SII values compared with those in the no lymph node metastasis group ($p < 0.05$). Previous studies have shown the correlation of SII with poor prognosis in various malignancies [25], including cervical cancer, where high SII values correlate with poor patient prognosis [26]. These findings suggest that the SII is closely related to the lymph node metastasis status in cervical cancer, and high SII values may indicate a higher risk of lymph node metastasis.

The findings from transvaginal ultrasonography revealed that SAD, LS, the blood flow parameter PSV, and SII are independent risk factors for lymph node metastasis in cervical cancer patients, while the blood flow parameters PI and RI are protective factors. SAD, reflected in ultrasound images as abnormal proliferation of tissue structure, was found associated with the invasive growth of cervical cancer cells. Tumor cells invasion into surrounding tissues leads to thickening and morphological changes of the local tissue [27]. A reduced LS suggests a transition in lymph node morphology from oval to round, potentially reflecting morphological changes in lymph nodes due to tumor cell infiltration [28]. Such abnormal changes in tumor morphology provide a potential biological basis for lymph node metastasis in cervical cancer, as tumor cells invasiveness and proliferative capacity are key factors influencing metastatic spread. Blood flow parameters from ultrasonography can directly assess changes in tumor hemodynamics. Increased PSV, an important parameter for tumor angiogenesis, may indicate abundant blood vessels and fast blood flow within the tumor, this facilitates the nutritional supply and removal of metabolic waste and convenient conditions for tumor cell dissemination [29]. Unlike PSV, decreased PI and RI appear protective factors for lymph node metastasis in cervical cancer, likely due to alterations in intratumoral hemodynamics. Lower PI and RI may reflect more mature intratumoral blood vessels and reduced blood flow resistance, conditions that are less favorable for shedding and metastasis of tumor cells [30]. Additionally, decrease in these parameters may also be associated with the immune regulatory mechanisms of the body, which can reduce the invasiveness and metastatic ability of tumor cells by improving the tumor

microenvironment.

As a comprehensive indicator of systemic inflammation and immune status, an elevated SII indicates significant inflammatory responses and immunosuppression in patients. Tumor-associated inflammation can promote the invasiveness, angiogenesis, and immune escape ability of tumor cells, thereby increasing the risk of metastasis [31, 32]. The ROC curve analysis in this study showed that the predictive model incorporating SAD, LS, PSV, PI, RI, and SII achieved an AUC of 0.946, with a Youden index of 0.762, and sensitivity and specificity of 85.70% and 95.00%, respectively. These findings indicate that the model exhibits excellent performance in distinguishing cervical cancer patients with and without lymph node metastasis. Mechanistically, tumor metastasis involves the local lymph node microenvironment (SAD, LS), angiogenesis (PSV, PI, RI), and SII. A combined analysis can integrate this information and provide a comprehensive assessment from molecules to organ systems. Moreover, individual indicators may be significantly influenced by individual differences or external interference, resulting in a low signal-to-noise ratio. In contrast, multi-indicator model combined diagnosis employ cross-validation and weighted analysis, reducing the impact of interfering factors and improving diagnostic reliability.

Despite important findings, this study also has certain limitations. Firstly, the relatively limited sample size may restrict the widespread applicability and accuracy validation of the model. Future research needs to further expand the sample size to more comprehensively assess the model's performance. Secondly, although this study reveals the important role of transvaginal color Doppler ultrasound parameters and the systemic immune-inflammation index in predicting the risk of lymph node metastasis, the specific interaction mechanisms among these parameters and their relationship with tumor biological characteristics still require in-depth exploration. Third, this study did not use a matching design, mainly due to the limited sample size (172 cases), as matching may reduce statistical power. Future studies will consider propensity score adjustment to balance confounding factors between groups and verify model stability. Additionally, we will endeavor to expand the sample size and include more diverse gynecological tumors and cervical cancer patients with different pathological types to further validate and optimize this prediction model. These efforts aim to provide a more precise and comprehensive tool for predicting the risk of cervical cancer lymph node metastasis and offer strong support for individualized treatment and prognosis assessment of cervical cancer patients.

5. Conclusions

This study conducted an in-depth predictive analysis of the cervical cancer lymph node metastasis risk through the combined application of transvaginal color Doppler ultrasound parameters (including lymph node size, SAD, PSV, PI, RI) and the SII. The combined prediction model demonstrated significant advantages in assessing the risk of cervical cancer lymph node metastasis and shows considerable potential for clinical application.

AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

DEL, XHX—designed the study and carried them out; interpreted the data; prepared the manuscript for publication and reviewed the draft of the manuscript. DEL, XHX and LY—supervised the data collection; analyzed the data. All authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of Ningbo Yinzhou No.2 Hospital (Approval no. 2025034). Written informed consent was obtained from legally authorized representatives for anonymized patient information to be published in this article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

- [1] Ikeda M, Shida M, Shigeta S, Nagase S, Takahashi F, Yamagami W, *et al.* The trend and outcome of postsurgical therapy for high-risk early-stage cervical cancer with lymph node metastasis in Japan: a report from the Japan Society of Gynecologic Oncology (JSGO) guidelines evaluation committee. *Journal of Gynecologic Oncology*. 2021; 32: e44.
- [2] Tewari KS. Cervical cancer. *The New England Journal of Medicine*. 2025; 392: 56–71.
- [3] Perkins RB, Wentzensen N, Guido RS, Schiffman M. Cervical cancer screening: a review. *JAMA*. 2023; 330: 547–558.
- [4] Nicolai L, Yigit R, Bleeker MCG, Bart J, van der Velden J, Mom CH. The risk of lymph node metastasis in the new FIGO 2018 stage IA cervical cancer with >7 mm diameter. *Journal of Gynecologic Oncology*. 2023; 34: e75.
- [5] Cao L, Kong W, Li J, Song D, Jin B, Liu T, *et al.* Analysis of lymph node metastasis and risk factors in 975 patients with FIGO 2009 stage IA–IIA cervical cancer. *Gynecologic and Obstetric Investigation*. 2023; 88: 30–36.
- [6] Yang XL, Wang MM, Kou LN, Lai H, Wu DJ. Conditional survival for high-risk early-stage cervical cancer patients with lymph node metastasis after hysterectomy. *Current Problems in Cancer*. 2021; 45: 100756.
- [7] Peng Y, Liu J, Xie J, Li Q. Diagnostic value and efficacy evaluation value of transvaginal color doppler ultrasound parameters for uterine scar pregnancy and sub-type after cesarean section. *BMC Medical Imaging*. 2024; 24: 239.
- [8] Guo S, Liu L, Li Y, Shi H, Cong AN. Correlation between nm23-H₁ expression and transvaginal color Doppler ultrasound performance after radiotherapy for cervical cancer. *Translational Cancer Research*. 2022; 11: 1354–1361.
- [9] Liu P, Jiang Y, Zheng X, Pan B, Xiang H, Zheng M. Pretreatment systemic immune-inflammation index can predict response to neoadjuvant chemotherapy in cervical cancer at stages IB2–IIB. *Pathology and Oncology Research*. 2022; 28: 1610294.
- [10] Shao X, Bai L, Liang J, Li M. Diagnostic value and clinical significance of serum miR-4534 combined with transvaginal color Doppler ultrasound in cervical cancer. *Discover Oncology*. 2024; 15: 403.
- [11] Meng L, Yang Y, Hu X, Zhang R, Li X. Prognostic value of the pretreatment systemic immune-inflammation index in patients with prostate cancer: a systematic review and meta-analysis. *Journal of Translational Medicine*. 2023; 21: 79.
- [12] Morrison J, Balega J, Buckley L, Clamp A, Crosbie E, Drew Y, *et al.* British Gynaecological Cancer Society (BGCS) uterine cancer guidelines: recommendations for practice. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 2022; 270: 50–89.
- [13] Verit FF, Bese T, Demirkiran F. Correspondence on: the risk of lymph node metastasis in the new FIGO 2018 stage IA cervical cancer with >7 mm diameter by Nicolai *et al.* *Journal of Gynecologic Oncology*. 2024; 35: e91.
- [14] Guani B, Mahiou K, Crestani A, Cibula D, Buda A, Gaillard T, *et al.* Clinical impact of low-volume lymph node metastases in early-stage cervical cancer: a comprehensive meta-analysis. *Gynecologic Oncology*. 2022; 164: 446–454.
- [15] Olthof EP, van der Aa MA, Adam JA, Stalpers LJA, Wenzel HHB, van der Velden J, *et al.* The role of lymph nodes in cervical cancer: incidence and identification of lymph node metastases—a literature review. *International Journal of Clinical Oncology*. 2021; 26: 1600–1610.
- [16] Yang S, Liu C, Li C, Hua K. Nomogram predicting lymph node metastasis in the early-stage cervical cancer. *Frontiers in Medicine*. 2022; 9: 866283.
- [17] Xu M, Xie X, Cai L, Xie Y, Gao Q, Sun P. Risk factor assessment of lymph node metastasis in patients with FIGO stage IB1 cervical cancer. *Frontiers in Oncology*. 2022; 12: 809159.
- [18] He H, He M, Zhou Q, Tang Y, Wang J, Li X, *et al.* Genetic analysis of cervical cancer with lymph node metastasis. *Journal of Gynecologic Oncology*. 2024; 35: e102.
- [19] Wenzel HHB, Schnack TH, Van der Aa MA, Jensen PT, Høgdall CK, Hardie AN, *et al.* Risk factors for lymph node metastasis in women with FIGO 2018 IA cervical cancer with a horizontal spread of >7 mm. *European Journal of Cancer*. 2024; 212: 115063.
- [20] Liu X, Xiao W, Qiao J, Luo Q, Gao X, He F, *et al.* Prediction of lymph node metastasis in endometrial cancer based on color Doppler ultrasound radiomics. *Academic Radiology*. 2024; 31: 4499–4508.
- [21] Xu M, Xie X, Cai L, Liu D, Sun P. Preoperative scoring system for the prediction of risk of lymph node metastasis in cervical cancer. *Scientific Reports*. 2024; 14: 23860.
- [22] Borges AC, Veloso H, Galindo P, Danés A, Chacon E, Mínguez JA, *et al.* Role of ultrasound in detection of lymph-nodes metastasis in gynecological cancers: systematic review and meta-analysis. *Ultrasound in Obstetrics & Gynecology*. 2024; 64: 155–163.
- [23] Wang Y, Yang J, Wang Y. Serum miRNA combined with transvaginal color Doppler ultrasound diagnosis clinical research on cervical cancer. *Journal of Ultrasound in Medicine*. 2024; 43: 791–798.
- [24] Kou J, Huang J, Li J, Wu Z, Ni L. Systemic immune-inflammation index predicts prognosis and responsiveness to immunotherapy in cancer patients: a systematic review and meta-analysis. *Clinical and Experimental Medicine*. 2023; 23: 3895–3905.
- [25] Atasever Akkas E, Erdis E, Yucel B. Prognostic value of the systemic immune-inflammation index, systemic inflammation response index, and prognostic nutritional index in head and neck cancer. *European Archives of Oto-Rhino-Laryngology*. 2023; 280: 3821–3830.
- [26] Wang HB, Xu XT, Tian MX, Ding CC, Tang J, Qian Y, *et al.* Prognostic values of the prognostic nutritional index, geriatric nutritional risk index, and systemic inflammatory indexes in patients with stage IIB–III cervical cancer receiving radiotherapy. *Frontiers in Nutrition*. 2023; 10: 1000326.
- [27] Zhu Y, Shen B, Pei X, Liu H, Li G. CT, MRI, and PET imaging features in cervical cancer staging and lymph node metastasis. *American Journal of Translational Research*. 2021; 13: 10536.

- [28] Ran C, Sun J, Qu Y, Long N. Clinical value of MRI, serum SCCA, and CA125 levels in the diagnosis of lymph node metastasis and para-uterine infiltration in cervical cancer. *World Journal of Surgical Oncology*. 2021; 19: 343.
- [29] Sun X, Wei Z, Luo Y, Wang M. Exploration of the evaluation value of combined magnetic resonance imaging and ultrasound blood flow parameters in cervical lymph node metastasis of thyroid cancer. *Cancer Management and Research*. 2025; 17: 651–659.
- [30] Zhao J, Cai J, Wang H, Dong W, Zhang Y, Wang S, *et al*. Region-specific risk factors for pelvic lymph node metastasis in patients with stage IB1 cervical cancer. *Journal of Cancer*. 2021; 12: 2624–2632.
- [31] Zhang H, Lin J, Huang Y, Chen Y. The systemic immune-inflammation index as an independent predictor of survival in patients with locally advanced esophageal squamous cell Carcinoma Undergoing Neoadjuvant Radiotherapy. *Journal of Inflammation Research*. 2024; 17: 4575–4786.
- [32] Guo J, Lv W, Wang Z, Shang Y, Yang F, Zhang X, *et al*. Prognostic value of inflammatory and nutritional markers for patients with early-stage poorly-to moderately-differentiated cervical squamous cell carcinoma. *Cancer Control*. 2023; 30: 10732748221148913.

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