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ARTICLE

Clinicopathological Determinants of Lymph Node Metastasis in Early-Stage Cervical Cancer: A Retrospective Cohort Study

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Abstract

Aims/Background Accurate identification of lymph node metastasis is critical for optimising surgical strategies in early-stage cervical cancer. This study aimed to analyse multiple clinicopathological factors which are potentially associated with lymph node metastasis to guide personalised lymphadenectomy decisions.

Methods This retrospective cohort study included 266 patients with early-stage cervical cancer (International Federation of Gynecology and Obstetrics [FIGO] stage IA1 to IIA2) who underwent surgical treatment at Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, between 1 December 2014 and 31 December 2019. Patients were followed up every 3 months for the first 2 years, every 6 months for the next 3 years, and annually thereafter. The presence of lymph node metastasis was included as the primary outcome, while the associated factors as secondary outcomes. The univariate and multivariate logistic regression were performed to identify risk factors associated with lymph node metastasis.

Results The mean age of the study participants (n = 266) was 44.26 years (standard deviation [SD] = 10.19), and the median follow-up duration was 48.7 months (range 12–72 months). Lymph node metastasis was observed in 15.41% of patients. The metastatic rates increased with advancing FIGO stage: IA1 and IA2 (0%), IB1 (13.44%), IB2 (15.00%), IIA1 (23.33%), and IIA2 (66.67%). Univariate analysis identified FIGO stage ($p < 0.001$), depth of stromal invasion ($p < 0.001$), tumour size ($p = 0.017$), parametrial invasion ($p < 0.001$), and lymphovascular space invasion (LVSI) ($p < 0.001$) as significantly associated risk factors for lymph node metastasis. Multivariate analysis identified tumour size $\geq$4 cm (adjusted odds ratio [OR]: 3.857; 95% confidence interval [CI]: 1.530–9.728; $p = 0.004$), FIGO stage II (adjusted OR: 8.247; 95% CI: 3.171–21.455; $p < 0.001$), LVSI (adjusted OR: 2.974; 95% CI: 1.344–6.632; $p = 0.008$), and parametrial invasion (adjusted OR: 5.585; 95% CI: 1.900–16.415; $p = 0.002$) as independent risk factors for nodal metastasis.

Conclusion This study identifies several key clinicopathological factors associated with lymph node metastasis in early-stage cervical cancer. These findings underscore the importance of meticulous preoperative risk assessment and offer an evidence-based foundation for tailored surgical planning to improve patient outcomes.

Key words: cervical cancer; metastasis; parametrial invasion; lymphadenectomy

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Introduction

Cervical cancer remains a significant global health challenge, ranking as the fourth most common cancer among women (Bray et al, 2018). In 2020, there were an estimated 604,000 new cases and 342,000 deaths, underscoring the urgent need for comprehensive research and enhanced management strategies (Sung et al, 2021). The etiology of cervical cancer is well established. It results from persistent infection with high-risk human papillomavirus (HPV) types, with HPV types 16 and 18 accounting for approximately 70% of cases (de Sanjose et al, 2010; Ferenczy and Franco, 2002; Kombe et al, 2023).

Despite considerable advancements in understanding the pathogenesis of cervical cancer, significant gaps remain, particularly regarding the mechanisms underlying lymph node metastasis (Ji et al, 2023). Lymph node involvement is a critical prognostic factor influencing treatment decisions and outcomes. Metastatic lymph nodes are associated with a higher risk of recurrence and reduced overall survival, highlighting the significance of accurately assessing lymph node status for proper staging and treatment planning (Bhatla et al, 2018).

In early-stage cervical cancer, the presence of lymph node metastasis is associated with an approximately 30% reduction in 5-year overall survival rates (Peters et al, 2000). While pelvic lymphadenectomy is considered standard surgical management for young patients, the utility of para-aortic lymph node dissection remains a subject of debate. This is primarily due to its invasive nature, the potential for serious complications, and the technical expertise required to perform it safely (Park et al, 2008). While systematic lymphadenectomy aims to remove potentially metastatic nodes and mitigate recurrence risk, it is associated with substantial perioperative and long-term morbidity that can markedly diminish quality of life. Therefore, the accurate identification and targeted removal of metastatic lymph nodes while limiting surgical complications remains a crucial clinical objective.

Despite the established prognostic relevance of lymph node status, comprehensive data on clinicopathological predictors of lymph node metastasis remain limited. This limited understanding impedes the development of individualised surgical strategies. To address this knowledge gap, we conducted a comprehensive analysis of risk factors associated with lymph node metastasis in a large cohort of patients with cervical cancer who underwent relatively standardised surgical interventions.

Methods

Study Design and Population

This retrospective cohort analysis included 266 cervical cancer patients who underwent primary surgical treatment at Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, between 1 December 2014 and 31 December 2019. The study was approved by the Ethics Committee of Sir Run Run Shaw Hospital and conducted in accordance with the principles of the Declaration of Helsinki, and informed consent was obtained from each participant.

The inclusion criteria for patient selection were as follows: (1) histologically confirmed primary cervical cancer cases; (2) International Federation of Gynecology and Obstetrics [FIGO] 2009 (Pecorelli, 2009) clinical stages IA1 (with lymphovascular invasion), IA2, IB1, IB2, IIA1, or IIA2; (3) patients with no evidence of distant metastasis confirmed through preoperative imaging; (4) no history of neoadjuvant chemotherapy or radiation therapy; and (5) those with complete medical records and pathological data available. Exclusion criteria encompassed: patients with (1) recurrent cervical cancer, (2) other concurrent malignancies, (3) non-epithelial malignancies, and (4) incomplete lymphadenectomy.

Surgical Procedures and Pathological Evaluation

All patients underwent radical hysterectomy combined with bilateral salpingo-oophorectomy and systematic pelvic lymphadenectomy. In cases where gross lymph node metastasis was found intraoperatively, pelvic lymph node dissection and para-aortic lymph node dissection were generally conducted. The decision to proceed was based on intraoperative assessments, patient condition, and input from a multidisciplinary team. Pelvic lymphadenectomy included bilateral removal of lymph nodes from the external iliac, internal iliac, obturator fossa, common iliac, and presacral areas. Para-aortic lymphadenectomy was selectively performed based on preoperative imaging and intraoperative findings, particularly when suspicious para-aortic nodes were observed or when pelvic lymph nodes were found grossly enlarged. Lymph node specimens were labelled according to anatomical location and submitted separately for histopathological examination.

All specimens were independently reviewed by two experienced gynecologic pathologists who were blinded to the patient's clinical information. The pathological assessment included histological type, tumour grade, tumour size, depth of stromal invasion, lymphovascular space invasion (LVSI), parametrial involvement, vaginal margin status, and lymph node metastasis. Lymph nodes were entirely processed for microscopic examination using interval sectioning and stained with hematoxylin-eosin (H&E) for comprehensive analysis.

Data Collection and Outcome Measures

Patient-related data were obtained from medical records using a standardised form. Preoperative data included patient demographics, gynaecological history, and tumour marker levels (CA125). Postoperative pathological information consisted of FIGO stage, tumour size, histological type, and grade, depth of stromal invasion, LVSI, parametrial involvement, vaginal margin status, and details of lymph node metastasis. The primary outcome was the presence of pathologically confirmed lymph node metastasis, while secondary outcomes included factors associated with lymph node metastasis.

Statistical Analysis

Continuous variables were presented as mean $\pm$ standard deviation, while categorical variables were expressed as frequencies (percentages) and analysed using the chi-square test or Fisher's exact tests. The normality of continuous variables was assessed using the Shapiro-Wilk test. Univariate and multivariate logistic regression analyses were performed to identify factors associated with lymph node metastasis. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Confidence intervals for proportions were calculated using the Clopper-Pearson exact method for small sample sizes or proportions close to 0 or 1 and the Wilson score method for larger samples with proportions away from extremes, as appropriate for each subgroup. The Clopper-Pearson method provides more conservative intervals in extreme cases, whereas the Wilson score method offers better coverage probability in moderate sample sizes. Variables with a p-value < 0.05 in the univariate analysis were included in the multivariate logistic regression model. A backwards stepwise selection method was used, retaining variables with a threshold of a p-value of <0.05 in the final model. Statistical significance was considered at a p-value of <0.05. All analyses were conducted using SPSS version 21.0 (IBM Corp, Armonk, NY, USA).

Results

Analysis of Baseline Characteristics Across Study Participants

This analysis included 266 cervical cancer patients (Table 1), with a mean age of 44.26 years (SD = 10.19; range, 26–69 years). The mean age at menarche was 14.26 years (SD = 1.63), and at menopause was 50.05 years (SD = 4.17). Histologically, 210 patients (78.95%) were diagnosed with squamous cell carcinoma, while 56 (21.05%) had adenocarcinoma. Tumour differentiation was categorised as well-differentiated in 144 cases (54.13%), moderately differentiated in 80 (30.08%), and poorly differentiated in 42 (15.79%). Tumours measuring $\geq$4 cm were found in 39 patients (14.66%). Deep stromal invasion ($\geq$50% of stomal thickness) was observed in 106 patients (39.85%). Most patients (186 [69.92%]) had FIGO stage IB1 disease. No cases of ovarian metastasis were identified in this cohort.

A bilateral salpingo-oophorectomy was routinely performed in all cases undergoing radical hysterectomy, following institutional protocols for early-stage cervical cancer. Regarding the surgical approach, 198 patients (74.4%) underwent open surgery, while 68 (25.6%) received laparoscopic procedures. No significant difference in lymph node metastasis rates was observed between the two surgical approaches (p = 0.840) (**Supplementary Table 1**). Postoperative adjuvant therapy was administered to 87 patients (32.7%). Among them, 56 cases (21.1%) received concurrent chemoradiotherapy, 19 (7.1%) received only radiotherapy, and 12 (4.5%) received only chemotherapy. All patients with positive lymph node metastasis received adjuvant therapy.

HPV testing was performed in 218 patients (82.0%), with 187 (85.8%) testing positive for high-risk HPV types. The most frequently observed types were HPV 16 (52.9%) and HPV 18 (17.7%). No significant association was found between HPV infection status and the presence of lymph node metastasis (p = 0.382). Preoperative imaging employing computed tomography (CT) or magnetic resonance imaging (MRI) identified suspicious lymph nodes in 53 patients (19.9%), among

Table 1. Demographic and clinical characteristics of the cervical cancer patients [n (%)].

Variables	Cervical cancer patients (n = 266)
Mean age (years)	44.26 $\pm$ 10.19
Mean age at menarche (years)	14.26 $\pm$ 1.63
Mean age at menopause (years)	50.05 $\pm$ 4.17
Pathological type	
Cervical squamous cell carcinoma	210 (78.95%)
Cervical adenocarcinoma	56 (21.05%)
Pathological grade	
Well-differentiated	144 (54.13%)
Moderately differentiated	80 (30.08%)
Poorly differentiated	42 (15.79%)
Tumour size	
$\geq$4 cm	39 (14.66%)
$<$4 cm	227 (85.34%)
Depth of stromal invasion	
$\geq$1/2	106 (39.85%)
$<$1/2	160 (60.15%)
FIGO stage	
IA1	5 (1.88%)
IA2	16 (6.02%)
IB1	186 (69.92%)
IB2	20 (7.52%)
IIA1	30 (11.28%)
IIA2	9 (3.38%)

FIGO, International Federation of Gynecology and Obstetrics.

whom metastatic involvement was confirmed in 21 cases (39.6%) through pathological assessment (**Supplementary Table 1**).

Analysis of Lymph Node Metastasis Among Study Participants

Pelvic lymph node metastasis was observed in 41 patients (15.41%). The anatomical distribution of metastatic nodes was as follows (Table 2): obturator nodes in 29 (10.90%) patients, internal iliac in 17 (6.39%), external iliac in 4 (1.50%), parametrial in 4 (1.50%), common iliac in 2 (0.75%), and para-aortic in none (0%). Among patients with lymph node metastasis, 32 (78.0%) had metastasis limited to a single nodal group, while 9 (22.0%) had involvement of multiple nodal groups. The median number of positive nodes per patient was 2 (range: 1–8), and bilateral lymph node involvement was observed in 12 patients (29.3%).

The pattern of lymphatic spread followed a sequential progression, with no cases of skip metastasis to the common iliac nodes without involvement of more distal nodes. This distribution pattern supports the concept of orderly lymphatic dissemination from the primary tumour to adjacent nodal basins. The incidence of lymph node metastasis increased significantly with advancing FIGO stage (Ta-

Table 2. Anatomical distribution of metastatic nodes in cervical cancer patients [cases (%)].

Site of lymph node metastasis	Number of cases (n = 266)
Parametrial	4 (1.50%)
Obturator	29 (10.90%)
Internal iliac	17 (6.39%)
External iliac	4 (1.50%)
Common iliac	2 (0.75%)
Para-aortic	0 (0.00%)

Table 3. Incidence of lymph node metastasis in different stages of cervical cancer.

FIGO stage	Number of cases (n = 266)	Lymph node metastasis, n (%)	95% CI	χ^2	*p*-value
IA1	5	0 (0.00%)	0.0–45.7 [a]		
IA2	16	0 (0.00%)	0.0–18.5 [a]		
IB1	186	25 (13.44%)	9.0–19.3 [b]		
IB2	20	3 (15.00%)	3.2–37.5 [a]	16.74	<0.001
IIA	39	13 (33.33%)	20.0–50.0 [b]		
IIA1	30	7 (23.33%)	11.5–40.3 [b]		
IIA2	9	6 (66.67%)	30.0–90.3 [a]		

Calculated with [a] Clopper-Pearson or [b] Wilson Score. CI, confidence interval.

ble 3): 0% (0/21) in stages IA1–IA2, 13.44% (25/186) in IB1, 15.00% (3/20) in IB2, 23.33% (7/30) in IIA1, and 66.7% (6/9) in IIA2.

Analysis of Factors Associated With Lymph Node Metastasis

In univariate analysis (Table 4), FIGO stage II, deep stromal invasion, tumour size ≥4 cm, parametrial invasion, and LVSI were significantly associated with lymph node metastasis. However, age and histological type demonstrated no significant association. Multivariate logistic regression analysis confirmed four independent predictors of lymph node metastasis (Tables 5,6): tumour size ≥4 cm (adjusted OR: 3.857; 95% CI: 1.530–9.728; $p = 0.004$), FIGO stage II (adjusted OR: 8.247; 95% CI: 3.171–21.455; $p < 0.001$), LVSI (adjusted OR: 2.974; 95% CI: 1.344–6.632; $p = 0.008$), and parametrial invasion (adjusted OR, 5.585; 95% CI, 1.900–16.415; $p = 0.002$). The Hosmer-Lemeshow goodness-of-fit test ($\chi^2 = 7.1$, $p = 0.526$) indicated adequate model fit.

Although the depth of stromal invasion was significantly associated with lymph node metastasis in univariate analysis, it was excluded from the final multivariate model due to its high correlation with other variables, particularly tumour size and FIGO stage, with Spearman correlation coefficients of 0.671 and 0.588, respectively (both $p < 0.001$). Including this variable would have reduced the model's statistical integrity.

Furthermore, the area under the receiver operating characteristic curve (AUC) of the model was 0.801 (95% CI: 0.752–0.851), demonstrating good discriminative performance of the model (Fig. 1).

Table 4. Univariate analysis of factors influencing lymph node metastasis in cervical cancer patients.

Influencing factor		No metastasis (n = 225)	Metastasis (n = 41)	χ^2	*p*-value
Age (years)	≥45	119	23	0.144	0.705
	<45	106	18		
Pathological type	Adenocarcinoma	48	8	0.069	0.793
	Squamous cell carcinoma	177	33		
FIGO stage	I	199	28	11.260	<0.001
	II	26	13		
Depth of stromal invasion	≥1/2	70	36	46.500	<0.001
	<1/2	155	5		
Tumour size	≥4 cm	28	11	5.735	0.017
	<4 cm	197	30		
Parametrial invasion	Yes	6	6	11.530	<0.001
	No	219	35		
Number of lymph nodes resected	≥15	101	15	0.972	0.324
	<15	124	26		
LVSI	Yes	45	19	13.170	<0.001
	No	180	22		

LVSI, lymphovascular space invasion.

These results provide a comprehensive analysis of the clinicopathological characteristics, patterns of lymph node metastasis, and key predictors of nodal involvement in our cohort of cervical cancer patients who received surgical therapy. The findings offer valuable insights for preoperative risk stratification and support a more individualised approach to surgical decision-making.

Discussion

Lymph node metastasis is a critical determinant of prognosis in cervical cancer, significantly impacting patient survival outcomes (Peters et al, 2000). The current analysis of 266 cervical cancer patients provides insights into the patterns of lymphatic dissemination and identifies key clinicopathological factors associated with a higher risk of nodal involvement. These findings are critical for improving preoperative risk stratification, optimising surgical approaches, and informing adjuvant therapy decisions.

The overall incidence of pelvic lymph node metastasis in our cohort was 15.41%, consistent with a previous study that reported rates between 15–20% in early-stage cervical cancer (Ferrandina et al, 2017). This relatively high rate of occult nodal involvement, even in clinically early-stage disease, underscores the limitations of current preoperative staging methods and highlights the need for meticulous surgical evaluation of regional lymph nodes. The significant difference in 5-year overall

Table 5. Assignment of values for each factor.

Factor	Value assignment
Lymph node metastasis†	No = 0, Yes = 1
Tumour size*	<4 cm = 0, ≥4 cm = 1
FIGO stage*	Stage I (IA1, IA2, IB1, IB2) = 0, Stage II (IIA1, IIA2) = 1
LVSI*	No = 0, Yes = 1
Parametrial invasion*	No = 0, Yes = 1
Depth of stromal invasion*	<1/2 = 0, ≥1/2 = 1

†Dependent variable, *Independent variable.

Table 6. Logistic regression analysis of factors influencing lymph node metastasis in cervical cancer patients.

Influencing factor	Regression coefficient	Standard error	OR (95% CI)	Wald χ^2	p-value
Tumour size	1.350	0.472	3.857 (1.530–9.728)	8.200	0.004
FIGO stage	2.110	0.488	8.247 (3.171–21.455)	18.700	<0.001
LVSI	1.090	0.409	2.974 (1.344–6.632)	7.100	0.008
Parametrial invasion	1.720	0.550	5.585 (1.900–16.415)	9.800	0.002

OR, odds ratio.

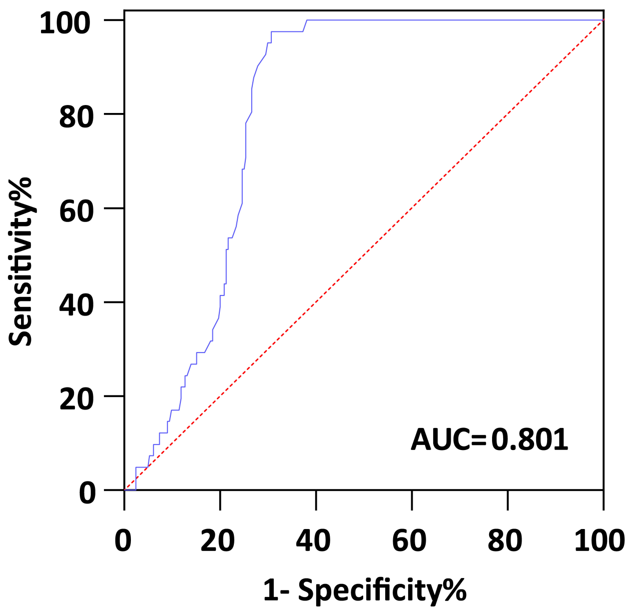

Fig. 1. ROC curve of multivariate predictive model for lymph node metastasis in cervical cancer. ROC, receiver operating characteristic; AUC, area under the receiver operating characteristic curve.

survival, approximately 50% in node-positive patients versus over 90% in node-negative patients, emphasises the prognostic significance of lymph node status and the potential of identifying patients at high risk for metastasis (Park and Bae, 2016). In our study, the obturator (10.90%) and internal iliac (6.39%) nodes were the most common sites of metastasis, a distribution that aligns with previous sentinel lymph node mapping studies. Smits et al (2023) reported that the most common locations for sentinel nodes were the common iliac (12.5%) and obturator (6.67%) regions, with a similar pattern observed for metastatic nodes. Similarly, Lührs et al (2022) found that sentinel nodes were predominantly located in the obturator fossa (54.1%) and internal iliac region (31%). Our results thus support the established anatomical patterns of lymphatic drainage in cervical cancer and the reliability and clinical significance of sentinel node mapping.

The absence of para-aortic metastases in our cohort differs from previous studies, suggesting an incidence of 1–5% in early-stage cervical cancer (Hwang et al, 2015). This discrepancy may be attributed to several factors, such as our stringent patient selection criteria, the relatively small sample size, and potential limitations in the sensitivity of detection methods. Conventional imaging techniques may have limited sensitivity in detecting micrometastases. Conversely, studies using more advanced detection methods, such as sentinel lymph node mapping combined with ultrastaging and immunohistochemistry, have reported higher identification rates of occult metastases. Future research should incorporate these advanced techniques to enhance diagnostic accuracy. Nonetheless, our finding is consistent with the perspective that routine para-aortic lymphadenectomy may not be necessary in early-stage cervical cancer, especially when preoperative imaging does not suggest para-aortic involvement.

Our multivariate analysis identified four independent predictors of lymph node metastasis: tumour size ≥4 cm, FIGO stage II, lymphovascular invasion, and parametrial invasion. These findings corroborate and extend previous studies by quantifying the individual effect of each factor on nodal risk. The strong association between lymphovascular invasion and nodal metastasis (adjusted OR: 2.974; 95% CI: 1.334–6.632) is particularly noteworthy, highlighting the significance of including LVSI in preoperative risk-stratification algorithms. Interestingly, while the depth of stromal invasion was a significant factor in univariate analysis, it did not emerge as an independent predictor in the multivariate model. This may reflect its close association with other variables, especially tumour size and parametrial involvement, indicating that its impact may be mediated through these relevant features.

The lack of significant association between lymph node metastasis and patient age or histological subtype in our study contrasts with results from some previous studies (Aslan et al, 2021). This discrepancy might be due to the relatively homogeneity of our cohort, defined by a narrow age range and a predominance of squamous cell carcinoma. These findings suggest that these factors may have limited significance in predicting nodal involvement among similarly selected patient cohorts and should be considered cautiously in nodal risk-assessment models.

A key strength of our investigation is the detailed anatomical mapping of lymph node metastases within the pelvic nodal basins. The predominance of obturator (10.90%) and internal iliac (6.39%) node involvement, with less frequent metastasis to the parametrial, external iliac, and common iliac nodes, provides a rational basis for guiding surgical dissection and sentinel node assessment. While the absence of isolated para-aortic metastases in our early-stage cohort is reassuring, this observation should be interpreted cautiously. It does not obviate the potential need for para-aortic assessment in higher-risk patients, particularly those with positive pelvic nodal involvement or advanced diseases.

The observed metastatic pattern in our study closely aligns with established lymphatic drainage pathways and supports the concept of sentinel nodes in cervical cancer. The obturator and internal iliac lymph nodes often serve as the primary echelon of nodal metastasis, a finding consistently validated by numerous sentinel node biopsy studies (Cibula et al, 2020; Mathevet et al, 2021; Zhang et al, 2021). Our data thus lend further credence to sentinel node mapping as a potential approach to tailor the extent of lymphadenectomy while maintaining staging accuracy. However, the presence of metastasis in multiple nodal groups in 21.95% of node-positive patients (9/41) highlights the limitations of depending solely on targeted or limited nodal sampling. This finding reinforces the need for thorough evaluation across all major pelvic nodal basins, especially in those with high-risk pathological characteristics, to ensure precise staging and treatment decision-making.

We acknowledge several potential sources of bias in our study. Selection bias is inherent to the retrospective design and may be compounded by institutional referral patterns. Information bias may have affected our assessment of lymph node metastasis, as the extent of lymph node dissection was partially guided by preoperative imaging evaluation and intraoperative findings. Patients with suspicious lymph nodes observed through imaging or during surgery may have undergone more extensive dissections, potentially increasing the likelihood of metastasis detection. Conversely, individuals without such observations may have undergone standard lymphadenectomy, potentially resulting in undetected microscopic metastases. To mitigate these biases, we included only patients who underwent systematic pelvic lymphadenectomy following standardised institutional protocols. However, we further state that these strategies cannot fully eliminate the potential impact of these biases on our results.

Despite the promising insights, our study has several limitations. First, the retrospective, single-institution design may limit the generalizability of our results to broader populations. Second, the small sample size within the FIGO IIA2 subgroup (n = 9) may affect the reliability of the observed 66.67% lymph node metastasis rate. To address this limitation, we conducted additional analyses by combining FIGO IIA1 and IIA2 into a single IIA group, resulting in a more statistically reliable metastasis rate of 33.33% (13/39). Future larger studies are needed to validate these results. Third, including low-risk patients (FIGO stages IA1 and IA2) with no lymph node metastases may have influenced the risk factor analysis. However, our stratified analysis excluding these patients yielded consistent results, supporting the validity of our observations. Fourth, the lack of standardised preoperative imaging protocols may have introduced variability in surgical decision-making and the degree of lymph node dissection. Fifth, our study did not incorporate molecular markers or genomic data, which could have provided additional insights into the underlying mechanisms of lymphatic dissemination. Sixth, despite the median follow-up of 48.7 months, longer follow-up would be beneficial for assessing the long-term prognostic impact of lymph node metastasis. Finally, tumour size measurements were based on final histopathology rather than preoperative imaging, which may limit the applicability of our findings to preoperative risk assessment. Additionally, survival outcomes, such as disease-free survival (DFS) and overall survival (OS), were not assessed and should be included in future research.

The translational implications of our findings are substantial. Using the identified predictors for preoperative risk stratification could guide therapeutic decisions, such as choosing between simple hysterectomy, radical hysterectomy, or primary chemoradiation. For individuals undergoing surgical intervention, these promising observations may help inform the extent of parametrial resection and lymph node dissection, potentially minimising surgical morbidity in low-risk patients while ensuring adequate oncological safety for those at high risk. Our findings align with recent results from the Simple Hysterectomy and Pelvic Node Assessment (SHAPE) trial published in The New England Journal of Medicine (Plante et al, 2024), suggesting that less radical surgical approaches may be sufficient for appropriately selected patients with early-stage cervical cancer. However, further research is needed to delineate and validate criteria for identifying patients who can safely undergo less extensive procedures. Additionally, the detailed mapping of the nodal metastatic roadmap provided in our study may improve the accuracy of radiotherapy planning by allowing for more targeted irradiation of high-risk nodal basins. Furthermore, this approach would improve therapeutic outcomes while alleviating damage to adjacent tissues.

Future research should include prospective, multi-institutional studies with larger cohorts and long-term follow-up periods to validate our findings and assess their impact on recurrence and survival outcomes. Incorporating molecular markers and advanced imaging techniques like sentinel node mapping using indocyanine green (ICG) could further enhance risk stratification and improve diagnostic accuracy. Additionally, investigating the biological mechanisms underlying the observed metastatic patterns may demonstrate critical insights into lymphatic spread and identify novel therapeutic targets.

While stage, tumour size, and LVSI are known risk factors for lymph node metastasis, our study offers several novel insights. First, it provides a comprehensive analysis of the relative contribution of these factors in an East-Chinese population, a demographic underrepresented in previous studies. Second, our detailed anatomical mapping of metastatic nodes offers valuable information for optimising sentinel node biopsy techniques. Third, by quantifying the risk associated with each factor, our observations further substantiate more personalised surgical planning and evidence-based decisions about the need for adjuvant therapy.

Conclusion

Our comprehensive analysis of lymph node metastasis in cervical cancer reaffirms its profound prognostic importance and provides an evidence-based framework for individualising nodal assessment strategies. By elucidating the complex relationships between clinicopathological risk factors and lymphatic spread patterns, we advance a step toward risk-adapted, precision management of this challenging malignancy. While many questions remain, our study brings us closer to the goal of improving patient outcomes through optimised local control and judicious use of adjuvant therapy.

Key Points

- Lymph node metastasis was observed in 15.41% of patients with early-stage cervical cancer, with increasing rates corresponding to higher FIGO stages.
- Tumour size $\geq$4 cm, FIGO stage II, lymphovascular space invasion, and parametrial invasion were identified as independent risk factors for lymph node metastasis.
- The obturator and internal iliac regions were the most common sites of nodal metastasis, supporting the anatomical basis for sentinel node mapping techniques.
- These findings provide a rational basis for preoperative risk assessment and individualised surgical planning in early-stage cervical cancer.

Availability of Data and Materials

All data included in this study are available from the corresponding author upon reasonable request.

Author Contributions

XZ and JY conceived this study. SS and ZM analysed the data. SS drafted the manuscript. All authors contributed to the important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The experimental protocol of the present study was reviewed and approved by the Institutional Review Board of Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University (Ethics-2024-1045). The study was conducted in accordance with the principles of the Declaration of Helsinki, and informed written consent was obtained from all participants.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://www.magonlinelibrary.com/doi/suppl/10.12968/hmed.2025.0175.

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