International Journal of Women's Health

Dovepress
Taylor & Francis Group

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ORIGINAL RESEARCH

Analysis of the Predictive Efficacy and Influencing Factors of Serum Tie-1, FoxO3a, and PKD1 for Lymph Node Metastasis in Cervical Cancer

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Objective: To investigate the factors affecting lymph node metastasis (LNM) in patients with cervical cancer and the predictive efficacy of serum tyrosine kinase receptor 1 (Tie-1), serum Forkhead Framing Protein O3a (FoxO3a), and protein kinase D1 (PKD1).

Methods: Cervical cancer patients were categorized into 60 cases of LNM-positive group and 320 cases of LNM-negative group according to whether LNM occurred or not. The levels of serum Tie-1, FoxO3a and PKD1 were tested. Multivariate logistic regression analysis was conducted to identify the risk factors for cervical cancer induced lymph node metastasis (LNM). Receiver operating characteristic (ROC) curves were plotted to analyze the predictive value of various indicators for LNM in cervical cancer.

Results: The percentage of patients with FIGO stage IIa, combined paracervical infiltration and myometrial infiltration was significantly higher in the LNM-positive group than in the LNM-negative group (P<0.05). Huanz serum levels of Tie-1 and PKD1 in the LNM-positive group were significantly higher than those in the LNM-negative group, and the relative expression of FoxO3a was significantly lower than that in the LNM-negative group (P<0.05). The results of logistic regression analysis showed that FIGO stage, parietal infiltration, myometrial infiltration, serum Tie-1, PKD1 were LNM-positive in cervical cancer patients (P<0.05), and low level of relative expression of serum FoxO3a was a protective factor (P<0.05). The cutoff of serum Tie-1, FoxO3a, and PKD1 levels for predicting the occurrence of LNM in cervical cancer were 1.97 ng/mL, 0.54, and 113.26 μg/L, and the area under the ROC curve (AUC) was 0.852, 0.827, 0.844, respectively.

Conclusion: Serum Tie-1, FoxO3a and PKD1 have certain predictive efficacy for lymph node metastasis, and the combination of these tests can improve the predictive accuracy.

Keywords: cervical cancer, lymph node metastasis, Tie-1, FoxO3a, PKD1, predictive efficacy

Introduction

Cervical cancer is one of the four most common cancers in the world and has the second highest incidence rate, especially among women.[1] In recent years, the overall incidence and mortality rates of cervical cancer have shown a decreasing trend with the increased awareness of screening and the worldwide use of human papillomavirus (HPV) vaccines.[2] However, the incidence of early-stage cervical cancer has increased, and 15–20% of these patients develop lymph node metastasis (LNM), which is one of the major risk factors affecting the prognosis of early-stage cervical cancer patients, and the survival rate of patients with lymph node metastasis is significantly decreased.[3] The evaluation of LNM is crucial for the development of the treatment plan for patients with cervical cancer and for determining the prognosis, and, according to the most recent guideline, the presence or absence of lymph node metastasis determines the stage of cervical cancer patients, and different stages directly affect the choice of treatment plan for patients.[4] Therefore, accurate preoperative assessment of whether lymph node metastasis is present is important for optimizing treatment strategies, reducing postoperative complications, and improving patient prognosis. Although there are several methods for the assessment of LNM, all of them have certain limitations. In recent years, with the deepening of molecular biology

Received: 15 December 2024
Accepted: 5 March 2025
Published: 1 May 2025

research, some serum markers have been found to play an important role in tumor development and metastasis. Tyrosine kinase receptor 1 (Tie-1) is a receptor tyrosine kinase expressed on cell membranes and plays an important role in the process of vascular development and neovascularization. Studies have shown[5] that Tie-1 is aberrantly expressed in a variety of cancers, including lung and breast cancers, and is closely related to the processes of angiogenesis, invasion, and metastasis of cancer, and may promote cancer progression. Serum forkhead box protein O3a (FoxO3a) serves as a central transcription factor that transcriptionally regulates a variety of physiological and pathological processes involved in apoptosis, cell proliferation, cell cycle, survival, and DNA damage.[6] FoxO3a plays an important role in a variety of cancers, and its aberrant expression is closely related to tumorigenesis, for example, in cancer, it is common to see the down-regulation of FoxO3a gene, which makes FoxO3a known as a tumor suppressor.[7] In addition, the expression level of FoxO3a is correlated with the degree of tumor differentiation, depth of infiltration, distant metastasis, staging and histological classification in some types of cancer (eg colorectal cancer).[8] Protein kinase D1 (PKD1) A serine/threonine protein kinase of the PKD family is involved in the regulation of cell proliferation and apoptosis processes. During cell proliferation, PKD1 can promote cell cycle progression, while during apoptosis, PKD1 may inhibit apoptosis by regulating the activity of apoptosis-related molecules.[9] In addition, by inhibiting the activity of PKD1, the proliferation and invasive ability of tumor cells can be inhibited, providing new ideas for cancer treatment. Although previous studies have revealed Tie-1 FoxO3a The role of PKD1 in cancer, but research on their specific role and predictive value in cervical cancer LNM is still relatively limited. This study aims to further explore the impact of these molecules on LNM in cervical cancer and analyze their potential value as predictive indicators. By collecting and analyzing the clinical characteristics and serum Tie-1 FoxO3a We hope that the expression level of PKD1 can provide new basis and ideas for early diagnosis, treatment selection, and prognosis evaluation of cervical cancer. In addition, this study also used methods such as multiple logistic regression analysis and ROC curve analysis to more accurately evaluate the predictive performance of these molecules, which is also the novelty of this study in terms of methodology.

Information and Methods

General Information

380 cases of cervical cancer patients diagnosed and treated in our hospital from January 2022 to May 2024 were selected for the study. Inclusion criteria: ① all meet the diagnostic and treatment criteria of cervical cancer[10] and are diagnosed as squamous carcinoma or adenocarcinoma by pathological tests; ② the score of physical status (ECOG) is not more than 2, and the score of Carpenter's score is more than 70; ③ all of them are the first time onset of the disease and have not received radiotherapy before participating in the study; ④ there are no malignant lesions of other tissues and organs except cervical cancer; ⑤ they can communicate normally, and have normal mental health and are clear consciousness. Exclusion criteria: ① combined with other malignant tumors; ② the presence of distant metastases; ③ heart, liver, kidney and other vital organs can tolerate radiotherapy; ④ contraindications to radiotherapy; ⑤combined with hemorrhagic disease; ⑥ allergic to contrast media; ⑦ bone marrow dysfunction can not tolerate radiotherapy. All patients were diagnosed by pathology and divided into 60 cases of LNM-positive group and 320 cases of LNM-negative group according to the occurrence of LNM.

Data Collection

This study collected detailed clinical and pathological characteristics of all patients, including age FIGO Stage (determined according to the classification criteria of the International Union of Obstetrics and Gynecology), degree of differentiation (high differentiation, moderate differentiation, low differentiation), tumor size (represented by maximum diameter), histological type (squamous cell carcinoma, adenocarcinoma, etc)., parametrial invasion, depth of muscular invasion, and vascular invasion. All data collection follows strict standardized processes to ensure accuracy and consistency of the data.

LNM Judgment: The diagnosis of lymph node metastasis is mainly based on pathological examination results. During the surgery, the excised lymph node tissue needs to undergo pathological section examination to confirm the presence of cancer cell infiltration. The specific diagnostic criteria include: ① visible cancer cell infiltration in lymph node tissue; ② The morphology and structure of cancer cells are consistent with the primary tumor; ③ Based on

imaging and clinical information, exclude the possibility of tumor metastasis from other parts. In this study, all diagnoses of lymph node metastasis were reviewed and confirmed by at least two pathologists to ensure accuracy and consistency of the diagnosis.

Detection Method

Serum Tie-1 and PKD1 levels were measured by enzyme-linked immunosorbent assay (ELISA): 10 mL of peripheral venous blood was collected from all subjects in an anticoagulation tube, and the required reagents and samples were prepared, including standards, test samples and detection antibodies. All reagents and samples should be equilibrated to room temperature. Pre-coagulate the specific antibody on a high affinity ELISA plate to ensure that the capture antibody binds specifically to the target antigen. Dilute serum samples appropriately using 1× Assay Buffer according to the kit instructions to ensure that the target protein concentration in the sample is suitable for detection. The diluted sample and standard are added to the wells of the enzyme plate and incubated to allow the target protein in the sample to bind to the solid phase antibody. After incubation, the enzyme plate needs to be washed thoroughly to remove unbound material to minimize background noise. Horseradish peroxidase-labeled detection antibody is added and incubated to bind the detection antibody to the target protein. The plate is washed again after incubation to remove unbound detection antibody. The color development substrate TMB is added and the color is developed away from light. The intensity of the color reaction is proportional to the concentration of the target protein in the sample. Terminate the reaction and read the absorbance: add the termination solution to terminate the color reaction, then read the absorbance value on the enzyme marker and calculate the concentration of target protein in the sample by comparing with the standard curve.

The relative expression of FoxO3a was detected by real-time quantitative PCR: 10 mL of peripheral venous blood was collected from all the study subjects in anticoagulation tubes, and the serum was separated, frozen, resuscitated and purified according to the steps prompted by the assay kit (Invitrogen, USA), and the RNA (RNA) was measured by an ultramicro spectrophotometer (Thermo Fisher Scientific, USA, model: Nano-Drop-2000). 2000) was used to determine the concentration of ribonucleic acid (RNA). The extracted RNA was reverse transcribed to generate cDNA, which was performed under low temperature conditions to ensure the accuracy and stability of the reaction. Specific primers and probes were designed according to the target gene (FoxO3a). The reaction solution was prepared at low temperature according to the instructions of the PCR kit, including the addition of template cDNA, primers, probes, dNTPs, MgCl2 and other components. The configured reaction solution was placed in a PCR instrument for the reaction. The real-time quantitative PCR reaction consisted of three phases: pre-denaturation, PCR cycle and melting curve, and each cycle consisted of three steps of denaturation, annealing and extension, and 40 cycles were run. The fluorescence signal intensity of each cycle was collected by the real-time quantitative PCR instrument and the Ct value curve was plotted. The relative expression of target genes was calculated using the ΔΔCt method or the 2^-ΔΔCt method.

Statistical Methods

SPSS25.0 software was used for data processing and the measurement data was expressed as "$\overline{x} \pm s$". Independent sample *t* test was used for comparison between two groups. The count data were expressed as n%, and $\chi 2$ test was used. Multivariate Logistic regression analysis was used to analyze the risk factors for LNM in cervical cancer, and the working curve (ROC) of the subjects was drawn. The area under the curve (AUC) was calculated to test the value of serum Tie-1, FoxO3a, and PKD1 in predicting the occurrence of LNM in cervical cancer. Test level α=0.05.

Results

Comparison of Clinical Features of Patients Between LNM Positive Group and LNM Negative Group

The proportion of patients in the LNM positive group with FIGO stage IIa and concomitant para-uterine infiltration and muscular layer infiltration was significantly higher than that in the LNM negative group ($P < 0.05$), as shown in Table 1.

Table 1 Comparison of Clinical Features of Patients Between LNM-Positive and LNM-Negative Groups ($\bar{x} \pm s$, %)

Factor		LNM Positive Group (n=60)	LNM Negative Group (n=320)	$t/\chi 2$	*P*
Age (years)		52.26±6.12	50.73±7.49	1.491	0.137
FIGO staging	Stage Ia	0 (0.00)	52 (16.25)	39.712	<0.001
	Stage Ib	19 (31.67)	179 (55.94)		
	Stage IIa	41 (68.33)	89 (27.81)		
Degree of differentiation	Low	13 (21.67)	67 (20.94)	1.548	0.461
	Middle	41 (68.33)	201 (62.81)		
	Tall	6 (10.00)	52 (16.25)		
Tumor size (cm)		4.23±1.22	4.09±1.97	0.531	0.596
Histological type	Squamous carcinoma	51 (85.00)	260 (81.25)	0.478	0.490
	Non-squamous cell carcinoma	9 (15.00)	60 (18.75)		
Parauterine infiltration	Have	24 (40.00)	52 (16.25)	17.813	<0.001
	Without	36 (60.00)	268 (83.75)		
Muscular layer infiltration	Have	30 (50.00)	82 (25.63)	14.442	<0.001
	Without	30 (50.00)	238 (74.38)		
Vascular infiltration	Have	6 (10.00)	15 (4.69)	2.731	0.098
	Without	54 (90.00)	305 (95.31)		

Table 2 Comparison of Patient Serum Tie-1, FoxO3a, and PKD1 Levels Between the LNM-Positive and LNM-Negative Groups ($\bar{x} \pm s$)

Group	Number of Cases	Tie-1 (ng/mL)	FoxO3a	PKD1 (μg/L)
LNM positive group	60	2.22±0.88	0.44±0.08	163.52±24.26
LNM negative group	320	1.82±0.49	0.90±0.11	94.36±16.11
t		4.999	30.882	27.881
P		<0.001	<0.001	<0.001

Comparison of Serum Tie-1, FoxO3a, and PKD1 Levels Between the LNM-Positive Group and the LNM-Negative Group

The levels of serum Tie-1 and PKD1 of huanz in the LNM positive group were significantly higher than those in the LNM negative group, and the relative expression level of FoxO3a was significantly lower than that in the LNM negative group ($P < 0.05$), as shown in Table 2

Multivariate Logistic Regression Analysis of Risk Factors for LNM of Cervical Cancer

The positive or negative LNM of cervical cancer patients was taken as the dependent variable ("1" = LNM positive, "0" = LNM negative, and FIGO stage, intrauterine infiltration, muscular layer infiltration, serum Tie-1, FoxO3a, and PKD1 were taken as the independent variables (FIGO stage II A, intrauterine infiltration, and muscular layer infiltration were all 1= "Yes", 0= "No", serum Tie-1, FoxO3a, and PKD1 were all continuous variables). Logistic regression analysis showed that FIGO stage, parauterine infiltration, muscular layer infiltration, serum Tie-1 and PKD1 were the independent risk factors for LNM positivity in cervical cancer patients ($OR > 1$, $P < 0.05$). The low relative expression of serum FoxO3a was the protective factor ($OR < 1$, $P < 0.05$). See Table 3 and Figure 1

Table 3 Risk Factors for LNM of Cervical Cancer by Multivariate Logistic Regression Analysis

Influencing Factor	*B*	*SE*	*Wald*	*P*	*OR*	95% Confidence Interval
FIGO staging	0.712	0.156	20.684	<0.001	2.037	1.149–2.768
Parauterine infiltration	1.083	0.339	10.228	0.001	2.954	1.521–5.736
Muscular layer infiltration	1.065	0.407	6.859	0.009	2.901	1.307–6.436
Tie-1	0.791	0.152	27.227	<0.001	2.205	1.638–2.967
FoxO3a	−2.922	0.663	19.448	<0.001	0.054	0.015–0.197
PKD1	1.256	0.429	8.590	0.003	3.510	1.135~10.257
Constant	−5.334	1.068	24.942	<0.001	–	–

ROC Curve Analysis of Serum Tie-1, FoxO3a, and PKD1 in Predicting the Clinical Value of LNM in Cervical Cancer

The optimal cutoff points for serum Tie-1, FoxO3a, and PKD1 levels to predict LNM in cervical cancer were 1.97 ng/mL, 0.54, and 113.26μg/L, respectively, the sensitivities were 81.80%, 86.30%, and 81.72%, and the specificities were 86.55%, 79.80%, and 73.10%, respectively. The areas under the ROC curve (AUC) were 0.852, 0.827, and 0.844, respectively, and the sensitivity, specificity, and AUC for the combined prediction of the three were 81.72%, 96.23%, and 0.932, respectively, as shown in Figure 2 and Table 4

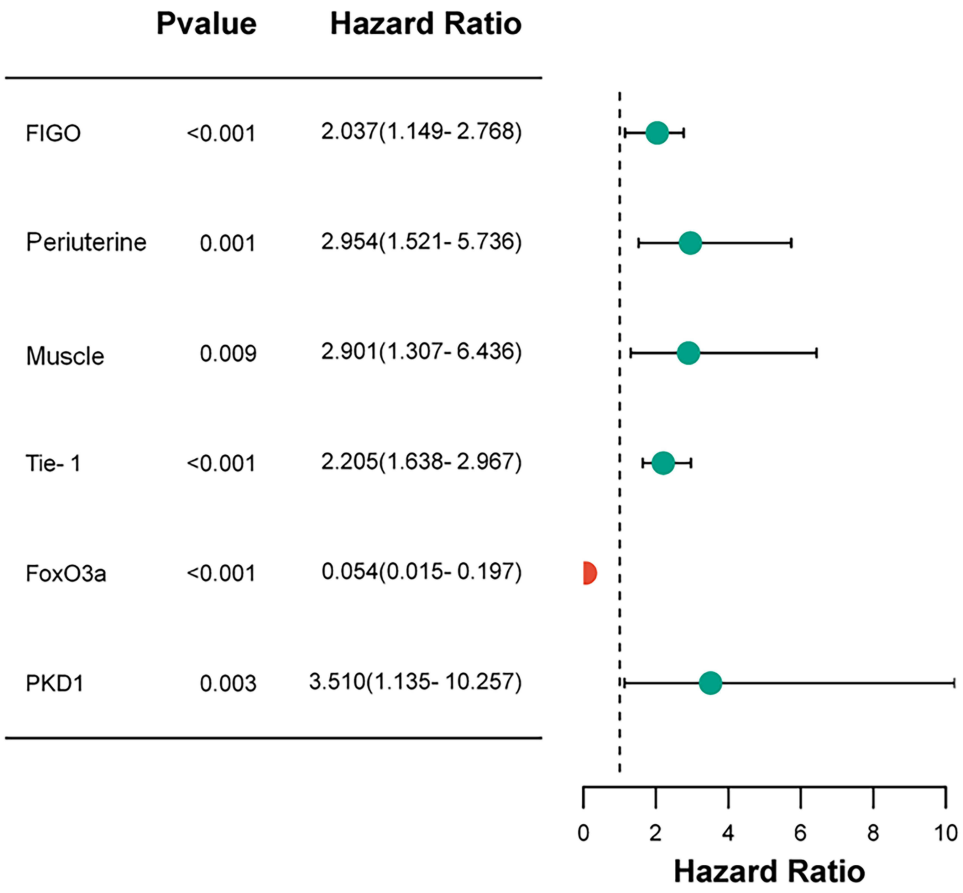

Figure 1 Forest map for risk factors of LNM of cervical cancer by multivariate Logistic regression analysis.

https://doi.org/10.2147/IJWH.S512411

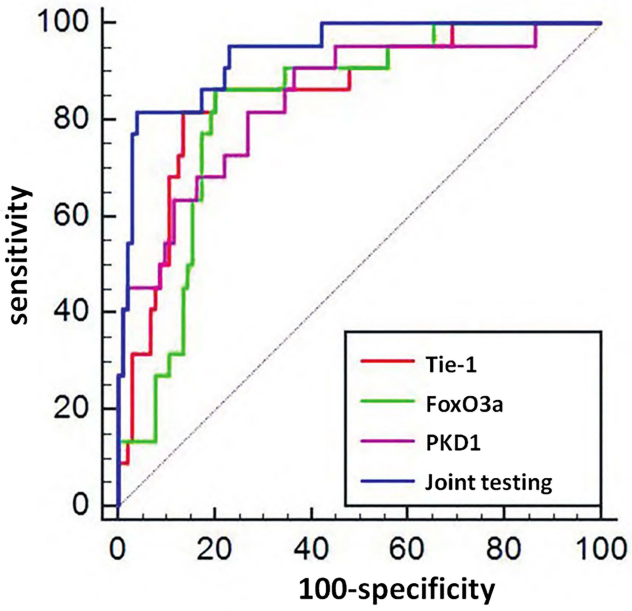

Figure 2 ROC curve analysis diagram.

Discussion

Cervical cancer is one of the common malignant tumors among women worldwide, and its incidence and mortality rates remain high, especially in developing countries. With the advancement and popularization of screening technology, the early diagnosis rate of cervical cancer has improved, but in many regions, patients with advanced cervical cancer still account for a significant proportion.[11] Lymph node metastasis is one of the major metastatic modes of cervical cancer, which has an important impact on patients' prognosis and choice of treatment options. Several studies have shown[12,13] that lymph node metastasis is an important independent risk factor for the prognosis of cervical cancer, and that patients with lymph node metastasis have a significantly lower survival rate and a higher recurrence rate compared with those without lymph node metastasis. The status of nodules, especially sentinel lymph nodes, is one of the most important prognostic factors for cancer patients. As the first stop lymph nodes for tumor drainage, the status of sentinel lymph nodes is of great significance for evaluating whether tumors have lymph node metastasis, predicting patient prognosis, and developing personalized treatment plans. Therefore, a deep understanding and accurate assessment of the status of sentinel lymph nodes is crucial for optimizing treatment strategies for cervical cancer patients. A study[14] suggests that precise sentinel lymph node localization and biopsy can more effectively assess lymph node metastasis in cervical cancer patients, providing more accurate prognostic information and personalized treatment recommendations for patients. These studies emphasize the importance of sentinel lymph node status in the treatment decisions of cervical cancer patients.

Serum Tie-1 is a protein expressed only on the surface of vascular endothelial cells, and its main function is involved in angiogenesis and vascular stability. In recent years, the role of Tie-1 in a variety of diseases has gradually gained

Table 4 Clinical Value of ROC Curve Analysis of Serum Tie-1, FoxO3a, and PKD1 in Predicting the Occurrence of LNM in Cervical Cancer

Index	AUC	95% CI	Sensitivity	Specificity	*P*	Truncated Value	Youden's Index
Tie-1	0.852	0.771~0.912	81.80	86.55	<0.001	1.97 ng/mL	0.684
FoxO3a	0.827	0.750~0.887	86.30	79.80	<0.001	0.54	0.661
PKD1	0.844	0.769~0.902	81.72	73.10	<0.001	113.26μg/L	0.548
Joint testing	0.932	0.882~0.967	81.72	96.23	<0.001		0.780

attention, especially in the field of cancer therapy, where the expression of Tie-1 is significantly increased in ovarian cancer and correlated with platinum drug resistance.[15] It was found[16] that Tie-1-positive tumor regions were significantly increased in platinum drug-resistant patients. In addition, knockdown of Tie-1 was found to significantly reduce the expression of key molecules of the PI3K/Akt signaling pathway, such as p110α and phosphorylated-Akt, after treatment of ovarian cancer cells with siRNA, which resulted in the inhibition of cell proliferation, suggesting that Tie-1 may be a key component of the PI3K high expression in ovarian cancer cells, suggesting that Tie-1 may be a novel therapeutic target in PI3K-overexpressing ovarian cancer cells.FoxO3a is an important transcription factor that is widely involved in a variety of biological processes such as cell proliferation, apoptosis, autophagy and oxidative stress. Relevant data show[17] that FoxO3a usually acts as a tumor suppressor in breast cancer, inhibiting the proliferation and invasiveness of tumor cells by regulating cell cycle, apoptosis and metabolism. In addition, FoxO3a also affects the sensitivity of breast cancer cells to endocrine therapy by regulating the expression of Thioredoxin interacting protein (TXNIP).[18] Studies have shown[19] that inactivation or low expression of FoxO3a is closely associated with epithelial mesenchymal transition (EMT) in prostate cancer cells, a process that is associated with increased cancer invasiveness and metastasis, and furthermore that aberrant expression of FoxO3a may contribute to the development of prostate cancer by affecting the PI3K/Akt signaling pathway.PKD1, a serine/threonine kinase that affects cancer cell proliferation, apoptosis and drug sensitivity by regulating different signaling pathways.[9] In oral squamous carcinoma, high expression of PKD1 is associated with increased expression of the cell proliferation and anti-apoptosis related protein Bcl-2, whereas PKD1 gene silencing significantly reduces the expression of these proteins, thereby inhibiting tumor cell growth and increasing apoptosis.[20] In addition, PKD1 is also involved in regulating the glycolysis process in oral squamous carcinoma cells, and its gene silencing can inhibit the glycolysis of tumor cells, which in turn inhibits the proliferation of tumor cells.[21] In breast cancer, PKD1 regulates the proliferative ability of breast cancer cells through MEK/ERK and PI3K/AKT signaling pathways.[22] Studies have shown that interfering with the PKD1-mediated signaling pathway can inhibit the proliferation of breast cancer cells, in addition, the PKD1 signaling pathway plays a key role in breast cancer progression and lung metastasis, and the overall survival rate of patients with high expression of PKD1 is lower.[23]

The results of this study showed that FIGO stage, paracervical infiltration, myometrial infiltration and elevated levels of serum Tie-1 and PKD1 were independent risk factors for the development of LNM in cervical cancer, and FoxO3a was a protective factor.FIGO stage reflects the degree of tumor progression, and the higher the stage is, the wider the scope of tumor invasion is, and the higher the risk of lymph node metastasis is. Paracervical infiltration is an independent risk factor for lymph node metastasis in patients with cervical cancer. Several studies have shown that cervical cancer patients with paracervical infiltration are more likely to develop lymph node metastasis, probably because paracervical infiltration indicates that the tumor has broken through the limitations of the uterus and has stronger invasiveness and metastatic ability. Deep myometrial infiltration is an independent risk factor for lymph node metastasis of cervical cancer, probably because deep myometrial infiltration indicates that the tumor has penetrated deeper into the myometrium, which has stronger invasiveness and metastatic ability. Elevated levels of serum Tie-1, PKD1, and FoxO3a are associated with lymph node metastasis of cervical cancer.Tie-1 is a tyrosine kinase receptor, which plays an important role in angiogenesis and lymphangiogenesis.Tumor cells can secrete Tie-1 to promote lymphangiogenesis, thus increasing the risk of lymph node metastasis.PKD1 is a protein kinase, which participates in a variety of cellular signal transduction pathways. PKD1 is a protein kinase that participates in a variety of cell signaling pathways, and studies have shown that PKD1 plays an important role in tumorigenesis, development and metastasis. We also evaluated in detail the sensitivity, specificity, and predictive values of serum Tie-1, FoxO3a, and PKD1 in predicting lymph node metastasis in cervical cancer. Sensitivity reflects the ability of biomarkers to correctly identify LNM positive patients, while specificity reflects the ability of biomarkers to correctly identify LNM negative patients. As shown in Table 4, the sensitivity and specificity of serum Tie-1 are 81.80% and 86.55%, indicating its high accuracy in distinguishing LNM positive and negative patients. Similarly, the sensitivity and specificity of serum FoxO3a were 86.30% and 79.80%, respectively, while the sensitivity and specificity of PKD1 were 81.72% and 73.10%, respectively. These data further support the potential of serum Tie-1, FoxO3a, and PKD1 as predictive biomarkers for cervical cancer lymph node metastasis. In addition, we also calculated the predictive values of these biomarkers, including positive and negative predictive values, to more comprehensively evaluate their clinical

applicability and relevance. These predicted values will help clinical doctors make more informed decisions when developing personalized treatment plans. Our research findings are consistent with existing literature reports, further confirming that FIGO staging, parametrial invasion, myometrial invasion, and elevated serum Tie-1 and PKD1 levels are independent risk factors for cervical cancer lymph node metastasis, while FoxO3a is a protective factor. For example, Bai[24] In their study, they found that serum Tie-1 levels were significantly elevated in cervical cancer patients and were associated with lymph node metastasis and poor prognosis. Similarly, the study by Meguro[25] et al also showed that PKD1 is abnormally expressed in various cancers and participates in the processes of tumor proliferation, apoptosis, and metastasis. Our research not only validated these findings, but also evaluated the diagnostic performance of these biomarkers in detail through ROC curve analysis, and found that joint detection can further improve prediction accuracy. These results not only deepen our understanding of the mechanism of lymph node metastasis in cervical cancer, but also provide new ideas and methods for clinical diagnosis and treatment. The results of this study revealed that FIGO staging, parametrial invasion, myometrial invasion, and elevated serum Tie-1 and PKD1 levels are independent risk factors for lymph node metastasis in cervical cancer, while FoxO3a is a protective factor. These findings are somewhat consistent with existing literature reports, but also provide new insights into the understanding of gynecological oncology. Especially, we found that serum Tie-1 FoxO3a The combined detection with PKD1 has high accuracy in predicting cervical cancer lymph node metastasis, which may be of great significance for optimizing treatment strategies, reducing postoperative complications, and improving patient prognosis. Although the results of this study are relatively simple, it emphasizes the value of multi indicator combined detection in predicting lymph node metastasis in cervical cancer, which to some extent supplements the shortcomings of existing literature and provides new ideas for further research in this field. In recent decades, significant progress has been made in the treatment of cancer due to the continuous improvement of early diagnosis, molecular pattern recognition, surgical techniques, and adjuvant therapy. In particular, Tullio Golia D'Aug è, Violante Di Donato, and Andrea Giannini proposed strategic approaches for early cervical cancer management in their recent study,[26] which provide new ideas for optimizing patient treatment outcomes and improving survival rates.

In summary, this study indicates that serum Tie-1 FoxO3a PKD1 has certain predictive performance for cervical cancer lymph node metastasis and is closely related to the progression free survival (DFS) and overall survival (OS) of patients. High clinical stage, concomitant parametrial infiltration, muscular infiltration, and elevated serum Tie-1 and PKD1 levels are independent risk factors for lymph node metastasis, while serum FoxO3a is a protective factor. Joint detection of these three biomarkers can improve prediction accuracy and provide important references for developing personalized treatment plans in clinical practice. Although this study has made some progress in exploring the influencing factors and predictive performance of cervical cancer lymph node metastasis, there are still some limitations. It is worth noting that due to time constraints and the original design intention of this study, we were unable to statistically analyze progression free survival (PFS) and overall survival (OS). PFS OS is an important indicator for evaluating the effectiveness of cancer treatment and patient prognosis, and is crucial for a comprehensive understanding of the biological behavior and treatment strategies of cervical cancer.

Data Sharing Statement

The raw data supporting the conclusions of this article will be made available by the corresponding author, without undue reservation.

Ethics Approval and Consent to Participate

The study was approved by the Ethics Committee of the First Affiliated Hospital of China Medical University (No. 2022023312), and informed consent was obtained from all patients. This study was conducted in accordance with the Declaration of Helsinki.

Funding

There is no funding to report.

Disclosure

The authors declare that they have no competing interests.

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