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ORIGINAL RESEARCH

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Diagnostic value of dynamic enhanced multi-slice spiral CT in lymph node metastasis of cervical cancer and analysis of the causes of missed diagnosis

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Abstract

We aimed to explore the diagnostic value of multi-slice spiral computed tomography dynamic enhanced scanning (MSCT) for the lymph node metastasis of cervical cancer and the causes for missed diagnosis. A total of 283 patients with cervical cancer treated from March 2019 to March 2022 were selected. Lymph node metastasis was observed by MSCT. The results were compared with those of surgical and pathological examinations to analyze the diagnostic value of MSCT. The patients with confirmed lymph node metastasis were divided into a missed diagnosis group (n = 41) and a non-missed diagnosis group (n = 128). The factors for missed diagnosis by MSCT were explored by multivariate logistic regression analysis. A back propagation (BP) neural network model was constructed and evaluated. Results: The positive coincidence rate of MSCT diagnosis was 92.75%, the negative coincidence rate was 71.72%, and the total coincidence rate was 81.98%. The area under the receiver operator characteristic curve of MSCT was 0.741 (95% confidence interval: 0.723–0.826), indicating a high diagnostic value. A high degree of differentiation, negative Ki-67 expression, and interstitial infiltration depth of <one half were independent risk factors for the missed diagnosis of lymph node metastasis by MSCT ($p < 0.05$), and tumor size was an independent protective factor ($p < 0.05$). The BP neural network model has good discrimination and high accuracy. MSCT has a high diagnostic value for the lymph node metastasis of cervical cancer.

Keywords

Multi-slice spiral CT; Cervical carcinoma; Lymph node metastasis; Missed diagnosis; Back propagation neural network model

1. Introduction

Cervical cancer is a common female malignant tumor with a mortality rate of over 50% [1], seriously threatening women's health. The lymph node metastasis of cervical cancer has a high incidence rate [2]. Lymph node metastasis not only dramatically increases the difficulty of treatment but also adversely affects the prognosis. The progression of lymph node metastasis is a long-term process. If screening can be carried out early, the onset and progression of cancer can be effectively prevented. Therefore, the early diagnosis of lymph node metastasis in patients with cervical cancer is crucial for improving the prognosis [3].

In recent years, imaging has been reported to play an essential role in the clinical screening of lymph node metastasis of cervical cancer [4], among which magnetic resonance imaging (MRI) and computed tomography (CT) have been most widely used. Compared with MRI, CT is not easily affected by tumor and is better for diagnosing the lymph node metastasis of cervical cancer [5]. Multi-slice spiral CT (MSCT) is a novel CT technology. It can reconstruct images at multiple levels with high quality and clearly show lymph node involvement [6]. Although MSCT has a higher diagnostic value than that of traditional CT, missed diagnosis still occurs [7]. Therefore, the purpose of this study was to explore the diagnostic value of MSCT dynamic enhanced scanning for the lymph node metastasis of cervical cancer and the related factors of missed diagnosis and to provide a valuable basis for noninvasive examination.

2. Materials and methods

2.1 Subjects

From March 2019 to March 2022, 283 patients with cervical cancer admitted to our hospital were selected as the subjects. They were aged from 33 to 67 years, with an average age of (50.33 $\pm$ 4.36) years. The pathological types included squamous cell carcinoma (236 cases), adenocarcinoma (25 cases), and adenosquamous cell carcinoma (22 cases). Lymph node metastasis was observed by MSCT before surgery and patho-

logical examination after surgery. According to the missed diagnosis by MSCT, the patients with lymph node metastasis were divided into a missed diagnosis group (n = 41) and a non-missed diagnosis group (n = 128).

2.2 Inclusion and exclusion criteria

Inclusion criteria: patients diagnosed with cervical cancer by pathological examination [8]; patients receiving surgical treatment; patients with complete clinical data. Exclusion criteria: pregnant or lactating patients; patients receiving other treatments before surgery; patients without receiving pathological examination after surgery; patients with other malignant tumors; patients with unclear pathological classification or clinical stage. All patients or their family members in this study were informed, agreed and signed the informed consent form.

2.3 Data collection

The clinical data of patients were obtained by collecting their electronic medical records, including age, menstrual cycle, tumor size, body mass index, the International Federation of Gynecology and Obstetrics (FIGO) stage, and differentiation degree. The expression of cell proliferation nuclear antigen 67 (Ki-67) in biopsy specimens was detected by immunohistochemistry.

2.4 MSCT detection method

The patient was detected using LightSpeed VCT 64-slice spiral CT scanner (GE, Chicago, IL, USA). The patient was instructed to hold the urine to fill the bladder and to take the supine position. The scan range was from the diaphragm to the level of the pubic symphysis. Scan parameters: tube voltage = 120 kV, tube current = 200–300 mA, slice thickness = 5–10 mm, pitch = 1 and reconstruction interval = 0.5–2.5 mm. After the plain scan, 80–100 mL of contrast agent iohexol was injected through the cubital vein at a rate of 3.0–4.0 mL/s. Meanwhile, angiography tracing was started, and the arterial phase scan was performed after the CT value of the abdominal aorta reached the set threshold of 170–180 HU. The parenchymal phase scan was conducted after a delay of 65 s, and the bladder and ureter were imaged after a delay of 3–4 min. The images were interpreted by two experienced radiologists. (1) Stage II cervical cancer: Stage IIa involved the upper two-thirds of the vagina without parametrial invasion; Stage IIb had parametrial invasion but without reaching the pelvic wall. (2) Stage III cervical cancer: Stage IIIA had tumor invasion into the lower one-third of the vagina, but without invading the pelvis; Stage IIIB had tumor invasion into the pelvic wall and/or hydronephrosis or renal nonfunction, involving pelvic lymph nodes and/or para-aortic lymph nodes regardless of tumor size or degree of invasion. (3) Stage IV cervical cancer: CT showed invasion into the bladder or rectal mucosa and/or extension beyond the true pelvis.

MSCT criteria [9]: Criteria for lymph node metastasis: the maximum transverse diameter of lymph nodes was $>$10 mm or low-density necrotic areas can be observed in lymph nodes. Criteria for necrotic areas: the enhancement value of a lesion before and after scanning was $<$20 Hu.

2.5 Pathological diagnosis

None of the patients included in MSCT had undergone surgery, radiotherapy, chemotherapy, immune therapy, or other related treatments. All patients were subjected to lymph node dissection immediately after MSCT. The common iliac artery, internal iliac artery, external iliac artery, and abdominal aorta were marked according to the anatomical and physiological locations, and the metastasis of lymph nodes in different anatomical locations was recorded.

After abdominal exploration, radical hysterectomy (wide hysterectomy + pelvic lymph node dissection) was performed for all cases. Bilateral pelvic lymph node dissection was started from 3 or 5 cm above the bifurcation of internal and external iliac arteries, from top to bottom and from outside to inside. Sequentially, common iliac, external iliac, deep inguinal, internal iliac and obturator foramen lymph nodes and adipose tissues on both sides were dissected. If abdominal aortic enlargement was found during exploration, lymph node resection or sampling was performed. The metastasis of lymph nodes in each anatomical position, numbers of positive, false positive and false negative cases diagnosed by MSCT, as well as the diameter and length of lymph nodes, were recorded [10].

2.6 Diagnostic criteria

True positive: each group of lymph nodes was diagnosed by MSCT as positive, and pathological examination also showed positive characteristics. False positive: each group of lymph nodes was diagnosed by MSCT as positive, but no positive lymph nodes were detected by pathological examination. True negative: each group of lymph nodes was diagnosed by MSCT as negative, and no lymph node metastasis was found by pathological examination. False negative: each group of lymph nodes was diagnosed by MSCT as negative, but lymph node metastasis was found by pathological examination.

2.7 Statistical analysis

SPSS 22.0 software (IBM Inc., Armonk, NY, USA) was utilized for statistical analysis. The count data were expressed as rates (%), and the comparison between groups was performed using the χ^2 test. Using postoperative pathological examination as the gold standard, the positive coincidence rate, negative coincidence rate, total coincidence rate, sensitivity, specificity, missed diagnosis rate, and misdiagnosis rate of MSCT examination were calculated. The receiver operating characteristic (ROC) curve was plotted to evaluate the diagnostic value of MSCT for the lymph node metastasis of cervical cancer. Multivariate logistic regression analysis was used to determine the influencing factors of missed diagnosis by MSCT. A back propagation (BP) neural network model was constructed, and the number of nodes in the hidden layer was determined by repeated cross-validation. The ROC curve was used to analyze the discrimination degree of the model prediction. The inspection level α was set at 0.05.

3. Results

3.1 Pathological examination results

The results of surgical and pathological examinations showed that there were 169 cases with lymph node metastasis and 114 cases without metastasis, with the metastasis rate of 59.72%. Besides, 128 cases of lymph node metastasis were detected by MSCT, and 41 cases were missed. Using postoperative pathological examination as the gold standard, the positive and negative coincidence rates of MSCT diagnosis were 92.75% (128/138) and 71.72% (104/145), respectively. The total coincidence rate, sensitivity, and specificity were 81.98% (232/283), 75.74% (128/169), 91.23% (104/114), 24.26% (41/169: 41 true positive patients were not diagnosed by MSCT) and 8.77% (10/114: 10 true negative cases were misdiagnosed as positive by MSCT), respectively. Collectively, MSCT diagnosis had a high consistency with pathological examination (Table 1).

TABLE 1. MSCT findings and pathological examination results in patients.

CT	Pathological diagnosis		Total
	Positive	Negative	
Positive	128	10	138
Negative	41	104	145
Total	169	114	283

CT: computed tomography.

3.2 Diagnostic value of MSCT for lymph node metastasis of cervical cancer

The area under the ROC curve (AUC) of MSCT was 0.741 (95% CI: 0.723–0.826), indicating a high diagnostic value (Fig. 1).

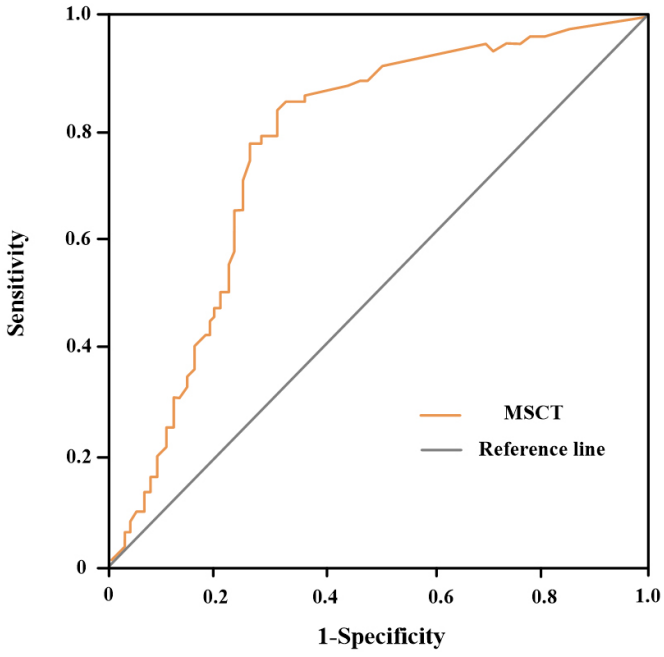

FIGURE 1. ROC curve of MSCT. MSCT: Multi-slice spiral CT.

3.3 Univariate analysis results of missed diagnosis by MSCT

MSCT showed lymph node metastasis in 128 cases and missed diagnosis in 41 cases. There were significant differences between missed diagnosis and non-missed diagnosis groups in terms of tumor size, FIGO stage, differentiation degree, vaginal margin, Ki-67 expression, parauterine invasion, interstitial invasion depth, and vascular invasion ($p < 0.05$) (Table 2).

3.4 Multivariate analysis results of missed diagnosis by MSCT

Multivariate logistic regression analysis was performed using the factors with significant differences between the two groups as independent variables and missed diagnosis (non-missed diagnosis = 0, missed diagnosis = 1) as the dependent variable. The results showed that a high degree of differentiation, negative Ki-67 expression, and interstitial infiltration depth of <one half were independent risk factors for the missed diagnosis by MSCT ($p < 0.05$), and tumor size was an independent protective factor ($p < 0.05$) (Fig. 2).

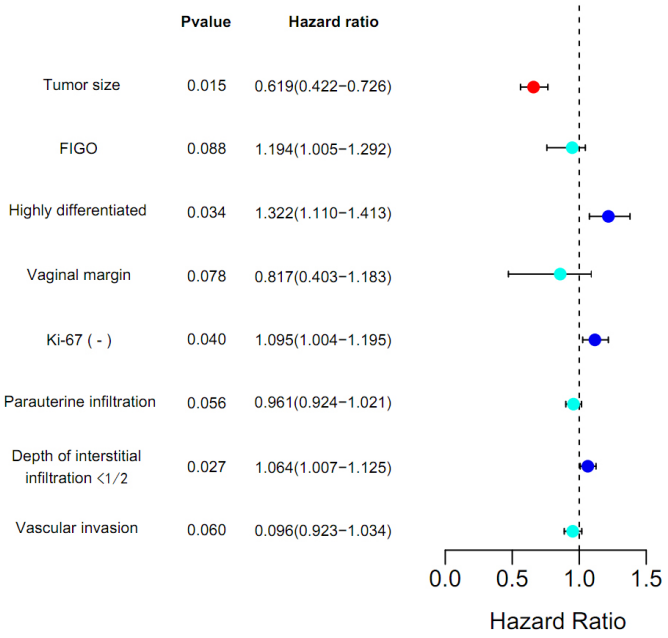

FIGURE 2. Forest map for missed diagnosis by MSCT in the diagnosis of cervical cancer lymph node metastasis through multivariate Logistic regression analysis. FIGO: the International Federation of Gynecology and Obstetrics.

3.5 Model establishment

The risk factors and protective factors that affected the missed diagnosis by MSCT were included in the BP neural network model using the input layers. The number of hidden layer nodes was determined through repeated cross-validation. When the node number was three, the root mean square error of cross-validation was the smallest (Fig. 3). With missed diagnosis as the output layer, the BP neural network model for predicting MSCT missed diagnosis was constructed (Fig. 4).

TABLE 2. Univariate analysis of missed diagnosis by MSCT.

	Missed diagnosis group (n = 41)	Non-missed diagnosis group (n = 128)	χ^2	*p*
Age				
<50	18 (43.90%)	56 (43.75%)	0.000	0.986
≥50	23 (56.10%)	72 (56.25%)		
Body mass index (kg/m^2)				
<25	20 (48.78%)	62 (48.44%)	0.001	0.969
≥25	21 (51.22%)	66 (51.56%)		
Gravidity				
<2	19 (46.34%)	59 (46.09%)	0.001	0.978
≥2	22 (53.66%)	69 (53.91%)		
Postmenopausal women				
No	23 (56.10%)	72 (56.25%)	0.000	0.986
Yes	18 (43.90%)	56 (43.75%)		
Tumor diameter (cm)				
<4 cm	36 (87.80%)	39 (30.47%)	41.357	<0.001
≥4 cm	5 (12.20%)	89 (69.53%)		
Histological type				
Squamous carcinoma	33 (80.49%)	105 (82.03%)	0.049	0.824
Glandular cancer	5 (12.20%)	13 (10.16%)		
Adenosquamous carcinoma	3 (7.32%)	10 (7.81%)		
FIGO				
I∼II	28 (68.29%)	35 (27.34%)	22.270	<0.001
III∼IV	13 (31.71%)	93 (72.66%)		
Degree of differentiation				
High	30 (73.17%)	33 (25.78%)	29.826	<0.001
Medium and low	11 (26.83%)	95 (74.22%)		
Growth mode				
Endogenous type	14 (34.15%)	46 (35.94%)	1.082	0.298
Exogenous type	21 (51.22%)	67 (52.34%)		
Others	6 (14.63%)	15 (11.72%)		
Vaginal margin				
Without	15 (36.59%)	13 (10.16%)	15.692	<0.001
With	26 (63.41%)	115 (89.84%)		
Ki-67				
Negative	34 (82.93%)	12 (9.38%)	84.802	<0.001
Positive	7 (17.07%)	116 (90.63%)		
Parauterine infiltration				
No	25 (60.98%)	29 (22.66%)	20.971	<0.001
Yes	16 (39.02%)	99 (77.34%)		
Infiltration depth				
<One-half layer	35 (85.37%)	15 (11.72%)	80.849	<0.001
≥One-half layer	6 (14.63%)	62 (48.44%)		
Full layer	0 (0)	51 (39.84%)		
HPV infection				
No	5 (12.20%)	16 (12.50%)	0.003	0.959
Yes	36 (87.80%)	112 (87.50%)		
Vascular invasion				
Without	38 (92.68%)	13 (10.16%)	100.373	<0.001
With	3 (7.32%)	115 (89.84%)		

FIGO: the International Federation of Gynecology and Obstetrics; HPV: human papillomavirus.

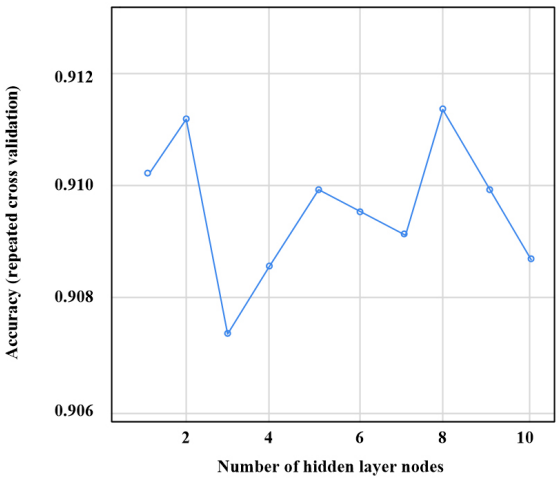

FIGURE 3. Determination of the number of hidden layer nodes (cross-validation).

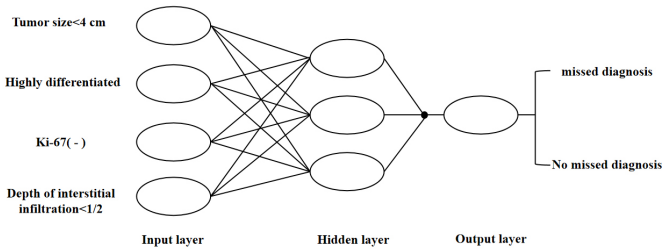

FIGURE 4. Construction of BP neural network model.

3.6 Model verification

AUC of the missed diagnosis by MSCT predicted by the BP neural network model was 0.842 (95% CI: 0.801–0.893, $p < 0.001$), and the sensitivity and specificity were 87.64% and 86.27%, respectively, showing good discrimination (Fig. 5). Then the patients were divided into five categories according to the quintiles of actual probability of missed diagnosis and used as the abscissa to plot the probability calibration curve, by which the accuracy of the model was evaluated. The predicted probabilities of missed diagnosis by the BP neural network model were 9.23%, 17.31%, 32.50%, 48.49% and 68.46%, respectively, and the corresponding observed probabilities were 10.05%, 18.14%, 31.81%, 48.97% and 67.29%, respectively. The Hosmer-Lemeshow analysis showed that $p > 0.05$, and the accuracy of the model prediction was high (Fig. 6).

4. Discussion

In recent years, researchers have endeavored to improve the clinical treatment of cervical cancer [11]. However, the five-year survival rate of patients is still only about 50% [12]. Wang *et al.* [13] reported that lymph node metastasis was the most important factor affecting the prognosis of patients with cervical cancer. Compared with patients without lymph node metastasis, the five-year survival rate of cases with metastasis greatly reduces, and the recurrence rate significantly increases. The five-year survival rate of patients with cervical cancer decreases with increasing number of metastatic lymph nodes [14]. Therefore, determining the lymph node metastasis in

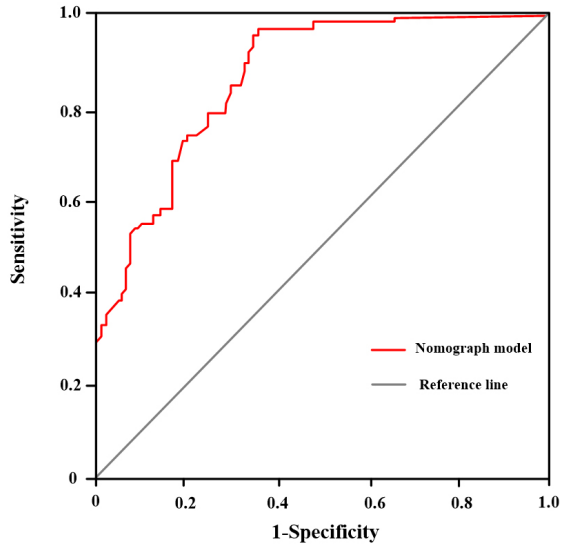

FIGURE 5. ROC curve of BP neural network model.

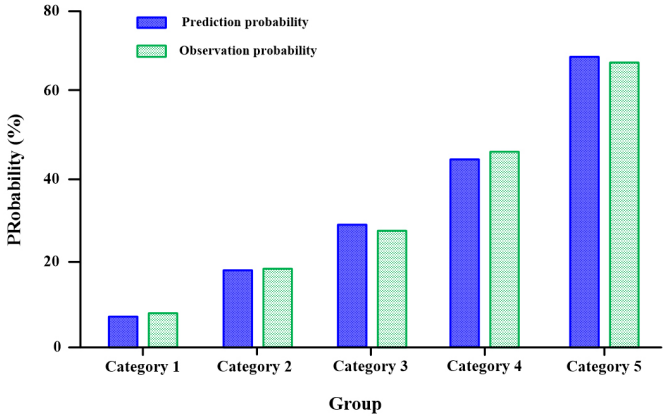

FIGURE 6. Accuracy evaluation of BP neural network model.

patients with cervical cancer before treatment is of great significance to the selection of an appropriate treatment plan and prognostic evaluation.

Ultrasound, CT and MRI examination methods have been widely used to diagnose the lymph node metastasis of cervical cancer. Among them, CT has a high spatial resolution and can clearly show the anatomic sites of lymph nodes with high sensitivity and specificity. Compared with traditional CT, MSCT has more slices and clearer single-slice imaging. Recently, MSCT has been widely used in the clinical diagnosis of lymph node metastasis of cervical cancer. There is no significant difference between the positive coincidence rates of MSCT and pathological examination in the diagnosis of lymph node metastasis of cervical cancer [15]. Additionally, the specificity and sensitivity of MSCT for detecting the lymph node metastasis of cervical cancer are 88.43% and 71.56%, respectively [16]. In this study, the positive and negative coincidence rates of MSCT diagnosis were 92.75%% and 71.72%, respectively, and the total coincidence rate, sensitivity, and specificity were 81.98%, 75.74% and 91.23%, respectively, which were consistent with those of pathological examination. In addition, AUC of MSCT diagnosis was 0.741, indicating

that MSCT had a high diagnostic value for the lymph node metastasis of cervical cancer.

Although MSCT can accurately position the lesion through multi-axial observation, missed diagnosis may still occur in the case of lymph node metastasis. Therefore, exploring the influencing factors of missed diagnosis by MSCT is of great clinical significance. Xu *et al*. [17] reported that tumor size was a key predictive factor for missed diagnosis by CT examination. Cohen *et al*. [18] found that tumor diameter was inversely related to the missed diagnosis rate. In this study, the tumors of patients with missed diagnosis were mostly <4 cm, probably because they had smaller lesions, shallower invasion depth, and less obvious change of cervical tissue [19]. Deng *et al*. [20] reported that the depth of interstitial infiltration <one half was an independent risk factor for the missed diagnosis of cervical cancer. In this study, 85.37% of patients in the missed diagnosis group had the interstitial infiltration depth of <one half. Multivariate Logistic regression analysis showed that the interstitial infiltration depth of <one half was an independent risk factor for the missed diagnosis of lymph node metastasis by MSCT. Possibly, the patients with the interstitial infiltration depth of <one half were often accompanied by smaller tumor diameters [21] and less prone to lymph node metastasis. The prognosis of cervical cancer is closely related to the degree of tumor differentiation. The five-year survival rate of patients with well-differentiated tumors is significantly higher than that of patients with moderately and poorly differentiated tumors [22]. We herein found that the degree of differentiation of the missed diagnosis group was high, and a high degree of differentiation was an independent risk factor for the missed diagnosis of lymph node metastasis by MSCT, which may be attributed to the weak diffusion of well-differentiated tumor tissues [23] and inconspicuous lymph node metastasis. In addition, we also found that the negative expression of Ki-67 was closely related to the missed diagnosis by MSCT, as an independent risk factor. Probably, the patients with negative Ki-67 expression had lower cell proliferation [24], better prognosis and weaker lymph node metastasis [25]. Moreover, the model established based on the above independent influencing factors had high discrimination, accuracy, and predictive value.

Regardless, this study is still limited. This is a single-center retrospective study with a small sample size, which increases the risk of selection bias among subjects. Some confounding factors which may also affect the missed diagnosis by MSCT, such as genetic inheritance, are not included in this study.

5. Conclusions

In conclusion, MSCT had a high diagnostic value for the lymph node metastasis of cervical cancer. However, the patients with tumor size of <4 cm, a high degree of differentiation, negative Ki-67 expression and interstitial infiltration depth of <one half may suffer from missed diagnosis, and should be diagnosed in combination with other auxiliary examinations.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

HH designed and performed this study, and prepared this manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study has been approved by the ethics commit of The Third Affiliated Hospital of Jinzhou Medical University. Written informed consent has been obtained from all patients.

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CONFLICT OF INTEREST

The author declares no conflict of interest.

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