Original Article

The Diagnostic Accuracy of MRI Pelvis in Parametrial Invasion in Patients with Cervical Cancer keeping Histopathology as Gold Standard

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Abstract

Objective: To determine the diagnostic accuracy of MRI pelvis in parametrial invasion in patients with cervical cancer (CC) keeping histopathology as gold standard.

Methodology: This cross-sectional study was conducted at department of Radiology, Liaquat University of Medical and Health Sciences (LUMHS), Hyderabad, from April 2022 to October 2022. All women aged 31–70 years with a diagnosis of cervical cancer, including both premenopausal and postmenopausal women, who underwent pelvic MRI for pretreatment local staging before surgery and subsequently underwent radical hysterectomy with histopathological examination of the surgical specimen were included in the study. MRI scans were assessed by a consultant radiologist to evaluate the presence or absence of parametrial invasion in cervical cancer, and the findings were further compared with the histopathological findings of hysterectomy specimens, to assess the diagnostic accuracy of MRI by using 2 x 2 tables keeping histopathological findings as gold standard.

Results: Overall mean age of 134 enrolled patients was 49.67±11.99 years, with majority of pre-menopausal women. The MRI pelvis exhibited an overall diagnostic accuracy around 88.06% with sensitivity 86.49% and specificity 88.66%, for detecting parametrial invasion, compared to the histopathology as the gold standard. Additionally, the diagnostic accuracy was some higher noted among women aged >45 years and with post-menopausal status, while not significant.

Conclusion: MRI showed higher sensitivity, specificity and overall diagnostic accuracy in diagnosis parametrial invasion in cases of cervical cancer, based on histopathology as gold standard.

Key words: Cervical cancer, MRI, Sensitivity, Specificity, Diagnostic accuracy.

Cite this article as: Sualeha, Aijaz S, Sajid E, Ana U, Keenjhgar. The Diagnostic Accuracy of MRI Pelvis in Parametrial Invasion in Patients with Cervical Cancer keeping Histopathology as Gold Standard J Soc Obstet Gynaecol Pak. 2026;16(3):237-242. DOI. 0.71104/jsogp.v16i3.1104

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Introduction

The Cervical cancer is ranked fourth among the most common cancers diagnosed among women around the world. It is a significant cause of cancer-related global morbidity and mortality, with around 660,000 newly diagnosed cases during 2022 and annual death of 350,000 female patients worldwide.[1,2] Resources limited low and middle-income nations where interventions remain largely ineffective, share a substantial burden of avoidable cervical carcinoma, with fresh cases up to 85% and cervical-cancer associated death in 87% of patients.[2,3] Cervical cancer's development is most commonly linked to being persistently infected with high-risk human papillomavirus (HPV), Human Immunodeficiency Virus (HIV) infection, diethylstilbestrol exposure, and history of squamous intraepithelial lesion.[4] The two most common high-risk oncogenic types of HPV 16 and 18 are the predominant cause of cervical cancer.

Persistent infection with these HPV variants can alter cellular mechanism in cervix. These cellular changes in

Authorship Contribution: [1,5]Substantial contributions to the conception or design of the work or the acquisition, [1,2,3] Drafting the work or revising it critically for important intellectual content, [3]Final approval of the version to be published. [4]Active participation in methodology.,

Funding Source: none
Conflict of Interest: none

Received: April 27, 2026 Revised: July 22, 2026
Accepted Aug 03, 2026

a woman exposed to HPV infection may take 15-20 years to progress through precancerous lesions to cervical cancer.[5] Despite the contribution of prophylactic vaccination and screening to the reduction in cervical cancer incidence, many women still continue to struggle with clinically significant burden of this disease, especially in low resource settings.[6]

The prognosis of cervical cancer is strongly influenced by the size and extent of tumor spread and presence of high-risk pathological features. Such high-risk pathological findings include Lymph node metastasis and parametrial invasion that are frequently linked to the large tumor size. These factors are significantly associated with recurrence risk, treatment response, and clinical outcomes in patients with cervical cancer.[7,8]

Cervical cancer may extend locally to parametrium, uterosacral ligaments, vagina, bladder, and rectum. On the other hand, distant spread most frequently affects the pulmonary, hepatic, intestinal, and osseous regions. Lymphatic spread of cervical cancer commonly involves the parametrial and pelvic lymph nodes, which may progress to paracaval and para-aortic nodes. Parametrial involvement and lymph node metastasis are more frequently associated with tumors exceeding 2 cm. The extent of both local and distant spread may significantly influence patient survival. Tumor size, stromal invasion, and lymphovascular space invasion are the important prognostic factors.[9,10] Accurate assessments of parametrial involvement is therefore essential for pretreatment staging of cervical cancer and the choice of appropriate therapeutic approach.

Traditionally, clinical examination has played an important role in assessing the local extent of cervical cancer. However, modern imaging techniques are superior to clinical examination in differentiating cervical tumors from surrounding soft tissues and provide better assessment of local tumor extension.[10,11] Magnetic resonance imaging (MRI) of the pelvis is a widely recognized important imaging modality for local staging of cervical cancer. It can provide detailed visualization of the cervix and adjacent pelvic structures due to its excellent soft-tissue contrast and multiplanar imaging capability, without exposing patients to ionizing radiation. MRI, on T2-weighted sequences, can demonstrate the presence of an irregular tumor margin, disruption of the low-signal-intensity stromal ring, and extension into the parametrial fat. Combined application of diffusion-weighted imaging (DWI) and apparent diffusion coefficient mapping facilitates differentiation of tumor from oedema and fibrosis, which can enhance the assessment of parametrial invasion. The correct identification of parametrial invasion in cervical cancer is often challenging to diagnose and essential for choosing between surgery and chemoradiation. Histopathological examination serves as a gold standard in identifying microscopic invasion that may not always be apparent clinically or radiologically, [8-12] while MRI is a promising non-invasive alternative, its diagnostic accuracy needs to be validated against histopathology, the gold standard. This study was aimed to determine the diagnostic accuracy of MRI in detecting parametrial invasion, facilitating the appropriate treatment selection and avoid unnecessary surgical intervention.

Methodology

This was a cross-sectional descriptive study, conducted at Radiology department of Liaquat University Hospital Hyderabad. This study was conducted after obtained ethical approval from April 2022 to October 2022. A sample size of 134 patients was calculated by taking proportion (sensitivity=84.5% and specificity=84.2%)[13] of MRI in detecting parametrial invasion in cases of cervical cancer, Prevalence of parametrial invasion by cervical cancer=73%[5] and desired precision of 8% for sensitivity and 12% for specificity. Non probability consecutive sampling technique was used. All the women aged 31–70 years, diagnosed with cervical cancer, both pre- and post-menopausal women, who underwent MRI pelvis for pre-treatment local staging prior to surgery, and who were planned for and subsequently underwent radical hysterectomy with histopathological examination of the surgical specimen, were included. All the pregnant women; biopsy-proven patients of other pelvic malignancies such as ovarian cancer; patients with a history of previous surgery for uterine pathology; patients with a contraindication to MRI; women with recurrent cervical cancer; patients in whom the histopathological specimen was inadequate/incomplete for parametrial assessment; women who did not undergo surgery; and those not willing to participate in the study were excluded. After obtaining the informed consent, all the eligible women underwent MRI for pelvis, and the images were evaluated by the consultant radiologist to identify the presence or absence of parametrial invasion. Subsequently all the included patients were underwent planned radical hysterectomy and the surgical specimens were sent to the hospital laboratory for histopathological evaluation. Furthermore, the MRI findings regarding parametrial invasion were

subsequently compared with the histopathological findings of the hysterectomy specimens, taken as the gold standard, in order to determine the diagnostic accuracy of MRI pelvis in terms of (sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy) in the detection of parametrial invasion among patients with cervical cancer. All the relevant data were analyzed using SPSS version 26. Qualitative data variables were expressed as number and percentage, while quantitative variables were expressed as mean and standard deviation. Two by two tabulation was utilized to calculate the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of MRI pelvis in detection of parametrial invasion in cases of cervical cancer taking histopathology as gold standard. Effect modifiers like age and menopausal status were controlled through stratification.

Results

Mean age of the patients was 49.67 ± 11.99 years, with majority of patients (83.6%) were older than 45 years, while 16.4% were aged ≤45 years. According to menstrual status, the majority of women (67.2%) were pre-menopausal, while 32.8% were post-menopausal. According to MRI, parametrial invasion was found positive among 51 (38.1%) of patients and negative in 83 (61.9%). On histopathological examination, parametrial invasion was positive in 44 (32.8%) of patients and negative in 90 (67.2%). Table I.

The MRI pelvis showed good overall diagnostic accuracy for parametrial invasion in the cervical carcinoma, sensitivity (86.49%), specificity (88.66%) and overall accuracy around 88.06% with the positive MRI finding highly likely to be accurate (PPV= 94.51%), along with a negative finding carried a somewhat higher chance of missing of true invasion (NPV=74.42%). Table II

Table I: Demographic and clinical characteristics of the patients. (n=134)

Variable	Category	N (%)
Menstrual status	Pre-menopausal	68 (50.7%)
	Post-menopausal	66 (49.3%)
Clinical FIGO Stage	IIA	20 (14.9%)
	IB	43 (32.1%)
	IIB	71 (53.0%)
MRI findings	Positive	51 (38.1%)
	Negative	83 (61.9%)
Histopathology findings	Positive	44 (32.8%)
	Negative	90 (67.2%)
Mean age (mean+SD)		49.67 ± 11.99 years

Table II: Diagnostic accuracy of MRI taking Histopathology as gold standard. (n=134)

MRI	Histopathology		
	Positive	**Negative**	**Total**
Positive	86	5	91
Negative	11	32	43
Total	97	37	134
Sensitivity: 86.49%, Specificity: 88.66%, PPV: 94.51%, NPV: 74.42%, Diagnostic accuracy: 88.06%			

Based on post stratification MRI showed some higher diagnostic accuracy among >45 years aged women (89.87%) compared to those <45 years (85.45%), with some better sensitivity, specificity, and NPV along with NPV (60%). However, it also showed some higher overall diagnostic accuracy in post-menopausal women (90.63%) compared to pre-menopausal women (85.71%), while not significant as shown in table III &IV.

Table III: Diagnostic accuracy of MRI taking Histopathology as gold standard according to age groups. (n=55)

Age groups	MRI findings	Histopathology		
		Positive	Negative	Total
Women aged ≤45 years	Positive	38	2	40
	Negative	6	9	15
	Total	44	11	55
Sensitivity = 86.36%, Specificity = 81.82%, PPV = 95%, NPV = 60%, Overall DA =85.45%				
Women aged >45 years	Positive	48	3	51
	Negative	5	23	28
	Total	53	26	79
Sensitivity = 90.57%, Specificity = 88.46%, PPV = 94.12%, NPV = 82.14%, Overall DA =89.87%				

Table IV: Diagnostic accuracy of MRI taking Histopathology as gold standard according to premenopausal status. (n=55)

Age groups	MRI findings	Histopathology		
		Positive	Negative	Total
Pre-menopausal women	Positive	45	2	47
	Negative	8	15	23
	Total	53	17	70
Sensitivity = 84.91%, Specificity = 88.24% PPV = 95.74%, NPV = 65.22%, Overall DA = 85.71%				
Post-menopausal women	Positive	41	3	44
	Negative	3	17	20
	Total	44	20	64
Sensitivity = 93.18%, Specificity =85.0%, PPV = 93.18%, NPV = 85.00%, Overall DA= 90.63%				

Discussion

The cervical carcinoma remains one of the leading gynecological cancers and accurate pre-treatment measurements of parametrial invasion plays an essential role in the determination of the most appropriate management strategy. Present study evaluated the diagnostic performance of MRI in detecting parametrial invasion in 134 suspected cervical cancer cases, using histopathological examination as the gold standard, with an overall, mean age of study subjects was 44.67 ± 11.99 years, with majority of subjects comprising pre-menopausal (67.2%) patients and older than 30 years (83.6%). The demographic findings of the present study are consistent with study conducted by Yang Q et al[13] who reported that mean age of cervical cancer patients was 47.33 ± 8.42 and predominance of non-menopausal (64.9%) patients. Similarly, in the study conducted by Dabi Y et al[14] in patients with parametrial invasion, mean age was 58.5 years, with greater proportion comprising menopausal women (67.9%).

In this study, parametrial invasion was identified in 51 (38.1%) patients on MRI and confirmed in 44 (32.8%) patients on histopathological examination. Thus, MRI detected most of the cases confirmed by histopathology, while some cases of parametrial invasion that were not detected on MRI may be attributed to the subtle or microscopic extent of invasion. In line with our findings, Hassan S et al.[15] reported a similar incidence of parametrial invasion on MRI compared with histopathological findings, with 68 (50.0%) cases detected on MRI and 67 (49.3%) confirmed on histopathological examination. Similarly, Yang K et al.[17] reported a considerably higher detection rate of parametrial invasion on MRI compared with surgical pathology. In their cohort of 303 patients, parametrial invasion was identified in 24.1% of patients on MRI, compared with 17.2% on surgical pathology. The differences in findings across studies may be attributed to variations in MRI interpretation criteria, imaging protocols, tumour stage, and radiologist experience. These factors may contribute to the overestimation of parametrial invasion on MRI rather than reflecting a true higher prevalence of disease.[16]

In this study, pelvic MRI demonstrated good overall diagnostic accuracy for detecting parametrial invasion in patients with cervical carcinoma, with a sensitivity of 86.49%, specificity of 88.66%, and overall accuracy of 88.06%. A positive MRI finding was highly likely to represent true parametrial invasion (PPV = 94.51%), whereas a negative MRI finding had a relatively higher likelihood of missing true invasion (NPV = 74.42%). In line with these findings, Hassan S et al.[15] reported a similar sensitivity of 89.55% and a lower false-negative rate (5.14%) for MRI in detecting parametrial invasion. Their findings, similar to ours, suggest that a negative MRI finding does not completely exclude parametrial invasion. In contrast, Ditto A et al.[18] reported 28 histopathologically confirmed cases of parametrial invasion, while MRI showed an overall sensitivity of approximately 49.8% for detecting parametrial involvement in the neoadjuvant-treatment group, which was considerably lower than that observed in the present study.

This difference may be related to treatment-associated changes, such as fibrosis, inflammation, and alterations in tissue characteristics, which can make residual or microscopic parametrial invasion difficult to distinguish on MRI.[16]

Comparable findings were reported in the study by Ditto A et al[18] who found 67.3% specificity of MRI for detecting parametrial involvement in the neoadjuvant-treatment group. In agreement with these findings, in a recent study carried out by Li XX et al[19] combined model based intravoxel incoherent motion diffusion-weighted and dynamic contrast-enhanced MRI achieved 86.3% specificity for predicting parametrial invasion, which is higher than that of our findings. The higher specificity in their study may be attributable to the application of combined model based MRI, which can improve discrimination between malignant invasion and non-malignant tissue changes by providing additional functional information. In contrast, the study carried out by Yang K et al.,[17] showed 82.1% specificity of MRI for detecting parametrial invasion, which is higher than that observed in the present study. The higher specificity in their study may be associated with differences in the prevalence and extent of disease, which may have affected the ability of MRI to correctly identify patients without parametrial invasion.

In this cohort, some higher positive predictive value (PPV) of MRI indicates that MRI is highly reliable in detecting parametrial invasion and help treatment decisions making by providing valuable information regarding locally advanced disease. On the contrary, the study of Steiner A et al[20] reported considerably lower PPV of 46% for MRI alone in detecting parametrial invasion compared to our study, indicating that a substantial proportion of MRI-positive findings in

their study were not confirmed by the reference standard. Similarly, in the study of Yang K et al[17] MRI showed PPV of 38.4% for the detection of parametrial invasion, which is also substantially lower than our findings. The lower positive predictive values in the reported studies may be explained by differences in disease prevalence, MRI acquisition protocols, and criteria used to define parametrial invasion.

In comparison with our findings, Cibula D et al.[21] reported an NPV of 95.3% for parametrial involvement on MRI, which was substantially higher than that observed in the present study. However, parametrial involvement was identified in only 25 (4.7%) of 536 patients on final histopathology, indicating a considerably lower disease prevalence than in our cohort. Similarly, Hassan S et al.[15] reported an NPV of 89.71% for MRI, which was also higher than that observed in our study. The higher NPVs reported in these studies may be partly explained by differences in disease prevalence, as NPV is influenced by the prevalence of the condition being assessed. Variations in MRI protocols, image interpretation criteria, and patient characteristics may have also contributed to the differences in diagnostic performance. The findings of this study were also consistent with the study carried out by Hassan S et al.,[15] who reported a slightly higher diagnostic accuracy of 88.97%, supporting overall good performance of MRI for detecting parametrial invasion.

In contrast, the study conducted by Ditto A et al.[18] reported lower accuracy of 65.8% for MRI in detecting parametrial invasion compared to our study. Treatment-related changes in their patient population may have made MRI assessment of parametrial involvement more challenging, leading to lower accuracy. Similarly, study conducted by Yang K et al.[17] reported accuracy of MRI for detecting parametrial invasion was 77.2%, which was somewhat lower than that observed in the present study. These findings indicate that MRI has an overall good diagnostic accuracy for assessing parametrial invasion, despite possible differences in the performance of MRI based on clinical and technical factors. Moreover, partially aligning with our finding, the study of Park JJ et al[22] reported good diagnostic performance for MRI in detecting parametrial invasion, with sensitivity ranging from 67.6% to 81.1%, specificity from 95.7% to 99.1%, and accuracy from 89.5% to 93.4%. The differences in specificity and accuracy may be related to the MRI technique, as the application of high-b-value diffusion-weighted imaging and image fusion in their study may have improved diagnostic performance. Comparably, the study of Qu JR et al[23] reported an overall sensitivity of 62%, specificity of 88%, PPV of 53%, NPV of 91%, and accuracy of 83% for predicting pathological parametrial invasion. The difference in the study findings may be attributable to the disease prevalence and sample selection criteria.

Present study was limited by its single-center design, relatively limited sample size, and lack of blinding between radiologists and pathologists may influence the generalizability of the findings. Hence further larger multi-center, blinded prospective studies incorporating advanced MRI techniques are recommended to further validate and strengthen the findings of this study.

Conclusion

MRI pelvis revealed a higher overall diagnostic accuracy in the detection of parametrial invasion among women with cervical cancer based on histopathology as the gold standard, with sensitivity and specificity as (86.49% and 88.66%) respectively. Overall findings support the usage of MRI as a reliable, non-invasive pre-treatment staging diagnostic tool that may meaningfully support the selection of appropriate management strategy in clinical practice.

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