

ROLE OF MRI IN STAGING OF CARCINOMA CERVIX

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ABSTRACT

CONTEXT

Cervical carcinoma continues to be staged according to the clinical FIGO classification system which is not accurate. In our study, we determined the diagnostic accuracy of MRI in staging carcinoma cervix with same parameters as FIGO staging.

AIMS

In our study, we determined the diagnostic accuracy of MRI in staging carcinoma cervix, adjoining organ infiltration and delineating stage IIA and below from rest of the stages in carcinoma cervix.

SETTINGS

Study was done in the Department of Radiodiagnosis, in a tertiary care government hospital on 70 female patients diagnosed with carcinoma cervix.

DESIGN

Hospital based observational study.

MATERIALS AND METHODS

MRI staging was correlated with surgico-pathological findings when patient underwent surgery. MRI staging was compared to the non-pathological staging when patient underwent radiotherapy or neoadjuvant chemotherapy.

STATISTICAL ANALYSIS

Univariate and bivariate frequency tables are generated. Sensitivity, specificity and accuracy of MRI in staging of carcinoma cervix are calculated. Interclass correlation is done with Pearson's correlation co-efficient, p value ≤ 0.05 was considered statistically significant.

RESULTS

MRI has a sensitivity, specificity, PPV, NPV and accuracy of 88.7%, 87.5%, 98.2%, 50% and 88.6% respectively [with interclass correlation coefficient $r=0.982$, $p<0.01$ 95% CI (0.972 –0.989)] in staging of carcinoma cervix.

CONCLUSIONS

MRI in staging carcinoma cervix is preferred to clinical FIGO staging for deciding on the treatment modality. However, MRI is not a good modality in detecting carcinoma in situ [stage 0] and stage I of carcinoma cervix.

KEYWORDS

Carcinoma cervix, MRI, Accuracy, Staging.

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INTRODUCTION: Cervical cancer is the 2nd most common cancer in women aged 15 to 44 years in India.¹ Because of its epidemiologic characteristics, cervical carcinoma continues to be staged according to the FIGO classification system. However, there are significant error rates in FIGO

staging which depends on the experience of the examining physician.²

Owing to its superior soft tissue resolution, magnetic resonance (MR) imaging is widely accepted as the single most effective modality for detection of primary tumour and local spread and it is optimal for the selection of a therapeutic strategy for cervical cancer as well.³

In our study, we determined the diagnostic accuracy of MRI in staging carcinoma cervix, adjoining organ infiltration and delineating stage IIA and below from rest of the stages in carcinoma cervix.

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MATERIALS AND METHODS: This was a hospital based observational study done in the Department of Radiodiagnosis, in a tertiary care government hospital on 70 female patients diagnosed with carcinoma cervix by biopsy and Pap smear and were referred for MRI. Permission for the study was obtained from the Ethical Committee of the Institution.

Patients having contraindications for MRI examination and treated cases of carcinoma cervix were excluded from the study. Study was performed with 1.5 Tesla Philips Achieva MRI machine using Torso XL coil. The MRI findings were interpreted by a radiologist with 8 years of experience. The clinical examination was performed by gynaec-oncosurgeons with 10 to 20 years of experience.

Patient Preparation: Fasting for a minimum of 6 hours prior to the examination is recommended to reduce bowel motion artefacts. Tampon is kept in the vagina to assess the vaginal involvement in imaging. Patients are asked to empty the urinary bladder prior to MRI to reduce bowel motion artefact.

Imaging: The MRI of abdomen and pelvis is done from upper border of diaphragm till pubic symphysis. The sequences performed were T1 axial, T2 (axial, coronal and sagittal), T1 post contrast (axial and sagittal) for pelvis. T1 axial, T2 (axial, coronal and sagittal), T1 postcontrast axial for abdomen.

The patients are first staged according to clinical FIGO staging noting the clinical examination findings. They are then subjected to MRI abdomen and pelvis based on the protocol followed in our institution and staged according to revised FIGO classification.

For those early cases of carcinoma cervix where surgery is done as the initial modality of treatment MRI staging is correlated with surgico-pathological findings which are taken as the gold standard. For those cases where the initial treatment modality was not surgery (i.e., treatment given being either RT or neoadjuvant chemotherapy), the MRI findings are correlated with other findings like examination under anaesthesia (for parametrial and pelvic side wall invasion), Ultrasound $\pm$ cystoscopy (for urinary bladder involvement) and per rectal $\pm$ proctoscopy/colonoscopy (for rectal involvement) where these findings are taken as the gold standard.

A final staging is made based on the surgico-pathological staging and the non-pathological staging as mentioned above for correlation of MRI staging.

STATISTICS: For statistical calculations, data is spread in excel sheet and analysis is done with the help of R software v.2.15.1. Univariate and bivariate frequency tables are generated. Sensitivity and specificity of MRI in assessing the extensions and accuracy in staging of carcinoma cervix is calculated. Interclass correlation is done to assess the relationship between MRI staging and the surgico-pathological and/or the non-pathological staging (wherever applicable depending upon the stage and treatment given) using Pearson's correlation co-efficient, p value ≤ 0.05 was considered statistically significant.

RESULTS: Among these 70 cases of carcinoma cervix in our study, 66/70 (94.3%) were squamous cell carcinoma, with the rest being adenocarcinoma. Most of the lesions (35%) were endophytic and were seen to arise from the endocervix, while 16% were seen arising exophytically away from the squamo-columnar junction and 17% cases had both endophytic and exophytic component on MRI. 12 cases were not detected on MRI. Only 29% were less than or equal to 4 cm in the greatest dimension and 54% cases were more than 4 cm in the greatest dimension it was found that 51% of the patients had extension to uterus (either into the corpus or into the lower uterine segment (LUS)), 9% of the patients had involvement of urinary bladder (either muscular or mucosal involvement of urinary bladder) and 44% patients had vaginal involvement in the form of extension to fornix of vagina (3%), upper 1/3rd of vagina (27%) upper 2/3rd of vagina (9%) and full length if vagina up to introitus in 6% of the patients. The involvement of vagina, urinary bladder and rectum are considered when the hypointense wall is replaced by high signal intensity tumour on T2WI. MRI could detect significant lymph nodes by size criteria (short axis ≥ 10 mm). But the findings of lymph nodes could not be compared since neither biopsy nor PET was done for the inoperable cases. So MRI diagnosis of lymph node according to size criteria was considered for further treatment planning. Two patients had hepatic metastasis, one had pulmonary metastasis and one had both hepatic and pulmonary metastasis being detected on MRI and proven by FNAC later.

It was observed that 90 % of the cases were staged the same by MRI but 9% (6/70) patients were under-staged and 1% (1/70) patients were over-staged by MRI. Compared to this, clinical FIGO staging could correctly stage only 63% patients and it led to over-staging in 20% and under-staging in 17% patients.

MRI has a sensitivity, specificity, PPV, NPV and accuracy of 88.7%, 87.5%, 98.2%, 50% and 88.6% respectively [with interclass correlation coefficient $r=0.982$, $p<0.01$ 95% CI (0.972 – 0.989)] in staging of carcinoma cervix. MRI has an accuracy of 98.5% in differentiating stage $\leq$ IIA, thereby correctly delineating operable from inoperable stages of carcinoma cervix, thereby helping in appropriate treatment planning. The sensitivity, specificity, PPV, NPV and accuracy of MRI in predicting various site infiltrations in carcinoma cervix is tabulated in table 1. MRI could detect significant lymph nodes by size criteria in 43/70 patients (61%) in iliac region and in para-aortic region in 5.7% cases.

DISCUSSION: Carcinoma cervix is the third most common malignancy in women.⁴ In current study, majority of patients were in age group of 41-50 years (48%) (table 2), with age of patients ranging from 29 years to 86 years. The most common pathological subtype in our study is SCC representing 94.3% of the total patients being studied. This incidence is almost comparable with the previous studies done by Colletini et al.⁵

Most of the cervical masses in our study were endophytic (36%); 17% were endo-exophytic and 15%

were exophytic. This is in agreement with Okamoto et al who explained the growth pattern of cervical carcinoma as follows: In younger women, the SCJ is located outside the external uterine os, and the tumour tends to grow outward (exophytic growth pattern); in contrast, in elderly patients, the SCJ is located within the cervical canal. In these patients, cervical cancer tends to grow inward along the cervical canal (endophytic growth pattern).⁶

In the current study, 14.3% patients were stage IB, 2.9% stage IIA, 40% were stage IIB, 2.9% were stage IIIA, 10% were stage IIIB, 7.1% were stage IVA and 5.7% were stage IVB on MRI (table 3). 17.1 % cases didn't show any altered signal on MRI and corresponded to stage 1A or lesser. Acquisition in axial, sagittal, and coronal planes is sufficient for staging in most of the cases of carcinoma cervix. In our study, 83% cases showed high signal on T2WI replacing the low signal of cervical stroma. Okamoto et al in 2003 and Mahajan et al in 2013 reported same about the appearance of cervical carcinoma in T2WI.^{6,7} Also our study found that the lesion could be isointense or intermediate signal or hypointense on T1WI. T2WI is the minimum required sequence for imaging of carcinoma cervix, especially if lesion is large where the lesion appears as a hyperintense mass. Contrast enhanced imaging and DWI can be advantageous in case of very early stages of carcinoma cervix, where there was a case in our study which was detected only on post contrast T1WI and the same is proven pathologically. In patients with early stage cervical cancer, contrast-enhanced T1-weighted imaging was superior to T2-weighted imaging in terms of cervical cancer tumour localisation and tumour margin detection as well as overall conspicuity.⁸

The sensitivity, specificity PPV and NPV of MRI in detecting vaginal involvement in carcinoma cervix as per the current study was 70%, 94%, 92% and 61% respectively. This was almost in agreement with the study done by Sheu et al.⁹ The involvement of lower 1/3rd of vagina changes the staging from IIA to IIIA and vice versa which affects the treatment plan. One of the case was associated with vesico-vaginal fistula.

MRI findings suggesting bladder invasion include focal or diffuse disruption of the normal low-signal intensity posterior bladder wall, nodular or irregular bladder wall, mass protruding into the lumen of the bladder. Rectal invasion is rare and appears as segmental thickening and loss of the anterior rectal wall normal intensity. Prominent strands between the tumour and the rectal wall may also indicate rectal invasion. The reported sensitivity of MRI in the evaluation of bladder or rectal invasion is 71–100%, and the specificity is 88–91%.^{10, 11}

The absence of bladder or rectal invasion can be diagnosed with sufficient confidence using MRI (NPV=100%) to safely obviate invasive cystoscopic or endoscopic staging in most patients with cervical cancer. The current study detected extension of the mass in cervix into corpus of uterus in 51.4% patients, into rectal musculature or mucosa in 5.7% patients and into mucosa or muscle of urinary bladder in 8.6% patients. The accuracy,

specificity and NPV is almost agreeing with the studies of Shweel et al and Shirazi et al.¹²

Parametrial extension in a case of carcinoma cervix can be excluded if the hypointense stromal signal intensity is preserved on T₂WI. Parametrial involvement is said to be present when there is a spiculated margin replacing the hypointense signal on T2WI. Tumour extending to involve the internal obturator, piriformis, or levator ani muscles, with or without a dilated ureter, indicates pelvic wall invasion.¹³ Irrespective of the stage of carcinoma cervix, MRI has a sensitivity of 69.9% specificity of 91.7%, NPV of 61.1% and PPV of 94.1% and an accuracy of 77% in assessing the parametrium. A 15.7% (11/70) of the patients had hydroureteronephrosis which is an indirect evidence for pelvic sidewall involvement.

In our study, it is found that MRI has a sensitivity, specificity, PPV, NPV and accuracy of 88.7%, 87.5%, 98.2%, 50% and 88.6% respectively [with interclass correlation coefficient $r=0.982$, $p<0.01$ 95 % CI (0.972 –0.989)] in staging of carcinoma cervix. According to our study, in stage IA and stage 0, MRI has no major role. But MRI has better accuracy in diagnosing stage IB or above. In our study, MRI could correctly detect stage IB and IIA (i.e., 10/11 cases of stage IB and IIA were staged correctly). But the accuracy of MRI in staging increased in advanced cases of carcinoma cervix where MRI correctly staged 46/47 cases of advanced carcinoma cervix ($\geq$ stage IIB). The accuracy of MRI in delineating stage IIA and below from the rest of the stages was 98.6%. The result is in agreement with the previous studies reviewed.⁹

In our study, MRI has over-staged 1/70 case and under-staged 6/70 cases, but MRI staging was correlating with the final FIGO staging in all the other cases. This is in comparison to Shweel et al where there was under-staging of 6% cases. Although lymph nodal involvement is not a criterion in FIGO staging of carcinoma cervix, it is an important criterion to plan for adjuvant RT or chemotherapy for including the region before an RT planning.¹⁴ In our study, MRI could detect significant lymph nodes by size criteria (short axis ≥ 10 mm) in 43/70 patients (61%) in iliac region and in para-aortic region in 5.7% (4/70) cases.

The revised FIGO staging system for cervical carcinoma was implemented on June 1, 2009. In the new FIGO staging system, the use of diagnostic imaging, including CT and MR imaging, to stage cervical tumours is recommended but remains nonmandatory. Examinations performed with anaesthesia, including cystoscopy and proctoscopy, are optional and no longer mandatory, T2-weighted MR imaging findings may be used to confidently exclude bladder or rectal involvement obviating the need for invasive procedures, these findings are similar to the results of our study.²

Current study results concur with literatures being reviewed. In conclusion, MRI is a non-invasive test with high accuracy in staging of carcinoma cervix.

CONCLUSIONS: Based on MRI findings, we could do staging in carcinoma cervix. Need of cystoscopy, proctoscopy & sigmoidoscopy, bone scan in carcinoma cervix

can be mitigated using MRI. In patients with carcinoma cervix, where the lesion is very small, we recommend the use of contrast enhanced imaging in addition to T2WI. Contrast enhanced MRI has no better advantage over conventional T2WI in $\geq$ stage IIA carcinoma cervix. MRI in staging carcinoma cervix is preferred to clinical FIGO staging

for deciding on the treatment modality where there is a dilemma in assessing the parametrium, clinically obviating tedious procedures like examination under anaesthesia. However, MRI is not a good modality in detecting carcinoma in situ [stage 0] and stage I of carcinoma cervix and is an expensive modality with limited availability.

Organ involvement	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)
Urinary bladder	83.3	98.4	83.3	98.4	97.1
Rectum	75	98.5	75	98.5	97
Vagina	70	94	92	61	
Parametrium	70	92	77	94	61

Table 1: MRI assessment of various sites of infiltration by carcinoma cervix

Age	Number of patients	Percentage of patients
≤ 40	17	24.3
41 – 50	22	31.4
51 – 60	21	30.0
> 60	10	14.3
Mean $\pm$ SD	49.3 $\pm$ 11.0	

Table 2: Age wise distribution of patients

MRI stage	Number of patients	Percentage of patients (%)
Normal Study	12	17.1
Stage IB	10	14.3
Stage IIA	2	2.9
Stage IIB	28	40.0
Stage IIIA	2	2.9
Stage IIIB	7	10.0
Stage IVA	5	7.1
Stage IVB	4	5.7
TOTAL	70	100

Table 3: Distribution of patients according to MRI staging

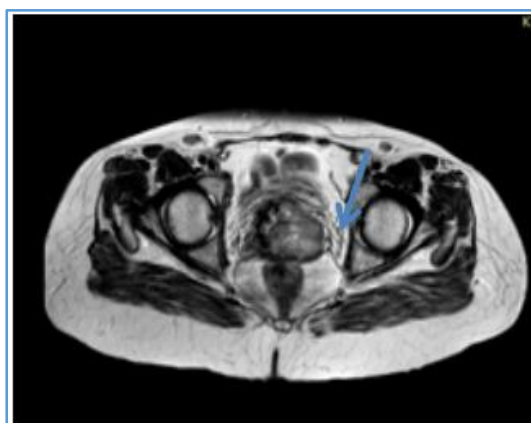


Fig. 1: Biopsy proven case of carcinoma cervix (stage IIA): MRI shows preserved surrounding stromal signal intensity (arrow) on axial

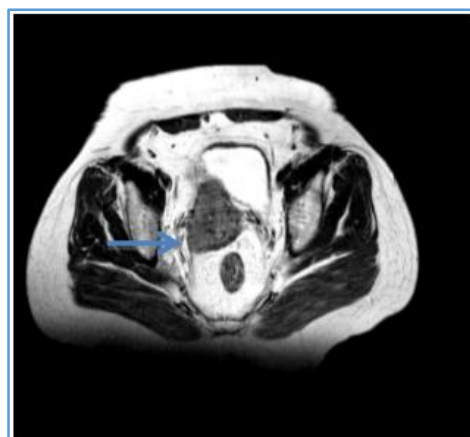


Fig. 2: Proven as squamous cell carcinoma cervix on HPE. MRI shows mass lesion in the cervix with interrupted stromal signal intensity and spiculated right lateral margin suggestive of involvement of right medial parametrium. Stage II B



Fig. 3: A 46-year-old female, proven as squamous cell carcinoma cervix on HPE. MRI shows mass lesion in the cervix with interrupted stromal signal intensity with involvement of lower 1/3rd of vagina (arrow). Lateral pelvic wall appears spared

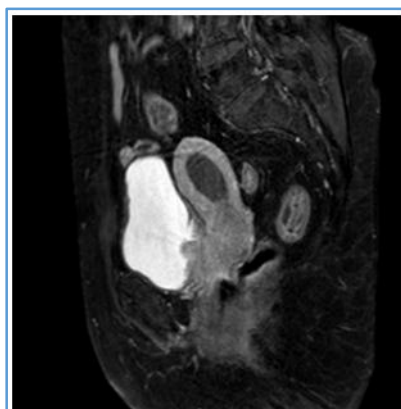


Fig. 4: Case of squamous cell carcinoma cervix. Post contrast Fat Sat images T₁ WI shows enhancing mass in cervix invading the urinary bladder and extending into the lumen of urinary bladder

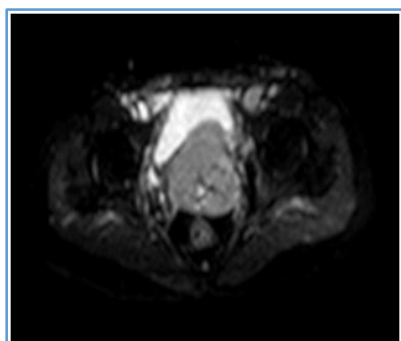


Fig. 5: STIR hyperintense lesion in cervix infiltrating bladder base

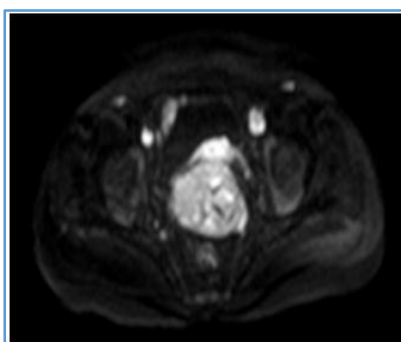


Fig. 6: Hyperintense cervical lesion in DWI (b 1000)

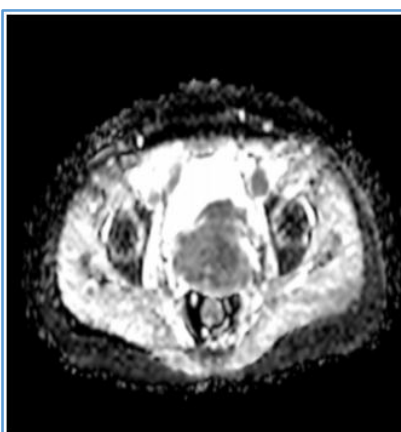


Fig. 7: ADC map showing inversion in cervical mass intensity suggestive of restricted diffusion

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