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ORIGINAL RESEARCH

Role of Magnetic Resonance Imaging in Pre and Post Chemo & Radio Therapy Irradiated Patients in Locally Advanced Cervical Cancer

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Abstract

Background: Cervical cancer is becoming a subject of concern in medical science as it is a serious health problem in developing countries. Carcinoma cervix is primarily staged clinically as per FIGO guideline with minimal permissible usage of diagnostic modalities, even though it has several pitfalls. As we consider the importance of tumor size measurement, we must take into account that, although a necessary step in the evaluation of patients with cervical cancer, physical examination is not a very accurate assessment of tumor size. MRI offers the best imaging tool to determine tumor size, as well as vaginal involvement and parametrial involvement. In patients with cervical cancer, pretreatment MRI provides higher spatial soft tissue resolution which can define pelvic tumor extent, including a more accurate assessment of tumor size, parametrial invasion, pelvic sidewall invasion, and adjacent pelvic organ invasion. We wanted to determine and compare the role of magnetic resonance imaging in pre and post chemotherapy irradiated patents in locally advanced cervical cancer.

Methods: A total of 50 patients diagnosed as a case of locally advanced Cervical carcinoma in the Radiotherapy Department of Burdwan Medical College were included in the study. The present study was aimed to evaluate the use of pre and post chemoradiotherapy MRI for advanced cervical cancer for assessing alteration of tumor volume, lymph nodal assessment and metastasis status in accurate way.

Results: In this study we evaluated pre chemo radiotherapy patients and the agreement between clinical stage (FIGO Classification) and MRI by using Kaplan-Meir Survival Curve showed significant agreement between these two (p value = <0.0001).

Correlation of response rate in post chemo radiotherapy patients using clinical methods and MRI was evaluated by Kaplan-Meir Survival Curve and it showed there was a positive correlation but this was not statistically significant (p value = 0.15).

Conclusions: MRI is more accurate in determining tumour location, tumour size, depth of stromal invasion and extension into lower uterine segment it can modify treatment options and may provide clinically important prognostic information not available from current FIGO staging.

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Keywords: MRI, DWI, ADC, FIGO, FSE, FOV, CRT.

Background

Cervical cancer is becoming a subject of concern in medical science as it is a serious health problem in developing countries. Carcinoma cervix is primarily staged clinically as per FIGO guideline with minimal permissible usage of diagnostic modalities, even though it has several pitfalls. As we consider the importance of tumor size measurement, we must take into account that, although a necessary step in the evaluation of patients with cervical cancer, physical examination is not a very accurate assessment of tumor size. MRI offers the best imaging tool to determine tumor size, as well as vaginal involvement and parametrial involvement. In patients with cervical cancer, pretreatment MRI provides higher spatial soft tissue resolution which can define pelvic tumor extent, including a more accurate assessment of tumor size, parametrial invasion, pelvic sidewall invasion, and adjacent pelvic organ invasion. We wanted to determine and compare the role of magnetic resonance imaging in pre and post chemotherapy irradiated patients in locally advanced cervical cancer.

Material &Methods

A total of 50 patients diagnosed as a case of locally advanced Cervical carcinoma in the Radiotherapy Department of Burdwan Medical College were included in the study.

Study Design

Institutional Prospective observational study.

Inclusion Criteria

- Biopsy proven cases of Cervical carcinoma.
- Locally advanced Cervical carcinoma diagnosed at baseline MRI (Pre CRT MRI)
- Patients will have to receive chemoradiation as per dose for treatment (from department of radiotherapy, BMCH).

Exclusion Criteria

- Early cervical carcinoma (IA).
- Lack of consent to participate.
- Age <18 yrs.&>70 yrs.
- Previous History of radiation.
- History of another carcinoma.
- Patients with metallic prosthesis.

Study Design

Institutional Prospective observational study.

Period of Study

From 1st MAY 2020 to 31st JULY 2021

Study Tools

1.1.5 Tesla MRI machine made by GE HEALTH CARE [MODEL NUMBER – BRIVOMR355] with other required accessories.

Statistical Analysis

Statistical analysis was performed using SPSS statistical software version 19.0. Continuous variables were expressed as mean & SD and categorical variable as counts and percentage. The Kaplan Meir survival analysis was done to compare the survival accuracy.

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Results

Regarding size of the tumour, the mean size at diagnosis was 5.64cm while after chemo radiation the mean size of tumor was 1.3cm with a mean reduction of 4.34cm.

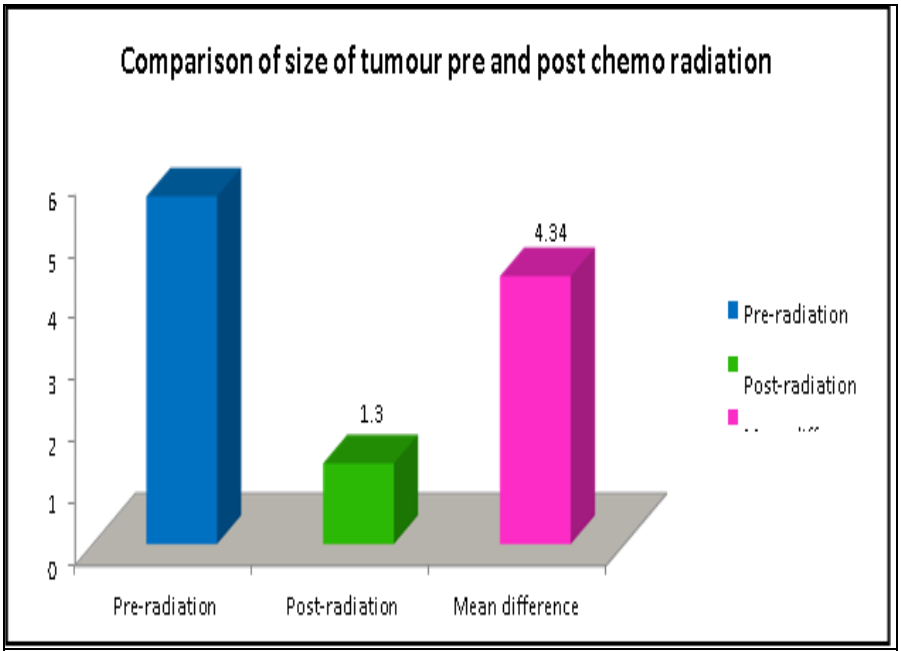

Figure 1: Comparison of size of tumour pre and post chemoradiation

Regarding nodal involvement we found 40 patients (80%) had either clinically or pathologically confirmed lymph node metastasis out of them 21 (42%) patients had pelvic nodes while 19 (38%) patients had paraaortic nodes.

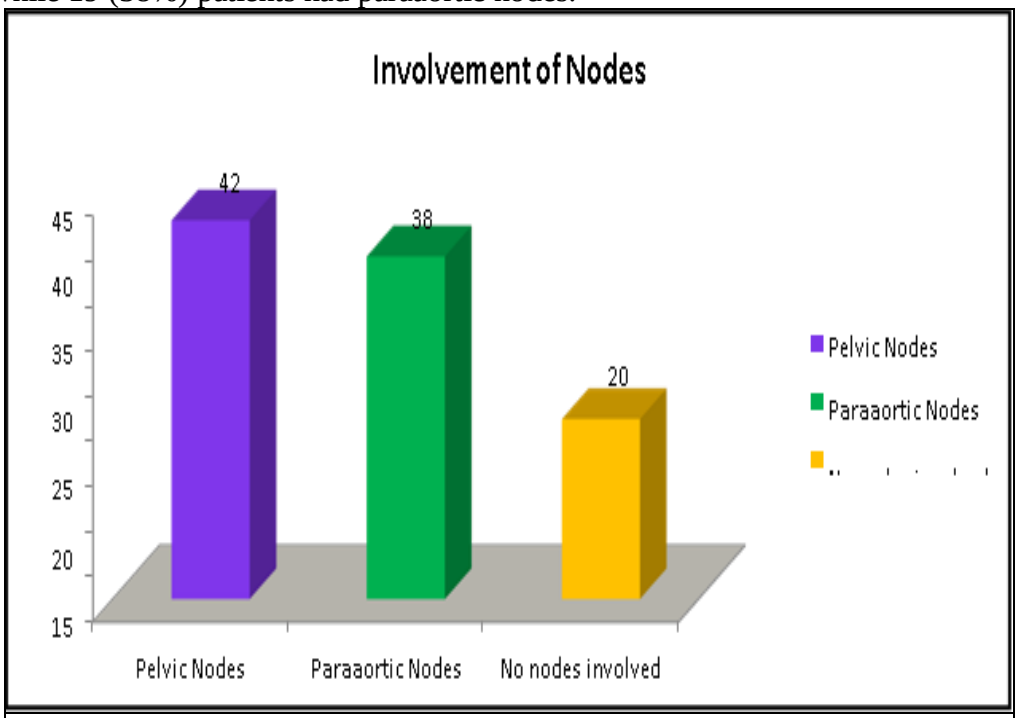

Figure 2: Involvement of Nodes

All patients were initially staged clinically as per the FIGO staging. Most common stage among the study participants was stage IIB (26%) followed by stage IIIB (18%) and IIIA and

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IIA which was 18%. Stage IIA1 involves 12% patients while stage IB2 and IVA involved 4% and 2% patients respectively.

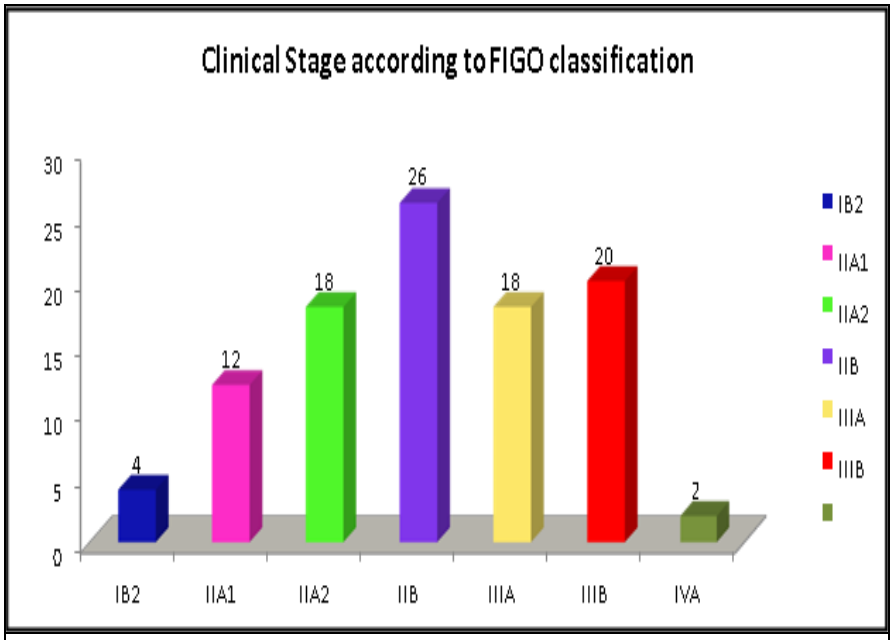

Figure 3: Clinical Stage according to FIGO classification

MRI evaluation was done after FIGO staging and we observed change in the FIGO stage after this evaluation. After combination of MRI, 35 (70%) cases remained unchanged, 12 (24%) cases were upstaged, while 3 (6%) cases were down staged.

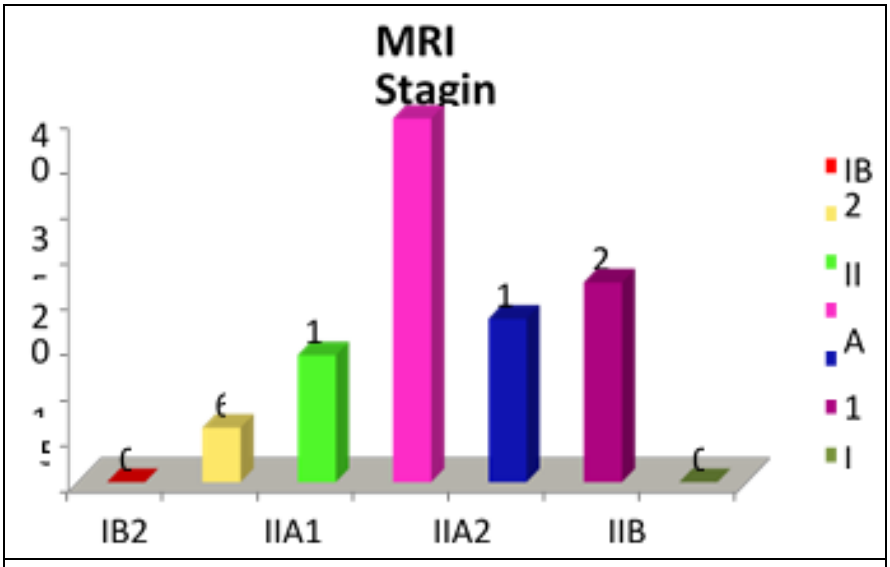

Figure 4: MRI Staging

The agreement between clinical stage (FIGO Classification) and MRI stage in pre-CRT patients by using Kaplan-Meir Survival Curve showed significant agreement between these two (p value =<0.0001).

According to MRI assessment of post CRT patients majority of the patients 56% showed complete response, 40% patients showed partial response and 4% patients had stable disease. None of the patients showed progression of disease.

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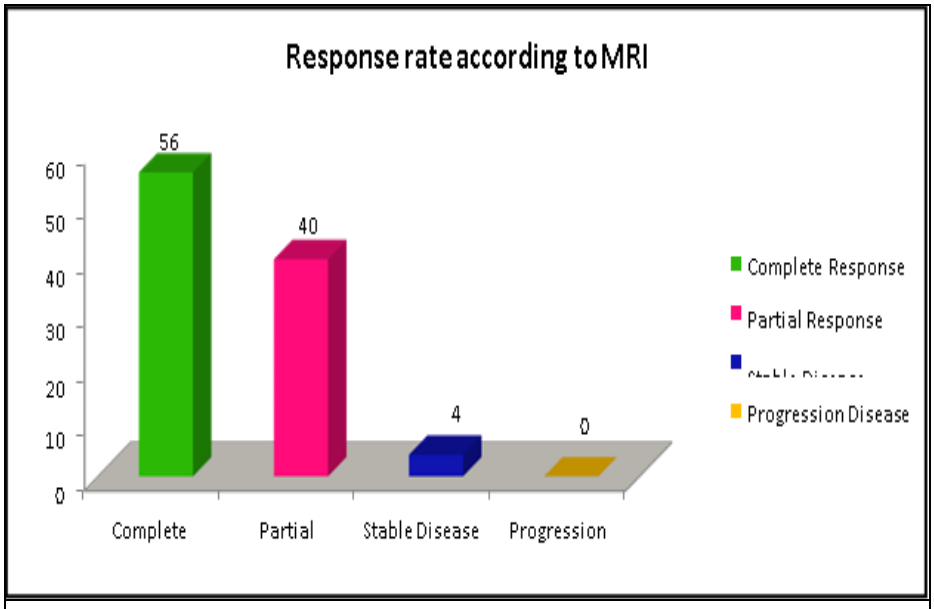

Figure 5: MRI Staging

According to clinical assessment majority of the patients i.e. 37 (74%) showed complete response, 24% (12) patients showed partial response and 2% (1) patient had stable disease. None of the patients showed progression of disease.

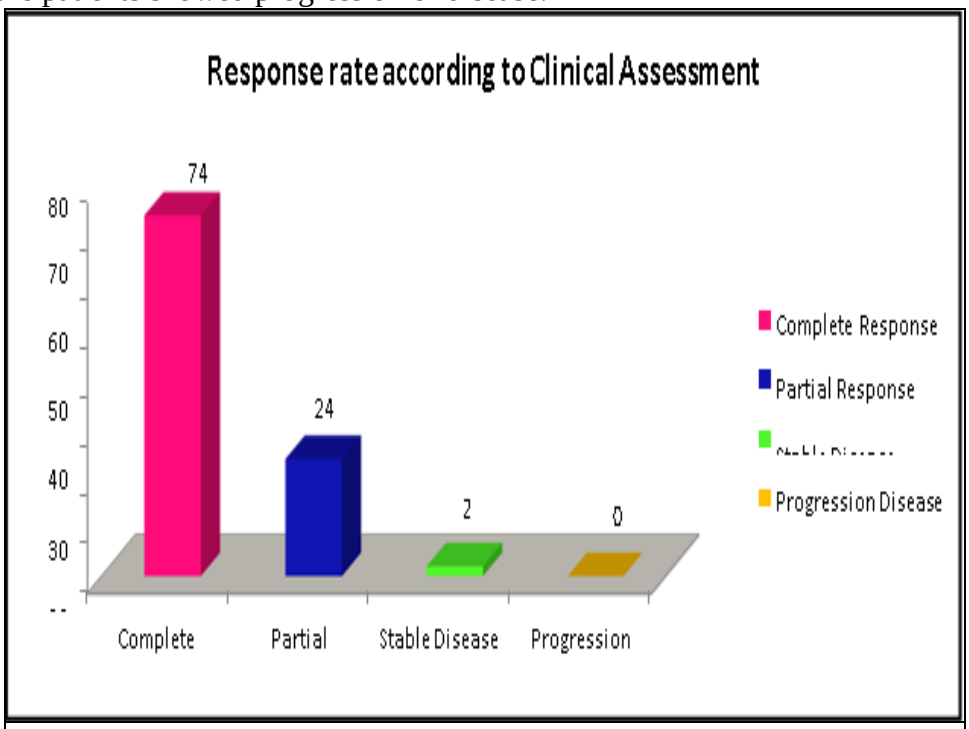

Figure 6: Response rate according to Clinical Assessment

Correlation of response rate was evaluated according to clinical and MRI assessment by Kaplan-Meir Survival Curve and it showed there was a positive correlation (p value = 0.15).

Discussion

Cervical cancer is third most common malignancies of the genital tract in women. With the implementation of cervical screening programs, such as the Pap test, and HPV DNA test, the incidence of cervical cancer in developed countries has decreased; however, it remains the third most common cancer in developing countries.[1] Persistent, recurrent, and metastatic

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cervical cancers have a poor prognosis, so cervical cancer is still a major cause of morbidity and mortality for women.

Accurate staging of patients with cervical cancer is crucial for appropriate treatment planning. The use of magnetic resonance imaging (MRI) for the evaluation of cervical cancer before and after treatment is well established but there are some important and difficult issues that must be addressed. Some of them are the evaluation of tumor response to therapy and the distinction between post radiation changes and viable tumor.

The differential between residual tumor and radiation changes cannot be done with conventional magnetic resonance images especially in the first 3 months after therapy. So, use of DWI and ADC is encouraged to detect early response to chemo-radiation. We know that MRI may be superior to computed tomography (CT) for residual tumor detection because of its high contrast resolution. The residual disease has a high signal intensity on T2-weighted images, similar to the corresponding primary tumor with early contrast uptake on DCE sequence, bright and dark areas on DWl and ADC maps. Therefore, MRI is considered the method of choice for follow-up after surgery or radiation treatment recommended by the FIGO guidelines because of its usefulness in the detection of local disease recurrence. However, physician experience with radiological post-treatment changes is essential to prevent misinterpretations. For these reasons, imaging techniques, especially magnetic resonance imaging, are widely used as a complement to the pelvic exam.

Hence the present study was aimed to evaluate the use of pre- and post- chemoradiotherapy MRI for advanced cervical cancer for assessing alteration of tumor volume, lymph nodal assessment and metastasis status in accurate way.

Regarding size of the tumor at diagnosis we observed that the mean size at admission was 5.64cm while after chemo radiation the mean size of tumor was 1.3cm with a mean reduction of 4.34cm.

Regarding nodal involvement we found 40 patients (80%) had either clinically or pathologically confirmed lymph node metastasis out of them 21 (42%) patients had pelvic nodes while 19 (38%) patients had paraaortic nodes.

Nodal involvement of the study by Aravindh SA et al revealed the involvement of the loco regional lymph nodes were evaluated in MRI and is reported as the farthest lymph node involved as seen in MR. 40 % patients were found to have no loco regional lymph node involvement.15.6 % patients had involvement up to the Para cervical lymph nodes only. Internal iliac was seen involved in 12.5 %, external iliac in 25% and common iliac in 6.3 % of patients.[2]

As per the FIGO staging we found the most common stage among the study participants was stage IIB (26%) followed by stage IIIB (18%) and IIIA and IIA which was 18%. Stage IIA1 involves 12% patients while stage IB2 and IVA involved 4% and 2% patients respectively.

Kumari et al in their study found according to FIGO staging of carcinoma cervix 7.1% patients were in stage I A, 40.5% in stage I B, 21.4% in stage II A, 16.7% in stage II B, 4.8% in stage III, and 9.5% in stage IV.[3]

MRI evaluation was done after FIGO staging and we observed change in the FIGO stage after this evaluation. After combination of MRI, 35 (70%) cases remained unchanged, 12 (24%) cases were upstaged, while 3 (6%) cases were down staged. In this study we evaluated the agreement between clinical stage (FIGO Classification) and MRI by using Kaplan-Meir Survival Curve. While observing it showed significant agreement between these two (p value = <0.0001).

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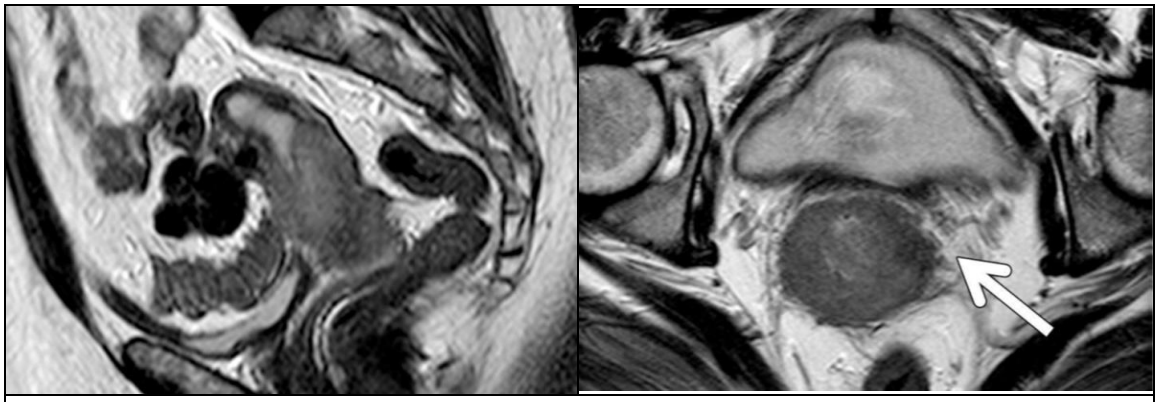

Image 1- Pre-Chemo & Radio Therapy Irradiated Patient with Cervical Cancer

Sagittal (a) and axial (b) T2-weighted fast spin- echo MR images show a stage IIB primary cervical tumor with parametrial invasion (arrow in b).

Zhang et al in their study reported after combination of MRI, 607 (59.7%) cases remained unchanged, 175 (17.2%) cases were upstaged, while 234 (23.0%) cases were down staged.[4]

We evaluated the response rate among the study participants by MRI. Our study revealed majority of the patients (56%) showed complete response, 40% (20) patients showed partial response and 4% (2) patients had stable disease. None of the patients showed progression of disease. According to clinical response assessment majority of the patients i.e., 37 (74%) showed complete response, 24% (12) patients showed partial response and 2% (1) patient had stable disease. None of the patients showed progression of disease.

Correlation of response rate was evaluated by Kaplan-Meir Survival Curve and it showed there was a positive correlation but this was not statistically significant (p value = 0.15).

IzaskunValduvieco et al in their study revealed the assessment of local response to treatment with physical exam and MRI correlated in 45 patients (60%) and was discordant in 26 patients (34.7%). According to the Spearman's rho test, the correlation of clinical–radiological assessment at 3 months was considered good ($r= 0.658$, $p < 0.0001$).[5]

Image 2 - Post Chemo & Radio Therapy Irradiated Same Patient with Cervical Cancer

Sagittal ***(c)*** *and axial* ***(d)*** *T2-weighted MR images obtained 12 months after the start of chemoradiotherapy show that the cervix is contracted. There is reconstitution of the low signal intensity of the stroma (arrow), a finding consistent with complete response to treatment. Note the fatty replacement of the sacral bone marrow after radiation therapy.*

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MRI is accurate for evolution of tumor size usually with 0.5 cms of the surgical size in 90% cases. An important pitfall of MRI staging is over estimation of parametrial invasion on T2 weighted images in large tumors with accuracy of 70% compared with small one's accuracy of 96% due to stromal edema caused by tumor compression or inflammation. This may lead to higher rate of false positive assessment of parametrical invasion in patients with large tumors, which must be considered when making the treatment decisions in their patients.

Accurate evaluation of local tumor response is essential to determine the probability of disease control in locally advanced cervical cancer. The lack of local control usually precedes the development of widespread disease.

The incorporation of MRI in a routine practice has provided a more precise evaluation of cervical tumors in terms of volume, localization, presence of parametrial and/or uterosacral infiltration and regional lymph node involvement. To accurately localize relapse, clinical examination may not be enough and there are no established MRI parameters for the same purpose.

MRI (before, during and after treatment) represents an invaluable tool because it allows differentiation of healthy tissue, tumor and post-irradiation fibrosis.

Ma et al. observed the signal intensity changes through the implementation of MRI- T2 before treatment and at week 4 (a half of treatment). These authors concluded that persistent high signal intensities in the tumor at mid treatment predicted a high risk for treatment failure, while a large reduction in signal intensity predicted a favorable outcome. These authors did not perform an evaluation at the end of treatment.

As pointed out by Vincens et al, MRI assessment of residual post-ChT/RT disease continues to be difficult and the risk of false positives is high. These authors reported a false positive rate of up to 50%.[6]

Rizzo et al reviewed the post-irradiation MRI in a series of 17 patients and concluded that at 3 months conventional MRI inadequately differentiates the post- irradiation changes of the residual tumor. They concluded that Diffusion Weighted Magnetic Resonance (DWMR) should be considered as an additional tool in the follow-up of non-surgical cases.[7] Levy et al reported a similar conclusion.[8]

Saida et al studied a series of 46 cases measuring the volume of the areas of high signal intensity in T2 immediately after finishing the treatment. They concluded that local control depends more on the diminishment of volume registered than the initial volume. As in other trials, no mention was made of the clinical–radiological correlation.[9]

In a series of 14 patients Zhang et al also studied the value of DWMR in the immediate evaluation of radiological response without assessing the grade of reliability on posterior outcome.[10]

Much more recently, the criteria of the American College of Radiology insisted on MRI and PET scan as the most effective method for post-CT–RT follow-up of locally advanced cervical cancers.[11]

Conclusion

At the end of the study, we come to the conclusion that:

Cervical cancer is becoming a subject of concern in medical science as it is a serious health problem in developing countries. Carcinoma cervix is primarily staged clinically as per FIGO guideline with minimal permissible usage of diagnostic modalities, even though it has several pitfalls.

As we consider the importance of tumor size measurement, we must take into account that, although a necessary step in the evaluation of patients with cervical cancer, physical examination is not a very accurate assessment of tumor size.

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In conclusion it can be said that as MRIs more accurate in determining tumor location, tumor size, depth of stromal invasion, extension into lower uterine segment and early response assessment so it can modify treatment options and may provide clinically important prognostic information not available from current FIGO staging.

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