

Efficacy and Diagnostic Value of MRI in Assessment of Cervical Stroma Invasion in Cervical Cancer

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Abstract

Objective: Studies have shown that globally, cervical cancer is the third most occurring malignancy in females. Precise diagnosis is imperative for the accurate and optimal treatment of the disease. The objective of this review paper is to analyze the efficacy and diagnostic properties of magnetic resonance imaging (MRI) in the assessment of cervical stroma invasion in cervical cancer and identifying various staging techniques.

Materials and Methods: 40 females were added in the study with untreated uterine cervical malignancy. Their cases were pathologically supported. Most of these female patients were between 38 and 64 years of age and the average age of these patients was 40 years. These patients were subjected to MRI for assessment of their disease stages and preoperative staging methods.

Results: It was observed that metastasized lymph nodes showed 49% sensitivity to MRI and 88% specificity, however, in the detection of parametrial infiltration, MRI showed 99% sensitivity and 84% specificity. Similar fashion was observed in the detection of vaginal

infiltration. In case of tumor size evaluation, significant error occurred, but in the rectum, stroma and urinary bladder, tumor extension was detected by MRI with 99% specificity and sensitivity. It has been found that MRI is efficient in spotlighting endometrial involvement in myometrial cancer detection, but, primary cervical cancer detection has restricted accuracy specifically when it comes to parametrial and lymph node invasion. MRI played significant role in staging of cervical carcinoma in IB & IVA along with IIA & IIB carcinoma stages. This was observed according to the histopathologic staging.

Conclusion: MRI is a significant non-invasive method for diagnosing uterine cervical malignancy. However, it is crucial in specifying accurately the finest treatment planning.

Keywords: MRI, cervical cancer, diagnosis, staging, stroma invasion.

Introduction

In the under developed and developing countries, cervical cancer is the third most common cancer in females. This high occurrence ratio is owing to the fact that routinely

screening tests are very less performed. It is quite imperative to accurately diagnose the stage of disease on the basis of which optimal treatment strategy is developed.^{1,2}

FIGO, Federation of Gynecology and Obstetrics, is an international organization that has provided guidelines for cervical cancer staging procedure. This includes proper inspection, palpation, endocervical curettage, hysteroscopy, cyst observation, urinary observation, proctoscopy, ileostomy, and radiographic assessment of skeleton and lungs of the patient. However, error is always present in every system, so as it is in FIGO staging system with 23 to 40% rate.^{3,4}

In the case of patients with cervical malignancies, MRI is the most commonly used pre-operative evaluation method. Assessment of prognostic factors like lesion size, stroma invasion and metastatic indulgence, are carried out by MRI. Thence, MRI specifies the use of different operative methods and procedures like cystoscopy and hysteroscopy. It is also useful in the process of cervical cancer staging in its early as well as in advanced level. Study of previously published papers in the past years have revealed that MRI gained immense importance for cervical cancer staging and its efficacy in detection of cervical stroma invasion, however, it can not be still accepted as 100% accurate as an engraved standard.

This review paper focuses on spotlighting the efficacy and diagnostic properties of MRI in evaluation of cervical stroma invasion in cervical cancer and its staging system.⁵

Modus Operandi and Material

Patients: This review paper is based upon the study of 40 female patients who had pathologically proven cervical cancer which was untreated. The study was authorized as per the hospital guidelines defined by the ethical committee, and it was carried out during the term between

February 2016 to July 2017. Colposcopic biopsy was carried out in the patients for pretreatment histopathologic disease diagnosis. The patients who were under observation had ages between 38 to 64, and average age was 40 years. Routine checkup and staging procedure was carried out including chest radiography, pelvic examination, physical examination, sonography of lower entire abdominal region, urography and other similar clinical protocols. MRI was carried out in all patients for specifying preoperative staging. However, after carrying out MRI a few patients had to be excluded. The reason was the transfer of one patient from the hospital to another one, contraindication against MRI in one patient, and surgery right after 30 days of MRI in the third patient.

MRI Mechanism

The MRI was carried out with the help of phased-array coil and 1T MR Closed Imager. Patients were asked to stop eating and drinking 6 hours before the performance of MRI so that it will minimize movement in the intestine. Pulse sequences and multiple scan plans were assessed. Moreover, a committee of radiologists was called on to study the MRI images. Those radiologists were kept unaware about the clinical results and pathological elaborations to prevent any issues in the final results. A consensus of the committee threw light upon multiple MRI characteristics regarding cervical malignancies and its efficacy in assessment of cervical stroma invasion. Diameters, margins (symmetrical and asymmetrical), origin, shape of tumor (elliptical, circular, lobular or oval), severity of its growth and pattern, heterogeneous or homogeneous internal appearances; the invasion of tumor cells into the surrounding tissues, vagina, parametrium and other adjacent organs, were all observed by the radiologists.

It was examined that origin of the tumor was from stroma or from the endocervical canal. On T1 weighted image (T1WI) the appearance of cervical tumor was insointense and it had a mass with strong signal intensity encapsulated by the cervical stroma which had less signal intensity, which appeared on T2WI, T2 weighted image. This imaging process is the most efficient one in identification of tumors; for instance if there is stromal invasion in cervical cancer then a ring of strong intensity signal generating tumor encapsulates the low signal intensity producing mass. Moreover, when the stromal invasion reaches to the apex then the tumor covers the entire region along with the natural low signal intensity mass of the vaginal wall.

When asymmetrical or nodular cancer cells disturb the stromal ring then the signal intensity rises and reach to the parametrium which points out towards the parametrial invasion of tumor. On the other hand, when T2WI depicted disturbance in the natural signal intensities of the hypointense walls of bladder and rectum, it was stated that this was the sign of bladder and rectal tumor invasion into the lumen. It was also observed that 1 cm or greater size of lymph nodes were a depiction of presence of pathological intranodal necrosis.

Histopathology Assessment

Lymphadenectomy and hysterectomy were applied to 20/40 patients with following division; modified and developed hysterectomy was carried out on 7 out of 20 patients, and radical hysterectomy on 13 out of 20 patients. Other 20 patients were subjected to colposcopic biopsy of vagina and laparoscopic staging. Sampling of lymph nodes also underwent deep study. 6 out of these 20 patients had former assessment and 14 underwent the latter assessment method. All gathered specimens were

subjected to careful evaluation by a pathologist without giving him the MRI results.

Statistical Evaluation

Comparative evaluation was made between MRI results and final pathological findings as the referencing standard. SPSS software was used for data entry and evaluation figures. Excel was used for graphing and McNemar's test was utilized for the comparison of PPV, sensitivity, NPV and specificity.

Results

This review paper encapsulates the study of 40 females who had untreated cervical cancer at primary stage, with average 40 years of age, in the Mayo Hospital. Staging was done as per the FIGO set guidelines. According to these guidelines, 6% patients fell under IB stage, 41% into IIA stage, 25% into stage IIB, and 27% were in stage IVA. Histopathologic diagnosis showed that 20% patients had adenocarcinoma, 73% had squamous cell carcinoma, and 7% had anaplastic cancer. Moreover, 87% patients had asymmetrical uterine bleeding issues.

Through MRI 40 cervical cancerous uterine images were obtained which assured that 12% out of them were endocervical while 87% were exophytic. Almost 92% of these were present at the posterior and anterior sides of cervical walls, and only 8% were present on the posterior side. Moreover, the depth of tumor cells was also revealed by the MRI into extra and intrauterine areas. The increase in size of lymph nodes were also diagnosed effectively by MRI in almost 34% patients.

When it comes to the efficacy of MRI it showed variable results. For instance, lymph nodes that were metastasized depicted 88% specificity and 49% sensitivity to MRI, on the other hand, MRI depicted 99% sensitivity and 88% specificity about parametrial infiltration. Similar trend was observed in vaginal infiltration detection. However,

sensitivity and specificity of MRI was 99% in case of stroma invasion, urinary bladder observance and tumor extension, but tumor size diagnosis showed some errors. endometrial involvement was found in myometrial cancer detection by MRI but the accuracy was significantly restricted by primary cervical cancer diagnosis when lymph node invasion was involved. As per histopathologic staging sequence, similar results were gathered by MRI images. Here it played important role in staging of cervical cancer into IB, IIA, IIB, and IVA cancerous stages.

Discussion

Cancer of the cervical region is one of the leading cancer in females in the under-developed and developing countries. About 80% of newly tested women with cervical cancer are from the developing countries and most of them have advanced disease form.^{1,2}

Medical scholars named Zand, Stenstedt and Collettini from an International Institute of Health Department had elaborated the MRI impact upon staging of the uterine cervical cancer and its pre-operative management. They stated that MRI had proved so far as one of the most reliable modus operandi for treatment workup and cancer staging in cervical malignancies. It provides fine results and answers for local disease evaluation. They mentioned that MRI is suitable in tumor detection in pregnant and obese ladies along with pre-operative assessment specifically for tumors greater than 2cm.^{3,4,5}

In this paper, based upon the examination results, the most common type of cervical mass under observation was squamous cell carcinoma. It was 73% of all the studied malignancies in 40 patients. Surprisingly, this occurrence was similar to the results of Sahdev and Collentini who stated that almost 79 to 91% uterine cervical malignancies are of squamous cells.^{5,6}

Study of the patients showed that cancerous cells encapsulated both the anterior and posterior walls of the cervical region, they were of exophytic nature. Upon comparison of these results with the research paper of Okamoto, published in 2003, the stance was further consolidated that 73% of the carcinoma growth is at the squamo columnar junction which is found outside the os of external uterine in young females. In our study, sensitivity and specificity of MRI images were keenly observed and compared with histopathology results for authentication. MRI was found with 99% accurate results in diagnosis of urinary bladder, rectum and stroma invasion. In 2000, report was published by Morimura who put forward similar results about MRI accuracy in cervical stromal invasion diagnosis.^{6,7}

Vagina is usually divided into two portions, upper 2/3rd and lower 1/3rd for definite staging purpose. Invasion of the cancerous cells in these portions define the type of stage the patient is in. For instance, the most frequent place for extrauterine cancerous invasion is in the upper 2/3rd of vagina. The incidence rate of this occurrence is 42% almost similar to the report of Chen, published in 1984, who stated that the incidence ratio of overall cervical carcinoma of vaginal invasion was 34%. Stage is proceeded IIA to IIIA when invasion of the tumor reaches lower 2/3rd of the vagina.^{7,8}

In our study, MRI showed some errors in vaginal invasion diagnosis, but only in 3 patients put of 20. This was owing to the large exophytic tumor size, but pathological test detected no such vagina invasion. Such concerns were also put forward by Sheu, Nicolet and Zand, in 2001, 2000, and 2007, respectively, that MRI overestimate cancerous invasion in vagina due to the presence of exophytic tumors. Vagina's fornix is thin and stretched so

it is difficult to find that either it is intact or disturbed by the tumor.⁸

One of the imperative factors in pre-operative cervical cancer evaluation and its staging is the diagnosis of invasion of the parametrium. In the present time, MRI has 86% accuracy in parametrial invasion detection, and this result is consolidated by multiple previous studies.^{9,10}

Furthermore, when cervical tumor is encapsulated by hypointense fibrous stromal ring, then the T-2 weighted MR images with high resolution depict a large negative Predictive Value (NPV). This NPV is generally considered as a diagnostic sign for the absence of the parametrial invasion. In our study, MRI showed false positive results about parametrial invasion only in patients who had big exophytic tumor. Histopathology results revealed that this large tumor had full thickness and complete stromal intrusion with edema but no parametrial indulgence.^{11,12}

Research of Kinkle in 2010 and Scheidler in 1998 elaborated that T2 weighted imaging proved more accurate in parametrial invasion diagnosis in comparison to T1 enhanced material weighted images. When it came to the rectum and bladder invasion diagnosis, it was observed on only 9 patients, it came up equal to the researched report of Rockall (2006), where he mentioned that such rectum and bladder invasion is very rare in case of cervical cancer. This rarity is owing to the Douglas pouch that separates the rectum and posterior fornix. This separation makes direct cancer invasion quite rare and uncommon.^{13,14}

Staging of cervical cancer is not affected by the metastasis of lymph nodes as per the FIGO criteria. Nevertheless, the treatment of cervical cancer is modified owing to its presence. When paraaortic node is involved then mortality rate rises, thus nodal metastasis in each stage of cancer

depicts poor prognosis. Tumor in stage IIIB, present to pelvic side wall, is considered equal in damage to the presence of pelvic lymph node metastases. Moreover, paraaortic indulgence is considered to be equal to stage IVB of extrapelvic tumor spread. In our patients, no paraaortic node involvement was found, and pelvic lymph node indulgence was diagnosed in only 11 patients. Size for prediction of metastatic lymph node was taken as a short axis diameter of 10mm. This size for comparison was as per the widely accepted criteria verified in Choi's paper (2006).¹⁵

Tumor size, stage and nodal involvement are considered as the most imperative factors in cervical cancer. Other factors include tumor grade, depth of indulgence, and lymphatic vascular involvement. In this study, staging of cervical cancer by MRI ranged between IB to IVA in consolidation with the Zand's study. The anomaly enhancement in axial scan were considered as the detection of stage IB. Clinically, this stage has no vaginal and parametrium invasion but involves the cervix tumor invasion. When the tumor is visible it indicates the presence of stage IB or greater, and T2WI detects the 5mm or higher stromal invasion.

As per FIGO standard, histopathologic system of staging cervical cancer provides comparable data for MRI staging procedure. However, in our study, exaggerated staging was observed by MRI due to wrong estimation of upper 2/3rd vaginal indulgence. These errors in staging arise due to the struggle in differentiating tumor cells from the nearby tissue edema, especially when the tumor size is large.¹⁵

Conclusion

MRI is used for pre-operative assessment and identification of the cancer stages in patients suspected of having uterine cervical cancer. It not only diagnose the

tumor but also aids in defining its size, invasion ratio, areas affected, effective staging, damage ratio, characteristics of tumor and abdominal as well as pelvic lymphadenopathy. MRI do shows some erros, but these errors are specifically confined to only a limited number of cases where the tumor size is too large.

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