Vol. 4 No. 1 (2025)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

DIAGNOSTIC ACCURACY OF DIFFUSION-WEIGHTED MEGNATIC RESONANCE IMAGING IN DETECTING CERVICAL CANCER TAKING HISTOPATHOLOGY AS GOLD STANDARD

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Keywords: Cervical Cancer, Diffusion-Weighted Imaging, Magnetic Resonance Imaging, Histopathology, Diagnostic Accuracy, Apparent Diffusion Coefficient

Received on 10 Jan 2025
Accepted on 25 Mar 2025
Published on 31 Mar 2025

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Abstract

Background: Cervical cancer is still a big public health problem in many parts of the world, especially in low and middle income countries. Prompt and correct diagnosis is crucial to prompt treatment and better patient outcomes. Diffusion-weighted magnetic resonance imaging (DWI-MRI) is a new non-invasive imaging method which has proved to be a promising approach in the diagnosis of cervical malignancies. **Objective**: To determine the diagnostic accuracy of MRI DWI in detecting cervical cancer taking histopathology as gold standard. **Method:** This descriptive cross-sectional study was carried out in Department of Diagnostics Radiology, Jinnah Hospital, Lahore, during January 2024 to September 2024. A non-probability consecutive sampling method was used to enroll a total of 100 women in the age range 25-65 years with suspected cervical cancer. DWI-MRI was performed on all the subjects, and ADC was measured. Histopathological examination of cervical biopsy specimens was used as the reference standard. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and overall diagnostic accuracy of DWI-MRI were computed. **Results:** Cervical cancer was confirmed by histopathology in 24% of the patients. The sensitivity, specificity, PPV, NPV and overall diagnostic accuracy of DWI-MRI were 87.5%, 85.5%, 65.6%, 95.6% and 86.0% respectively. The age of the participants was 47.3±9.8 years. **Conclusion:** The sensitivity, specificity, and diagnostic accuracy of DWI-MRI for detecting cervical cancer were high. It is an important non-invasive imaging modality in the evaluation of malignancy in the cervical region as well as in the work up of a suspected malignancy in the neck.

INTRODUCTION

In 2020, an estimated 604,000 new cases of cervical cancer and 342,000 deaths were reported globally; cervical cancer is the fourth most common cancer in women worldwide. The great majority of these cases and deaths (around 90%) take place in low and middle income countries where there are huge disparities in access to screening, vaccination and healthcare services [1]. The burden of cervical cancer is growing in Pakistan over the years. The prevalence of cervical cancer among Pakistani women increased from 9 per 100,000 women in 2002 to 19.5 per 100,000 women in 2008. Every day, it is estimated that almost 20 women are diagnosed with cervical cancer in Pakistan and the country ranks among the countries with the highest mortality rate for women from cervical

cancer [2]. World Health Organization (WHO) estimates that by 2030, cervical cancer deaths will surpass half a million a year, with over 98% of these cases taking place in developing countries [3].

High risk human papillomavirus (HPV) is the most important etiologic agent of cervical cancer. HPV-16 and HPV-18 are the most oncogenic and are responsible for over 50% and 10% of cervical cancer cases, respectively [4]. Patients often complain of abnormal vaginal bleeding such as postcoital bleeding, heavy periods and/or prolonged vaginal discharge. Later advanced disease may present with pain in the pelvis, in the lower back, urinary symptoms, and/or hematuria, hematochezia or a fistula formation caused by invasion of surrounding organs [5].

The first step in the clinical evaluation is the detailed inspection of the pelvis. On speculum exam some patients may have a visible cervical lesion, while others may have a normal appearing cervix. Another way to find cervical cancer is to have a routine screening with an abnormal Papanicolaou (Pap) smear. The colposcopy is the most accurate diagnostic test in women with abnormal findings on the cervical exam, or abnormal cervical cytology results [6]. The gold standard for diagnosis is still histopathological examination of cervical biopsy specimens. Squamous cell and adenocarcinoma and adenosquamous carcinomas are present in about 70–85% of cases, and are also the minor lesions in most of the remaining cases [7].

Cervical cancers are mostly preventable, and can be prevented by good HPV vaccination programs and regular cervical screening. Such prevention measures have greatly lowered the incidence and mortality of cervical cancer in countries that have established screening programs [8]. However, imaging has a significant role in determining the extent of disease, disease stage, in treatment planning, and in determining response to treatment. Cone biopsy and endocervical curettage (ECC) may be indicated for non-visible lesions, while clinical examination and cervical biopsy is sufficient for visible lesions. Imaging techniques like ultrasound, transvaginal ultrasound, magnetic resonance imaging (MRI) and computed tomography (CT) can give important information about the extent of the tumour in the area and the spread of tumour to the distance [9].

Diffusion-weighted imaging (DWI) is a promising functional MRI tool to assess the movement of water molecules in tissues, among the available imaging techniques. DWI quantitatively assesses by apparent diffusion coefficient (ADC) values, depending on tissue cellularity and nuclear-to-cytoplasmic ratio. ADC values for malignant lesions are usually lower and the diffusion is usually restricted, compared to benign lesions and normal tissue [10]. The usefulness of DWI-MRI in the detection and characterization of the cervical cancer has already been shown from previous studies. An ADC value less than 0.945×10^{-3} mm^2/s was strong evidence of malignancy, according to Abd Elsalam et al. [11]. In addition, Shen et al. found that DW-MRI had sensitivity and specificity values of 86% and 84%, respectively, for diagnosing malignancy of the cervical region [12]. Song et al. found that the prevalence of cervical cancer was 23.5% among women who had been assessed for suspected cancer [13].

DWI-MRI could be a useful non-radiative technique for the diagnosis and preoperative evaluation of cervical cancer. Hence, this study is designed to find out the diagnostic efficacy of diffusion weighted MRI compared to histopathology in cervical cancer diagnosis. The evaluation of its diagnostic efficiency can help to support its frequent use in routine clinical practice, aid in early detection of the disease, guide treatment planning and eventually decrease the morbidity and mortality from cervical cancer.

OBJECTIVE

To determine the diagnostic accuracy of MRI DWI in detecting cervical cancer taking histopathology as gold standard.

METHODOLOGY

This descriptive cross sectional study was carried out in the Department of Diagnostic Radiology, Jinnah Hospital, Lahore, during January 2024 to September 2024. A non-probability consecutive sampling method was used for the selection of 100 women aged 25–65 years who were suspected to have cervical cancer. Patients had detailed history taking, clinical examination, laboratory tests and DWI-MRI examination performed in a 1.5 Tesla MRI scanner. ADC measurements were performed by placing the regions of interest in the solid components of cervical lesions. The gold standard was the histopathological examination of cervical biopsy specimens. The clinical and histopathological results were not provided to the radiologists who made the interpretation of the MR scans. The sensitivity, specificity, positive predictive value, negative predictive value and overall accuracy were calculated.

INCLUSION CRITERIA

Patients who met the criteria of suspected cervical cancer as per the operational definition of suspected cervical cancer, i.e. those with symptoms suggestive of cervical cancer for more than 1 month, and suspected on clinical examination and/or ultrasonographic examination and were referred from the Gynecology Out Patient Department to the Department of Radiology, Jinnah Hospital Lahore, were included.

EXCLUSION CRITERIA

Patients who had contraindications to MRI (metallic implants, pacemakers, aneurysmal clips, prosthetic valves, severe renal impairment (GFR <30 mL/min), severe claustrophobia, or known gadolinium-based contrast agent allergy) were excluded.

DATA COLLECTION PROCEDURE

Eligible patients who satisfied the inclusion criteria were recruited following approval from the IRB.Following approval by IRB (Institutional Ethical Review Committee), eligible patients who met the inclusion criteria were recruited. A structured proforma was used to record the demographic data, clinical history, duration of symptoms, BMI and menopausal status. The MRI examinations were performed in all patients with standardized sequences and sequences: T1-weighted, T2-weighted, diffusion-weighted, ADC mapping and post-contrast sequences. ADC measurements were acquired from solid areas of lesions, excluding areas of necrosis and cyst. Pictures from MRI scans were subjected to independent evaluation by expert radiologists who did not know the histopathological findings. Thereafter, cervical biopsy samples were taken and examined by experienced pathologists. Histopathological findings were used as the reference standard. All gathered information was documented and kept confidentially during the study.

DATA ANALYSIS

Data were entered and analyzed using SPSS version 26.0. The quantitative variables such as age, body mass index and duration of symptoms were expressed as mean ± standard deviation. Qualitative variables like menopausal status, DWI-MRI findings and histopathological diagnosis were presented as frequencies and percentages. A 2×2 contingency table was set up to compare DWI-MRI results and the histopathologic results. Sensitivity, specificity, positive predictive value, negative predictive value and overall diagnostic accuracy were computed with 95% confidence intervals. Possible effect modifiers included: age, body mass index, duration of symptoms and menopausal status. A p-value of <0.05 was deemed as statistical significance.

RESULTS

To investigate the diagnostic value of diffusion-weighted magnetic resonance imaging (DWI-MRI) in diagnosing cervical cancer, 100 women were included in this study by the institution of histopathology as a gold standard. The mean age of the participants was 47.3 ± 9.8 years, and the mean length of symptoms was 4.7 ± 2.3 months. Of the study population, 58 (58.0%) were post and 42 (42.0%) were premenopausal women.

Baseline Characteristics

Parameter	Total (n = 100)
Mean Age (years)	47.3 ± 9.8
Mean Duration of Symptoms (months)	4.7 ± 2.3
Premenopausal	42 (42.0%)
Postmenopausal	58 (58.0%)

Demographic and clinical features of the patients in this study were typical of those women with clinically suspected cervical malignancy.

Detection of Cervical Cancer

Diagnostic Method	Positive	Negative
DWI-MRI	32 (32.0%)	68 (68.0%)

Histopathology	24 (24.0%)	76 (76.0%)

The histological diagnosis confirmed cervical cancer in 24 (24.0%) patients, and DWI-MRI in 32 (32.0%) patients.

Diagnostic Performance of DWI-MRI

Histopathology	DWI-MRI Positive	DWI-MRI Negative	Total
Positive	21 (TP)	3 (FN)	24
Negative	11 (FP)	65 (TN)	76
Total	32	68	100

There were 21 true positive, 65 true negative, 11 false positive, and 3 false negative cases when the DWI-MRI results were compared with the histopathological results.

Diagnostic Accuracy Indices

Parameter	Value (%)
Sensitivity	87.5
Specificity	85.5
Positive Predictive Value (PPV)	65.6
Negative Predictive Value (NPV)	95.6
Diagnostic Accuracy	86.0

The sensitivity and specificity of DWI-MRI for detecting cervical cancer were 87.5% and 85.5% respectively. The PPV was 65.6% and the NPV was 95.6%. The diagnostic accuracy of DWI-MRI was 86.0% overall.

Histopathological Types of Cervical Cancer

Histological Type	Frequency (n=24)	Percentage (%)
Squamous Cell Carcinoma	19	79.2
Adenocarcinoma	4	16.7
Other Histological Types	1	4.1

In these histopathologically proven cases, squamous cell carcinoma was the most frequent (79.2%), followed by adenocarcinoma (16.7%) and other histological variants (4.1%).

Stratification Analysis

DWI-MRI had a high sensitivity and specificity in all age groups, menopausal status, and symptom duration groups. There was no statistical difference for the stratification ($p > 0.05$). A greater percentage of cervical cancers was observed in postmenopausal women, however, compared to premenopausal women.

Interpretation

This study has shown that DWI-MRI is a promising imaging method for the diagnosis of cervical cancer. This technique had a very high sensitivity, specificity and overall accuracy in comparison to the histopathological findings. The high negative predictive value suggests that DWI-MRI can be an important tool to rule out malignancy in patients with suspected cervical lesions. The most common histological type found was squamous cell carcinoma. The study results indicate that DWI MRI could be a reliable non-invasive technique for the diagnostic assessment and surgical planning of cervical cancer.

DISCUSSION

Cervical cancer is still a major health problem, especially in low- and middle-income countries. Cervical cancer is a very common cancer in women and it occurs more frequently in developing countries where screening and preventive services are not maximized [1]. Some of the factors for late diagnosis and poor outcomes in Pakistan are lack of awareness, sociocultural issues and absence of organized screening programs [2,3].

Cervical cancer is the most commonly accepted etiological cause of the pathogenesis is high-risk human papillomavirus (HPV). A number of large epidemiological studies have shown that many of the cervical cancers that are seen in the world are caused by the oncogenic strains of the HPV infection which warrants vaccination and early detection programmes [4]. The current screening and management approaches rely on pathophysiological events that occur in the transition from HPV infection to invasive carcinoma, such as cellular dysplasia and stromal invasion.

Cytological screening (Pap smear) has proven to be effective but it is not widely used in low resource settings due to low uptake, problems with follow-up and infrastructure needs [2,6]. In this regard, cervical cancer has been increasingly reported as a global health emergency, where there are considerable disparities in prevention, diagnosis and treatment between high income and low-income countries [7]. The global public health experts still recommend screening uptake and its inclusion in the primary health service [8].

Magnetic resonance imaging (MRI) plays an important role in the management of cervical cancer in the local staging, an assessment of the extent of the tumour and in treatment planning. Conventional MRI has a high contrast resolution in soft tissues and allows for a precise diagnosis of tumour size, parametrial invasion and involvement of adjacent organs [9]. Diffusion weighted imaging (DWI) has extended the use potential of MRI, which now gives functional information regarding cellularity of tissues.

The DWI-MRI has also been shown to have high diagnostic accuracy for the detection of cervical malignancy, similar to previous studies in this study, which achieved a sensitivity and specificity of 80 % and 93 % respectively. According to Liu et al. [10] the most important consideration for the observed restricted diffusion in malignant cervical tumors is the decrease in ADC values in tumors due to the increase in cell density and reduction in the extracellular space. Their finding that quantitative ADC analysis can significantly aid in differentiating between benign and malignant cervical lesions [11] is extremely helpful.

Meta-analysis showed that DWI-MRI had good diagnostic performance in detecting the spread of disease and metastatic lymph nodes, which confirms the accuracy of DWI-MRI in the diagnosis of cervical cancer [13]. Additionally, MRI imaging is increasingly being accepted as an important component of the initial work up and is helpful in achieving a correct staging as well as identifying optimal treatment [12].

Imaging has come a long way from diagnosis and staging to the importance it plays in the advanced imaging technologies like MRI. Radiomics and other quantitative imaging features derived from DWI and other MRI modalities have been successfully applied in the prediction of clinical outcomes of cervical cancer including the response to treatment, recurrence, and survival [15-18]. Since 2020, some studies have demonstrated that the combination of clinical parameters and MRI features can improve the accuracy of the prognostic stratification and guide to individualized clinical treatment [15–18].

However, there are DWI-MRI limitations to be acknowledged. A restriction of diffusion can also be seen in non-cancerous situations like inflammation, fibrosis, other post biopsy changes etc. which can result in false positive with low positive predictive value [11]. Therefore, DWI findings should be correlated with conventional MRI sequences and clinical findings, which is why it is crucial.

Lastly, DWI-MRI could be used in a regular assessment of the cervical cancer, and help with improved diagnosis, staging and prognosis. If paired with a successful screening and prevention program, advanced imaging may play an important role in the clinical management of women diagnosed with cervical cancer to ensure optimal clinical management and outcome [1–18].

CONCLUSION

In the present study, we have shown that DW-MRI is a precise and trustworthy diagnostic tool for the diagnosis of cervical cancer. Overall, DWI-MRI showed high sensitivity and specificity and good diagnostic accuracy with the histopathological findings, thus proving the usefulness of this non-invasive imaging modality in the assessment of suspected cervical malignancy. The ADC can be quantified because of DWI, making the imaging modality more useful in the characterisation of the lesions and in differentiating malignant forms from benign ones in cervical abnormalities. Furthermore, the high NPV of DWI-MRI in this study showed that DWI-MRI is a useful tool to exclude

malignancy and can reduce unnecessary invasive diagnostic procedures. Due to its promising diagnostic and functional capabilities, DWI-MRI is a valuable tool in diagnosis and pre-operative assessment of cervical cancer. The findings reported here indicate that larger multicenter trials are warranted in the future to corroborate these findings and to give a standard ADC cut-off value for clinical practice.

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