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QUANTITATIVE APPARENT DIFFUSION COEFFICIENT VALUES IN PRE-OPERATIVE ASSESSMENT OF CERVICAL CANCER

Radiodiagnosis

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ABSTRACT

Introduction: Cervical cancer is a common gynaecological malignancy worldwide and is one of the leading causes of cancer related female deaths in developing countries. Quantitative evaluation of ADC values might be useful in differentiating benign from malignant cervical tissue and serves as a biomarker for post treatment assessment.

Aim: To differentiate normal cervical tissue from malignant lesions preoperatively, based on the apparent diffusion coefficient (ADC) values and whether there was any correlation between the mean ADC values at different stages of cervical cancer.

Materials and Methods: This is a prospective observational study. The present study included patients/subjects from south Indian population. Mean ADC values of 25 histopathologically proven cervical cancer patients (study group), and that of 20 patients (control group) with otherwise normal uterine cervix were compared. Mean ADC values of early (FIGO IB & IIA) and late stages (FIGO IIB, III & IVA) of cervical cancer were compared. Difference with a *p* value of less than 0.05 was considered statistically significant.

Results: The mean ADC values (0.900×10^{-3} mm^2/s) of cervical cancer patients (study group) were statistically lower than that of the control group (1.633×10^{-3} mm^2/s) ($p<0.05$). The mean ADC values in early stage (FIGO IB & IIA) cervical cancer (0.802×10^{-3} mm^2/s) were lower than the mean ADC values in late stage (FIGO IIB, III & IVA) disease (0.965×10^{-3} mm^2/s).

Conclusions: Quantitative ADC values provide added information in the diagnosis of cervical cancer as well as in the preoperative assessment of tumor stage which serves as a biomarker for post treatment evaluation.

KEYWORDS

Diffusion weighted imaging (DWI), apparent diffusion coefficient (ADC), Magnetic Resonance Imaging (MRI), cervical cancer.

INTRODUCTION:

Cervical cancer is the fourth most common cancer in women worldwide, typically seen in their fourth or fifth decades of life[1]. It has a high incidence in countries with low socioeconomic status and represents a significant public health problem. Various imaging modalities are used in the preoperative evaluation of cervical cancer. Magnetic Resonance Imaging (MRI) is an excellent modality for depicting invasive cervical cancer. MR Imaging (MRI) provides better soft tissue details, helps in the identification of stromal and parametrial invasion. The International Federation of Gynecology and Obstetrics (FIGO) staging system [2,3] is used for the staging of cervical cancer which helps in treatment planning. However, it is inadequate in the evaluation of prognostic factors such as tumor volume and nodal status.

Recent advances in MRI include diffusion-weighted imaging (DWI) commonly employed in detection and evaluation of acute stroke. Diffusion-weighted imaging (DWI) is a technique whose contrast is derived from the random motion of water molecules within the tissues. The image contrast is derived from the inherent difference in restriction of the movement of water molecules, so no exogenous contrast medium administration is required. Diffusion weighted magnetic resonance imaging has now been used in various abdominal and pelvic diseases. Apparent diffusion coefficient (ADC) maps are calculated from DWI images and it has been reported that quantitative evaluation of ADC values might be used for distinguishing benign from malignant tissue[4]. Lymph node assessment is not included in the FIGO staging system; however, it is an important prognostic factor in the choice of adjuvant radiation therapy in cervical cancer[5]. DWI improves the detection rate of lymph node involvement – accurate preoperative assessment of lymph node metastases is very important in patients with cervical cancer. Many studies showed decreased ADC value in malignant lymph nodes when compared to benign lymphadenopathy [6,7]. Few studies have also reported that there was an increase in ADC values after radiotherapy, which indicated that DWI might be used to monitor the response to therapy [8,9,10].

MATERIALS AND METHODS:

Prospective observational study conducted at JSS Medical College and Hospital from January 2018 – September 2018 for a period of 9months. The study included 25 histopathologically proven cervical cancer patients who were sent to the department of radiology for routine preoperative MR Imaging. All patients underwent diffusion-weighted imaging (DWI) in addition to routine non-contrast MR imaging. Post-operative cases and patients with general contraindication to MRI (pacemakers, cochlear implants, and claustrophobic patients) were excluded. Twenty patients who had routine MRI imaging of the pelvis for other benign pelvic pathologies were used as controls.

Routine pelvic MR images were obtained using a 3T Philips MRI scanner (Ingenia, Netherlands). Transverse, coronal and sagittal high resolution T2W fast spin-echo with TR/TE = 4468/100 ms, field of view = 240 x 240 mm, matrix size= 336 x 268, slice thickness 4 mm with slice gap of 0 mm. Transverse T1W fast spin-echo with TR/TE = 524/10 ms, field of view = 240 x 240 mm, matrix size= 256 x 204, slice thickness 4 mm with slice gap of 0 mm. STIR sequence is obtained in the axial plane using TR/TE = 2000/54 ms, field of view = 300 x 250 mm, matrix size= 176 x 144, slice thickness 4 mm with slice gap of 0 mm. Imaging parameters for DWI obtained through a multi-section single shot spin-echo type echo planar imaging (EPI) sequence in the transverse plane with sensitivity encoding (SENSE) technique. Parameters used are as follows: b values of 0, 800 and 1000 mm2/s; TR/TE = 6000/100 ms, field of view = 240 x 240 mm, matrix size= 177 x 112, slice thickness 5 mm with no gap.

Statistical analysis:

Statistical analysis was performed by using the software SPSS 22.0.

Descriptive statistics were used to describe clinical demographics using range, means and standard deviation (mean ± SD). Student's *t*-test was used to analyze comparisons and a difference with a *p* value of less than 0.05 was considered statistically significant.

RESULTS:

Twenty five cervical cancer patients with mean age of 53.7 years (ranging from 36-71 years). Seven patients were in premenopausal (28%) and eighteen patients in postmenopausal status (72%). The most common presenting complaint was bleeding per vagina which was seen in 26 patients (64%) followed by foul smelling discharge per vagina seen in 9 patients (36%). Histopathologically, 20 (80%) patients had squamous cell carcinoma and 5 (20%) patients had adenocarcinoma [Table 1]. Comparisons of mean ADC values between the various histopathological subtypes were excluded from the study since all the subtypes were not encompassed during the study period.

[Table 1]: Patient and tumor characteristics comparison

Patient characteristics	Study group (total n=25)
Mean age	53.7 years.
FIGO staging	
Early stage (FIGO IB & IIA)	10 (40%)
Late stage (FIGO IIB, III & IVA)	15 (60%)
Histopathology subtype	
Squamous cell carcinoma	20 (80%)
Adenocarcinoma	5 (20%)
Pelvic lymph nodes	
Positive	12 (48%)

Twenty patients who had undergone MR imaging for other benign pelvic pathologies, in whom there was no detectable cervical pathology, these patients were taken as controls. The mean age was 42.4 years (ranging from 29-55 years). 15 (75%) patients were premenopausal and 5(25%) patients were in post menopausal status. Most common benign pelvic pathology was uterine leiomyoma seen in 14 patients (70%) followed by benign ovarian pathologies seen in 5 patients (25%).

All the cases of cervical cancer showed restricted diffusion on DWI images. The mean ADC value of cervical cancer patients (study group) was $0.900 \pm 0.15 \times 10^{-3}$ mm^2/s, and that of the control group cervical tissue was $1.633 \pm 0.07 \times 10^{-3}$ mm^2/s as depicted in [Table/Fig-3].

[Table 2]: Comparison of ADC values of normal and carcinoma cervix with other recent studies.

Author (year)	Mean ADC values (x 10^{-3} mm^2/s)	
	Normal cervix	Ca cervix
Demirbas T et al., (2014) [14]	1.67 ± 0.17	0.96 ± 0.15
Abd elsalam SM et al.,(2020) [15]	1.56	0.82 ± 0.10

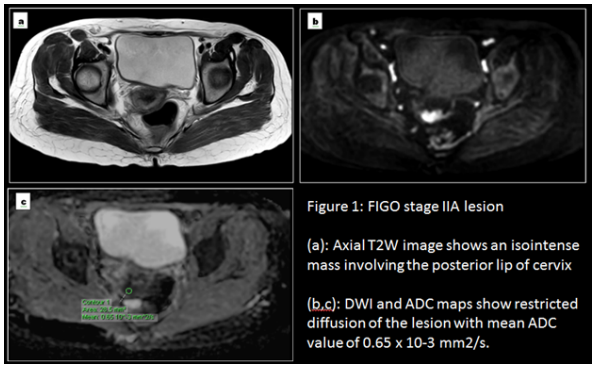
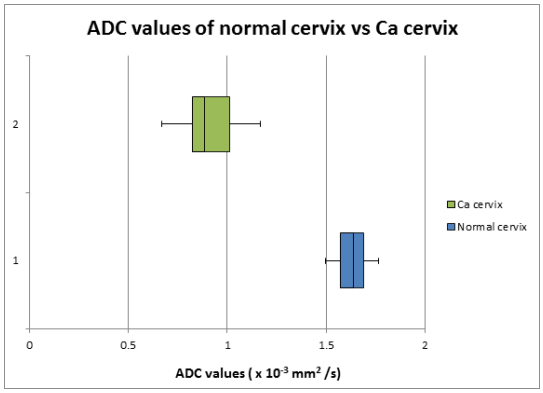


Figure 1: Cervical Carcinoma: FIGO stage IIA

The difference in the mean ADC value was statistically significant ($p < 0.05$). According to the FIGO classification, 10 patients (40%) were in the early stage (FIGO IB & IIA) and 15 (60%) patients in the late stage disease (FIGO IIB, III & IVA) on MR imaging [Table 1, Figure 1].

The mean ADC value in early stage of cervical cancer was found to be $0.802 \pm 0.11 \times 10^{-3}$ mm^2/s, and that of the late stage disease was $0.965 \pm 0.13 \times 10^{-3}$ mm^2/s as depicted in [Graph 1, Figure 2/3].



[Graph 1]: The mean ADC value of cervical cancer patients (study group) was 0.900 x 10^{-3} mm^2/s, and that of the control group cervical tissue was 1.633 x 10^{-3} mm^2/s ($p < 0.05$).

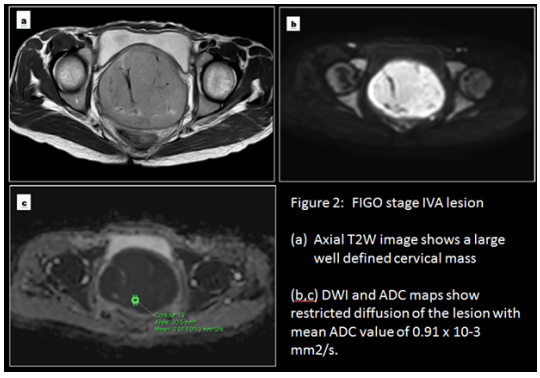


Figure 2: Cervical Carcinoma: FIGO stage IVA

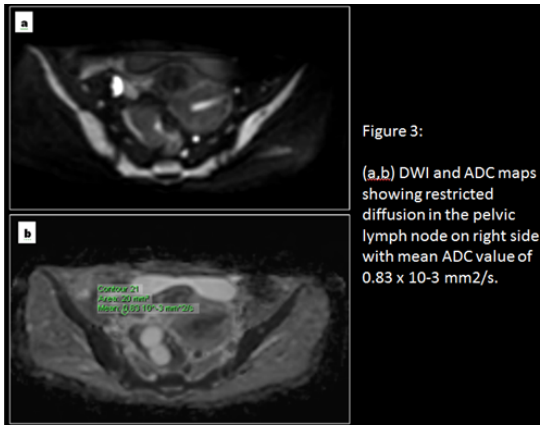


Figure 3: Cervical Carcinoma: Diffusion and ADC maps

The values in the early stages of cervical cancer were lower than the ones in the late stages of the disease and the difference was statistically significant ($p < 0.05$).

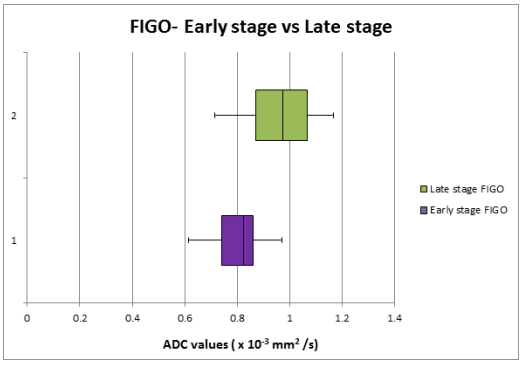
Lymph nodes which showed restricted diffusion were seen in 12 patients (48%). The mean ADC value of the lymph nodes which showed restricted diffusion was 0.89×10^{-3} mm^2/s.

DISCUSSION:

Among the various imaging modalities, Magnetic Resonance Imaging provides high soft-tissue resolution in the assessment of tumour volume, depth of cervical invasion and extent of loco-regional tumour spread in the staging of cervical cancer [11,12]. DWI has been recently used in the staging of cervical cancer and in detection of metastatic lymph nodes [13]. In this study, quantitative ADC values were evaluated for differentiating benign from malignant cervical tissue. In our study, all the cervical cancers showed diffusion restriction on DWI

and the ADC value of these lesions were calculated from the corresponding ADC maps. The ADC value of cervical cancer was less than that of the normal uterine cervix as shown in Table 1. Similar results were shown in previous studies as shown in Table 2.

The mean ADC values in early-stage cervical cancer (0.802 x 10^{-3} mm^2 /s) were significantly lower than the mean ADC values in the late stage (0.965 x 10^{-3} mm^2 /s) of the disease. The comparison of mean ADC values for early and late stage cervical cancer according to FIGO classification is given in Graph 2.



[Graph 2]: The mean ADC value in early stage of cervical cancer was found to be 0.802 x 10^{-3} mm^2 /s, and that of the late stage disease was 0.965 x 10^{-3} mm^2 /s ($p < 0.05$).

There was a statistically significant difference between early and late stage cervical cancer ($p < 0.05$). Similar results were shown in previous studies as depicted in Table 3.

[Table 3]: Comparison of ADC values of early and late stage cervical cancer with other recent studies.

Author (year)	Mean ADC values (x 10^{-3} mm^2/s)	
	Early stage(FIGO IB & IIA)	Late stage(FIGO IIB,III &IVA)
Hasan DI et al., (2015) [12]	0.83 ± 0.05	0.98 ± 0.06
Demirbas T et al., (2014) [14]	0.86 ± 0.05	0.98 ± 0.06

In the study group, the mean ADC values of the regional lymph nodes which showed restricted diffusion was 0.89 x 10^{-3} mm^2/s. Few studies have shown the increase in the mean ADC values of the cancer tissue and metastatic nodes during post treatment follow up [9,10]. Lymph node involvement is a significant prognostic factor in deciding the treatment plan. The 5 year survival rate for lymph node positive patients is 39–54%, as compared to 67–92% in patients without lymph nodal involvement [16].

No similar studies with larger sample size have been carried out previously; existing studies along with this study indicate that ADC values may provide additional data for the diagnosis of cervical cancer as well as for preoperative assessment of the tumor stage.

Limitation(s):
1. Relatively small sample size.
2. Post treatment follow up was not employed as a part of our study.

CONCLUSION:
The apparent diffusion coefficient (ADC) values calculated from diffusion weighted imaging (DWI) images provide added information in diagnosis of cervical cancer as well as in preoperative assessment of tumor stage. It serves as a biomarker for assessment of post treatment response following chemo-radiotherapy or surgery.

Conflict of interest:
The authors declare that there is no conflict of interest.

Financial Disclosure:
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