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Diffusion-weighted MRI as a Predictor of Outcome in Cervical Cancer Following Chemoradiation

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Abstract

Purpose—Diffusion weighted magnetic resonance imaging (DWI MRI) is emerging as a useful diagnostic and prognostic imaging technique in cervical cancer. We aimed to determine if apparent diffusion coefficient (ADC) value is predictive of survival following definitive chemoradiation for cervical cancer independent of established imaging and clinical prognostic factors.

Methods and Materials—Between 2011–2013, the pre-treatment MRIs for 69 patients treated with definitive chemoradiation for newly diagnosed cervical cancer were retrieved. Scans were acquired with a 1.5 T magnetic resonance scanner, including DWI sequences. Mean ADC value was measured within a region of interest in the primary cervical cancer on the baseline MRI. Baseline tumor maximum standardized uptake value (SUV) on the PET/CT was determined by the reading radiologist. Treatment included external beam radiation therapy to the pelvis followed by brachytherapy in 97%, and with concurrent weekly cisplatin in 99% of patients. Univariate and multivariate analyses were done to investigate the association of clinical and imaging variables with disease control and survival endpoints using a Cox proportional hazard test.

Results—Median follow-up was 16.7 months (range 3.1–44.2). The 1-year overall survival, locoregional recurrence-free survival, and disease-free survival (DFS) were 91%, 86% and 74%,

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Conflict of Interest: none

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respectively. The median ADC value was $0.941 \times 10^{-3} \text{ mm}^2/\text{s}$ (range $[0.256\text{--}1.508] \times 10^{-3} \text{ mm}^2/\text{s}$). The median SUV in the primary tumor was 15 (range 6.2–43.4). In multivariate analysis, higher ADC value (HR 0.36 [0.15–0.85], $p=0.02$), higher stage (HR 2.4 [1.1–5.5], $p=0.033$), and non-squamous histology (HR 0.23 [0.07–0.82], $p=0.024$) were independent predictors of DFS.

Conclusion—The mean ADC value of the primary tumor on pre-treatment MRI was the only imaging feature which was an independent predictor of DFS in cervical cancer patients treated with chemoradiation. Further validation will be needed to determine if ADC values may prove useful in identifying cervical patients at high risk of recurrence.

Introduction

Cervical cancer is the eleventh most common cancer and ninth most common cause of cancer related death in developed countries, with approximately 13,000 new cases and 4,100 cancer related deaths per year in the United States (1,2). In developing countries, cervical cancer is the second most common cancer and third most common cause of cancer death (2). Concurrent chemoradiation is the recommended treatment for patients with locally advanced disease, based on several randomized trials (3–7). Five year survival varies from approximately 75% in patients with FIGO stage IB2 disease to 22% in those with stage IVA disease (8). In patients treated with concurrent chemoradiation, approximately 30% experience disease recurrence (3–7). Besides stage, other clinical and pathologic factors such as histology, ethnicity, tumor size, tumor grade, lymph node status have been shown to be prognostic (9)

Functional magnetic resonance imaging (MRI) techniques such as diffusion weighted imaging (DWI) provide a metabolic and physiologic view of the tumor microenvironment (10). DWI is a noninvasive imaging technique that measures the mobility of water, providing information on architecture with a resolution of millimeters, and with a sensitivity to changes at the cellular level (11). It is quantified in the apparent diffusion coefficient (ADC). In general, malignant tumors have a lower ADC, reflecting the restricted motion of water molecules, which is thought to be due to higher cellularity and tissue disorganization in tumors (11). ^{18}F -FDG Positron emission tomography/computed tomography (PET/CT) is another functional imaging modality that is commonly used in the work up of cervical cancer, often quantified using the maximum standardized uptake value (SUV). Compared to traditional clinical and pathologic prognostic factors, these functional imaging techniques may better characterize individual tumor biology and serve as useful imaging biomarkers. We therefore investigated the utility of DWI MRI compared to other established imaging and clinical factors on predicting recurrence and survival in cervical cancer patients treated with definitive chemoradiation.

Methods and Materials

Patient Selection

Following institutional review board approval, our institution's tumor registry and radiation oncology databases were used to identify patients with cervical cancer who were treated with definitive chemoradiation between 2011 and 2013. Patients were included if they had

an MRI with DWI sequence performed at baseline, before the start of any treatment. In addition, all included patients had a PET/CT performed at baseline, and at follow-up after the completion of chemoradiation. All patients who received definitive chemoradiation, which included patients with stage IB1-IVB cancer, who met these requirements were included if they were treated with curative intent, as determined at the time of initial consultation. One patient with stage IVB disease was included who had an initial PET that was suspicious for distant metastasis, but still received definitive chemoradiation to her primary tumor and pelvic and paraortic lymph node basins after initial chemotherapy. No patients who received postoperative radiation were included. Sixty-nine patients who met these criteria were included in this retrospective analysis. Institutional and radiation oncology records were used to obtain data regarding patient, pathology, and imaging characteristics, radiation treatment plans, recurrences and survival.

Imaging Analysis

MRI was performed on a 1.5T GE whole body MRI system (Signa; GE Healthcare, Waukesha, Wisconsin). All the studies used body coil transmission and an 8-channel phased array pelvic RF coil for signal reception. Unenhanced axial T1 weighted images, sagittal and axial T2 weighted images, and post contrast axial T1 weighted images were obtained following administration of intravenous gadolinium injection. Vaginal gel was instilled in all patients prior to scanning. For the diffusion sequence three b values were used: 0, 50 and 800. 0–50 was the perfusion component of the diffusion, and 50–800 was the diffusion. EDWI was used and the ADC map was automatically generated from the scanner, and sent to the Advantage work station. The ADC maps were calculated using all three B values. Mean ADC value was recorded retrospectively by a single physician, who was blinded to outcome, from segmenting a region of interest (ROI) of the primary cervical tumor on the baseline MRI (Figure 1). ROI segmentation was performed using available T2-weighted images to assist in ROI selection; manual segmentation included the tumor extent as observed on matched T2 images, as well as reference to DWI acquisitions, avoiding any visible necrotic or cystic areas. The ROI measurements were documented. Three-dimensional segmentation of the primary tumor was performed based on T2 axial images in Velocity AI v.3.01 (Varian Medical Systems, Atlanta, GA), and tumor volume was extracted.

A PET/CT was obtained one hour after injection of approximately 15 mCi [555 MBq] radiolabeled FDG on an integrated PET/CT scanner (Discovery ST-8, GE Healthcare). The patients underwent fasting for 6 hours prior to the study. Blood glucose levels were measured and patients underwent imaging only if the baseline blood glucose level was <150 mg/dl (8.3 mmol/L). Baseline tumor maximum standardized uptake value (SUV) was determined on the PET/CT by the reading radiologist and that was documented from the MIM Vista workstation.

Treatment

All patients first received external beam pelvic radiation, with the final dose, treatment fields, technique, and use of a boost at the discretion of the treating radiation oncologist, based on factors such as nodal or parametrial/sidewall involvement. Radiation was given at 1.8 Gy per fraction to a total dose of 43.2 to 45 Gy, using a four-field 3D-conformal

technique and 15 or 18 MV photons in 55 (80%) patients, using a four-field pelvic field matched to an intensity modulated radiation therapy (IMRT) paraortic field in 10 (14%) patients, and using an IMRT plan alone in 4 (6%) patients. Within one week after completion of external beam radiation therapy, most patients received two pulsed-dose-rate intracavitary pulsed dose rate brachytherapy treatment using an after-loaded tandem and ovoid system, delivered 10–14 days apart. Each brachytherapy session lasted approximately 44–48 hours, with a goal total dose delivered of 85–90 Gy. Brachytherapy treatment planning was performed either using volume-based dosimetry, or point-based dosimetry. For volume-based treatment planning, the high-risk CTV was defined similarly to the GEC-ESTRO guidelines using a post-implant, same-day CT scan, and included the entire cervix, as well as any gross residual disease present at the time of brachytherapy, and any intrauterine or intravaginal extent of disease at diagnosis (12). For point-based dosimetric planning, the point A dose goal was 18–22 Gy per implant, and planned according to standard methods as described previously (13). Fifty (72%) patients received an external beam boost to areas of initial nodal or parametrial involvement, usually given in between brachytherapy treatments, and 30 of those patients received this boost using an IMRT technique (Table 1). Cisplatin was typically delivered weekly, at a dose of 40 mg/m² (maximum dose 70 mg), during external beam radiation therapy and at the time of the second brachytherapy treatment, as prescribed by the treating gynecologic oncologist.

Follow-up

After completion of chemoradiation, patients were typically followed with a PET/CT every 3–4 months for 2–3 years, then at 6 month intervals, and eventually yearly. Patients no longer followed at our institution were contacted annually to obtain information about survival, disease and treatment status.

Recurrence

Follow up PET/CTs were used to assess for recurrence, with any uptake above background activity (typically around 3) considered to be concerning for recurrence. All suspicions for recurrence were subsequently followed by biopsy for pathologic confirmation, unless there was unequivocal imaging evidence of widely metastatic disease. Central recurrence was defined as any recurrence in the original primary cervical tumor region. Nodal recurrence was defined as any recurrence within the pelvic region that was included in the external beam radiation fields. Locoregional recurrence included either central and/or nodal recurrence. Distant metastases were any recurrences outside the original radiation fields.

Statistical Analysis

Endpoints assessed included overall survival, central recurrence free survival, locoregional recurrence free survival, disease free survival, and distant metastasis free survival. All survival rates were calculated from the start date of radiation. For disease free survival, central recurrence, locoregional recurrence, distant metastases, and death were scored as events.

Data analysis was performed using Stata/MP 13.0 statistical software. Fisher's exact test assessed measures of association in frequency tables. The equality of group medians was

assessed with a nonparametric test for equality. The survival function was carried out using Kaplan-Meier estimates. The log rank test assessed the equality of the survivor function across groups. A p-value of 0.05 or less was considered to be statistically significant. Statistical tests were based on a two-sided significance level.

The Cox's proportional hazard model assessed the effect of factors of significance on the survival end points for univariate and multivariate analysis. The estimated hazard ratio is reported. Variables such as age, baseline SUV, baseline mean ADC, and MRI volume were analyzed both continuously as well as by categorizing above and below the median. Multivariate analysis was performed on all factors found to have a p-value of 0.25 or less on univariate analysis. Backwards elimination was performed with the least significant factor eliminated in a step-wise manner until the most significant variables were identified.

Results

Patient, Tumor, and Treatment Characteristics

Baseline patient, imaging, and treatment characteristics are listed in Table 1. Forty-eight (70%) patients had squamous cell carcinoma. The remaining twenty-one patients (30%) had adenocarcinoma (n=16), adenosquamous (n=2), clear cell (n=2), and small cell (n=1). Forty-eight (70%) patients had positive lymph nodes at diagnosis: 39 (57%) with pelvic lymph node involvement, and nine patients (13%) with paraortic lymph node involvement. The median maximum SUV of the primary tumor on baseline PET/CT was 15 (range 6.2 to 43.4). The median ADC of the primary tumor on baseline DWI MRI was $0.941 \times 10^{-3} \text{ mm}^2/\text{s}$ (range $0.256 - 1.508 \times 10^{-3} \text{ mm}^2/\text{s}$).

Sixty-seven (97%) patients received brachytherapy treatments after completion of external beam pelvic radiation therapy. One patient did not receive brachytherapy due to a fistula and instead received an external beam boost to the primary tumor using intensity modulated radiation therapy (IMRT) to a dose of 16 Gy in 8 fractions. Another patient's brachytherapy procedure was aborted due to technical difficulty, and instead was dispositioned to surgery. Concurrent weekly cisplatin was given in 68 (99%) patients. The remaining one patient did not receive concurrent cisplatin due to preexisting hearing loss.

Survival

At a median follow-up of 16.7 months (range 3.1–44.2 months), 24 (35%) patients had disease recurrence. Eight (12%) patients had a central recurrence, 11 (16%) patients had a locoregional recurrence, and 16 (23%) patients had a distant metastasis. Thirteen patients were alive with disease and 11 patients had died of their disease. The one-year and two-year overall survival rates were 91% (95% CI 81%–96%), and 81% (95% CI 66%–90%), respectively. The one-year and two-year locoregional recurrence free survival rates were 86% (95% CI 75%–93%) and 82% (95% CI 69%–90%), respectively. The one-year and two-year central recurrence free survival rates were both 88% (95% CI 77%–94%). The one-year and two-year disease free survival rates were 74% (95% CI 61%–83%) and 63% (95% CI 49%–75%), respectively.

Univariate Analysis

The 1-year and 2-year disease free survival rate were 63% (95% CI 45%–77%) and 51% (95% CI 31%–67%) for patients with a mean ADC $0.940 \times 10^{-3} \text{ mm}^2/\text{s}$, compared to 84% (95% CI 67%–93%) and 76% (95% CI 56%–88%) in those with a mean ADC $> 0.940 \times 10^{-3} \text{ mm}^2/\text{s}$ ($p=0.053$; Figure 2). In univariate analysis for disease free survival, histology and FIGO stage were significant factors, and ADC was borderline significant ($p=0.059$) (Table 2). There was no significant association found between age, tumor grade, dose to point A, nodal status, baseline tumor maximum SUV, and tumor volume and disease free survival.

There were no significant associations on univariate analysis found between these same factors and with overall survival, central recurrence free survival, or with locoregional recurrence free survival. There was improved distant metastasis free survival for patients with non-squamous histology (HR 0.12 [0.02–0.91], $p=0.041$) and those without lymph node involvement at diagnosis (HR 0.12 [0.02–0.95], $p=0.044$). In patients with a higher mean ADC value ($> 0.940 \times 10^{-3} \text{ mm}^2/\text{s}$) versus a lower one (ADC $0.940 \times 10^{-3} \text{ mm}^2/\text{s}$), the two-year overall survival rate was 89% (95% CI 67%–96%) versus 73% (95% CI 50%–87%), $p=0.291$, the two-year locoregional recurrence free survival rate was 86% (95% CI 66%–95%) versus 78% (95% CI 60%–89%), $p=0.260$, and the two-year central recurrence free survival rate was 94% (95% CI 78%–98%) versus 81% (95% CI 63%–91%), $p=0.124$ (Figure 2).

Multivariate Analysis

In multivariate analysis, mean ADC, FIGO stage, and histology were significantly associated with disease-free survival (Table 3). Patients with a higher stage (III or IV, compared to I or II), had a worse disease free survival (HR 2.4 [1.1–5.5], $p=0.033$). Patients with a higher mean ADC ($> 0.940 \times 10^{-3} \text{ mm}^2/\text{s}$, compared to $0.940 \times 10^{-3} \text{ mm}^2/\text{s}$), had an improved disease free survival (HR 0.36 [0.15–0.85], $p=0.02$). Patients with a non-squamous histology, compared to squamous, had an improved disease free survival (HR 0.23 [0.07–0.82], $p=0.024$).

In a multivariate model for distant metastasis free survival, non-squamous histology was significant (HR 0.12 [0.02–0.91], $p=0.041$). There were no multivariate models found for the other survival outcomes.

Discussion

Our results show that the mean ADC value of the primary tumor on pre-treatment MRI was a significant predictor of disease free survival in cervical cancer patients, independent of established clinical factors and SUV on FDG- PET. On multivariate analysis, only ADC, stage, and histology were significant predictors of disease free survival.

Diffusion weighted imaging is an MRI sequence that characterizes the Brownian motion of water molecules, which is reflected in the ADC measurement. Hypercellular tumors often have restricted diffusion compared to normal tissue, and low ADC values are thought to reflect more aggressive tumors and have been shown to confer a worse prognosis in other

cancer sites (14–16). DWI has been shown to be capable of distinguishing normal tissue from cervical cancer (17–19). In addition, it has been shown that poorly differentiated cervical tumors have a lower ADC than well or moderately differentiated ones (20,21).

Several studies have previously shown that the change in ADC over the course of chemoradiation for cervical cancer could be predictive of clinical or immediate response to treatment (22–26). However, there have only been a few studies with larger patient cohorts that have examined the utility of pretreatment ADC as a prognostic factor in longer term survival and recurrence outcomes in cervical cancer (27–30). Two studies demonstrated that lower pretreatment ADC was associated with worse disease free survival in early stage cervical cancer patients who were treated mostly with surgery (27,29). In another study examining 69 patients treated with definitive radiation or chemoradiation, lower pretreatment as well as lower posttreatment ADC were associated with worse disease free and overall survival rates, although on multivariate analysis, only posttreatment ADC was a significant predictor (30). In an analysis of 85 patients with locally advanced cervical cancer treated with definitive chemoradiation, Gladwish et al. found that a lower pretreatment 95% percentile ADC was associated with inferior disease free survival on multivariate analysis (31). However, those studies were limited in that they did not include pretreatment PET, or MRI-delineated tumor volume, both of which our study did examine as prognostic factors. We found pretreatment ADC to be a significant predictor of disease free survival on multivariate analysis, with the only other significant factors being stage and histology. Although mean ADC was not statistically significant on univariate analysis by log-rank test ($p=0.061$), it was significant by Wilcoxon test ($p=0.022$) (suggestive of a differential in early DFS, but not at later time points; Supplemental Figure 1), and significant on multivariate analysis. We also performed a post-hoc analysis and did not identify significant collinearity within our model. Therefore, we believe our finding of a lower ADC being associated with an inferior DFS on multivariate analysis as likely to represent a potential covariate of DFS, albeit given the limitations of the exploratory model we utilized and the necessary limitations of our sample size.

Functional imaging metrics, including SUV and ADC, have been reported to correlate with pathologic features, including tumor grade and histology as well as clinical outcomes. (19–21,32). The total metabolic tumor volume (MTV) and lesion glycolysis (TLG) have been associated with increased stage, size, and risk of lymph node involvement at diagnosis, as well as increased risk of relapse (33–36).” Higher SUV values have been reported to correlate with survival in some studies, while others have demonstrated no correlation of baseline SUV and disease recurrence. (35,37–40). In this series, we did not find any significant association with baseline tumor maximum SUV and survival. Volumetric quantification of SUV may be a more robust prognostic factor, which we did not assess in this study. In addition, we did not find that nodal status, a well-established prognostic factor, was associated with outcome in this study, which is likely due to the relatively small patient numbers in this study.

Although most cervical cancer cases occur in developing nations, where imaging is also less available, advanced technology such as MRI has been shown to play a major role in improving disease control outcomes (12). Our results support the use of DWI MRI in the

baseline evaluation of newly diagnosed cervical cancer patients. Most patients in the United States with locally advanced cervical cancer undergo diagnostic baseline MRIs for staging and evaluation of disease extent. The addition of DWI to conventional T1 and T2 sequences only minimally extends study time. Furthermore, our measurement of ADC on a two-dimensional region of interest in the primary tumor could be implemented easily in clinical practice without requiring significant extra time for analysis. In this manner, DWI could be a useful tool for identifying cervical cancer patients who have more aggressive tumors, and perhaps in the future be used to select patients for more aggressive treatment such as radiation dose escalation or adjuvant chemotherapy.

Although this study and others demonstrate promise for the prognostic value of ADC, the interpretation of the data has been complicated by the variability in ADC value cutoffs as well as the measures of ADC used. Given our limited patient size of 69, we decided to use the mean ADC of 940 as a cut off value for analysis. However, it would be valuable for future analyses with larger sample sizes to define more optimum ADC thresholds. Our study also has limitations, including its retrospective design and relatively limited patient size. In addition, only the mean ADC value from a single region of interest was used, and we did not analyze volumetric ADC values or other percentile measures. Also, we did not have mid or post treatment DWI MRI scans available, and therefore could not report on the significance of the change in ADC or of post-treatment ADC.

Like all imaging studies of tumor volumes, our data is subject to the inherent variability in manual image segmentation. To minimize these effects, we selected ROIs in the center of the tumor and used mean values, in order to derive a representative region. We found that a small percentage, 6%, of cases had regions of necrosis, which were excluded in the ROIs, so we do not suspect that inclusion of necrotic regions impacted our analysis. We avoided incorporation of non-tumor regions (e.g. intra-vaginal gel used in simulation) in the ROI. We recognize that there are inconsistencies in the process of sub-segmentation which may potentially skew distributional measures of ADC. However, use of mean ADC as a summary measure should mute the effects of these potential confounders and provide the most summative information given expected tumor heterogeneity. Similarly, both DWI and summary SUV (i.e SUV max) measures failed to account for potentially informative, but more methodologically complex measures of tumor biology and heterogeneity, and are a locus of future efforts (e.g. FDG-PET SUV- or MRI ADC-based radiomics profiling). Additionally, the utilized method is fairly reproducible due to its simplicity, as analysis did not require complex time-consuming calculations or extended segmentation efforts, but is potentially clinically applicable nonetheless.

Despite these limitations, we were able to show that pretreatment ADC was a significant predictor of disease free survival, with a trend toward significance in overall survival and local recurrence. Future prospective study should be performed to confirm these findings. In addition, simultaneous analysis of other functional imaging such as dynamic contrast enhanced MRI would be of interest.

In conclusion, the mean ADC value of the primary tumor on pre-treatment MRI was a significant predictor of disease free survival in cervical cancer patients on multivariate

analysis, independent of established clinical factors and SUV on FDG-PET, and appears to be a useful biomarker that should be further studied.

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Summary

This paper analyzed the prognostic value of the pretreatment diffusion weighted MRI in patients with cervical cancer treated with definitive chemoradiation. We found that a lower mean apparent diffusion coefficient ($0.940 \times 10^{-3} \text{ mm}^2/\text{s}$ versus $>0.940 \times 10^{-3} \text{ mm}^2/\text{s}$) on pretreatment MRI was a predictor of decreased disease free survival, independent of established clinical factors and SUV on FDG-PET. This technique can be easily incorporated in clinical practice to identify patients at increased risk of failure.

Figure 1.
Examples of a pre-treatment axial T2-weighted MRI image (A) and ADC map (B) showing the primary cervical tumor.

Figure 2.

Kaplan-Meier analyses of overall survival, disease free survival, local regional recurrence free survival, and central recurrence free survival, comparing patients with low mean pretreatment ADC ($< 0.940 \times 10^{-3} \text{ mm}^2/\text{s}$) versus high mean pretreatment ADC ($> 0.940 \times 10^{-3} \text{ mm}^2/\text{s}$).

Table 1**Patient Characteristics**

Characteristic	No. of patients (%)
Age	
Median (range)	50 (26–94)
Histology	
Squamous	48 (70%)
Adenocarcinoma/other	21 (30%)
Tumor differentiation	
Well/moderate	30 (44%)
Poor	26 (38%)
Unknown	13 (19%)
FIGO Stage	
IB1	4 (6%)
IB2	15 (22%)
IIA	7 (10%)
IIB	22 (32%)
IIIA	2 (3%)
IIIB	14 (20%)
IVA	4 (6%)
IVB	1 (1%)
Lymph Node Involvement	
Positive	48 (70%)
None	21 (30%)
Baseline PET SUV	
Median (range)	15 (6.2–43.4)
MRI Tumor Volume	
Median (range)	43 (3–894) cc
Mean ADC	
Median (range)	941 (256–1508)
Concurrent cisplatin	68 (99%)
Brachytherapy	67 (97%)
Pelvic Radiation Technique	
3D conformal	55 (80%)
3D conformal + IMRT	10 (14%)
IMRT	4 (6%)
Pelvic Radiation Dose	
45 Gy	52 (75%)
43.2 Gy	16 (23%)
40 Gy	1 (1%)
External Beam Boost	50 (72%)
IMRT Boost	30 (43%)

Characteristic	No. of patients (%)
3D Conformal Boost	20 (29%)
Median (range)	10 (4–17.4) Gy

Abbreviations: FIGO, International Federation of Gynecology and Obstetrics; PET SUV, positron emission tomography standardized uptake value; MRI, magnetic resonance imaging; ADC, apparent diffusion coefficient; IMRT, intensity modulated radiation therapy.

Table 2

Univariate Analysis for Disease Free Survival

Variable	Comparison	HR	95% CI	P-value
Age	Continuous	1.0	0.96–1.0	0.72
Non-squamous	Squamous	0.24	0.07–0.82	0.02
Poorly differentiated	Well/moderately	2.1	0.85–5.4	0.11
FIGO Stage III-IV	I-II	2.7	1.2–6.1	0.01
Lymph Node Status				
Positive	Negative	1.4	0.58–3.9	0.47
Baseline PET SUV	Continuous	1.0	0.97–1.1	0.49
>15	15	1.7	0.73–3.7	0.23
MRI Volume	Continuous	1.0	1.0–1.0	0.98
>42 cc	42 cc	1.5	0.67–3.4	0.32
Mean ADC	Continuous	1.0	1.0–1.0	0.28
>0.940 x 10 ⁻³ mm ² /s	0.940	0.45	0.2–1.0	0.06

Abbreviations: HR, hazard ratio; CI, confidence interval, FIGO, International Federation of Gynecology and Obstetrics; PET SUV, positron emission tomography standardized uptake value; MRI, magnetic resonance imaging; ADC, apparent diffusion coefficient.

Table 3

Multivariate Analysis for Disease Free Survival

Variable	Comparison	HR	95% CI	P-value
FIGO Stage				
III-IV	I-II	2.4	1.1–5.5	0.03
Mean ADC				
> 0.940 x 10 ⁻³ mm ² /s	0.940	0.36	0.15–0.85	0.02
Histology				
Non-squamous	Squamous	0.23	0.07–0.82	0.02

Abbreviations: HR, hazard ratio; CI, confidence interval, FIGO, International Federation of Gynecology and Obstetrics; ADC, apparent diffusion coefficient.