Correlation of Clinical Risk Factors with Diffusion-Weighted Magnetic Resonance Images in Prostate Cancer Patients Treated with Definitive Radiotherapy

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ABSTRACT

This study is aimed to correlate apparent diffusion coefficient (ADC) values and clinical T-stage, serum PSA, pathology Gleason scores. We also further analyzed whether ADC values could be used to appropriately define the risk groups. 135 biopsy-proven, radiotherapy-(RT)-treated, prostate cancer patients who underwent pre-RT DW-MRI and standard T2W pelvic MRI were included. ADC and normalized ADC (nADC) values were calculated from DW-MRI delivered a median 8.1 weeks after prostate biopsy. ADC values were correlated with clinical risk factor values by using Pearson correlation test. ADCs in low-, intermediate-, and high-risk patients were 0.873±0.122X10^{-3} mm^2/s, 0.763±0.124X10^{-3} mm^2/s, and 0.701±0.132X10^{-3} mm^2/s (p= 0.001), respectively. Patients with preRT PSA <10 ng/mL had significantly higher ADCs than patients with preRT PSA 10–20 ng/mL (p= 0.02) or >20 ng/mL (p< 0.001). Mean ADC for patients with Gleason score <7 was significantly higher than patients scoring 7 (p= 0.001) or >7 (p < 0.001). Clinical stage <T2b patients had significantly higher ADC values versus stage T2b (p=0.001) and T2b tumors (p< 0.001). ADC demonstrated stronger correlation with NCCN risk groups (R=–0.510; p< 0.001). All clinical factors except Gleason score had moderate inverse correlation with nADC. Best nADC correlation occurred with NCCN risk groups (R=-0.461; p< 0.001). ADCs measured by DW-MRI are noninvasive prognostic markers of clinical parameters and risk for prostate cancer in RT candidates.

Keywords: Prostate cancer, Diffusion-weighted MRI, Risk factors, Apparent diffusion coefficient, Prognostic factor

ÖZET

Definitif Radyoterapi ile Tedavi Edilen Prostat Kanserli Hastalarda Klinik Risk Faktörleri ve Difüzyon Ağırlıklı Manyetik Rezonans Görüntülerinin İlişkisi

Bu çalışmanın amacı klinik T evresi, serum prostat spesifik anijen (PSA) ve patolojik Gleason skoru ile apparent diffusion coefficient (ADC) değerlerinin ilişkisini araştırmak. Ayrıca ADC değerlerinin risk gruplarının tanımlanması için uygun olup olmayacağını analiz edilmiştir. Definitif radyoterapi (RT) ile tedavi edilen, tedavi öncesi DA-MRG ve standart T2 ağırlıklı MRG'si olan 135 prostat kanserli hasta çalışmaya dahil edildi. Prostat biyopsisinden medyan 8.1 hafta sonra çekilen DA-MRG' lerden ADC ve normalize edilmiş ADC (nADC) değerleri ölçüldü. ADC değerleri ve klinik risk faktörleri arasındaki ilişkiyi araştırmak için Pearson korelasyon testi kullanıldı. Düşük, orta ve yüksek risk hastalarda ADC değerleri sırası ile 0.873±0.122×10^{-3} mm^2/s, 0.763±0.124×10^{-3} mm^2/s ve 0.701±0.132×10^{-3} mm^2/s (p = 0.001) idi. RT öncesi PSA değerleri <10 ng/mL olan hastalar, RT öncesi PSA değerleri 10-20 ng/mL (p= 0.02) veya >20 ng/mL (p< 0.001) olan hastalara göre istatistiksel olarak anlamı derecede yüksek ADC değerlerine sahipti. Gleason Skoru <7 olan hastalar için ortalama ADC skoru, gleason 7 (p = 0.001) veya >7 (p < 0.001) olanlara göre anlamlı derecede yüksekti. Klinik evre <T2b olan hastaların ADC değerleri, evre 2b (p= 0.001) ve >2b (p < 0.001) hastalara göre anlamlı derecede daha yüksekti. ADC değerleri National Compheresive Cancer Network (NCCN) risk grupları ile kuvvetli bir korelasyon gösterdi(R=–0.510; p< 0.001). Gleason skoru hariç tüm klinik faktörler nADC değeri ile ılımlı ters bir korelasyon içindeydi. nADC' nin en iyi korelasyonu NCCN risk grupları ileydi. (R=–0.461; p< 0.001). DA-MRG ile ölçülen ADC değerleri, RT planlanan prostat kanserli hastalarda önemli bir non invaziv prognostik belirteç olarak değerlendirilebilir.

Anahtar Kelimeler: Apparent difüzyon katsayısı, Difüzyon ağırlıklı MRG, Prognostik faktör, Prostat kanseri, Risk faktörleri

INTRODUCTION

Prostate cancer is mostly an indolent tumor with slow disease progression. However one of six men had prostate cancer, but only one of 36 patients died with disease. Treatment strategies include watchful waiting, radical prostatectomy, or radiotherapy (RT) with or without hormonotherapy, depending on disease stage and risk factors.[1-3] The challenge of managing localized prostate cancer is to distinguish patients who may benefit from radical treatment from patients who do not need any intervention. Furthermore, in patients treated with RT, treatment strategies depend on clinical parameters and, notably, risk groups.

Currently, serum prostate-specific antigen (PSA), clinical T stage, and Gleason scoring are used for defining prostate cancer risk.[4,5] These risk factors have been used to predict the biochemical relapse after surgery or RT, and these parameters are also used to make treatment choices. Additionally, PSA doubling-time and PSA density are used to predict disease outcome, but they are nonspecific in determining diseases prognosis.[6,7] To predict tumor biological behavior, histological evaluation of the prostate is required. However, histological evaluation involves invasive biopsy procedure(s) and is subject to sampling error. Furthermore, histopathological findings of prostatectomy and biopsy specimens do not always accurately reflect actual disease status.[8,9] There may be discordance between clinical and pathological staging, and Gleason scores of biopsy and prostatectomy specimens may vary. For this reason, a thorough evaluation of entire prostate is essential before performing definitive RT, in which histopathological evaluation is based on prostate biopsy only, and staging is performed with clinical and radiological findings. Non-invasive methods to evaluate the entire prostate and the tumor biology before performing RT may be a promising alternative. Moreover, this approach would allow optimized treatment delivery to adequately stratified patient risk groups.

The best method of imaging prostate cancer is endorectal T2-weighted magnetic resonance imaging (MRI), which has 60-82% sensitivity and 55-70% specificity for detecting cancer.[10-12] Additionally, recent studies have aimed to determine the value of MR correlates of cellular density, metabolite concentration, and tumor vascularization for predicting tumor aggressiveness.[13-16] Diffusion-weighted MRI (DW-MRI) is advantageous in tumor localization.[17-19] DW-MRI may also provide qualitative information regarding the pathophysiological character of prostate cancer.[18,20,21] DW-MRI is sensitive to the microscopic motion of water molecules and allows biological characterization of tissues based on their water-diffusion properties. The degree of diffusion is quantified as the apparent diffusion coefficient (ADC).

Few clinical studies involving limited patient numbers have evaluated the potential value of pre-prostatectomy DW-MRI as a non-invasive marker of disease aggressiveness.[22,23] This study assessed the potential importance of ADC values obtained from DW-MRI in prostate cancer patients treated with definitive RT. Additionally; we analyzed the correlation between ADC values and clinical T-stage, serum PSA levels, and Gleason scores. We further analyzed whether ADC values could be used to appropriately define the risk groups.

PATIENTS AND METHODS

Study Design and Patient Population

This retrospective study was approved by Baskent University Institutional Review Board (Project No #KA13/146) and was supported by the Baskent University Research Fund. The requirement for receipt of written informed consent was waived due to the retrospective nature of this study and because all patient-identifying information was anonymized. All study protocols adhered to the tenets of the Declaration of Helsinki. We reviewed the records of 135 patients with biopsy-proven prostate cancer at the Baskent University Faculty of Medicine who were treated with curative intent using definitive RT between January 2012 and August 2013 and who had undergone both DW-MRI and standard T2W pelvic MRI before RT.

Patients were stratified into three risk groups according to the National Comprehensive Cancer Network (NCCN) guidelines.[24] The low-risk group contained patients with T1-T2a tumor, Gleason score <7, and PSA<10 ng/mL; intermediate-risk

patients were T2b tumor, Gleason score= 7, and PSA 10-20 ng/mL; and high-risk patients were ≥T3a tumor, Gleason score >7, and PSA >20 ng/mL. Pre-RT MRI scans were performed a median 8.1 weeks (range 4.3-34.1 weeks) after initial prostate biopsy and cancer diagnosis.

Magnetic Resonance Imaging

For all patients, T2W, fat-saturated T2W, DWI, and Dynamic Contrast Imaging- (DCE)-MRI exam were performed using a 1.5 T Siemens Avanto® MR scanner used as an 8-element, phased-array coil during the scans, without an endorectal coil. T2W images were acquired with a fast spin-echo sequence: repetition time/echo time (TR/TE)= 5480/55 ms, acquisition matrix 224×320, field of view (FOV)= 220 cm, slice thickness 4 mm, and intersection gap 1.6 mm. Fat-saturation turbo spin echo sequence imaging parameters were: TR/TE= 5480/55 ms, echo train length= 40, acquisition matrix 224×320, FOV= 220 cm, slice thickness=1.6 mm. DW-MRI scans were performed using a multi-slice, single-shot, spin-echo, planar imaging (SE-EPI) sequence (FOV= 365 cm, slice thickness= 4mm, EPI-factor= 192, intersection gap= 0 mm, TR/TE= 4400/83 ms, acquisition matrix= 192×100, 4 averages, sense factor= 2 in the anterior-posterior direction. The b-values of 0, 200, 600, and 1000 s/mm^2 were used to calculate ADC. The ADC maps were generated automatically using multi-exponential data fitting with manufacturer's software (syngo.via; Siemens Healthcare, Erlangen, Germany). The DCE-MRI protocol consisted of a three-dimensional, spoiled-gradient echo sequence (3 mm section thickness, TR/TE= 6.7/3.14 ms, flip angle 10^0, FOV= 200 cm, acquisition matrix= 154×256. For DCE imaging, a dose of 0.1 mL/kg gadoterate meglumine (Dotarem®; Guerbet Group, LLC., Villepinte, France) was injected at 2mL/s, followed by a saline flush.

Data Analysis

Prostate cancer localization was determined by consensus of the two experienced genitourinary radiologists (≥20-years experience) based on a comparison of digital rectal examination findings, pathologic biopsy results with four-quadrate and 12 core biopsy, and the presence of focal low-signal-intensity areas in the peripheral and/or transition zones on ADC maps, with using T2W. ADCs were determined and maps created using Siemens workstation software syngo.via. Diagnostic criteria of prostate cancer in MRI findings were: focal area(s) revealing low signal intensity on T2W images and focal lesion restriction on ADC maps,

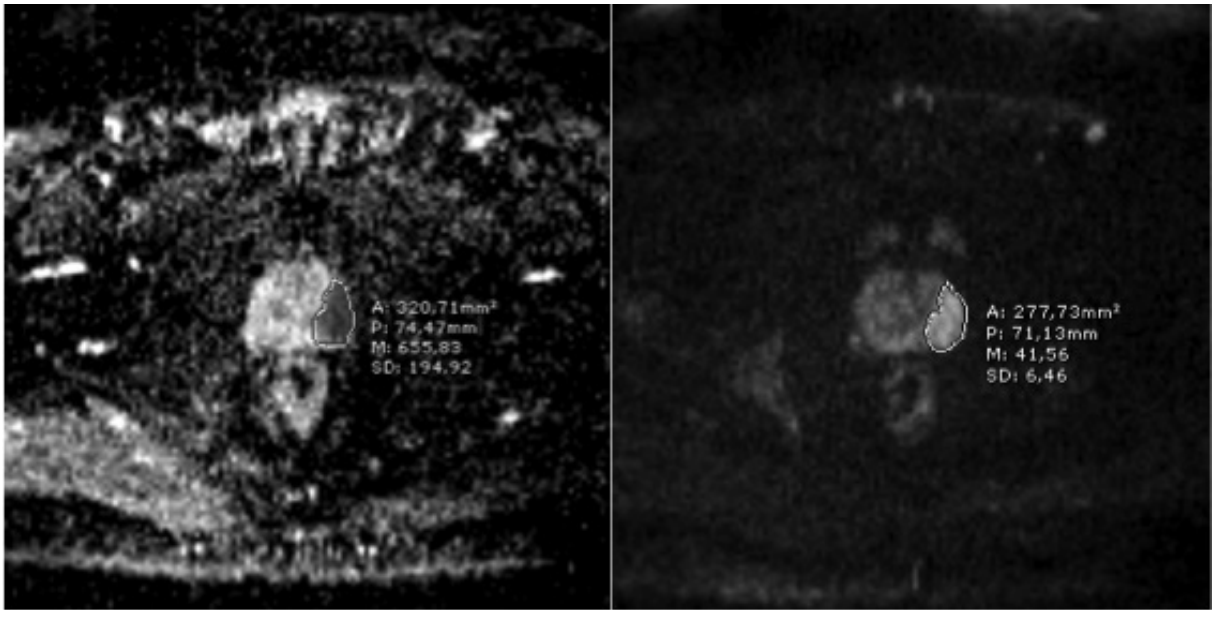

Figure 1. Axial apparent diffusion coefficient map of a corresponding patient demonstrating prostate tumor at left periheral zone.

Table 1. Patient characteristics

Characteristics	No of patients	Percent (%)
Age, median (range), yrs	68 (52 – 84)	
Stage		
T1c	66	49
T2a	8	6
T2b	26	20
T2c	7	5
T3a	6	4
T3b	22	16
Gleason score		
3+3	72	53
3+4	25	19
4+3	20	15
4+4	6	4
4+5	10	7
5+5	2	2
Risk groups		
Low	41	30
Intermediate	34	25
High	60	45

early contrast enhancement with fast washout, and high blood vessel permeability on dynamic contrast-enhanced images.[25,26] Additionally, prostate tumors were seen as hyperintense lesions with high b-values.

First, both hyperintense lesions at high b-values (especially b= 800 or b= 1000) and lesion with diffusion restriction on ADC maps were, when co-localized in the same area, determined to be focal prostatic cancer lesions (Figure 1). Before RT, regions of interest (ROIs) of the tumors in the peripheral and/or transition zones were drawn on ADC maps to include as much of the tumor as possible, calculations were performed twice in the same site, and the average of these two values was calculated. If a tumor was located in several ADC map imaging slices, ADC values were measured on both the biggest and the most homogenous regions of the same slice. When the ROIs were drawn, great care was taken to exclude both the neurovascular bundle and the urethra to reduce ADC calculation error. For measuring ADC values in the peripheral and/or transition zones of benign tissue, ROIs at the contralateral side of the tumor were selected. Additionally, the normalized ADC (nADC) was calculated as the ratio of tumor ADC to normal prostate tissue ADC.

Statistical Analysis

Statistical analyses were performed using SPSS software version 20 (SPSS Inc./IBM, Chicago, IL). Clinical risk factors including Gleason score, clinical T-stage, and serum PSA level were categorized into three groups. A paired Student t-test and an independent samples t-test with Bonferroni correction were used to assess differences between groups. Pearson correlation analysis was performed between ADCs, nADCs, and clinical risk factor values. Receiver operating characteristic (ROC) analysis was performed to assess the power of tumor ADC and nADC in discriminating between low-, intermediate-, and high-risk groups and a cut-off value for this parameter was determined. A p value of <0.05 was considered indicative of statistically significant differences.

RESULTS

Patient characteristics are summarized in Table 1. Almost half of the patients had clinical stage T1c tumors or Gleason score 3+3 tumors. Again almost one-third of patients were stratified into the low-risk group, while the remaining two-thirds of patients were in the intermediate- or high-risk group. The overall mean and median serum PSA levels were 23.3±8.0 ng/mL and 12.6 ng/mL (range 1.6–119.6 ng/mL), respectively.

ADC Measurements

The mean tumor ADC and nADC values were $(0.773\pm0.141)\times10^{-3}$ mm^2/s and $(0.581\pm0.122)\times10^{-3}$ mm^2/s, respectively. The ADC values in the central and peripheral normal prostate tissue were $(1.321\pm0.156)\times10^{-3}$ mm^2/s and $(1.338\pm0.152)\times10^{-3}$ mm^2/s, respectively.

Correlation with Serum PSA

The mean ADC values for PSA groups <10 ng/mL, 10-20 ng/mL and >20 ng/mL were $(0.836\pm0.122)\times10^{-3}$ mm^2/s, $(0.751\pm0.130)\times10^{-3}$ mm^2/s, and $(0.690\pm0.141)\times10^{-3}$ mm^2/s, respectively (Figure 2A). Patients with low preRT PSA levels <10 ng/mL had significantly higher ADC

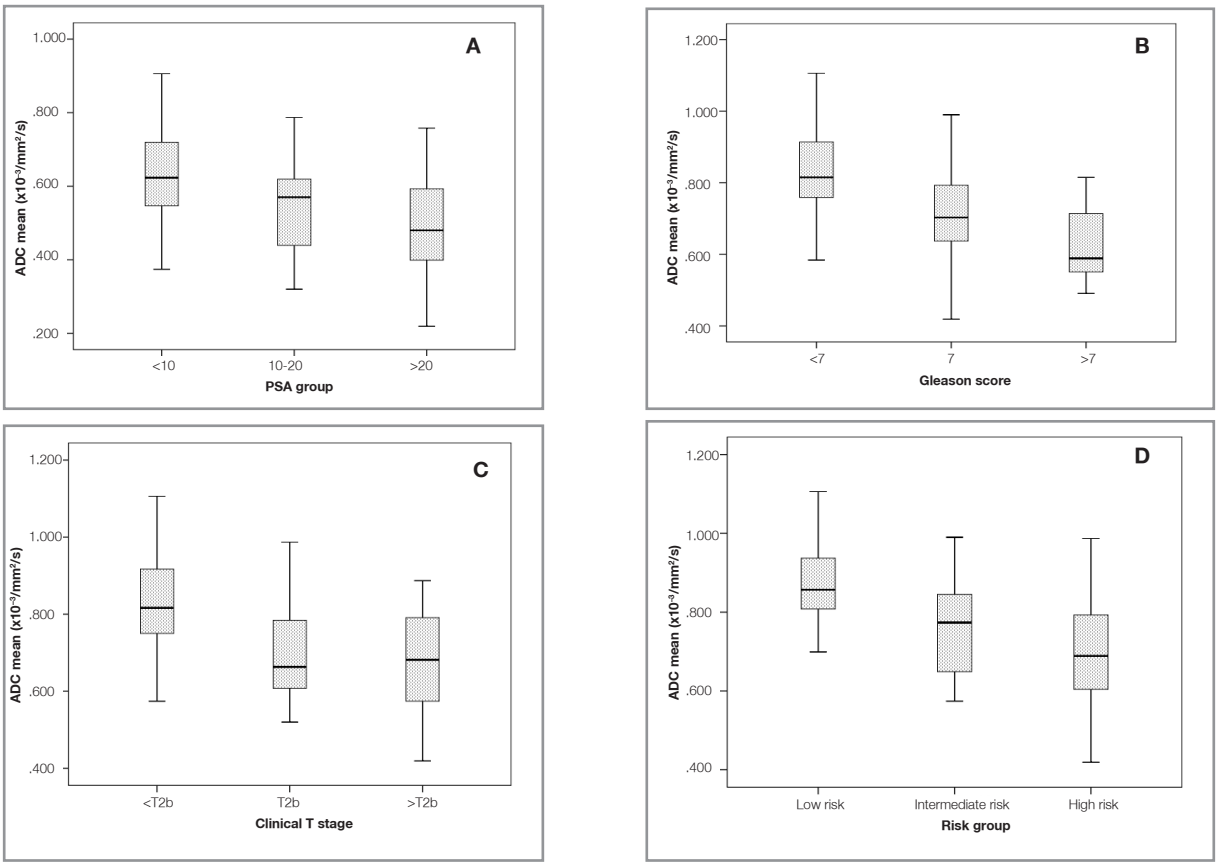

Figure 2. ADC values measured in diffusion-weighted magnetic resonance imaging before radiotherapy according to **(A)** PSA levels, **(B)** Gleason scores **(C)** clinical T-stage, and **(D)** risk groups.

values compared to patients with preRT PSA 10-20 ng/mL (p= 0.02), and PSA >20 ng/mL (p < 0.001). However there was no significant difference between ADC values of patients with intermediate PSA 10–20 ng/mL and PSA >20 ng/mL (p= 0.2) levels.

Correlation with Tumor Gleason Scores

The mean ADC for patients with Gleason scores <7 ($0.829\pm0.119\times10^{-3}$/mm²/s) was significantly higher than in patients with Gleason score 7 ($0.720\pm0.135\times10^{-3}$ mm²/s; p= 0.001) and patients with Gleason score >7 ($0.624\pm0.109\times10^{-3}$ mm²/s; p< 0.001) (Figure 2B). However, the difference between Gleason score 7 and Gleason score >7 approached statistical significance (p= 0.08).

Correlation with Tumor Stage

Patients with clinical stage <T2b tumors had significantly higher ADC values ($0.832\pm0.117\times10^{-3}$ mm²/s) compared to patients with stage-T2b tumors ($0.708\pm0.135\times10^{-3}$ mm²/s; p= 0.001), and stages >T2b tumors ($0.673\pm0.127\times10^{-3}$ mm²/s; p < 0.001) (Figure 2C). However there was no significant difference between ADC values of patients with clinical stage T2b tumor and >T2b tumors (p= 0.6).

Correlation with NCCN Risk Groups

We stratified patients into risk groups based on composites of Gleason score, serum PSA levels, and tumor stage. The ADC values in low-, intermediate-, and high-risk patient groups were $(0.873\pm0.122)\times10^{-3}$ mm²/s, $(0.763\pm0.124)\times10^{-3}$ mm²/s, and $(0.701\pm0.132)\times10^{-3}$ mm²/s, respectively (Figure 2D). The differences between all paired risk group comparisons were significant.

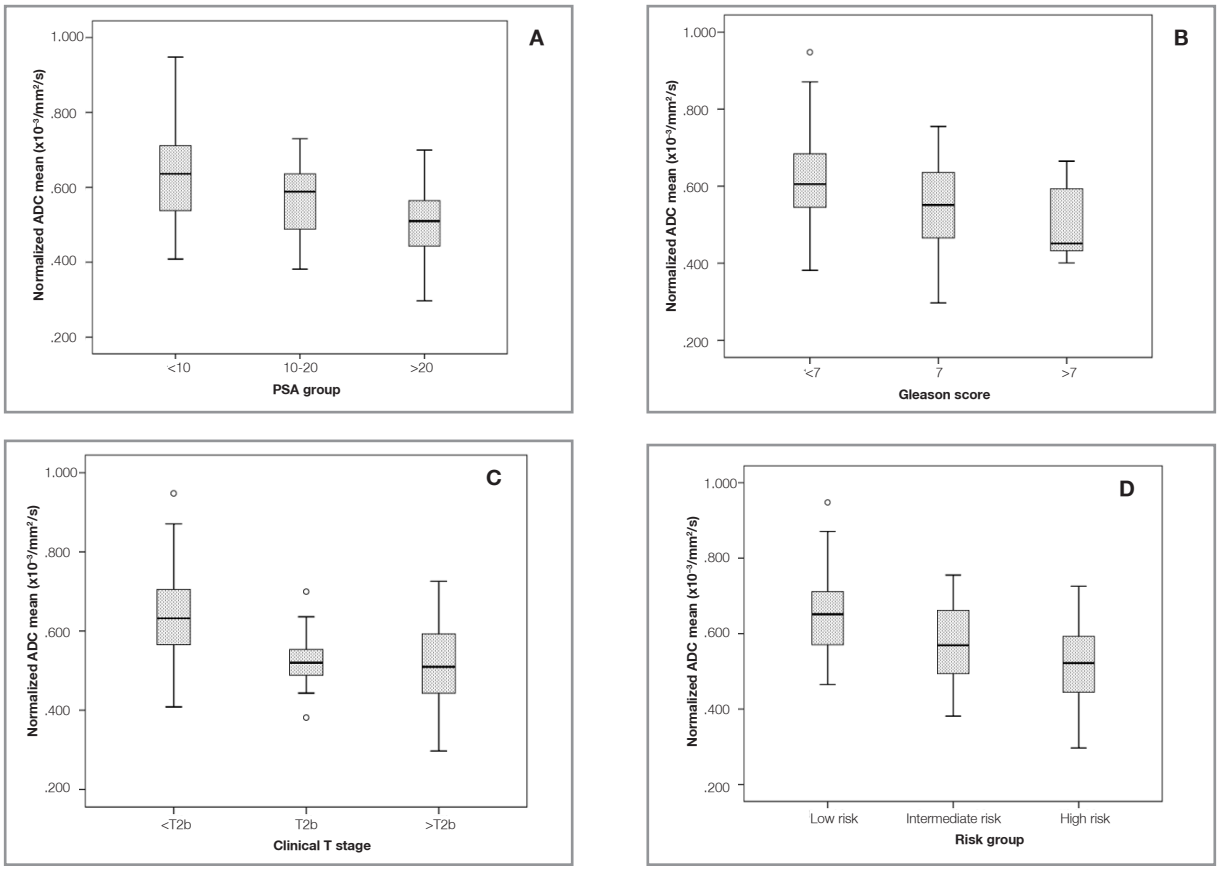

Figure 3. Normalized ADC values measured in diffusion-weighted magnetic resonance imaging before radiotherapy according to **(A)** PSA levels, (B) Gleason scores (C) clinical T-stage, and (D) risk groups.

Normalized ADC Measurements

The mean nADC values for PSA groups <10 ng/mL, 10-20 ng/mL, and >20 ng/mL were 0.63, 0.57, and 0.51, respectively (Figure 3A). The only significant difference in nADC values existed between patients with PSA <10 ng/mL versus patients with PSA >20ng/mL (p= 0.001). The mean nADC for patients with Gleason score <7 (0.62) was significantly higher than patients with Gleason score 7 (0.55; p= 0.04) and patients with Gleason score >7 (0.50; p= 0.03) (Figure 3B). However, the nADC difference between Gleason score 7 and Gleason score >7 groups did not reach statistical significance (p= 0.6). Patients with clinical stage <T2b tumors had significantly higher nADC values (0.63) compared to patients with clinical stage T2b tumors (0.53; p= 0.04) and stage >T2b tumors (0.51; p= 0.001) (Figure 3C). However, there was no significant difference between nADC values of patients with clinical stage T2b tumors versus >T2b tumors (p= 0.9). The nADC values in the low-, intermediate-, and high-risk patients were 0.66, 0.58, and 0.52, respectively (Figure 3D). The nADC differences between low- versus intermediate-risk groups (p= 0.04), and low- versus high-risk groups (p< 0.001) were significant. No significant difference in nADCs existed between the intermediate- and high-risk groups.

Correlation Between Clinical Factors

Significant and inverse moderate correlations between all clinical factors and ADCs were observed (Table 2). The ADC demonstrated the best correlation with the NCCN risk groups (Pearson=-0.510; p< 0.001). All clinical factors except the Gleason score were inversely and moderately correlated with nADCs. As with the ADC, the best correlation with nADC was observed with the NCCN risk groups (Pearson=–0.461; p< 0.001).

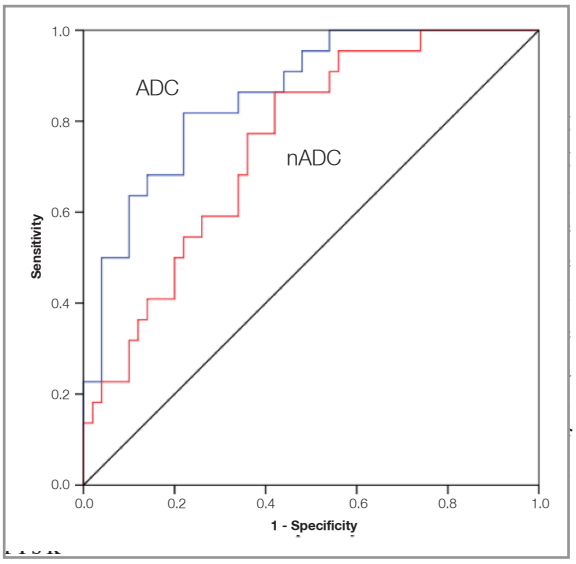

Figure 4. Receiver operating characteristic curve analysis in risk group prediction according to ADC and nADC.

prediction accuracy, a nADC cut-off value of 0.59 gave a sensitivity of 68% and specificity of 66%.

DISCUSSION

This study demonstrates that ADC values can distinguish between among the clinical parameters and define risk factors that are used when selecting RT strategies for treating prostate cancer. In low-risk patients, prostate RT is adequate treatment, whereas in intermediate- and high-risk patients, hormone therapy is delivered concurrently with RT. Additionally, negative correlations were found between ADC values and clinical parameters including serum PSA level, clinical T-stage, and Gleason score.

Water diffusion characteristics are substantially affected by cellular and structural changes within tissues, including cell density, vascularity and microvascular tortuosity, extracellular fluid viscosity, membrane permeability between intra- and extracellular compartments, active transport and flow, and directionality of tissue/cellular structures that impede water mobility.[27] These cellular and structural differences exist between low- and high-risk lesions, and they can be measured non-invasively in vivo using DW-MRI, which constructs images based on quantifying water molecule diffusion within tissues.[28]

The ADC is a quantitative parameter of the extent of water molecule diffusion. Due to increased cellularity, decreased extracellular space, and abnormal microvasculature, tumor ADCs are generally lower than surrounding normal tissues. Furthermore, ADC values can potentially be used to predict tumor aggressiveness.[22,29,30] Bae et al.[22] demonstrated that prostate cancer patients with a Gleason score ≥4+3, larger tumors (≥16 mm), and highly proliferating cancers had significantly lower ADC values in 29 patients treated with radical prostatectomy. Oto et al.[29] found a moderate negative correlation between Gleason score (r –0.376, p= 0.001) and tumor ADC values in 73 prostate cancer patients treated with radical prostatectomy. In 39 patients treated with radical prostatectomy, Thörmer et al.[21] found that nADC could be used as a valuable surrogate for predicting tumor aggressiveness. deSouza et al.[23] demonstrated significant differences in ADC values between patients at low-risk and those with higher-risk localized prostate cancer. We evaluated more patients compared to these previous studies, and we demonstrated a significant correlation between ADCs and diverse clinical parameters and NCCN risk groups.

Table 2. Correlation between ADC, nADC and clinical prognostic parameters

Parameter	ADC		nADC	
	Pearson correlation coefficient	p	Pearson correlation coefficient	p
PSA	-0.443	<0.001	-0431	<0.001
Gleason score	-0.496	<0.001	-0.351	<0.001
Clinical T stage	-0.501	<0.001	-0.430	<0.001
Risk groups	-0.510	<0.001	-0.461	<0.001

All patients had been treated with definitive RT. Therefore, we could not perform a detailed analysis of histopathological correlations with ADC values. In some cases, there may be discordance between histopathological findings in biopsy and prostatectomy specimens. Previous studies have shown significant pathologic upgrading at radical prostatectomy, with reported upgrading percentages ranging from 20.3%-54%.[15] This potentially creates a problem with accurately identifying and monitoring patients who are erroneously categorized as having low-risk disease before surgery. For defining NCCN risk groups, patients were stratified according to Gleason score, serum PSA level, and clinical T-stage. Although ADC values are known to correlate with tissue structure, the NCCN criteria rather than Gleason score were used to define risk groups, to reduce the effects of biopsy sampling variability and reflect that our ADC values were averaged over the whole tumor ROI. Averaging ADCs over the ROI is a limitation, as it does not account for ADC differences within the tumor itself; therefore, correlation of these differences with histopathology would be useful. Further study of DW-MRI in localized prostate cancer is also warranted to assess its correlative utility in relation to tumor histopathology and clinical outcomes.

Although several study evaluated ADCs for determining tumor aggressiveness, few studies defined the cut-off values to predict high-grade cancer foci.[21-23] Bae et al.[22] determined the cut-off ADC value of 0.52×10^{-3} mm^2/s as having low- versus high-grade tumors. deSouza et al.[23] found that ADC cut-off values of 1.33×10^{-3} mm^2/s (sensitivity 89%, specificity 58%) and $1.20\times10^{-3}/mm^2/s$ (sensitivity 55%, specificity 95%) provided 70% of risk prediction. Thörmer et al.[21] defined nADC values below 0.46 as the threshold for tumors with intermediate or high aggressiveness. The ADC cut-off values may vary between studies because of different enrolled patient numbers and varied ADC measurement techniques. In our study we evaluated both ADC and nADC values. We found that for 70% risk prediction, an ADC cut-off of 0.802×10^{-3} mm^2/s gave a sensitivity of 82% and specificity of 78%, and a nADC cut-off value of 0.59 gave a sensitivity of 68% and specificity of 66%. Although our ADC and nADC cut-off values were higher than previously reported findings, our results may be more reliable because we studied larger number of patients.

ADC value measurement has not been standardized yet. In some studies, minimum ADC values were correlated with tumor biological aggressiveness[31,32], whereas other researchers used mean ADC values as a surrogate for tumor aggressiveness.[22,33] Although there is intratumoral heterogeneity in prostate cancer, we used the mean ADC values. However, to minimize ADC measurement error, ADC was measured on much larger tumor volumes that previously studied, by averaging ADC maps of several imaging slices.

The main limitation of T2W imaging is false positivity for low-signal intensity lesions, where infection, inflammation, and fibrosis may mimic the tumor. In this study, to diminish false results, the radiologists delineating the ROI were aware of the tumor localization that was verified with biopsy. However, on post-biopsy T2W images, hemorrhage has low signal intensity that can mimic the tumor and lead to inaccurate measurements.[27] In previous studies analyzing the importance of ADC in prostate cancer patients[22,23], the MRI scans were delivered before prostate biopsy, which makes the result more accurate. We evaluated the patients before initiation of RT, and MRI scans were all taken before RT with biopsy proven prostate cancer. In suspected cases, T1W images of the whole pelvis were taken at the same time to differentiate hemorrhage and minimize artifactual error introduction into ADC measurements.

A major limitation of this study is the lack of correlating tumor ROIs with whole-mount histopathology sections, because all patients in this study were treated with definitive RT. In the high-risk cohort, all lesions were large and easily discernible on T2W imaging, so the likelihood of error in ROI selection is low. In the low-risk cohort, where all lesions were verified with biopsy data, the ADC values were likely to have been indistinguishable from adjacent non-malignant prostate tissue. In these cases, the lack of a visually identifiable lesion on the ADC map is also an indicator of the low-risk nature of the lesion. A more problematic feature is

that we used the averaged ADC from the entire tumor region, and this was often heterogeneous. It may be that the more diffusion-restricted areas within the tumor region are ultimately more predictive of outcome. Also, the absolute cut-off values for the ADC and nADC have not yet been appropriately defined and standardized, because prior studies used different measurement techniques and were prone to inter-observer variability. The images in our study were interpreted by consensus of two readers rather than by separate analyses. The purpose of this study, however, was not to assess ADC diagnostic accuracy for predicting localized prostate cancer by DW-MRI but to correlate the ADC values with clinical rsik factors using 1.5T MRI. Another study limitation was that all patient underwent transrectal sonography guided-biopsy with pretreatment MR examination, which might have had potential effects on subsequent ADC measurement due to hemorrhage or inflammatory changes in the normal prostate tissue.

In conclusion, DW-MRI offers potential to evaluate prostate cancer patients treated with definitive RT, where complete histopathological evaluation of the entire prostate is not possible. We found that ADC values measured using DW-MRI can noninvasively determine clinical parameters and risk groups for prostate cancer patients that have prognostic significance. However, further work is needed to conclusively determine the clinical significance of using ACDs to define risk groups and to evaluate treatment responses after definitive RT for prostate cancer.

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