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Original Article

Diffusion-weighted MRI in prostatic lesions: Diagnostic performance of normalized ADC using normal peripheral prostatic zone as a reference

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ABSTRACT

Aim of study: Evaluate the potential value of the normal peripheral zone as a reference organ to normalize prostatic lesion apparent diffusion coefficient (ADC) to improve its evaluation of prostatic lesions.

Patients and methods: This prospective study included 38 patients with clinical suspicion of cancer prostate (increased PSA levels (> 4 ng/ml, hard prostate in digital rectal examination) and who are scheduled to undergo a TRUS-guided biopsy. Conventional and DW-MRI was done and ADC was calculated. The normalized ADC value was calculated by dividing the ADC of lesion by ADC of reference site (healthy peripheral zone). DWI-MRI results were compared to the results of biopsy. Comparison of ADCs and nADCs of benign and malignant lesions was done. Receiver operating characteristics (ROC) curve analysis was done.

Results: The patients were classified by histopathology into non-malignant group (16 patients) and malignant group (22 patients). Significant negative correlation between ADC and normalized ADC (nADC) and malignancy was detected. There was no significant difference between the mean ADC of peripheral health prostatic zones (PZ) between benign and malignant cases (2.221 ± 0.356 versus $1.99 \pm 0.538 \times 10^{-3}$ mm^2/sec, $p = 0.144$).

There was significant difference between the mean ADC and mean nADC in benign and malignant lesions (1.049 ± 0.217 versus $0.659 \pm 0.221 \times 10^{-3}$ mm^2/sec, $p < 0.001$) and (0.475 ± 0.055 versus 0.328 ± 0.044, $p < 0.001$) respectively.

There was significant higher diagnostic performance of nADC than ADC with ADC Cut-off value 0.75×10^{-3} mm^2/sec and nADC cut-off value 0.39 could significantly differentiate between benign and malignant lesion with sensitivity, specificity, PPV,NPV of 86.36,75,82.61 and 80% respectively, $p < 0.0001$ for ADC and 95.45, 93.75, 95.45 and 93.75%, $p < 0.0001$ for nADC.

Conclusion: diagnostic performance of nADC using normal peripheral zone is higher than ADC in discrimination between cancerous and non-cancerous lesions of the prostate.

1. Introduction

Cancer prostate is considered the commonest cancer in males and first leading mortality cause in them. Its management depends upon various clinical parameters including patient age as well as the tumor aggressiveness with differentiation between indolent and aggressive lesions mainly at Gleason score using TRUS-guided biopsy [1–3].

TRUS guided biopsy has a main role in the diagnosis of cancer prostate. however its false negative results were assumed to be about 40%. This can partially attributed to limited accuracy of ultrasound in localization of cancer prostate which makes the biopsies of random not targeted pattern with subsequent drawbacks as sampling from normal tissue or missing of cancer site sampling [4–6].

So developing of reliable non-invasive techniques in cancer prostate evaluation is of important value. MRI is a growing tool in this. While prostate cancer can be detected as low signal intensity relative to normal bright peripheral zone signal, the central zone cancer is difficultly detected because of high signal intensity caused by benign prostatic hypertrophy [1,7–9].

Diffusion-weighted MRI (DWI) is a non-invasive tool that depends on the water molecules motion intra-, extra- cellular as well as through cell membrane. Apparent diffusion coefficient (ADC) value is a quantitative measurement of DW-MRI which has shown a promising role in the detection and localization of cancer prostate [3,10–16].

However the lack of standard parameters of DWI especially with variable b-value used as well as variable ADC in different prostatic

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zones leads to variation in the reported ADC [10–16]. To reduce this variability, normalized apparent diffusion coefficient (nADC) by using a reference organ is applied. Spleen and renal cortex was used as reference organs in hepatic pathologies [17–22]. Also the using of renal cortex showed a diagnostic accuracy improvement in detecting metastatic cervical cancer to pelvic lymph nodes [23].

The using of a reference location for calculation of nADC in prostate was tried in some previous studies and showed promising results [24–31].

The scope of the current study was to evaluate the potential value of using the normal peripheral zone as a reference organ to normalize prostatic lesion ADC in order to improve the performance of DWI in the evaluation of prostatic lesions.

2. Patients and methods

2.1. Patients

Approval for this prospective study from institutional review board as well as informed patient consent was obtained.

This study included thirty-eight consecutive patients (mean age 58 ± 13.4 years) with clinical suspicion of cancer prostate (increased PSA levels (> 4 ng/ml, hard prostate in digital rectal examination) done by expert surgeon (M.R.) (was not informed about imaging results) and who are scheduled to undergo a TRUS-guided biopsy to rule out carcinoma. The mean PSA: 28.65, range: 5.3–176 ng/ml)

The clinical presentation of the patients was dysuria, frequency, urgency, weak stream and urine retention or gross hematuria. All had no previous irradiation or hormonal therapy or MRI contraindications. TRUS was done before MRI in all patients.

2.2. MR imaging protocol

MR imaging was done using Philips Achieva machine (1.5 T) (Philips Medical system Nederland B.V., Best, The Netherlands) using a pelvic phased-array coil.

MR study included conventional MRI and DW imaging.

– Conventional images:

The patient was placed in the supine position. Localizer was taken then conventional images were obtained from the bifurcation of aorta down to the symphysis pubis including

– Axial T1-weighted spin-echo (repetition time (TR) ms/echo time (TE) ms, 520/15, slice thickness 4 mm; intersection interval 1 mm; field of view (FOV) 20 cm; matrix, 256 × 192 and flip angle 90 degree.
– high-spatial-resolution axial T2-weighted fast spin-echo for the prostate and seminal vesicles (TR/TE 3500/90, slice thickness 4 mm; slice interval 1 mm; FOV 25 cm; matrix 256 × 192 and flip angle 90 degree).
– Coronal and sagittal T2-weighted fast spine echo MR images of the prostate and seminal vesicles (TR/TE 4100–4500/90, slice thickness 3 mm; slice interval 1 mm; FOV 38 cm; matrix 256 × 192 and flip angle 90 degree).
– Diffusion-weighted imaging

Single shot echo-planar imaging with a pair of rectangular gradient pulses along three orthogonal axes to include whole prostate. The imaging parameters were (TR/TE: 2800/74; FOV = 38 cm2; slice thickness 3 mm and inter-slice interval of 1 mm. Matrix was 256 × 256 matrix. The b (diffusion sensitizing factor) values were 0 and 1000 s/mm^2 and flip angle 90 degree.

– Apparent diffusion coefficient (ADC):

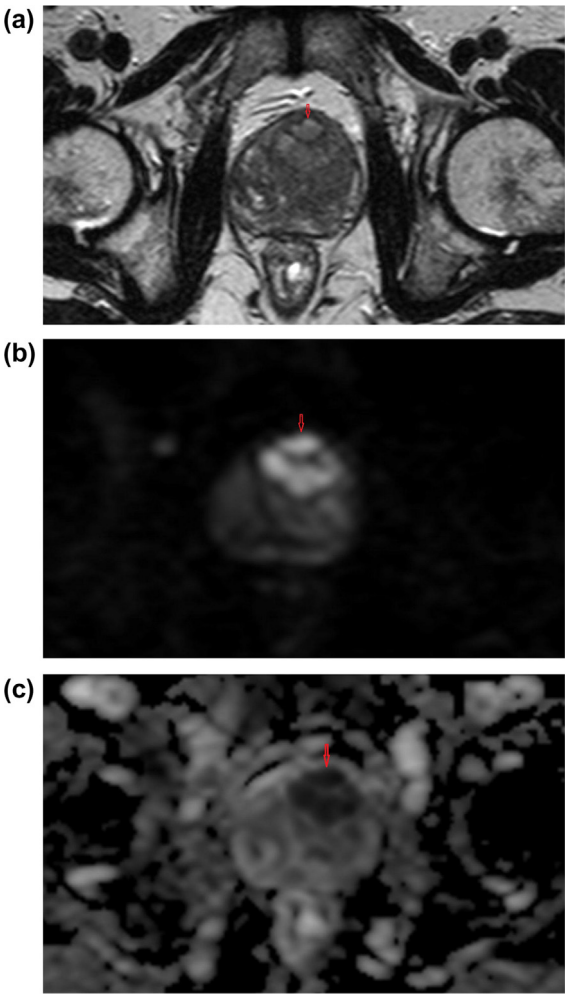

Fig. 1. Prostate cancer: axial T2WI (a) shows ill-defined hypointense focal lesion at central prostatic zone, more to the left side (arrow). It displays hyperintense signal at DWI (b = 1000) (arrow) (b) and low-signal intensity (arrow) at ADC map (c). ADC = 0.67 × 10^{-3} mm^2/sec and nADC of 0.33.

Apparent diffusion coefficient (ADC) maps were calculated by MRI machine incorporated software automatically. ADC values in prostatic lesions were calculated as the average of 3 ADC values assessed in the same site of the dominant lesion (The ROIs were chosen to be as large as possible with minimal contamination from normal tissue). The ADC values in normal peripheral zone (reference site) were calculated as the average of ADC in 3 different normal sites. In case of peripheral zone lesion, the contralateral peripheral zone was used as a reference site. If both lobes are involved healthy portion of the peripheral zone was used as reference site. Each ROI was a circle or oval, with an area of 6 to 24 mm^2. The mean normalized ADC value was calculated by dividing the ADC of lesion by ADC of reference site. The radiologists were blinded to results of histopathological examinations.

2.3. Histopathological study

DWI-MRI results were compared to the results of biopsy. All patients underwent transrectal ultrasound (TRUS)-guided biopsy of the prostate which was done 7–30 days after MR imaging. Biopsy specimens were fixed in formaldehyde, embedded in paraffin, and stained with hematoxylin-eosin. To match the biopsy cores with MR images, the prostate was divided into six zones (apical, mid, and basal zones) on each side. Additional 3 cores were taken from suspected focal lesions in the sonographic examination. Lesions were reported as cancer (and assigned Gleason score) or as benign tissue. The pathologists were blinded to