WORLD JOURNAL OF MEDICAL INNOVATIONS

The effect of 5-a-reductase inhibitor on apparent diffusion coefficient of MRI in the differential diagnosis of prostate cancer

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Article info

UROLOGY

Original paper

Article history:
Accepted September 21, 2021

Published online January 9, 2022

Keywords:
magnetic resonance imaging,
apparent diffusion coefficient,
prostate cancer,
5-a-reductase inhibitor,
finasteride

Abstract

Objectives. To study the effect of 5-a-reductase inhibitor on the parameter of the apparent diffusion coefficient of MRI in the differential diagnosis of prostate cancer. Material and methods. In total, the study involved 219 persons. The study included patients with histologically verified PCa and BPH, all patients before MRI and PBP were treated with 5-ARI - finasteride for lower urinary tract symptoms, 5 mg once daily for at least 4 months. The main group receiving finasteride treatment included patients of the following subgroups: 20 patients with PCa, of which 11 with clinically nonsignificant variant (nsPCa) and 9 with clinically significant variant (csPCa) of the disease and 12 patients with BPH. The comparison group included patients of the following subgroups: 102 patients with PCa, of which 23 with nsPCa, 79 with csPCa and 70 patients with BPH. In all patients MRI of the prostate (1.5 T) and biopsy were performed. Results. In patients treated with finasteride in both the subgroup with PCa and BPH, the mean ADC values were lower than in the corresponding comparison subgroups. At the same time, the statistical analysis did not reveal significant differences between the main and comparison subgroups of patients with PCa ($p > 0.05$) and between the respective subgroups of patients with nsPCa and csPCa ($p > 0.05$). In contrast, we observed significant differences between the mean values of ADC in subgroups of patients with BPH who did not receive and received finasteride treatment for lower urinary tract symptoms before MRI and biopsy: 1.16 ± 0.16 vs $0.84 \pm 0.12 \times 10^{-3}$ mm^2/s (<0.001). Conclusions. There is a link between administration of 5-ARI (finasteride) for symptoms of lower urinary tract and/or BPH, and values of ADC, which had a significant impact on the differential diagnosis between PCa and benign prostate disease using MRI.

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Introduction.

Prostate cancer (PCa) is the second most common diagnosis of malignancy in men. On average, about 1.1 million cases of PCa are diagnosed worldwide each year, which is 15% of all newly diagnosed cancers [1]. In addition, PCa is the second most common cause of death in men from cancer in the world [2]. The incidence of PCa in men aged 30-74 in Europe is growing by about 10-20% every 5 years, and in the USA - more than 25%[3]. The success of the treatment of PCa largely depends on the accurate diagnosis of this disease. With the introduction into clinical practice of active surveillance tactics in selected patients with very low and low risk PCa (ISPU 1, GS 6), accurate stratification into one group or another based on pre-op research methods is crucial to avoid over-treatment of patients in this category.[4-6]. However, given the above data and despite existing screening methods and diagnostic algorithms, the detection of PCa is still a serious and unresolved clinical problem.[7-9]. Significant shortcomings in the methods of diagnosis and screening of this pathology is a disease which in 44.7% of cases is detected in the late stages (III-IV), when radical treatment is no longer indicated [9]. In turn, overdiagnosis often leads to overt treatment of PCa, for example, when patients of very low and low risk (with a small localized tumor with a high degree of differentiation - 6 points on the Gleason scale) undergoes highly traumatic surgery with potentially disabling and minor complications [10]. According to numerous current studies, cross-sectional screening methods such as multidetector spiral contrast-enhanced CT and contrast-enhanced MRI play a leading role in the detection and local staging of cancer. High efficiency of MRI in local stage of PCa is proved: MRI had high accuracy of diagnosis of invasion of seminal vesicles according to histopathology data, which added value to clinical models of prediction based on Partin tables [11]. As previously demonstrated, apparent diffusion coefficient (ADC) of the of diffusion-weighted MRI images (DWI) is a valuable tool for non-invasive differential diagnosis of PCa with benign prostatic lesions [12]. It is known that treatment with 5-α-reductase inhibitors (5-ARI) for benign prostatic hyperplasia due to its mechanism of action has a significant effect on prostate tissue, causing apoptosis of epithelial cells, which leads to a decrease in prostate size, especially with prolonged use. In addition, according to recent data, finasteride has some effect on prostate vascularization [13.14]. In this context, an important and insufficiently studied issue is the impact on the detection and differentiation of PCa with potential imaging markers of MRI in patients previously treated with 5-ARI inhibitors for benign prostatic hyperplasia (BPH). Because, in clinical practice, it is not uncommon for a patient to be treated with 5-ARI for lower urinary tract symptoms and/or BPH before being diagnosed with PCa, it has been suggested that the use of these agents may affect ADC in prostate MRI and may be important in the detection and differential diagnosis of PCa.

Objectives.

To study the effect of 5-a-reductase inhibitor on the parameter of the ADC of MRI in the differential diagnosis of prostate cancer.

Material and methods.

Multiparametric MRI of the prostate was performed using a Signa HDxt 1.5T (General Electric®, USA) and an eight-channel coil based on Euroclinic medical centers (Lviv, Ukraine). Patients did not eat 5 hours before the examination. In the evening before the examination, a micro-enema (Microlax or similar) was used in all cases. Prostate PI-RADS version 2.1 recommended by the American College of Radiology and Clinical Guidelines was used to assess the results of prostate MRI. From the maps of diffusion-weighted images, which were automatically generated on the workstation, their quantitative parameter – ADC was calculated, which was used as a measure of diffusion of healthy and affected tissues. In total, the study involved 219 persons. In order to create the main group, the study included patients with histologically verified PCa and BPH, all patients before MRI and PBP were treated with 5-ARI - finasteride for lower urinary tract symptoms, 5 mg once daily for at least 4 months (average duration of treatment - 0.6 ± 0.9 years). We analyzed the indicators of ADC in subgroups of patients with PCa and BPH who were not treated with 5-ARI (comparison group), as well as in 15 healthy individuals without prostate pathology (control group). In the main group of patients when assessing the level of PSA used a factor of × 2, due to the ability of finasteride to reduce approximately 2 times the level of this marker. Baseline clinical data (mean age, mean prostate size, mean PSA levels after application of the coefficient) of the main and comparison groups were comparable and did not differ significantly. Thus, the main group receiving finasteride treatment included patients of the following subgroups: 20 patients with PCa, of which 11 with clinically nonsignificant variant (nsPCa) and 9 with clinically significant variant (csPCa) of the disease and 12 patients with BPH. The comparison group included patients of the following

subgroups: 102 patients with PCa, of which 23 with nsPCa, 79 with csPCa and 70 patients with BPH.

Results.

When analyzing the mean values of ADC in the studied groups and subgroups of patients, the following data were obtained: in patients treated with finasteride in both the subgroup with PCa and BPH, the mean ADC values were lower than in the corresponding comparison subgroups. At the same time, the statistical analysis did not reveal significant differences between the main and comparison subgroups of patients with PCa (p> 0.05) and between the respective subgroups of patients with nsPCa and csPCa (p> 0.05). In contrast, we observed significant differences between the mean values of ADC in subgroups of patients with BPH who did not receive and received finasteride treatment for lower urinary tract symptoms before MRI and biopsy: 1.16 ± 0.16 vs 0.84 ± 0.12× 10^{-3} mm^2/s (<0.001). Moreover, there were no significant differences in the mean values of ADC between the subgroups of patients with BPH who received 5-ARI, and subgroups of patients with nsPCa and csPCa who did not received finasteride (p>0.05), as well as with a subgroup of patients with nsPCa who received such treatment (p>0.05); at the same time, there was a significant difference in mean ADC values compared with the subgroup of patients with csPCa who received finasteride (p=0.001). It is especially important that the value of ADC of the suspicious areas of the prostate in patients with BPH who received treatment with 5-ARI to a large extent overlap with the indicators of ADC in patients with PCa, regardless of the use of finasteride. Given the above data, it should be noted that reducing the value of ADC under the influence of treatment 5-ARI in patients with BPH will increase the score when assessing a suspicious area of the prostate according to the PI-RADS system on diffusion-weighted MRI images, which in turn will increase the frequency of unnecessary biopsies. To avoid this, we should take into account the full range of patient clinical data, including the range of PSA-based markers, to determine the indications for biopsy. In addition, it was estimated that the mean value of ADC in the subgroup of BPH patients receiving finasteride was 27.59% lower, in the subgroup with BPH without such treatment, and the ratio between this indicator in these subgroups was 1.38 (1.66 / 0.84).

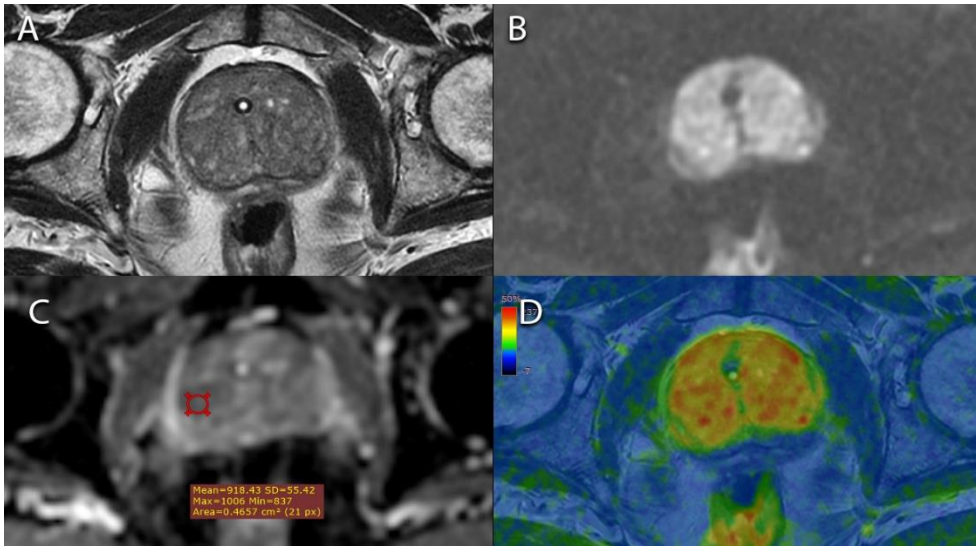

Figure 1. MRI of the prostate, axial images. A: T2-WW FRFSE; B: diffusion-weighted image (DWI), the areas of greatest restriction of diffusion have the brightest representation; C: ADC-map, ROI (red circle) is located above the zone of the greatest hypointensity of the MR signal, the ADC is 0.92 × 10^{-3} mm^2 / s; D: fusion map T2-WW and DWI, red color corresponds to the area of the greatest restriction of diffusion.

Discussion.

Our work was performed in order to study the effect of 5-a-reductase inhibitor on the parameter of the ADC of MRI in the differential diagnosis of prostate cancer. There is a lack of literature data on this topic. In a small study by Starobinets et al. (n = 17), it was reported that the increase in the homogeneity of prostate tissue in benign and malignant low-risk peripheral areas after administration of 5-ARI, reduced the variability of MR measurements after treatment. Discrimination of cancer was lower using T2-

weighted imaging, but was higher in functional MRI scores in the cohort receiving 5-ARI compared with controls, which contributed to the detection of PCa. However, a major drawback of this study was the lack of data on the transition zone of the prostate, the distinction of PCa in which is usually much more difficult compared to the peripheral zone, regardless of other factors [15]. In contrast, Kim et al. Demonstrated no such effect in the analysis of MRI data: there were no significant differences in the detection of PCa / csPCa between the 5-ARI and non-5-ARI groups (P> 0.05) [16]. In our study we found that there were no differences in the mean values of ADC between the subgroups of patients with BPH who received 5-ARI, and subgroups of patients with nsPCa and csPCa who did not received finasteride, as well as with a subgroup of patients with nsPCa who received such treatment; nevertheless, there was a significant difference in mean ADC values compared with the subgroup of patients with csPCa who received finasteride (p=0.001). We demonstrated the existence of a link between drug treatment with 5-ARI (finasteride) for symptoms of lower urinary tract and / or BPH, and values of ADC, which had a significant impact on the representation of prostate lesions on MRI images and hindered the differential diagnosis between PCa and benign prostate disease, due to the fact that the value of ADC suspicious areas of the prostate in patients with BPH who received treatment 5-ARI were superimposed with the indicators of ADC in patients with PCa, regardless of the intake of finasteride. To solve this problem, it is proposed to use a coefficient of × 1.38 when calculating the ADC value, which will allow to obtain a more accurate value of ADC for differential diagnosis with PCa.

Conclusions.

There is a link between administration of 5-ARI (finasteride) for symptoms of lower urinary tract and/or BPH, and values of ADC, which had a significant impact on the differential diagnosis between PCa and benign prostate disease using MRI.

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