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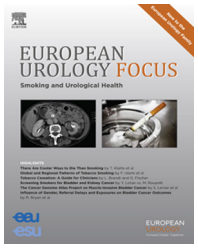

Prostate Cancer

Preliminary Diagnostic Accuracy of Multiparametric Magnetic Resonance Imaging to Detect Residual Prostate Cancer Following Focal Therapy with Irreversible Electroporation

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Abstract

Background: It is recommended to perform multiparametric magnetic resonance imaging (mpMRI) in the follow-up following focal therapy of prostate cancer (PCa).
Objective: To determine the diagnostic accuracy of mpMRI to detect residual PCa following focal therapy with irreversible electroporation.
Design, setting, and participants: Seventy-six patients with biopsy-proven localized PCa consented for primary irreversible electroporation between February 2013 and March 2016. Final analysis was performed on 50 patients that received follow-up mpMRI at 6 mo, serial prostate-specific antigen (PSA) testing, and transperineal template-mapping biopsies at 12 mo.
Outcome measurements and statistical analysis: Outfield regions of interest (ROI) were reported using PI-RADS version 2. A binary outcome (suspicious vs nonsuspicious) was given for the infield ablation zone. Sensitivity, specificity, positive predictive values, and negative predictive values were calculated for different definitions of significant PCa: (1) Gleason $\geq$4 + 3 or Gleason $\geq$3 + 3 with a maximum cancer core length $\geq$6 mm, (2) Gleason $\geq$3 + 4 or Gleason $\geq$3 + 3 with a maximum cancer core length $\geq$4 mm, for outfield and infield ROI. Multivariate linear regression analyses evaluated the additional value of nadir PSA.
Results and limitations: Sensitivity, specificity, positive predictive values, and negative predictive values of infield ROI was 43%, 86%, 33%, and 90% for definition 1 and 38%, 86%, 33%, and 88% for definition 2, respectively. For outfield ROI this was 33%, 82%, 20%, and 90% for definition 1 and 38%, 86%, 50%, and 80% for definition 2. PSA had no additional value in predicting residual significant PCa. Limitations include retrospective design, single reader, and low incidence of residual PCa.
Conclusions: Our preliminary data suggest that mpMRI can rule out high-volume residual PCa. However, follow-up biopsies should still be performed to determine oncological control.
Patient summary: Multiparametric magnetic resonance imaging is able to detect high-volume significant prostate cancer following focal therapy. Prostate biopsies are still required in the follow-up of focal therapy as (low-volume) significant prostate cancer is being missed by multiparametric magnetic resonance imaging.

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1. Introduction

Focal therapy is gaining traction as prostate cancer (PCa) treatment for carefully selected patients with localized disease [1]. A variety of focal ablative modalities are available, including irreversible electroporation (IRE) [1]. IRE ablates tumorous tissue by applying a direct current between two or more needle electrode pairs [2]. When the cell membrane is exposed to multiple consecutive electrical pulses, membrane instability and permeability is induced causing subsequent cell death [3]. Initial phase 1–2 trials have demonstrated the safety and feasibility of IRE for focal therapy in localized PCa [4–8].

Adequate PCa localization is the cornerstone for lesion-based ablative therapy. Multiparametric magnetic resonance imaging (mpMRI) of the prostate is the leading imaging modality to provide clinicians with information on lesion location and geometry. Consensus guidelines on the use of mpMRI with focal therapy recommend to perform mpMRI both for treatment planning and follow-up [9]. The diagnostic accuracy of mpMRI of PCa localization and diagnosis has been extensively evaluated in the past years. Among the studies [10] evaluating the PCa diagnostic value of mpMRI, the recently published PROMIS trial [11] showed a superior PCa detection rate of mpMRI over standard transrectal prostate biopsies in biopsy-naive patients, validated by use of transperineal template mapping biopsies (TTMB). The growing evidence for mpMRI in PCa care resulted in the application of mpMRI throughout focal therapy protocols. The follow-up of some trials even deferred standardized follow-up prostate biopsies, relying entirely on the diagnostic accuracy of mpMRI to detect residual PCa [12]. However, except for the study by Dickinson et al [13], no diagnostic accuracy studies have been published on mpMRI in the follow-up of focal therapy. These authors evaluated the diagnostic accuracy of prostate-specific antigen (PSA) and mpMRI for detection of infield (ie, prostate region previously ablated) residual PCa only, using targeted biopsy data (median 6 cores) from three different trials [13].

In order to advance the field of focal therapy, validation of the follow-up mpMRI needs to be achieved including both infield and outfield (ie, prostate tissue previously not ablated). Therefore, we aimed to determine the diagnostic accuracy of mpMRI to detect residual PCa following focal therapy with IRE.

2. Materials and methods

2.1. Ethical approval

Institutional review board approval was obtained from the Human Research Ethics Committee to acquire and analyze oncologic data (Human Research Ethics Committee approval: SVH 16/110). Written informed consent was obtained from all patients to perform focal IRE treatment and follow-up studies.

2.2. Study design and participants

Retrospective analysis of prospectively acquired data was performed on patients that underwent IRE for biopsy-proven, treatment-naïve localized PCa between February 2013 and March 2016. Preoperative diagnosis and disease localization were performed using PSA, mpMRI (in all patients), and transrectal prostate biopsies or TTMB. Treatment planning was based on biopsy and mpMRI results. Following IRE, patients underwent serial PSA testing, mpMRI (6 mo), and TTMB (~12 mo) as part of our institutional protocol following the consensus guidelines on trial design [14]. Patients that received both follow-up mpMRI and TTMB were included for final retrospective interpretation of prospectively acquired data (Fig. 1) following the Standards for Reporting Diagnostic accuracy studies [15].

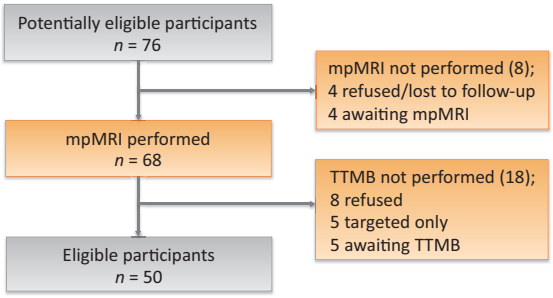

Fig. 1 – Inclusion flowchart of patients included for final analysis. mpMRI = multiparametric magnetic resonance imaging; TTMB = transperineal template mapping biopsies.

2.3. Study procedures

2.3.1. Irreversible electroporation

All patients were positioned in the lithotomy position under general anesthesia and deep-muscle paralysis. An indwelling catheter was placed to drain the bladder. Biplanar transrectal ultrasound (TRUS; BK Medical, Herlev, Denmark) and a template grid were used to place four to six electrode needles via the perineum to surround the PCa lesion. A 5–10-mm safety margin was applied surrounding the targeted lesion, which was based on biopsy and pretreatment mpMRI. The active tip length varied between 1 cm and 2 cm. The interelectrode distance was measured using TRUS and entered into the Nanoknife system (AngioDynamics, New York, NY, USA). Ten pulses were delivered to test the obtained direct current. The remaining 80 treatment pulses were delivered if the achieved current levels were appropriate (20–40 A). Patients underwent a trial of void either at 2 d or 5 d following IRE, depending on pre-existing lower urinary tract symptoms.

2.3.2. mpMRI

The index test used for this study was mpMRI, which was executed following the recommendations of the Prostate Imaging and Reporting and Data System (PI-RADS) Steering Committee (first and second version) [16]. The majority of patients had their follow-up mpMRI (43/50, 86%) done in a single center of expertise. Central review was done by an experienced radiologist for the remaining scans that were performed elsewhere (7/50, 14%). The radiologist was blinded to histopathology, had access to pretreatment biopsy, mpMRI and PSA data, and has reported more than 5000 mpMRIs (RS). All scans were performed on a 3.0 Tesla magnet, including T2-weighted, dynamic contrast enhanced (DCE), and diffusion weighted imaging (DWI; b-value 0, 800 s/mm^2, and 1500 s/mm^2), with the use of a cardiac coil. All mpMRIs were reported according to PI-RADS version 2 [16], using the standardized 5-point PI-RADS by lesion location to report the likelihood of significant PCa in untreated prostate tissue (ie, outfield). PI-RADS 3–5 was classified as significant disease and evaluated separately. Both treated prostate tissue (ie, infield) and adjacent regions of interest (ROI) were reported as part of the "infield region," as the original ablation zone is often not clearly defined at 6 mo

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