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Original article

Multiparametric magnetic resonance imaging vs. standard care in men being evaluated for prostate cancer: A randomized study

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Abstract

Objectives: To assess whether the proportion of men with clinically significant prostate cancer (PCa) is higher among men randomized to multiparametric magnetic resonance imaging (mp-MRI)/biopsy vs. those randomized to transrectal ultrasound (TRUS)-guided biopsy.

Methods: In total, 1,140 patients with symptoms highly suggestive of PCa were enrolled and divided in 2 groups of 570 patients to follow 2 different diagnostic algorithms. Group A underwent a TRUS-guided random biopsy. Group B underwent an mp-MRI and a TRUS-guided targeted + random biopsy. The accuracy of mp-MRI in the diagnosis of PCa was calculated using prostatectomy as the standard of reference.

Results: In group A, PCa was detected in 215 patients. The remaining 355 patients underwent an mp-MRI: the findings were positive in 208 and unremarkable in 147 patients. After the second random + targeted biopsy, PCa was detected in 186 of the 208 patients. In group B, 440 patients had positive findings on mp-MRI, and PCa was detected in 417 at first biopsy; 130 group B patients had unremarkable findings on both mp-MRI and biopsy. In the 130 group B patients with unremarkable findings on mp-MRI and biopsy, a PCa Gleason score of 6 or precancerous lesions were detected after saturation biopsy. mp-MRI showed an accuracy of 97% for the diagnosis of PCa.

Conclusions: The proportion of men with clinically significant PCa is higher among those randomized to mp-MRI/biopsy vs. those randomized to TRUS-guided biopsy; moreover, mp-MRI is a very reliable tool to identify patients to schedule in active surveillance.

Keywords: Magnetic resonance imaging; Prostate cancer; Biopsy; Ultrasonography; Prostate-specific antigen

1. Introduction

Prostate cancer (PCa) is the most commonly diagnosed cancer in men and the second cause of cancer-related death in men. The detection of PCa is traditionally based on digital rectal examination (DRE), serum prostate-specific antigen (PSA) level, and transrectal ultrasound (TRUS)–guided biopsies [1]. However, DRE fails to detect a substantial proportion of cancers and identifies predominantly large tumors and in a more advanced pathologic stage [2]. PSA level has a poor specificity (Spe) and a low positive predictive value (PPV), because benign conditions can cause an increase in serum PSA levels. TRUS is currently considered inadequate for diagnosing PCa, as at least 40% of neoplastic foci are isoechoic when compared with the surrounding parenchyma [3]. TRUS-guided biopsy, with 6- to 12-core sampling, 1 to 2 for each sextant, has been the diagnostic standard for PCa for many years. Because up to 30% of cancers are missed when performing sextant biopsies and 23% of those are high-risk PCas, the method has been extended to 45 cores for saturation biopsies [3-6]. Nevertheless, it does not solve

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the problem because of increased costs, complications, and a small but significant risk of missing high-grade cancer [4]. Patients with a suspected false-negative result on biopsy are a diagnostic challenge, because there is a progressively lower diagnostic yield from subsequent prostate biopsies. Second, third, and fourth rebiopsies are reported to detect cancer in only 25% to 27%, 5% to 24%, and 4% to 21% of cases, respectively. Furthermore, as PCa is multifocal in 85% of cases, TRUS biopsy may underestimate the extent and grade of cancer, which can result in Gleason upgrading after prostatectomy [7].

In summary, PSA levels, DRE, and TRUS-guided biopsy do not have the ability to correctly localize and stage PCa and to determine its volume and aggressiveness.

Currently, urologists use nomograms for decision making in the management of PCa. PSA levels, DRE, and TRUS-guided biopsy are the input for PCa nomograms, but these parameters are fairly imperfect [1,4]. There is a real need for clinicians to base therapeutic decisions not only on nomograms but also on advanced imaging findings.

Recently, a great interest has been shown for multiparametric magnetic resonance imaging (mp-MRI), which is an advanced diagnostic technique able to identify focal areas suggestive of PCa that could be considered as potential sites for targeted biopsies [3].

In this context, the aim of this study was to validate the role of mp-MRI as a first-line tool in the diagnostic examination of patients with symptoms highly suggestive of PCa to assess whether the proportion of men with clinically significant PCa is higher among those randomized to mp-MRI/biopsy vs. those randomized to TRUS-guided biopsy.

2. Materials and methods

2.1. Patient population and study design

This prospective study was approved by the local Ethics Committee, and all patients gave written informed consent.

In total, 1,140 consecutive male patients with any performance status and without any age limitation (average age of 64 y, age range: 51–82 y), with symptoms highly suggestive of PCa, who were referred to our institution from October 2011 to March 2014, were enrolled in the study. The following were the inclusion criteria:

(a) Total PSA level >4 ng/ml
(b) PSA density >0.15
(c) PSA velocity >0.75 ng/ml/y
(d) Free/total PSA ratio <0.10 when total PSA level was between 4 and 10 ng/ml.

The patients needed to meet all the 4 inclusion criteria to be included in the study.

Patients who previously underwent a prostate biopsy were excluded from the study.

The patient population was divided randomly in 2 groups to follow 2 different diagnostic algorithms. Group A included 570 patients who underwent a TRUS-guided biopsy according to a standard random scheme. Group B included 570 patients who first underwent an mp-MRI examination and, subsequently, underwent a TRUS-guided biopsy: if a suspicious lesion was detected on mp-MRI, the patient was referred to a targeted + random biopsy, otherwise if the finding on mp-MRI was unremarkable, the patient underwent a random standard biopsy. Group A patients with unremarkable findings on the first biopsy underwent an mp-MRI examination and subsequently a second TRUS-guided biopsy: if a suspicious lesion was depicted on mp-MRI, a targeted + random biopsy was performed, and if the finding on mp-MRI was unremarkable, the patient underwent a TRUS-guided biopsy with a saturation method. In group B, in patients with unremarkable findings for PCa at first biopsy, a TRUS-guided biopsy with a saturation technique was performed.

The patients who were successfully diagnosed for PCa underwent therapy according to their personal preferences and the European Association of Urology guidelines.

2.2. MR equipment and image acquisition protocol

MRI of the pelvis, focused on the prostate gland, was performed using a 3-T magnet (Discovery MR750, GE Healthcare, Milwaukee, and MAGNETOM Verio Siemens Medical Solutions) equipped with a phased-array coil and an endorectal coil. The MRI protocol included the following sequences:

T2-weighted (T2w) turbo spin-echo sequences (repetition time [TR], 4,500 ms; echo time [TE] 110 ms; thickness, 3 mm; and matrix, 352 × 352) in axial, sagittal, and coronal planes.

Diffusion-weighted imaging (DWI) sequences: slice thickness, 3 mm; TR, 3,100 ms; TE, 102 ms; and exponential b values of 0, 500, 1,000, and 3,000 s/mm^2.

Dynamic contrast-enhanced (DCE) MRI was obtained using a gradient-echo T1-weighted sequence in axial planes (TR, 3 ms; TE, 2 ms; thickness, 3 mm; time resolution, 12 sections/3 s; and matrix, 320 × 192).

The diagnostic accuracy of each technique alone and in combination with the others was evaluated.

2.3. Analysis of MR images

The images were evaluated in consensus by 2 genitourinary radiologists, with 13 and 4 years of experience, blinded to blood test results.

Each MRI technique (T2w, DWI, and DCE) was assessed relying on the prostate imaging reporting and data system (PI-RADS) score [8].