European Journal of Radiology 98 (2018) 107–112

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Research article

Seminal vesicle invasion on multi-parametric magnetic resonance imaging: Correlation with histopathology

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ARTICLE INFO

Keywords:
Prostate cancer
Magnetic resonance imaging
Tumor staging

ABSTRACT

Objectives: The pre-treatment risk of seminal vesicle (SV) invasion (SVI) from prostate cancer is currently based on nomograms which include clinical stage (cT), Gleason score (GS) and prostate-specific antigen (PSA). The aim of our study was to evaluate the staging accuracy of 3 T (3T) multi-parametric (mp) Magnetic Resonance Imaging (MRI) by comparing the imaging report of SVI with the tissue histopathology. The additional value in the existing prediction models and the role of radiologists' experience were also examined.

Methods: After obtaining institutional review board approval, we retrospectively reviewed clinico-pathological data from 527 patients who underwent a robot-assisted radical prostatectomy (RARP) between January 2012 and March 2015. Preoperative prostate imaging with an endorectal 3T-mp-MRI was performed in all patients. Sequences consisted of an axial pre-contrast T1 sequence, three orthogonally-oriented T2 sequences, axial diffusion weighted and dynamic contrast-enhanced sequences. We considered SVI in case of low-signal intensity in the SV on T2-weighted sequences or apparent mass while diffusion-weighted and DCE sequences were used to confirm findings on T2. Whole-mount section pathology was performed in all patients. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of MRI (index test) for the prediction of histological SVI (reference standard) were calculated. We developed logistic multivariable regression models including: clinical variables (PSA, cT, percentage of involved cores/total cores, primary GS 4–5) and Partin table estimates. MRI results (negative/positive exam) were then added in the models and the multivariate modeling was reassessed. In order to assess the extent of SVI and the reason for mismatch with pathology an MRI-review from an expert genitourinary radiologist was performed in a subgroup of 379 patients.

Results: A total of 54 patients (10%) were found to have SVI on RARP-histopathology. In the overall cohort sensitivity, specificity, PPV and NPV for SVI detection on MRI were 75.9%, 94.7%, 62% and 97% respectively. Based on our sub-analysis, the radiologist's expertise improved the accuracy demonstrating a sensitivity, specificity, PPV and NPV of 85.4%, 95.6%, 70.0% and 98.2%, respectively. In the multivariate analysis PSA (odds ratio [OR] 1.07, $p = 0.008$), primary GS 4 or 5 (OR 3.671, $p = 0.007$) and Partin estimates (OR 1.07, $p = 0.023$) were significant predictors of SVI. When MRI results were added to the analysis, a highly significant prediction of SVI was observed (OR 45.9, $p < 0.0001$). Comparing Partin, MRI and Partin with MRI predictive models, the areas under the curve were 0.837, 0.884 and 0.929, respectively.

Conclusions: MRI had high diagnostic accuracy for SVI on histopathology. It provided added diagnostic value to clinical/Partin based SVI-prediction models alone. A key factor is radiologist's experience, though no inter-observer variability could be examined due to the availability of a single expert radiologist.

Abbreviations: AUC, area under the curve; cT, clinical stage; CI, confidence interval; DCE, dynamic contrast-enhanced; EBRT, external beam radiotherapy; ECE, extracapsular extension; GS, gleason score; GU, genito-urinary; mp, multi-parametric; MRI, magnetic resonance imaging; NPV, negative predictive value; OR, odds ratio; PCa, prostate cancer; PPV, positive predictive value; PSA, prostate-specific antigen; RARP, robot-assisted radical prostatectomy; ROC, receiver operating curves; SV, seminal vesicle; SVI, seminal vesicle invasion 3T 3 tesla

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https://doi.org/10.1016/j.ejrad.2017.11.013
Received 25 September 2017; Received in revised form 11 November 2017; Accepted 17 November 2017

1. Introduction

Accurate prostate cancer (PCa) staging is critical in guiding a patient's treatment decision and it could prevent both under- and over-treatment. In case of suspected extracapsular extension (ECE) or seminal vesicle (SV) invasion (SVI) patients are usually not offered a radical prostatectomy due to the risk of irradical resection while brachytherapy is not an option due to the risk of under-dosage to the SV. In patients with suspected SVI who are treated with external beam radiotherapy (EBRT) the radiation field is recommended to include the base of the seminal vesicles [1]. However, this extended field will also increase the irradiated volume of rectal and bladder wall, affecting the complication rate as well.

Pre-treatment risk of SVI is currently based on prediction models, such as the Kattan nomogram [2] and the Partin tables [3]. In addition, patients are stratified into risk-groups [4], according to the clinical T stage (cT), Gleason score (GS) and prostate-specific antigen (PSA). Local staging with multiparametric (mp)-Magnetic Resonance Imaging (MRI) has become widely available and provides new diagnostic means to assess the local extent of prostate tumours. In the literature a wide range of sensitivity and specificity [5] for the detection of SVI is reported, mainly attributed to differences in technique, such as MR field-strength, coil-type and variation in radiologist's' experience [6].

We hypothesized that with contemporary, state of the art, high-quality mp-MRI and an experienced, dedicated genito-urinary (GU) radiologist, SVI can be detected accurately. The aim of our study was to evaluate the staging accuracy of 3 T (3T) multi-parametric (mp) magnetic resonance imaging (MRI) by comparing the imaging report of SVI with the tissue histopathology. The additional value in the existing prediction models and the role of radiologists' experience were also examined.

2. Materials and methods

2.1. Patient population

We performed a retrospective, single-institution cohort study. Institutional Review Board approval was obtained for the study, while the requirement for informed consent was waived. Between January 2012 and March 2015, a total of 688 patients with biopsy-proven primary prostate PCa were treated with a Robot Assisted Radical Prostatectomy (RARP) using the da Vinci S(i) Surgical system (Intuitive Surgical Inc., Sunnyvale, CA,USA). After excluding 37 patients who did not have a preoperative MRI and 123 patients with MRIs performed in other hospitals, the final study population consisted of 527 patients. Information on pathology and radiology were retrospectively collected from the electronic patient information system (Ezis, Chipsoft, Amsterdam, the Netherlands). Patient clinical and pathological data were entered into a prospective database at the time of diagnosis.

2.2. MRI technique

All patients were pre-operatively staged with an endorectal coil mp-3T MRI (Achieva, Philips). Sequences (Supplementary Table 1) consisted of an axial pre-contrast T1 sequence, three orthogonally-oriented T2 sequences, axial diffusion weighted and dynamic contrast-enhanced (DCE) sequences (using Dotarem, Guebet, France). We considered SVI in case of low-signal intensity in the SV on T2-weighted sequences or apparent mass while diffusion-weighted and DCE sequences were used to confirm findings on T2 (Fig. 1). Pre-contrast T1 images were used to exclude hematoma.

At the time of inclusion, MRIs were reported by a number of different radiologists, with varying experience in GU imaging. However, the majority of all scans (72%) were reported by one expert GU radiologist (SWH) with > 10 years of experience in reporting prostate MRI.

2.3. Pathology analysis and staging

Whole-mount section pathology was performed in all patients. The base of the SV was available in all specimens. Staging was done according to the 2009 TNM classification for staging of prostate cancer [7] based on the cT, GS and PSA. SVI was defined as cancer invasion into the extraprostatic portion of the seminal vesicles [8]. Risk group stratification was performed according to Ash et al. [4] into low risk ($\leq$cT2a, GS: 6, PSA < 10 ng/ml), intermediate risk (cT2b–T2c, GS: 7, PSA 10–20 ng/ml) and high risk (two or three intermediate risk-criteria and any combination of cT3, GS $\geq$8 or PSA > 20 ng/ml). Clinical characteristics were additionally entered into the most recent version of the Partin nomogram [9], based on patients treated from 2006 to 2011.

2.4. Subgroup analyses

In order to assess the extent of SVI and the reason for mismatch with pathology, a subgroup analysis was performed based solely on the MRI-reports from an expert GU radiologist (SH). Another analysis was done based on the revision results of 77 pathology specimens from an expert GU pathologist (JdeJ). The extent of SVI on pathology revision was scored ranging from small to large based on an extension length of 1 cm as cut-off. Finally, we examined whether the seminal vesicle lesion showed continuous growth, originating from the prostate tumor.

2.5. Statistical analysis

Baseline descriptive statistics were used to present demographics, tumor and MRI data. Only patients with complete data were included in the analysis. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of MRI (index test) for the diagnosis of histological SVI (reference standard) were calculated. We additionally developed logistic multivariable regression models including: clinical variables (PSA, cT, percentage of involved cores/total cores, primary GS 4–5) and Partin Table estimates. MRI results (negative/positive exam) were then added to the model and the multivariate modeling was reassessed. The predictive ability of each model was compared by receiver operating characteristic (ROC) curves based on the area under the curve (AUC) before and after the addition of MRI information to each model. In addition, a decision curve analysis was performed to evaluate and compare the net benefit for each model. A p value < 0.05 was considered significant. Statistical analysis was performed using the statistical package of social sciences (SPSS) version 22.0 (SPSS, Chicago, IL) and the R statistical package (R Foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1. Overall cohort

Patient's baseline clinical and pathological characteristics are presented in Table 1. 54 patients (10%) had SVI on pathology, whereas 67 patients (13%) were diagnosed with suspected SVI based on MRI. Based on the correlation of pre-operative MRI with pathology the sensitivity, specificity, PPV and NPV of MRI was 75.9%, 94.7%, 62% and 97%, respectively (Table 2).

When stratifying patients into risk groups (Table 3), according to the MRI-cT stage, a strong correlation (p < 0.0001) was found between high risk prostate cancer and SVI, with only 3 (0.05%) patients in the low and intermediate risk groups having SVI. However, the high risk group consisted of 67% of all patients and therefore high risk as a diagnostic criterion would have a PPV of only 14.6%. Based on Partin risk stratification with a 15% cut-off risk of SVI, as most often used in clinical practice, 34.7% of all patients would have been included in the increased SVI risk group with a sensitivity, specificity, NPV and PPV of 83.3%, 70.8%, 24,6% and 97.4% for the clinical prediction.