Prostate MRI to Evaluate Extra-Prostatic Disease: A Single Center Analysis

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Abstract
Introduction: To examine the use of prostate magnetic resonance imaging (MRI) for staging after a new diagnosis of prostate cancer in our hospital system. There are no universally accepted recommendations to guide the use of MRI for staging purposes. In practice, prostate MRI is used to help distinguish T2 and T3 cancer. Prostate MRI is a modality that could aid in the triage of patients to radical prostatectomy or non-surgical treatments via accurate identification of organ-confined disease.

Materials and Methods: We performed a retrospective review of prostate cancer patients who underwent staging MRI with 1.5T MRI with endorectal (ER) coil. We compared patient characteristics in patients who underwent surgery and those who did not, and used pathology reports from prostatectomy samples to calculate the negative predictive value (NPV) for extra-capsular extension (ECE) and seminal vesicle invasion (SVI).

Results: We found that patients who underwent radical prostatectomy were younger, had lower Gleason scores, and had lower PSA values at diagnosis than patients who were not treated surgically. We calculated a NPV of 93.7% for SVI and 69.5% for ECE. We found variation in rates of accurate identification of T3 prostate cancer across the seven radiologists who interpreted MRI images in our study.

Conclusions: 1.5T MRI with ER coil has a high NPV for SVI and a lower NPV for ECE. The utilization of 3T MRI may enable practitioners to more confidently rule out ECE. Future studies will be necessary to generate guidelines for use of MRI in prostate cancer staging.

Introduction

Prostate cancer is the most common male cancer in the United States⁴. Patients are often diagnosed at an early stage without symptoms. These patients generally have a prolonged disease course⁵. However, prostate cancer is a very heterogeneous disease, ranging from indolent to highly aggressive in nature, which emphasizes the importance of reliable risk stratification methods⁶. The most commonly used screening test remains the serum prostate-specific antigen (PSA), despite recent recommendations narrowing its use⁷. The diagnostic algorithm downstream of a positive PSA test is constantly evolving, but one well-accepted triage tool is the use of nomograms to predict ECE, SVI, and lymph node involvement⁸. In patients with cT3 or cT4 disease or for those patients with a greater than 10% likelihood of lymph node involvement by nomogram, the current National Comprehensive Cancer Network (NCCN) guidelines provide a category 2A recommendation for MRI for local staging⁹. In practice, the use of imaging in prostate cancer detection and staging extends beyond this recommendation, due to the reality that clinical assessment may underestimate local stage in 40-60% of cases⁷.

There is wide variation in the employment and acceptance of MRI as a staging tool⁸. One factor complicating the generation of high-level evidence for the use of MRI is the rapid advancement of MRI hardware and analysis techniques. MRI with ER coil was validated in the 1980’s; more recently, centers have been using higher field strength magnets (3T) as well as multi parametric analysis including diffusion weighted imaging and dynamic contrast-enhanced imaging⁹. The utilization of different MRI imaging techniques may have contributed to the wide variability in reporting the sensitivity, specificity, and predictive values of MRI for staging purposes⁹.

The ability of MRI to detect ECE has been reported with sensitivities ranging between 23 to 91% and specificities ranging between 84 to 97%¹⁰. One study reported a positive predictive value of 79% and a negative predictive value of 91% for ECE with 3T MRI with ER coil¹¹. Similar studies have been performed to evaluate MRI for the detection of SVI, reporting sensitivities ranging between 25 to 100% and specificities of 62 to 99%. Positive predictive values have been reported ranging between 20 to 83%, and negative predictive values range between 79 to 96%¹². The majority of these data were generated from large tertiary-care centers.

Keywords: Prostate Cancer; Extra-capsular extension; Seminal vesicle invasion; Magnetic Resonance Imaging (MRI)


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Materials and Methods

Patients

After approval by Rhode Island Hospital’s Institutional Review Board and receipt of a waiver for informed consent, we collected retrospective data for patients with biopsy-proven prostate cancer who underwent prostate MRI for staging between 2005 and 2010. We identified the subset of patients whom subsequently underwent radical prostatectomy in the Alpert Medical School of Brown University hospital system and whose post-prostatectomy pathology records were available for review. Patients were excluded from our final analysis if prostate MRI was ordered for an indication other than prostate cancer, prostate MRI was performed for restaging after biochemical relapse, or if the patient was enrolled in a clinical trial.

MRI Technique and Interpretation

All prostate MRI examinations were performed on a 1.5-T system (Signa Excite, GE Healthcare) with a gradient strength of 120mT/m and using both a pelvic phased-array coil and balloon-covered expandable endorectal coil. Glucagon, 1mg, was administered subcutaneously immediately before the start of the examination. All patients were imaged in the supine position. After the acquisition of localizing images, sagittal T2-weighted single shot fast spin-echo imaging through the pelvis was performed to confirm the position of the endorectal coil. Axial, coronal, and sagittal thin-section, high-spatial-resolution T2-weighted fast spin-echo (FSE) images through the prostate and seminal vesicles were obtained using the following parameters: TR range, 3,000–4,000 milliseconds; TE, 120 milliseconds; echo-train length, 16; field of view (FOV), 12cm; section thickness, 3mm; intersection gap, 0 mm; matrix, 256 × 192; and number of excitations (NEX), 4. Transverse axial T1-weighted spoiled gradient-echo images with a TR/TE of 325/4.2 and all other parameters matched to the axial high-resolution T2-weighted FSE sequence were obtained. Transverse axial T1-weighted spoiled gradient-echo images were also obtained from the aortic bifurcation to the symphysis pubis using the following parameters: 100/4.2; FOV, 38cm; section thickness, 5mm; intersection gap, 1mm; matrix, 256 × 192; and NEX, 1. DWI was performed using a single-shot echo planar imaging technique with a TR of 3,000 milliseconds and a minimum TE; FOV, 18cm; section thickness, 3mm; intersection gap, 0mm; matrix, 128 × 128; NEX, 6; ADC values were obtained from the DWI sequences performed with b values of 0 and 1,000 s/mm², and the ADC maps were generated by calculating the ADC value in each pixel of each slice. Seven radiologists, who were not blinded to the patients’ clinical characteristics, interpreted MRI images.

Statistical Analysis

Descriptive statistics were used to compare patient characteristics using simple t-tests. A p-value ≤ 0.05 was considered significant. Data for ECE and SVI were tabulated as binary variables (0 for absence of ECE or SVI, 1 for presence of ECE or SVI) and summary statistics were generated via two-by-two tables[13]. Pearson’s (chi)² analysis was performed to test for variance across MRI interpretation accuracy rates. All statistical analyses were performed with Med Calc software, version 12 (Ostend, Belgium).

Results

We identified 277 patients with prostate cancer who underwent prostate MRI between 2005 and 2010 whose medical records were under the purview of our IRB. We found that 75% of MRIs were ordered by urologists (n=207, 7 different providers), 15% of MRIs were ordered by radiation oncologists (n=41, 3 different providers), and 10% of MRIs were ordered by medical oncologists (n=29, 2 different providers). 129 patients underwent radical prostatectomy. Sixty-eight patients did not proceed to surgery, 12 patients were enrolled in a clinical trial, and 68 patients underwent MRI for restaging purposes. Pathology results from prostatectomy samples were used as the gold standard test in our analysis. We found that patients who underwent surgery were younger (61 vs. 67.2 years old), had lower Gleason scores (average score 7 vs. 7.5), and had lower average PSA values (6.08ng/mL vs. 15ng/mL) at the time of diagnosis (Table 1). Using pathology reports, we calculated the negative predictive value of MRI for SVI and ECE. We found that 1.5 T MRI with ER coil had a negative predictive value of 93.7% (95%CI 87.9% to 97.2) when evaluating for SVI, and a negative predictive value of 69.5% (95% CI 60.34 – 77.6) when evaluating for ECE.

Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Group</th>
<th>No Surgery (n=129)</th>
<th>Surgery (n=68)</th>
<th>t-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>n 129</td>
<td>68</td>
<td>p&lt;0.0001</td>
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<tr>
<td>Mean</td>
<td>61</td>
<td>67.2</td>
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</tr>
<tr>
<td>Range</td>
<td>44-75</td>
<td>48-92</td>
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<tr>
<td>Gleason Score</td>
<td>n 111</td>
<td>58</td>
<td>p=0.0006</td>
</tr>
<tr>
<td>Mean</td>
<td>6.99</td>
<td>7.47</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>6-9</td>
<td>6-9</td>
<td></td>
</tr>
<tr>
<td>PSA (ng/mL)</td>
<td>n 86</td>
<td>54</td>
<td>p=0.008</td>
</tr>
<tr>
<td>Mean</td>
<td>6.08</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>1.78 - 27</td>
<td>0.7 - 161.8</td>
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</tr>
</tbody>
</table>

We found significant variation in the accurate identification of ECE and SVI between radiologists, ranging from 0% accurate (of 3 prostate MRIs included in our study, with total of 20 interpreted during the study time period) to 92.3% accurate (13 prostate MRIs included in our study, with total of 45 interpreted during the study time period, p=0.012) (Figure 1).The rate of accurate identification of ECE or SVI did not correlate to the number of MRIs interpreted during the study period. Eight cases of seminal vesicle invasion identified by pathologic analysis were not identified by MRI analysis. Thirty-six cases of ECE seen on pathology were not identified by MRI, and 3 cases of ECE were reported in the MRI interpretation, but not present on pathologic analysis (Table 2). Overall, there were zero false positive interpretations of SVI and three false positive interpretations of ECE.
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present on initial biopsy. The absence of ECE on MRI is not yet nerve sparing procedures for intermediate- and high-risk disease ECE, the continued practice in our system is to perform non-period of our study. Given the significant false negative rate for variation in accuracy between radiologists, which did not cor-pelling NPV for ruling out T3a disease. We also demonstrate a false-negative reporting of ECE, which resulted in a less com-tomy. The most frequent inaccuracy in our study was the high for SVI, which can aid in triaging patients to radical prostatec-

Table 2. False positive and false negative interpretations for ECE and SVI

<table>
<thead>
<tr>
<th>Radiologist</th>
<th>Interpretation</th>
<th>ECE</th>
<th>SVI</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>False [+]</td>
<td>False [-]</td>
<td>False [+]</td>
</tr>
<tr>
<td>1</td>
<td>-</td>
<td>3</td>
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<td>-</td>
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</tr>
<tr>
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<td>1</td>
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<tr>
<td>6</td>
<td>-</td>
<td>7</td>
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</tr>
<tr>
<td>7</td>
<td>1</td>
<td>8</td>
<td>-</td>
</tr>
</tbody>
</table>

Discussion

In 2013, the American Cancer Society estimated 238,590 new diagnoses of prostate cancer, and 29,720 deaths from prostate cancer. The high prevalence and frequent diagnos-

References

3. Roobol, M.J., Carlsson, S.V. Risk stratification in prostate cancer staging can provide a good negative predictive value (NPV) for SVI, which can aid in triaging patients to radical prostatec-