Preoperative T Staging of Urinary Bladder Cancer: Efficacy of Stalk Detection and Diagnostic Performance of Diffusion-weighted Imaging at 3T

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(Received October 21, 2013; Accepted January 29, 2014; published online July 2, 2014)

Purpose: We evaluated the ability of diffusion-weighted imaging (DWI) at 3 tesla for diagnosing T stage and detecting stalks in bladder cancer.

Methods: In total, 39 consecutive patients with bladder tumors underwent magnetic resonance (MR) imaging that included T2-weighted imaging (T2WI) and DWI using a 3T MR scanner. Two radiologists interpreted T2WI plus DWI and T2WI for diagnosis of T stage and for detection of stalks. We used McNemar’s test to examine differences in diagnostic performance and Fisher’s exact test to evaluate differences in stalk detection frequency.

Results: Specificity and accuracy in differentiating T1 tumors from T2 to T4 tumors were significantly better with T2WI plus DWI (83% [20/24] and 85% [33/39]) than T2WI (50% [12/24] and 67% [26/39]; P = 0.02), and accuracy for diagnosing tumor stage was significantly better with T2WI plus DWI (82% [32/39]) than T2WI alone (59% [23/39]; P = 0.03). The observers identified stalks in 11 tumors by T2WI (48% [11/23]) and 17 by DWI (74% [17/23]) (P < 0.03).

Conclusion: DWI at 3T was superior to T2WI for evaluating the T stage of bladder cancer, particularly in differentiating T1 tumors from those T2 or higher, and in detecting stalks of papillary bladder tumors.

Keywords: bladder cancer, staging, diffusion-weighted imaging, MRI

Introduction

In the clinical management of urinary bladder cancer, non-muscle-invasive tumors (stage T1 or lower) are usually treated by transurethral resection (TUR), whereas muscle-invasive tumors (stage T2 or higher) are treated by radical cystectomy or by palliative chemotherapy or radiation therapy. Thus, preoperative imaging studies that could precisely differentiate the 2 types of tumor could play an important diagnostic role.

Several studies have suggested that diffusion-weighted imaging (DWI) is useful for diagnosing T stage. The configuration of urothelial carcinomas usually reflects tumor behavior. Cystoscopically, approximately 70% of urothelial tumors are papillary, and 30% are non-papillary. Histopathologically, most cases of papillary urothelial carcinoma demonstrate a stalk consisting of loose connective tissue. For T staging of urinary bladder cancer on magnetic resonance (MR) imaging, clear separation of the cancer from the bladder wall is important. Several studies have suggested that MR imaging at 1.5T facilitates the detection of stalks and staging of bladder tumors. However, we believe no study has compared MR imaging sequences with regard...
to the efficacy of stalk detection.

We undertook this study to evaluate the usefulness of DWI at 3T for diagnosing T stage in bladder cancer and to compare T2-weighted imaging (T2WI) and DWI with respect to stalk detection.

Materials and Methods

Patients

Our institutional review board approved this retrospective study and waived the requirement for informed consent.

Our primary selection criteria were (a) patients who underwent TUR or transurethral biopsy after MR imaging and (b) patients with suspected bladder cancer who underwent MR imaging examination that included T2WI and DWI with a 3T MR unit between June 2007 and September 2009. Based on these criteria, we selected 53 consecutive patients. Of these, we excluded 14 whose bladder cancer (a) was not proved (n = 6) and (b) appeared clinically noninvasive but was not histologically confirmed as invasive or noninvasive (n = 8). Consequently, 39 patients (35 men, 4 women; aged 43 to 90 years, mean, 70.7 years) were included. Nine underwent radical cystectomy, and the other 30 underwent TUR and additional deep muscle biopsy at the base of the tumor. If deep muscle biopsy revealed no cancerous tissue, the pathological stage was categorized as T1 or lower. In 6 patients with multiple tumors, the largest was evaluated. Cystoscopic configurations of bladder tumors (papillary or non-papillary) were recorded, but whether bladder tumors had stalks in cystoscopy was not. The bladder was divided into 6 segments; 4 tumors were located in the anterior segment, 13 in the posterior segment, four in the right side, ten in the left side, five in the dome, and three in the neck. The mean time interval between MR imaging and TUR or surgery was 18.8 days (range, 0 to 41 days).

MR imaging examination

All MR imaging examinations were performed using a 3T MR scanner (MAGNETOM Trio; Siemens Medical Solutions, Erlagen, Germany) with body-matrix and spine-matrix coils. Transverse DWI was obtained using a single-shot spin-echo echo-planar imaging sequence (repetition time [TR]/echo time [TE], 3800/82 ms; b-value, 0, 500, and 1000 s/mm2; matrix, 128 × 72; 3-mm section thickness with 0.6-mm intersectional gap; field of view [FOV], 35 cm; parallel imaging factor, 2; 40 sections obtained in 185 s). Conventional MR imaging was tailored to the clinical question, but all examinations included transverse and sagittal T2-weighted fast spin-echo imaging (TR/TE, 4500/82 ms; matrix, 384 × 230, 4-mm section thickness with 0.6-mm intersectional gap; FOV, 22 cm; parallel imaging factor, 2; 24 sections obtained in 185 s) of the entire bladder. All MR imaging examinations were performed without injection of butyl scopolamine or glucagon.

Image interpretation

We used 2 image interpretation protocols. One consisted of data from transverse and sagittal T2WI and the other, data from transverse and sagittal T2WI and transverse DWI. Image interpretation was performed on a picture archiving and communication systems workstation (SYNAPSE; FUJIFILM Medical, Tokyo, Japan). In consensus, 2 radiologists (JS and SS, each with 10 years’ experience reading body MR imaging) with knowledge of tumor locations but blinded to clinical, cystoscopic, and histopathological findings, interpreted each dataset. The 2 datasets were randomly interpreted in different sessions at 2-week intervals.

T staging on DWI

For DWI, we applied T staging criteria similar to those proposed by Takeuchi’s team.5 A thin, flat area of high signal intensity (SI) that corresponded to a tumor or a tumor with a stalk was considered stage T1 or lower (Fig. 1). A tumor with high SI without submucosal components and with a smooth tumor margin was considered stage T2 (Fig. 2), with high SI extending into the perivesical fat with an irregular margin, T3, and extending into adjacent organs, T4.

T staging on T2WI

For T2-weighted images, we applied staging criteria similar to those described previously.11–14 A lesion at the base of the tumor with intact muscle layer of low SI was considered stage T1 or lower and with focally disrupted muscle layer of low SI without perivesical infiltration, stage T2. A lesion extending into the perivesical fat was considered T3 and extending into adjacent organs, T4.

Stalk on MR imaging

The stalk was evaluated as present or absent, and its signal intensity in relation to the tumor was determined on T2WI and DWI. We defined a stalk as a structure that extended from the bladder wall to the tumor with different SI from that of the tumor, as Saito’s group proposed.9 The SI of the stalk was judged to be low when lower than that of the tumor and was otherwise considered high.
Statistical analyses

We evaluated differences in diagnostic performance and frequency of stalk detection using McNemar’s test with SPSS software (ver. 17.0 for Windows; SPSS Japan, Tokyo, Japan). We compared the diagnostic accuracy of staging with MR imaging with that using histopathological stage on a stage-by-stage basis and used the Mann-Whitney

Fig. 1. Stage T1 papillary urothelial carcinoma in a 63-year-old man. (a) Axial T2-weighted image shows tumor with a stalk of mixed high and low signal intensity (SI, arrow) that extends from the posterior bladder wall to the tumor. (b) Axial diffusion-weighted image shows a stalk with low SI (arrow) that is depicted clearly, compared with the T2-weighted image. (c) Photomicrograph of specimen shows a stalk (arrow) extending from the bladder wall into the tumor. The stalk consists of fibrous tissues, capillaries, inflammatory cell infiltration, and edema.

Fig. 2. Stage T2 non-papillary urothelial carcinoma in a 76-year-old man. (a) Axial T2-weighted image shows that low SI line of the bladder seems to be disrupted focally in the region underlying the tumor (arrow). (b) Axial diffusion-weighted image shows the high SI tumor (arrow) without submucosal components and with a smooth tumor margin.
U-test to compare the mean sizes of tumors between those with and without a stalk. \( P \leq 0.05 \) was considered to indicate statistical significance.

**Results**

**Tumor characteristics**

The stages of 32 of the 39 tumors were confirmed histologically. The remaining 7 tumors resected with TUR demonstrated invasion of tumor cells on deep muscle biopsy and were categorized as T2 or higher and not used to estimate the ability to differentiate tumors staged T2 and lower from those T3 and higher. The pathological stages of the 39 tumors were: T1 or lower in 61.5% (24 tumors), T2 in 5.1% (two), T3 in 7.7% (three), T4 in 7.7% (three), and T2 or higher in 17.9% (seven).

Based on cystoscopic findings, 23 of the 39 were papillary tumors (59.0%) and 16, non-papillary (41%). Table 1 summarizes histopathological T staging and the frequencies of papillary and non-papillary tumors based on cystoscopic findings. Maximum tumor size ranged from 4.1 to 67.1 mm (mean, 28.5 mm). Histopathological diagnoses were urothelial carcinoma \( (n = 38) \) and adenocarcinoma \( (n = 1) \). The pathological stages of the 39 tumors were: T1 or lower in 61.5% (24 tumors), T2 in 5.1% (two), T3 in 7.7% (three), T4 in 7.7% (three), and T2 or higher in 17.9% (seven).

**Tumor staging with MR imaging**

Table 2 summarizes diagnostic performance with respect to differentiating tumors staged T1 or lower from those staged T2 to T4. Specificity and accuracy were significantly better with T2WI plus DWI than with T2WI alone \( (P = 0.02) \). Table 3 summarizes diagnostic performances in differentiating T2 or lower tumors from T3 or higher tumors. Diagnostic performance did not differ significantly between T2WI plus DWI and T2WI alone. Table 4 summarizes diagnostic performance in terms of the overall accuracy of tumor stage diagnosis, which was significantly better for T2WI plus DWI than T2WI alone \( (P = 0.03) \).

**Stalk on MR imaging**

The pathological stages of the 23 papillary tumors were: T1 in 91.3% (21 tumors), T2 in 4.3% (one), T3 in 0% (zero), T4 in 0% (zero), and T2 or higher in 4.3% (one). Eleven papillary tumors on T2WI (47.8% [11/23]) and 17 on DWI (73.9% [17/23]) were assessed as having a stalk \( (P < 0.03) \) (Fig. 3). The pathological stages of 10 of the 11 tumors with a stalk on T2WI (90.9%) and 16 of the 17 tumors with a stalk on DWI (94.1%) were T1 or lower; that of the remaining tumor with a stalk on T2WI (9.1%) and DWI (5.9%) was T2 or higher (Fig. 4). On T2WI and DWI, all non-papillary tumors were assessed as having no stalk. On T2WI, the signal

<table>
<thead>
<tr>
<th>T stage</th>
<th>No.</th>
<th>Papillary tumor</th>
<th>Non-papillary tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>24</td>
<td>21</td>
<td>3</td>
</tr>
<tr>
<td>T2</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>T2 or higher</td>
<td>7</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>T3</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>T4</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>39</td>
<td>23</td>
<td>16</td>
</tr>
</tbody>
</table>

**Table 1.** Histopathological T staging and frequency of papillary and non-papillary tumors based on cystoscopic findings

<table>
<thead>
<tr>
<th>Diagnostic performance</th>
<th>T2WI</th>
<th>T2WI + DWI</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>14/15 (93.3%)</td>
<td>13/15 (86.7%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Specificity</td>
<td>12/24 (50.0%)</td>
<td>20/24 (83.3%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Accuracy</td>
<td>26/39 (66.7%)</td>
<td>33/39 (84.6%)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

**Table 2.** Diagnostic performance in differentiation of T1 or lower from T2 to T4 tumors on T2-weighted imaging (T2WI) and diffusion-weighted imaging (DWI)

<table>
<thead>
<tr>
<th>Diagnostic performance</th>
<th>T2WI</th>
<th>T2WI + DWI</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>5/6  (83.3%)</td>
<td>5/6  (83.3%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Specificity</td>
<td>19/26 (73.1%)</td>
<td>23/26 (88.5%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Accuracy</td>
<td>24/32 (75.0%)</td>
<td>28/32 (87.5%)</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

**Table 3.** Diagnostic performance in differentiation of T2 or lower from T3 to T4 tumors on T2-weighted imaging (T2WI) and diffusion-weighted imaging (DWI)

<table>
<thead>
<tr>
<th>Diagnostic performance</th>
<th>T2WI</th>
<th>T2WI + DWI</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accuracy</td>
<td>23/39 (59.0%)</td>
<td>32/39 (82.1%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Overdiagnosis rate</td>
<td>14/39 (35.9%)</td>
<td>6/39 (15.4%)</td>
<td>NA</td>
</tr>
<tr>
<td>Underdiagnosis rate</td>
<td>2/39 (5.1%)</td>
<td>1/39 (2.6%)</td>
<td>NA</td>
</tr>
</tbody>
</table>

**Table 4.** Diagnostic performance in overall accuracy for diagnosis of tumor stage on T2-weighted imaging (T2WI) and diffusion-weighted imaging (DWI)

NA, not applicable
intensity of the stalks of the 11 tumors was judged as low in nine (81.8%), high in one (9.1%), and mixed high and low in one (9.1%). On DWI, the signal intensity of the stalks of all 17 tumors (100%) was judged low.

On DWI, the maximum size of papillary tumors ranged from 4.1 to 67.1 mm (mean, 21.2 mm); without a stalk, they measured 4.1 to 13.7 mm.
(mean, 6.8 mm) and with a stalk, 12.8 to 67.1 mm (mean 26.2 mm). Papillary tumors were smaller without a stalk than with a stalk on DWI \( (P = 0.001) \). The pathological stages of papillary tumors without a stalk on DWI were T1 in 83.3% (5/6) and T2 in 16.7% (1/6). The maximum size of papillary tumors without a stalk on DWI of stage T1 or lower was 4.1 to 7.0 mm in (mean 5.5 mm), and that of the one tumor without a stalk on DWI at stage T2 was 13.7 mm.

The maximum size of papillary tumors without a stalk on T2WI ranged from 4.1 to 23.5 mm (mean, 13.8 mm), and that with a stalk from 12.8 to 67.1 mm (mean 29.2 mm) and did not differ significantly tumors without and with a stalk on T2WI \( (P = 0.16) \). The pathological stages of the 11 papillary tumors without a stalk on T2WI were T1 in 90.9% (ten) and T2 in 9.1% (one). The maximum size of papillary tumors without a stalk on a stalk on T2WI of stage T1 or lower ranged from 4.1 to 23.5 mm (mean, 12.2 mm), and that of the one tumor without a stalk on T2WI of stage T2 was 13.7 mm.

Discussion

Our findings suggested that T2WI plus DWI facilitated differentiation of tumors of stage T1 or lower from those T2 or higher at 3T MR imaging, and our clinical data demonstrated that the addition of DWI improved the accuracy of T staging. Our results were better than most previously reported T-staging accuracies for DWI at 1.5T\(^{4–7}\) and consistent with findings of previous studies.8 This might be due to the better image quality achieved by 3T MR imaging, which is able to increase the signal-to-noise ratio and acquire section of 3-mm thickness.

Our results were equal to previously reported T staging accuracies of dynamic contrast-enhanced MR imaging at 1.5T.15–17 This suggests that DWI plus T2WI at 3T has the potential to replace gadoxilinium-enhanced MR imaging at 1.5T for preoperative evaluation of urinary bladder cancer. We found DWI superior to T2WI in detecting stalks of papillary bladder tumors. Saito and associates10 and Takeuchi’s group5 reported that stalks extending from the bladder wall into the tumor consist of fibrous tissues, capillaries, inflammatory cells, edema, and mild inflammatory cell infiltration. Thus, on DWI, the stalks demonstrated low signal intensity because DWI shows fibrous and edematous lesions with low SI.18,19 Saito’s team reported T2WI as the best sequence for stalk detection but found some stalks difficult to separate from tumors because of their identical SI caused by edema.10

Our results revealed most bladder tumors with a stalk on MR imaging to be of pathological stage T1 or lower. This might be due in part to the greater specificity and accuracy of T2WI plus DWI than T2WI alone for differentiating tumors of stage T1 or lower from T2 to T4 tumors. Cystoscopically, 70% of urothelial bladder tumors are classified as papillary and 30% as non-papillary, according to the characteristics of the surface.9 Histopathologically, low grade urothelial neoplasms are recognized as such because their cells are arranged on fibrovascular stalks.9 As a result, papillary tumors with stalks tend to be of low grades and low stages compared with non-papillary tumors.20

Takeuchi and colleagues reported finding a tumor with high signal intensity with submucosal stalk of low SI on DWI that resembled an inchworm in all patients with pT1 disease. However, one tumor with a stalk on T2WI and DWI evaluated by the reviewers was histopathologically diagnosed as stage T2 or higher. In fact, Kobayashi’s group reported the histopathological diagnosis of 6 tumors with the “inchworm sign” on DWI as muscle-invasive bladder cancer.7 Although bladder tumors with stalks on MR imaging tend to be of low stages, thickness of the bladder wall at the base of the stalk should be evaluated carefully.

Papillary tumors without a stalk on DWI were smaller than those with a stalk. The maximum size of all papillary tumors without a stalk on DWI was less than 13.7 mm. Stalks were detected on DWI in all papillary tumors more than 13.7 mm and in one that measured 12.8 mm. Delineation of stalks on MR imaging using a 3T scanner may be difficult in cases of bladder tumors smaller than approximately 13 mm.

This study has some limitations. First, it was retrospective with a small sample size. The distribution of T stages was uneven and included few patients with tumors of stages T2, T3, and T4 because the number of total cystectomies was limited. This might be due in part to the lack of a statistically significant difference by which T2 tumors might be distinguished from T3 to T4 tumors. Second, we did not evaluate the apparent diffusion coefficient of tumors because the study aimed to assess the diagnostic performance for diagnosis of tumor stage and stalk detection on DWI at 3T. Third, our use of only a transverse plane with DWI might have reduced diagnostic performance and stalk detection; addition of a sagittal plane might improve them. Fourth, our use of different section thicknesses, 3 mm for DWI and 4 mm for T2-weighted fast spin-echo imaging, might have reduced diagnostic performance and stalk detection. Finally, we
did not perform dynamic contrast-enhanced MR imaging, and its addition to T2-weighted fast spin-echo imaging and DWI can improve overall diagnostic performance with 3T MR imaging.

Conclusion

In conclusion, DWI at 3T can provide useful information for evaluating the T stage of bladder cancer, particularly for differentiating tumors staged T1 or lower from those staged T2 or higher. On MR imaging at 3T, most bladder tumors with a stalk were of pathological stage T1 or lower. The ability to detect stalks of papillary bladder tumors was superior with DWI at 3T to that of T2WI.

Acknowledgements

We thank Chikara Noda, R.T. of the Department of Radiological Technology of Showa University Hospital for technical support.

References


