RESEARCH COMMUNICATION

Comparison of Cystoscopy with Diffusion-Weighted Magnetic Resonance Images Used in the Diagnosis and Follow-Up of Patients with Bladder Tumors

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Abstract

Purpose: To compare diffusion-weighted magnetic resonance imaging (DW-MRI) with cystoscopy in the diagnosis and follow-up of patients with bladder tumor and to investigate any histopathological correlation. Materials and Methods: Totally 59 patients, between 31-85 years (mean age 60±13) referred to our clinic due to a hematuria complaint were enrolled and evaluated by upper urinary system pathology and then DW-MRI (average 7 days) and cystoscopy. Apparent diffusion coefficients (ADCs) of images were calculated. Results: While a mass in bladder was determined with cystoscopy in 43 out of 59 patients,the mass was not deternined in 16 of the patients(n=34 malign,n=9 benign).While a mass was determined in 40 out of 59 patients with DW-MRI,the mass was not determined in 19 of the patients(n=40 malign,n=19 benign). Regarding ADC values, mean ADC values of 34 patients who were diagnosed with a bladder tumor (1.05±0.22 x 10^{-3}mm²/s), were significantly lower than the mean ADC values obtained from the normal bladder wall (1.830 ±0.18 x 10^{-3}mm²/s) whereas a statistically significant difference was found (p<0.001). ADC values in 9 patients with a benign lesion (1,73±0.12 x 10^{-3}mm²/s), were not found statistically different from the mean ADC values obtained from the normal bladder wall (1.78±0.2x10^{-3}mm²/s) (p>0.05).A significant difference was determined between ADC values of benign lesions and the ADC values of malign lesions (p<0.001). Conclusions: According to cystoscopy, values of DW-MRI's related with sensitivity, specificity and accuracy were found, respectively 90%, 93% and 91%. As the DW-MRI is a non-invasive and a rapid technique, and does not contain ionized radiation and because it is accepted as an important marker of tumor cellularity, it may be used as an alternative in future diagnosis and follow-up of bladder tumors.

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Introduction

Bladder tumor is a condition which can be frequently seen secondarily in the genitourinary system (Jemal et al., 2006). Urine cytology and cystoscopy are standard approaches in the diagnosis and treatment of bladder tumors (Walsh et al., 2005; Schmidbauer, 2008). However, cystoscopy is an invasive technique and may require anesthesia, and may have various disadvantages such as sensitivity dependent to the operator and negative effects of patient compatibility due to repeated cystoscopy (Wright and Jones, 2000; Tinzl and Marberger, 2003). Because of these disadvantages, there is an ongoing investigation for non-invasive and high sensitive methods. Accordingly, CT and MRI are frequently used to diagnose and follow bladder tumors (Lawler and Fishman, 2003).

It was shown that superficial and several numbers of tumors in dynamic images after a contrasted MRI study and the determination of an extension related with the extravesical tumor and its invasion to the surrounding organs were superior than CT (Amendola et al., 1986; Barentsz et al., 1996). The staging success of contrasted MRI in the literature was reported between 50% and 96% (Lawler and Fishman, 2003).

The aim of our study is to investigate the histopathological correlation by comparing cystoscopy and DW-MRI during the diagnosis and follow up of patients with a bladder tumor.

Materials and Methods

Totally 59 patients, who referred to our urology outpatient clinic between February 2008 and July 2009 due to hematuria complaint, during the follow up protocol for bladder tumor and with a primary hematuria complaint were enrolled into the study. Hematuria was found a primary complaint in 36 of the patients while bladder tumor was detected in 23 patients. The latter group of patients undergone a transurethral tumor resection were patients who were followed because of secondary hematuria.

Firstly, a DW-MRI was obtained from patients and then cystoscopy was performed under general or regional anesthesia in the terms and conditions of the operation

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unit. During cystoscopy, tissue samples were obtained by transurethral resection from lesions and doubtful areas and immersed into formol and submitted to the lab for a histopathological study. Cystoscopy findings and results obtained from biopsy were accepted as a standard reference.

DW-MRI studies were performed by a phase arrayed body coil with a Siemens Magnetom Symphony (Siemens, Erlangen, Germany) device and by the means of a lower abdomen MRI study. The field strength of the device was 1.5 Tesla (T) which is recognized as a high filed strength. Measurements were conducted by circular region of interest (ROI) applied on lesions. ADC value was re-measured by using ROI from the most hypo intense site of the tumor mass. The period of the study was 151 seconds.

Due to sustained variations, a One-Way Variance Analysis (One-way ANOWA) was used. Comparison of DW-MRI with cystoscopy and histopathology was carried out by diagnostic testing (sensitivity, specificity, positive erroneous ratio, negative erroneous ratio, accuracy ratio). A 5% ratio was considered during calculations related with statistical significance.

Results

The age of 59 patients was between 31 and 85 years old (mean 60.4±13.03) and the male/female ratio was 47/12.Primary hematuria was present in 36 cases while 23 cases were under a follow-up because of bladder tumor. A mass was determined in the bladder by cystoscopy in 43 patients while no any mass lesion was found in 16. Approximately 34 patients out of 43 who displayed a mass were diagnosed with bladder tumor while the tumor was benign in 9 patients.10 patients out of 16 who displayed no any lesions were patients under follow-up because of a previous diagnosis related with bladder tumor. The remaining 6 patients were cases with hematuria due to BPH and 1 patient suffered from secondary hematuria due to extensive use of coumadin.

One of the patients out of 34 who was diagnosed with bladder tumor passed away while 9 patients were muscle invasive, and one patient was unable to reach, therefore we failed to enroll these patients into a follow-up program. Relapses were determined in eleven patients out of 23 who were under a follow-up program.

A mass lesion was determined by DW-MRI in 40 patients out of 59. Thirty four patients out of 40 were considered malign while 6 were considered benign. Forty three patients displayed a mass in their cystoscopy studies. The histopathology studies of thirty four patients out of 43 were malign (TCC) while 9 were benign. However, 1 patient out of 34 who was diagnosed with carcinoma in cystoscopy and histopathological studies and undergone a TUR-TM application was not displayed by DW-MRI. Despite all of these, 1 patient was considered malign by DW-MRI while the histopathological study resulted benign. Mean ADC values of masses in 34 patients (1,05±0.22 x 10^{-3}mm²/s) was found significantly lower than the mean ADC values (1,85±0.18x10^{-3}mm²/s) obtained from the normal bladder wall (Figure 1 and 2) and a statistically significant difference were found

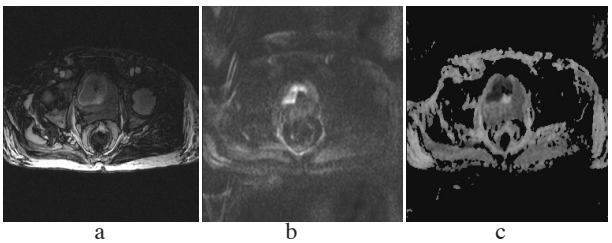

Figure 1. 76 Years Old, Male Patient, 3.5cm Size Mass at the Anterior of the Bladder (TCC). a) Hypo Intense mass at T2-Weighted Cross-Section, b) Hyper Intense at DAG c) Hypo Intense in ADC Images; ADC Value of Mass is 0.55 x 10^{-3} mm² /s, Normal Value of Bladder wall 1.69 x 10^{-3} mm²/s

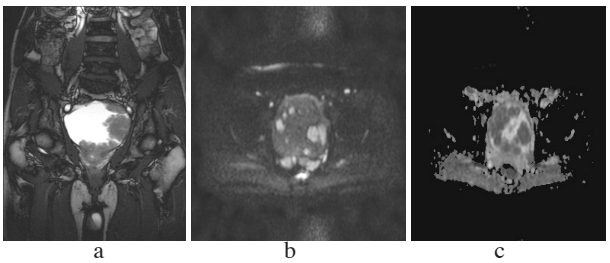

Figure 2. 54 Year Old, Male Patient, Diffused Mass that Extends Towards the Bladder Lumen (TCC). a) Hypo Intense Mass at T2 Weighted Cross-Section, b) Hyper Intense at DAG, c) Hypo Intense in ADC Images; ADC Value of Mass is 0.98 x 10^{-3}mm²/s, Normal Value of Bladder wall 1.78 x 10^{-3}mm² /s

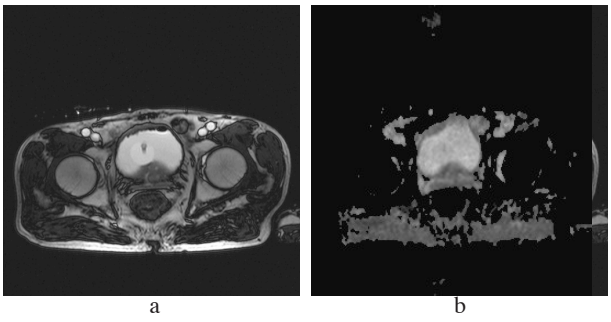

Figure 3. 70 Year Old, Male Patient, Irregular Place to Place wall Thickening (Diffused Place to Replace wall Thickening Due to Prostate Hyperplasia). a) Hypo Intense Irregular wall Thickening at the Anterior wall of the Bladder in T2-Weighted Cross-Section, b) Hypo Intense in ADC Images; ADC Value of Mass is 1.70 x 10^{-3}mm²/s, Normal Value of Bladder wall 1.79 x 10^{-3}mm²/s

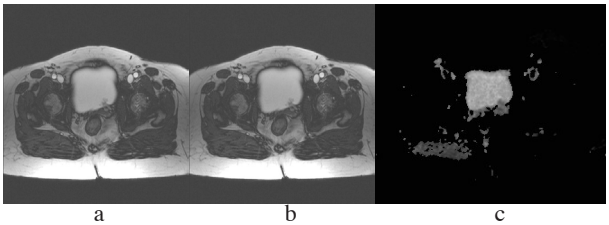

Figure 4. 38 Year old, Female Patient, Mass Extending in a Polyploidy Style Towards the Lumen with a Size of 1cm, Located at the Left Base of the Bladder. (polyploidy cystitis). a/b) DAG image, c) Hypo Intense in ADC Images; ADC Value of Mass is 1.75 x 10^{-3} mm² /s, normal value of bladder wall 1.7 x 10^{-3}mm² /s

Table 1. DW-MRI Diagnostic Testing According to Histopathology

	Sensitivity (%)	Specificity (%)	Erroneous Positive Ratio	Erroneous Negative Ratio	Accuracy (%)
DW-MRI	97,6	96	4	2.9	96.6

Table 2. DW-MRI Diagnostic Testing According to Cystoscopy

Sensitivity (%)	Specificity (%)	Erroneous Positive Ratio	Erroneous Negative Ratio	Accuracy (%)
90	93	6	9	91

Table 3. Cystoscopy Diagnostic Testing according to Histopathology

Sensitivity (%)	Specificity (%)	Erroneous Positive Ratio	Erroneous Negative Ratio	Accuracy (%)
100	64	36%	0%	84

between both values ($p<0.001$). The histopathology of these masses in 9 patients who were followed by cystoscopy was benign. By the means of DW-MRI, 8 of these masses were benign while malignity was determined in only one of the patients. No any statistically significant difference was found between mean ADC values of benign masses ($1,73\pm0.12x10^{-3}mm^2/s$) (Figure3) and the mean ADC values obtained from the normal bladder wall ($1.78\pm0.2x10^{-3}mm^2/s$) ($p>0.05$). ADC values of benign lesions were compared with the ADC values of malign lesions and a significant difference between both lesions was determined ($p<0.001$).No lesions were monitored by DW-MRI in the remaining 9 patients. Mean ADC value ($1.82\pm0.18x10^{-3}mm^2/s$) obtained from the bladder wall of the mentioned patients was higher than the ADC values obtained from malign masses ($p<0.001$). Histopathological results of nine patients who were diagnosed as benign: Acute cystitis (n=4), chronic cystitis (n=2, benign eosinophilic cystitis (n=1), inverted papilloma (n=1) and polyploidy cystitis (n=1). Polyploidy cyctitis for Figure 4.

When compared with histopathology, DW-MRI ratios for sensitivity, specificity, erroneous positiveness, erroneous negativeness and accuracy were respectively, 97.6%, 96%, 4%, 2.9% and 96.6%. Findings are summarized in Table 1.

When compared with cystoscopy, DW-MRI ratios for sensitivity, specificity, erroneous positiveness, erroneous negativeness and accuracy were respectively, 90%, 93%, 6%, 9% and 91%. Findings are summarized in Table 2.

When compared with the results submitted from the histopathology unit, sensitivity, specificity, erroneous positive ratio and negative erroneous and accuracy ratios were found, respectively 100%, 64%, 36%, 0% and 84%. Results are summarized in Table 3.

Discussion

Cystoscopy is a standard method used in the fol -up of patients with a bladder tumor (Walker et al., 1993) and is recognized for it's 90% sensitivity. However, cystoscopy is an invasive method and may require anesthesia, leading to extended periods of application and aggravate patient compatibility (Wright and Jones, 2000; Tinzl and Marberger, 2003).

The sensitivity of cytology in the diagnosis and follow-up of bladder tumors vary between 16-90%. Nevertheless, decreased sensitivity in low rated tumors (25-40%) and the diversity of views among cytologists may restrain its value (Landman et al., 1998; Konety et al., 1999; Leyh et al., 1999). Diagnosis and follow-up of cytology intend to increased when augmented with cystoscopy (Schmidbauer, 2008). In the present study, according to histopathological findings ratios of sensitivity, specificity, erroneous positiveness, erroneous negativeness and accuracy regarding cystoscopy are respectively, 100%, 64%, 36%, 0% and 84% (Table 3). Furthermore, according to cystoscopy, sensitivity, specificity and accuracy ratios of DW-MRI were determined respectively, 90%, 93% and 91% (Table 2).

There are a limited number of studies in English language related with the use of Diffusion-Weighted MRI (DW-MRI) in the diagnosis and follow-up of bladder tumors. In various studies carried out by Yoshida et al, in 10 patients with a upper urinary system urothelial carcinoma (Yoshıda et al., 2008), a retrospective study carried out by Matsuki et al, in 15 patients with bladder tumor (Matsuki et al., 2007) and by Assamy et al, in 43 patients with bladder tumor (El- Assamy et al., 2008), ADC values of the tumor tissue was found significantly low when compared to ADC values of the vicinity tissues. In our study, mean ADC values of masses in 34 patients diagnosed with bladder tumor ($1,05\pm0.22x10^{-3}mm^2/s$) were found lower than the mean ADC values obtained from a normal bladder wall ($1,85 \pm 0.18x10^{-3}mm^2/s$) and showed a statistically significant difference ($p<0.001$). The results of our study were compatible to the results in the literature.

Tumor relapse was monitored in 11 of these patients who were included in the bladder tumor follow-up protocol. The mean mass ADC value ($1,125\pm0.214x10^{-3}mm^2/s$) was significantly lower than the mean ADC value ($1,917\pm0.15x10^{-3}mm^2/s$) obtained from the normal bladder wall and a statistical significant difference between both values was determined ($p<0.001$).No any statistical difference was found between the mean ADC value ($1,125\pm0.214x10^{-3}mm^2/s$) of patients who displayed a relapse tumor and the mean ADC value ($1.007\pm0.218x10^{-3}mm^2/s$) of other patients who displayed a primary tumor ($p>0.05$). Accordingly, no any difference was determined between bladder tumors that were newly diagnosed and bladder tumors with relapses. In the three studies mentioned above, the availability at follow-ups was not investigated because no any comparison was carried out between the masses that were determined during the follow-up of patients with bladder tumors and

ADC values of masses obtained from patients who were newly diagnosed.

Furthermore, as much as we had the chance to investigate the English literature, we failed to encounter a study which was performed to compare the ADC values of benign and malign masses of the bladder. In our study, a significant difference was found between ADC values of benign and malign masses (p>0,001).

In a study carried out by Abou-El-Ghar et al, on 130 patient with hematüria, cystoscopy was considered as a standard and the sensitivity, specificity, positive predictive value (PPD), negative predictive value and accuracy of DW-MRI were found respectively, 98.5%, 93.3%, 100%, 92.3% and 97% (Abou-El-Ghar et al., 2009). Our findings were compatible with these findings.

DW-MRI appears as an alternative to cystoscopy because it possesses a non-invasive nature, provides a proximate relationship of diagnostic value for cystoscopy, requires a short time to take an image (151 seconds), it has no any necessities for a contrast and enables uncomplicated patient compatibility.

We assume that DW-MRI is a safe and confident method in the differentiation of malign-benign bladder masses and can be used in the follow-up period. The method may reduce the number of unnecessary efforts to carry out a cystoscopy. Yet cystoscopy and biopsy are inevitable studies in histopathological studies in patients whom a malignity in DW-MRI is considered. Unfortunately, the method may have some disadvantages as the urethral lumen cannot be studied by DW-MRI and it's use in patients with a metallic prosthesis or implant can be limited.

DW-MRI may be an alternative method in the diagnosis and follow-up of bladder pathologies against cystoscopy and cytology, however extensive studies are necessary.

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