

Role of Diffusion-Weighted MRI and Dynamic Contrast-Enhanced MRI in Early Staging of Bladder Cancer

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ABSTRACT

Objective: study the role of Dynamic contrast-enhanced (DCE), and Diffusion-weighted (DWI) MRI for preoperative early staging of urinary bladder cancer and compare their diagnostic accuracy with histopathological diagnosis.

Materials and Method: Thirty-seven patients with bladder cancer included in this study. All patients underwent Magnetic Resonance Imaging (MRI) on a 1.5-T scanner. MR images were evaluated and assigned a stage which compared with the histopathological staging depending on transurethral resection of bladder tumor (TURBT).

Results: There was substantial agreement between DCE- and DWI-MRI for T staging ($\kappa = 0.943$, $p < 0.001$), both MRI modalities had similar specificity for diagnosing stage T1 bladder CA with DWI offered slightly higher sensitivity (SN), positive predictive value (PPV), negative predictive values (NPV) and accuracy. Both MRI modalities show fair specificity for stage T2 with DWI offered slightly higher specificity and similar sensitivity for both with good accuracy.

Conclusion: MRI is an excellent modality for preoperative early staging as well as grading of the bladder cancer. Both Diffusion-weighted MR imaging and dynamic contrast-enhanced MRI offer excellent agreement for T-staging of bladder cancer with DWI as the preferred modality without the use of contrast media.

Keywords: Bladder cancer; diffusion-weighted, dynamic contrast-enhanced. MRI, transurethral resection

INTRODUCTION

Bladder tumors are the second most common tumor that can occur in the reproductive and urinary tract (prostate tumor is the most common)¹, and when diagnosed in the early stages, it is highly treatable². It accounts for 6-8% of overall malignancy in men and 2-3% in women and typically occurs in patients over the age of 50. They classified into either epithelial or nonepithelial (mesenchymal) tumor, on an average 90-95% of bladder neoplasms arise from the epithelium; the most common subtype is transitional cell carcinoma (90%)¹.

Urothelial tumors are classified as either invading muscle (nonpapillary) or not invading muscle (superficial or papillary)³. Approximately 80%–85% of urothelial tumors are non-muscle invasive. These are low-grade lesions, can be multifocal, and arise from a hyperplastic epithelium. They generally have a good prognosis and rarely evolve into invasive cancer, although urothelial recurrence rates are about 50%. Approximately 20%–25% of bladder cancers are muscle invasive, arise from severe dysplasia or carcinoma in situ, and have a higher histologic grade. Non-muscle-invasive urothelial tumors have a higher rate of recurrence than do the muscle-invasive variety³. Mesenchymal tumors represent the remaining 5% of bladder tumors, with the most common subtypes being rhabdomyosarcoma, in children, and leiomyosarcomas, in adults⁴.

Magnetic resonance imaging (MRI) is the best imaging modality for bladder cancer local staging⁵. Currently, for local staging of bladder cancer, a

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multiparametric approach with conventional and functional sequences is useful⁶. Diffusion-weighted imaging (DWI) imaging provides both qualitative and quantitative information that reflects changes at the cellular level concerning tumor cellularity and cell membrane integrity. Most of the bladder tumors manifest as areas increased signal intensity on diffusion-weighted images with a reduced apparent diffusion coefficient (ADC) at quantitative analysis^{6,7}. DW MRI, therefore, has the potential for monitoring treatment response to chemotherapy or radiotherapy with the identification of early non-responders who may benefit from a change in treatment approach⁸.

Dynamic contrast-enhanced (DCE)-MRI is a useful technique in which rapid enhancement of tumor by uptake of the contrast agent is compared to the bladder wall, assisting in differentiating tumor from surrounding normal tissue⁹. Dynamic MRI staging of bladder shows high accuracy in differentiating superficial tumors from invasive tumors and organ-confined tumors from non-organ-confined tumors of bladder¹⁰. The current study aimed to study the role of DWI- and DCE-MRI for the early staging of urinary bladder cancer and compare their diagnostic accuracy in correlation with histopathology.

METHOD

A cross-sectional study conducted in the MRI unit of an oncology teaching hospital, Baghdad Medical city, the study involved 37 patients diagnosed as having bladder tumor (31 males and six females) with their age ranged from (41–78 years) in the period between January 2017 and December 2017.

Patients with recent bladder biopsy (<20 days), patient with bladder CA having radiological T-stage more than T2 (T3 and T4), patients with multiple bladder masses, patients with impaired renal function (abnormal glomerular filtration rate (GFR<90)), patients who received radio or chemotherapy and the common contraindication to MRI (pacemaker, metallic foreign body, etc.) excluded from the study. All the patients had histopathological confirmation of CA bladder by conventional cystoscopy and biopsy.

MRI examination: It was done using 1.5 Tesla MRI machine (Magnetom Aera, Siemens medical system, Germany) using body surface coil. The examination

was done in the supine position with adequate bladder distention by instructing the patient to start drinking water 30 minutes before MRI study. In patients with a urethral catheter, 250-400 ml sterile saline was used to distend the bladder. During the imaging procedure fullness of the bladder was checked at the localizer images and the examination delayed if the bladder was not full.

Statistical Analysis: The categorical data compared by applying a Chi-Square test; Independent unpaired student t-test was used to analyze the differences in the values of ADC at different pathological regions. Cohen's kappa analysis of agreement was used to assess the possible agreement (or disagreement), and its magnitude for similarity between 2 discrete variables. Receiver operator curve used to see the validity of different parameters in separating active cases from control. The statistical analysis was performed using SPSS 20.0.0, MedClac 14.8.1 software package. A $P < 0.05$ considered statistically significant.

RESULTS

The study included 37 patients with bladder cancer, mean age was 61.59 ± 8.89 years, 83% were males, and 75.7% were smokers. The majority of cases (24 patients (64.9%)) had a high grade (III) of bladder cancer while 13 patients (35.1%) had a low-grade tumor. Mean ADC was significantly lower in patients with higher grade tumor compared to low grade (0.758 ± 0.202 vs. 0.970 ± 0.158 , p -value = 0.002), as illustrated in figure 1.

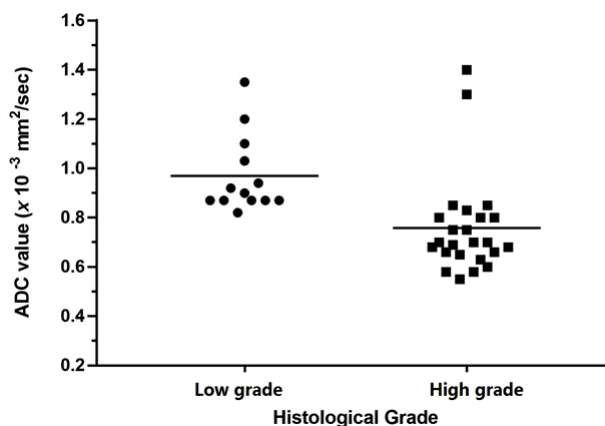


Figure 1: dot plot of ADC vs. histological grade

There was a substantial agreement between DCE and DWI in diagnosis of T-staging, as illustrated in table 1.

Table 1: comparison of the agreement of both MRI methods (DWI and DCE) in T-staging of bladder cancer

		DCE	
		T ₁ (15)	T ₂ (22)
DWI	T ₁ (14)	14	0
	T ₂ (23)	1	22
Kappa = 0.943, p < 0.001			

There is good agreement between DWI and DCE with TURBT, as illustrated in table 2.

Table 2: agreement between DWI and DCE and histopathological staging

		TURBT	
		T ₁ (19)	T ₂ (18)
DWI	T ₁ (15)	14	1
	T ₂ (22)	5	17
Kappa = 0.677, p < 0.001			
DCE	T ₁ (14)	13	1
	T ₂ (23)	6	17
Kappa = 0.624, p < 0.001			

ROC analysis revealed diagnostic utility of DWI and DCE for diagnosing T1 and T2 staging, it revealed that both have similar SN, SP, AC, PPV and NPV, as illustrated in table 3. Figures 2 and three show images of some patients in this study.

Table 3: Diagnostic efficacy of T staging by DWI and DCE based on histopathological T staging by TURBT

		Sensitivity	Specificity	Accuracy	PPV	NPV
DWI	T ₁	73.7%	94.4%	83.8%	93.3%	77.3%
	T ₂	94.4%	73.7%	84.3%	77.3%	93.3%
DCE	T ₁	68.4%	94.4%	81.0%	92.9%	73.9%
	T ₂	94.4%	68.4%	81.8%	73.9%	92.9%

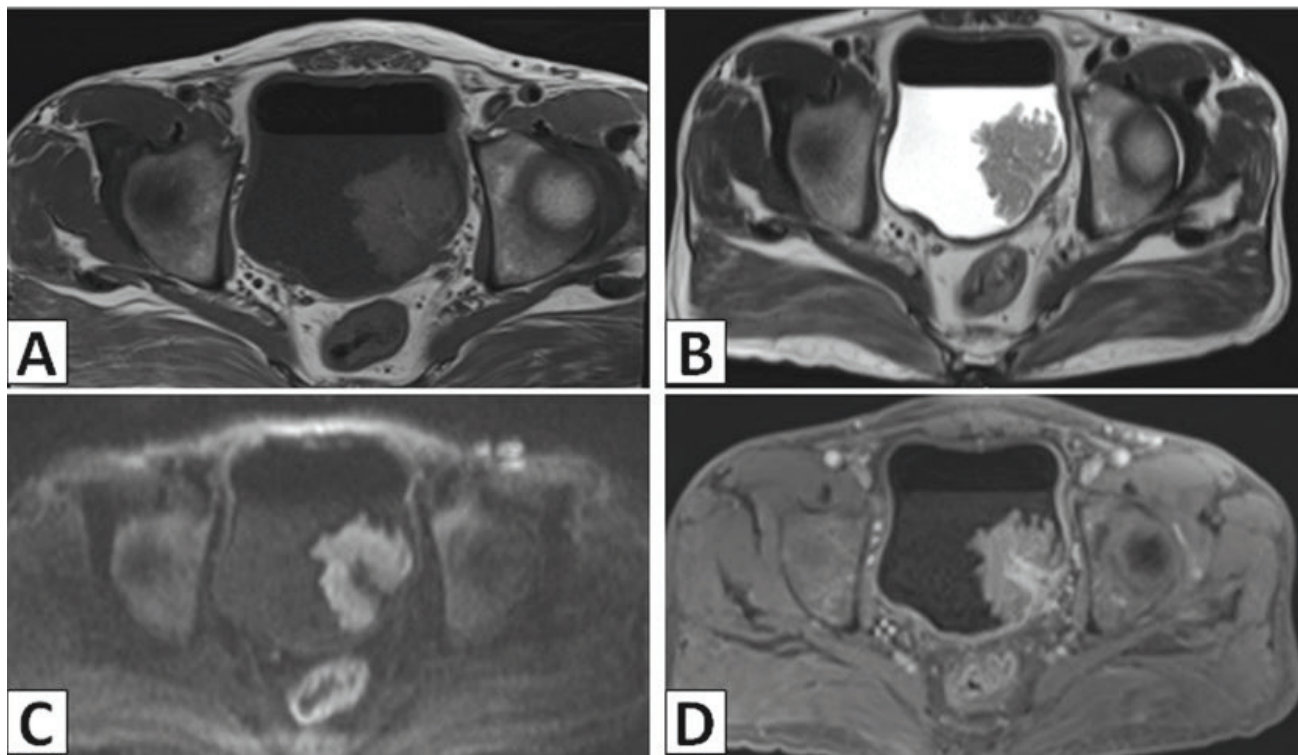


Figure 2: pelvic MRI for a 51 years old male presented with painless hematuria. A and B: are axial T1WI and T2WI show intermediate SI mass seen in Lt posterior-lateral wall of UB. C: axial DWI shows the mass with restricted diffusion. D: immediate sequence of DCE T1 WI with fat suppression show moderately enhancing tumor. MRI stage I bladder cancer which is proved by histopathology

DISCUSSION

Correct staging of the bladder carcinoma especially in the pre-operative period is critical, the clinical spectrum of bladder cancer classified into three categories (these classes have different prognosis, management, and therapeutic decisions), first non-muscle invasive bladder cancer which is best treated using transurethral resection, secondly muscle-invasive bladder cancer with goals to determine the need for complete or partial cystectomy, and finally metastatic group¹¹.

In the current study, about 91.9% of the patients were above 50 years, with a mean age at diagnosis 61.59 ± 8.89 years with a male to female ratio was 5.2:1, these findings were similar to previously reported studies^{1,12,13}.

In this study, 51% of patients had non-muscle invasive, and 49% had an invasive muscle disease, these results were slightly higher than the results of previously reported studies regarding high prevalence of muscle-invasive disease¹⁴⁻¹⁸.

The current findings showed that 35.1% of the cases presented with low-grade bladder cancer and 64.9% with high-grade bladder cancer, these results were similar to a previously reported study in Iraq which show that 63.27% having muscle-invasive and 42.9% had grade II disease, and 44.9% had grade III disease¹⁹, Sfakianos et al.²⁰ study showed that 75.3% had high-grade tumor, Divrik et al.¹⁶ study revealed 78.7% had high grade, and Herr et al.¹⁷ study revealed 97.3% had high-grade tumor, on the other hand, Gupta et al.¹ study show different results with 41.7% had low grade and 25% presented with high grade. This disagreement between different studies can be attributed to the difference in social, environmental and genetic predisposing in the different population.

In the current study both DWI and DCE show almost perfect agreement (kappa = 0.943) with T staging using transurethral resection, both MRI modalities showed excellent specificity (94.4% for DWI and 94.4% for DCE), good sensitivity (73.7% and 68.4% sensitivity), and accuracy (83.8% to 81.0%) for T1 staging, these findings were similar to that reported by Gupta et al⁽¹³⁾ which reported 100% specificity, 62.5% sensitivity, 90% accuracy for both DCE and DWI in diagnosing T1 disease, with both MRI modality showing substantial agreement with histopathological staging, Tuncbilek et al²¹ reported an accuracy of 62.5%, Tekes et al.²² reported 62% accuracy.

In the current study both DWI and DCE show 94.4% sensitivity of T2 staging and fair specificity (73.7% and 68.4%), which was in agreement with Gupta et al.¹ in which the specificity was 72.2%, while the sensitivity was 83.3% and 91.7% (DCE and DWI). DWI MRI provides information on diffusion in any organ and can be used to differentiate normal and abnormal structures of any tissues better, and it might help in the characterization of various abnormalities. DW MRI of the urinary bladder seems to be a feasible and reliable method to diagnose bladder carcinoma²³.

CONCLUSIONS

MRI is an excellent modality for preoperative early staging as well as grading of the bladder cancer. Both Diffusions weighted MR imaging, and dynamic contrast-enhanced MRI offers excellent agreement for T-staging of bladder cancer with DWI preferred without the use of contrast media.

Conflict of Interest: None

Ethical Clearance: Informed written consent was obtained from all the participants in the study, and the study and all its procedure were done in accordance with the Helsinki Declaration of 1975, as revised in 2000. The study was approved by the oncology teaching hospital, Baghdad Medical city.

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