Section: General Surgery

Original Research Article

ROLE OF DIFFUSION WEIGHTED MAGNETIC RESONANCE IMAGING IN BLADDER CANCER

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ABSTRACT

Background: Bladder cancer is a prevalent urological malignancy, with accurate preoperative staging being crucial for effective treatment planning. Diffusion-weighted magnetic resonance imaging (DW-MRI) is an emerging imaging modality that enables tumor characterization based on water molecule diffusion properties. This study evaluates the role of DW-MRI in preoperative staging and grading of bladder cancer and its correlation with clinical, radiological, and histopathological findings.

Materials and Methods: A prospective cross-sectional diagnostic study was conducted at Rajiv Gandhi Government General Hospital, Chennai, from March 2022 to March 2024. A total of 46 patients with bladder cancer were enrolled, with exclusion criteria including prior transurethral resection of bladder tumor (TURBT), intravesical therapy, systemic chemotherapy, or radiotherapy. All patients underwent DW-MRI of the kidney, ureter, and bladder (KUB) region using a 1.5-T MR system, followed by TURBT or radical cystectomy. Apparent diffusion coefficient (ADC) values were measured and correlated with histopathological staging and grading. Statistical analysis was performed using SPSS software, with a p-value of ≤ 0.05 considered significant.

Results: The study consisted of 42 males (91.3%) and 4 females (8.7%), with a mean age of 59.6 years. Muscle-invasive bladder cancer (MIBC) was observed in 27 (58.7%) patients, while 19 (41.3%) had non-muscle-invasive bladder cancer (NMIBC). Mean ADC values were significantly lower in tumors ($1.23 \pm 0.18 \times 10^{-3}$ mm²/sec) compared to normal bladder wall (1.91 ± 0.09), seminal vesicles (1.90 ± 0.13), and prostate (1.85 ± 0.11). High-grade tumors exhibited significantly lower ADC values (1.04 ± 0.10) than low-grade tumors (1.36 ± 0.06, $p < 0.001$). DW-MRI demonstrated excellent accuracy in differentiating T and N stages, with sensitivity and specificity of 94.74% and 100% for T staging and 97.3% and 100% for N staging, respectively. The overall diagnostic accuracy for staging was 97.83%.

Conclusion: DW-MRI is a valuable non-invasive imaging tool for preoperative staging and grading of bladder cancer. The strong correlation between ADC values and tumor grade suggests its potential utility in risk stratification. Given its high sensitivity and specificity, DW-MRI may serve as an alternative to contrast-enhanced imaging, particularly for patients with renal impairment, enhancing the accuracy of bladder cancer diagnosis and treatment planning.

Keywords: Bladder cancer, diffusion-weighted MRI, apparent diffusion coefficient, tumor staging, tumor grading, urothelial carcinoma.

INTRODUCTION

Bladder cancer is a common malignancy of the genitourinary tract, ranking as the second most prevalent urological malignancy worldwide after prostatic adenocarcinoma.[1] Urothelial tumors are primarily associated with environmental factors and aging, with major risk factors including smoking and exposure to industrial toxins.[2] The disease predominantly affects males, with a male-to-female ratio of 3:1, and is rare in individuals under 40 years of age.[3]

According to the WHO 2004 classification, bladder cancer is categorized into muscle-invasive and non-muscle-invasive types based on detrusor muscle invasion.[4] Approximately 80% of urothelial cancers are non-muscle-invasive, exhibiting various growth patterns. Muscle-invasive bladder cancer (MIBC) is characterized by high-grade tumors that infiltrate the lamina propria and deeper muscle layers. Histologically, urothelial carcinoma accounts for 90% of bladder cancers, whereas squamous cell carcinoma comprises 5%, and adenocarcinoma and other rare tumor types account for less than 5%.[5]

The management of bladder cancer depends on its invasiveness. Non-muscle-invasive bladder cancer (NMIBC) is primarily treated with transurethral resection of the tumor (TUR) followed by intravesical chemotherapy or immunotherapy. MIBC requires more aggressive treatment, including radical cystectomy, chemotherapy, radiotherapy, or a multimodal approach.[6] Accurate preoperative staging is crucial for guiding management and determining prognosis. While contrast-enhanced computed tomography (CECT) and magnetic resonance imaging (MRI) are the primary imaging modalities, dynamic MRI has shown superior staging capabilities, though it may lead to overstaging.[7] However, contrast agents pose risks, particularly in patients with renal impairment. Diffusion-weighted MRI (DW-MRI) is a novel, non-invasive imaging technique that evaluates molecular diffusion within tissues. The apparent diffusion coefficient (ADC), derived from DW-MRI, correlates with tumor grade and prognostic factors, aiding in risk stratification.[8]

This study was conducted to determine the pathological stage and grade of bladder cancer preoperatively using diffusion-weighted magnetic resonance imaging and to assess the correlation of DW-MRI findings with clinical, radiological, and pathological findings.

MATERIALS AND METHODS

This prospective cross-sectional diagnostic study was conducted in the Department of Urology at Rajiv Gandhi Government General Hospital, Madras Medical College, Chennai. The study period extended from March 2022 to March 2024. Approval for the study was obtained from the institutional ethical review board (No. 33032013).

All new patients presenting with total hematuria were initially evaluated using ultrasonography of the abdomen and pelvis. 46 Patients who were diagnosed with carcinoma of the bladder were included in the study. Exclusion criteria comprised patients who had undergone previous Transurethral Resection of Bladder Tumor (TURBT) and those who had received intravesical therapy, systemic chemotherapy, or external beam radiotherapy.

Informed consent was obtained from all patients after a detailed explanation of the study. The clinical details were recorded in a structured proforma during their inpatient stay, and data analysis was carried out prospectively. All patients with carcinoma of the bladder were evaluated through clinical examination, renal function tests, urine cytology, and imaging studies, including ultrasonography (USG) and contrast-enhanced computed tomography (CECT) of the kidney, ureter, and bladder (KUB) region. Diffusion-weighted magnetic resonance imaging (DW MRI) of the KUB region was performed at the time of hospital admission. TURBT was scheduled within one week following the imaging procedure.

For MR imaging, bladder distension was ensured before obtaining the DW MRI scans. Imaging was conducted using a 1.5-T clinical MR system (Magnetom Siemens Medical Solutions, Germany) with an eight-element body phased-array coil. Initially, axial T2-weighted images of the kidney, ureter, and urinary bladder were obtained with a bandwidth of 40–80 kHz, an echo time (TE) of 90–100 milliseconds, a repetition time (TR) of 8000 milliseconds, and a slice thickness of 3 to 5 mm, with an intersecting gap of approximately 1 mm. DW MRI was then performed using a bandwidth of 142 kHz, minimum TE, a TR of 8000 milliseconds, and a slice thickness of 3 to 5 mm without intersecting gaps. Imaging was conducted with b values of 0 and 800 sec/mm², and up to 54 slices were obtained within 1 to 2 minutes.

Apparent diffusion coefficient (ADC) calculations were performed at the MRI console using a linear regression analytic function. ADC values were determined by selecting tumor boundaries based on their appearance on T2-weighted imaging. ADC values were also measured for bladder tumors and surrounding structures, including the seminal vesicles, prostate, urine, and normal urinary bladder wall. Mean ADC values of the tumors were measured, and at least two or three ADC measurements per lesion were recorded, depending on the lesion size.

Following imaging, all patients underwent TURBT or cystectomy within one week. The resected specimens were sent for histopathological examination. The findings from DW MRI were then correlated with clinical, imaging, and pathological results.

Statistical analysis was conducted using the Statistical Package for the Social Sciences (SPSS) software, version 11.5 (SPSS Inc., Chicago, IL,

USA). Multivariate analysis was performed to compare ADC values of bladder tumors, normal bladder wall, urine, seminal vesicles, and prostate. A p-value of ≤0.05 was considered statistically significant.

RESULTS

Table 1: Profile of subjects with bladder cancer

		Number (n = 46)	Percentage
Gender	Males	42	91.30%
	Females	4	8.70%
Male: Female Ratio		10.5:1	
Mean Age (years)		59.6 ± 10.7	
Elevated Renal Parameters		10	21.70%
Tumor Base	Sessile	28	61%
	Pedunculated	18	39%
Histology	Urothelial Carcinoma	46	100%
Invasion	Muscle Invasion	27	58.70%
	Lamina Invasion	19	41.30%
Grade of Tumor	Low Grade Tumor	30	65%
	High Grade Tumor	16	35%
Type of procedure	Radical Cystectomy	10	21.8
	TUR Biopsy	17	36.9%
	TURBT	19	41.3%

Tumor measurement ranged from 2 to 12 cms (mean 4.7 cms). Out of 46 subjects, 19 (41.3%) patients who had T1 tumours following by TUR of tumour were subjected to intravesical immunotherapy, 27 (58.7%) patients had muscle invasive bladder tumour, of which 10 (21.7%) were subjected to radical cystectomy and urinary diversion procedure, of the remaining 17 patients, 10 patients (21.7%) were not willing for definitive surgical procedure and 7 (15.2%) were unfit for major surgical procedure and was advised palliative radiotherapy.

The ADC values ($\times 10^{-3}$ mm²/sec) for different structures showed distinct distributions. The tumour had a mean ADC of 1.23 ± 0.18, which was significantly lower compared to the normal bladder wall (1.91 ± 0.09), seminal vesicle (1.90 ± 0.13), and prostate (1.85 ± 0.11). Urine exhibited the highest ADC values, with a mean of 3.61 ± 0.32, distinctly higher than all other structures. The minimum and maximum ADC values also varied, with the tumour ranging from 0.81 to 1.48, while other structures had higher values, reinforcing the differentiation potential of ADC in distinguishing tumour tissue from normal anatomical structures. [Figure 1]

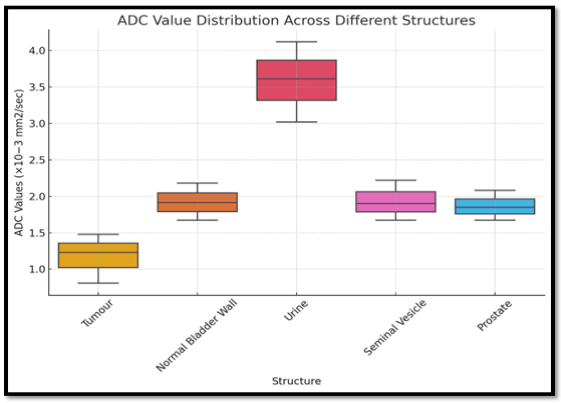

Figure 1: Box plot showing ADC Values with respect to different structures

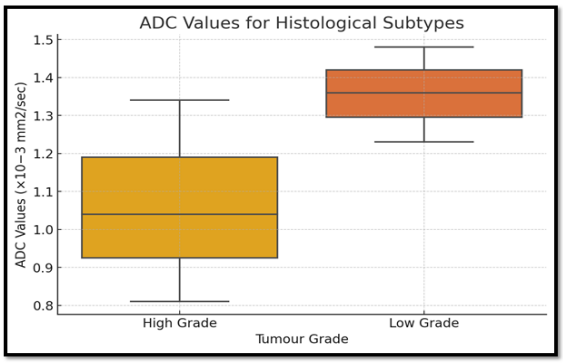

Figure 2: Box plot showing ADC values with respect to Tumor Grade

Table 2: ADC Value with respect to Tumor grade, T stage and N stage

		N	Mean ADC	SD	P value
Tumour Grade	High Grade	16	1.04	0.1	<0.001*
	Low Grade	30	1.36	0.06	
T Stage	T1	18	1.23	0.15	<0.001*
	T2	16	1.2	0.14	
	T3	12	1.04	0.1	
N Stage	N0	37	1.23	0.14	0.004*
	N2	9	1.04	0.1	

The ADC values ($\times 10^{-3}$ mm²/sec) showed a significant correlation with tumour grade, T stage, and N stage. High-grade tumours had a significantly lower mean ADC (1.04 ± 0.10, $p < 0.001$) compared to low-grade tumours (1.36 ± 0.06). Similarly, among T stages, T3 tumours had the lowest ADC (1.04 ± 0.10), while T1 and T2 stages had progressively higher values (1.23 ± 0.15 and 1.20 ± 0.14, respectively), with a statistically significant p value of <0.001. For N stages, ADC values were significantly lower in N2 patients (1.04 ± 0.10) compared to N0 patients (1.23 ± 0.14), with a p value of 0.004, indicating a clear distinction in diffusion characteristics based on tumour progression. [Table 2]

Table 3: DW-MRI in differentiating T staging with respect to HPE as Gold standard

		HPE		Total	P value
		T1	T2, T2, T3		
DW-MRI T staging	T1	18	0	18	<0.001*
	T2, T2, T3	1	27	29	
	Total	19	27	46	

Parameter	Estimate	Lower - Upper 95% CIs
Sensitivity	94.74%	(75.36, 99.06)
Specificity	100%	(87.54, 100)
Positive Predictive Value	100%	(82.41, 100)
Negative Predictive Value	96.43%	(82.29, 99.37)
Diagnostic Accuracy	97.83%	(88.66, 99.62)
Cohen's kappa (Unweighted)	0.9548	(0.6661 - 1.244)

Table 4: DW-MRI in differentiating N staging with respect to HPE as Gold standard

		HPE		Total	P value
		N0	N2		
DW- MRI N staging	N0	36	0	36	<0.001*
	N2	1	9	10	
	Total	37	9	46	

Parameter	Estimate	Lower - Upper 95% CIs
Sensitivity	97.3%	(86.18, 99.52[1])
Specificity	100%	(70.08, 100[1])
Positive Predictive Value	100%	(90.36, 100[1])
Negative Predictive Value	90%	(59.58, 98.21[1])
Diagnostic Accuracy	97.83%	(88.66, 99.62[1])
Cohen's kappa (Unweighted)	0.9337	(0.6454 - 1.222)

DW-MRI also showed high accuracy in differentiating nodal staging (N staging) relative to HPE. Among the 37 cases classified as N0 by HPE, DW-MRI correctly identified 36 cases, with only one false-negative case. Similarly, all 9 cases classified as N2 by HPE were accurately detected by DW-MRI, with no false positives. This resulted in a sensitivity of 97.3% (95% CI: 86.18 - 99.52) and a specificity of 100% (95% CI: 70.08 - 100). The PPV was 100% (95% CI: 90.36 - 100), and the NPV was 90% (95% CI: 59.58 - 98.21), demonstrating a high level of confidence in correctly diagnosing both N0 and N2 cases. The overall diagnostic accuracy was 97.83% (95% CI: 88.66 - 99.62), similar to the accuracy in T staging. The Cohen's kappa coefficient was 0.9337 (95% CI: 0.6454 - 1.222), further indicating a strong agreement between DW-MRI and HPE for N staging ($p < 0.001$) [Table 4]. These findings confirm that DW-MRI is a highly reliable imaging modality for accurately staging bladder cancer, with excellent sensitivity, specificity, and diagnostic agreement when compared to histopathological examination.

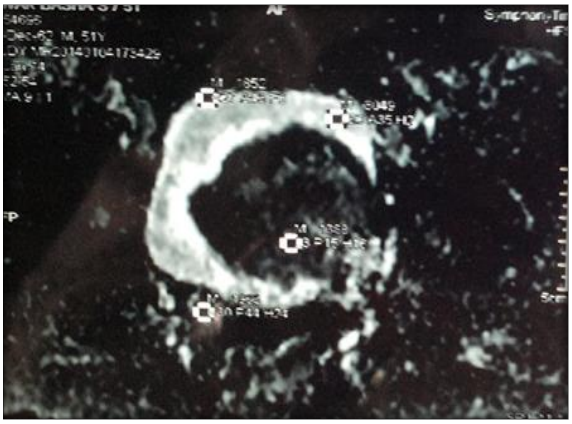

Figure 3: ADC Mapping showing tumour with low SI

DISCUSSIONS

The urothelium of the bladder is traditionally lined by transitional cells, which can transform into various benign and malignant tumors. Following prostatic adenocarcinoma, bladder carcinoma represents the second most common urological malignancy.[1] The literature describes bladder cancer as a disease influenced by environmental factors and aging, with an incidence three to four

times higher in males than females, peaking in the seventh decade of life. The most common histologic subtype worldwide is urothelial carcinoma, whereas in Egypt, squamous cell carcinoma is more prevalent due to the endemicity of Schistosomiasis.[9] Urothelial tumors are broadly classified into non-muscle-invasive and muscle-invasive tumors based on detrusor muscle invasion.

It has been established that tumor grade is more critical than stage in predicting prognosis for urothelial cancers. Additional prognostic factors include tumor size, multifocality, tumor nature, and angiolymphatic permeation.[10] Bladder tumors exhibit a high recurrence rate after primary treatment, which depends on these prognostic factors.

Under anesthesia, cystoscopic assessment followed by transurethral resection (TUR) provides a pathological evaluation. However, TUR has a high likelihood of underestimating tumor extent.[11] If histopathology suggests a non-muscle-invasive tumor, patients are managed with intravesical therapy, with high-risk cases requiring aggressive treatment. Muscle-invasive tumors are categorized into organ-confined, locally advanced, and metastatic disease. Treatment options include radical cystectomy, radiation therapy, chemotherapy, or a combination.[12]

DW-MRI is an advanced imaging technique based on the diffusion of water molecules, allowing for tissue characterization. Unlike T1- and T2-weighted imaging, DW-MRI utilizes the principle of Brownian motion to assess cellular density and diffusion restriction.[13] The apparent diffusion coefficient (ADC), derived from DW-MRI, reflects both water diffusion and capillary perfusion in extracellular extravascular space.[14] In highly cellular tumors with dense membranes, restricted proton movement results in high DW-MRI signal intensity and correspondingly low ADC values.[15] Thus, DW-MRI enables better differentiation between normal and abnormal tissue structures.

DW-MRI has long been used in neuroradiology, particularly in diagnosing cerebral ischemia.[16] Its application in extracranial organs has expanded, allowing for tumor detection, treatment response monitoring, and organ function evaluation.[17] Motion artifacts caused by breathing and bowel movements initially posed challenges for abdominal DW-MRI, but free-breathing imaging techniques, as suggested by Takahara et al., have improved image quality.[18]

Various imaging modalities are available for preoperative bladder cancer staging. In our study, 46 patients were evaluated using blood tests, radiological imaging, and DW-MRI. Based on DW-MRI findings, 18 patients were diagnosed with NMIBC, while 28 had MIBC. TURBT histopathology later confirmed that 19 patients had NMIBC and 27 had MIBC. The correlation between DW-MRI and histopathology demonstrated a sensitivity of 94.4%, specificity of 100%, and a positive predictive value (PPV) of 100%, indicating significant diagnostic accuracy.

The feasibility of DW-MRI under free-breathing conditions was validated by Matsuki et al., who demonstrated 100% sensitivity and specificity for detecting bladder cancers.[19] Similar to previous studies, our findings showed that bladder tumors exhibited high DW-MRI signal intensity and low ADC values relative to surrounding structures. Tumor invasion and nodal metastasis were clearly distinguished due to differential ADC values.

Additionally, our study confirmed a strong correlation between lower ADC values and high-grade tumors, a factor not assessed in prior studies. Takeuchi et al. reported that mean ADC values were significantly lower in grade 3 (G3) tumors compared to grades 1 and 2, improving overall staging accuracy from 67% to 88% when DW-MRI was incorporated.[20] Our results were consistent, showing an average ADC of $1.04 \pm 0.10 \times 10^{-3}$ mm^2/sec for high-grade tumors.

Despite its advantages, our study had limitations, including a small sample size and difficulty assessing superficial tumors. Post-therapy DW-MRI assessments were not performed, highlighting the need for further research to differentiate between tumors and reactive tissue. Nonetheless, our findings demonstrated that DW-MRI significantly correlated with histopathology in differentiating bladder cancer stages and grades.

DW-MRI is a rapid, contrast-free imaging modality suitable for patients with renal impairment or contrast allergies. Given its ability to accurately stage and grade bladder tumors preoperatively, DW-MRI is a valuable tool for treatment planning.

CONCLUSION

DW MRI findings significantly correlate with histopathology in differentiating non muscle invasive bladder tumours from muscle invasive bladder tumours and also in local nodal staging. Grading of bladder tumour could be assessed with DW MRI as high-grade tumours had significantly lower ADC values compared to low grade tumours. Hence in the preoperative evaluation of bladder cancers, DW MRI is a useful diagnostic imaging study both for grading and local staging of bladder cancers.

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