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Role of MR Diffusion-Weighted Imaging in Assessment of Urinary Bladder Masses

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Abstract: Background: Bladder cancer is the most common tumor, occupying the 4th and the 10thin males and females, respectively. one of the valuable imaging technique is the magnetic resonance imaging (MRI) which characterized by multiplanar imaging capabilities, high tissue contrast, and the opportunity of tissue characterization. Another diagnostic technique which are applied in the evaluation of various abdominal lesions is the diffusion-weighted imaging (DWI). **Aim of the work:** to assess role of MR Diffusion Weighted imaging in evaluation of urinary bladder masses. **Patients and Methods:** Fifty (50) consecutive patients (43 men and 7 women) with the range of age between (34–70 years) with suspected bladder lesions, underwent MR imaging through the period between March 2016 and December 2019. These patients presented with gross (macroscopic) hematuria or had urinary bladder mass, detected on U/S and/or CT examinations. **Results:** As regards the detection of urinary bladder carcinoma, the accuracy of DW in differentiating between neoplastic and non-neoplasticlesion was 100%, the mean ADC value in non-neoplastic lesion 1.7and in neoplastic lesion 0.8 -/+0.13 and the cut off value was1.2, accuracy of T2WI for proper tumor staging was 100%,50%, 88.9%, and 100 % for stages T1, T2, T3 and T4, respectively. Precision of DWI for accurate cancer stagingwas100%, 75%, 100%, and 100% for stages T1, T2, T3 and T4 respectively. **Conclusion:** MR imaging has high dependability for the diagnosis of bladder cancers and differentiate between neoplastic and non-neoplastic lesions, and assess stage & grades of bladder cancer with high degree of accuracy. More precise extrapolations can be made around the malignant potential of urinary bladder lesions by using ADC quantification.

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1. Introduction:

Worldwide, the urinary bladder tumor are representing the 2ndmost common tumor of the urinary tract. It accounts for 6-8% of overall malignancy in men and 2-3% in women. It is more common in men than women (3:1) and typically occurs in patients over the age of 50 ***(Yaxley.2016).*** Radiological evaluation is a significant part of diagnosis and staging of bladder tumor. Magnetic resonance imaging (MRI) and Computed tomography (CT) are the foremost radiologic tools which are applied in the estimation of subjects with bladder tumor ***(Bouchelouche et al., 2012).*** Whereas, there are a recent functional MR-imaging methods are introduced for detection of bladder cancer such as determination of the apparent diffusion coefficient values (ADC) and diffusion-weighted magnetic resonance imaging (DW-MRI) ***(Al Johy et al., 2018).*** DWI has a higher overall precision matched to both T2WI and post contrast T1WI in T staging of bladder tumor, and similarly ADC map can forecast the cancer grade. There fore, DWI can be optional as talented MRI sequence in urinary bladder T grading and staging ***(Abdel-Rahman et al.,2015).*** **Aim of the work:** is to evaluate role of MR Diffusion Weighted imaging in evaluation of urinary bladder masses.

2. Patients and Methods:

Through the period between March 2016 and December 2019, fifty (50) consecutive patients (43 men and 7 women) with the range of age between (34–70 years) with suspected bladder lesions, underwent MR imaging. These patients presented with gross (macroscopic) hematuria or had urinary bladder mass, detected on U/S and/or CT examinations. This study excluded patients with upper urinary tract stones or neoplasma and in patients with history of urinary tract disturbance, patients with contraindications to MR scanning (eg, pacemaker or metallic prostheses), and patients who refuse to write the consent before the study.

All 50 patients underwent transurethral cystoscopic biopsy after imaging, and 4 patients were of non-neoplastic nature. The tumor was histologically confirmed in the remaining 46 patients, Pathologic stage was determined in the 46 patients and all subjects endured surgical operation within 35 days after MR scanning. A further deep muscle biopsy was done at the base of the tumor in cases that underwent TUR. The pathologic stage was classified as T1 or less in case of no tumor cells were present. 4b1 patients who underwent TUR show positive deep muscle biopsy, so they shifted into invasive bladder cancer and underwent radical cystectomy.

MR Imaging Technique:

Patients were advised to start drinking water to moderately distend the bladder, at least 1hr before the MR scanning examination. MR scanning was done by applying a 1.5-T imager (Gyroscan Intera; Philips Medical Systems, Best, the Netherlands) equipped with a radiofrequency coil (Quadrature body coil; Philips Medical Systems).

ADC and Histological Grade:

The ADC values were measured to assessment the degree of diffusion. ADC maps were created in the 50 lesions that were larger than 5 mm to comprise the area of attention.

Histopathology Analysis:

The specimens were stained with hematoxylin-eosin stain for conventional histopathology evaluation.

Statistical analysis:

Data were collected, coded, revised and entered to the Statistical Package for Social Science (IBM SPSS) version 20.

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following: P > 0.05: Non-significant (NS). P < 0.05: Significant (S), P < 0.01: Highly significant (HS).

3. Results:

In this study, 86% of patients were males, mean of age were 57.22 with range from 34 to 70 years.

As regard the clinical history, results showed that 84% of patients had hematuria, 8% had frequency and 4% had vaginal bleeding.

Results also revealed that 56% of lesions were thickening, 42% were single and 2 were multiple. In DWI 92% of lesions showed restricted diffusion and 8% showed no diffusion restriction, the mean of ADC were 0.94 with range from 0.49 to 2.

According to the nature of the lesions, 92% were neoplastic and 8% were non-neoplastic.

Table (2) showed that there was statistically significant increase in ADC value in non neoplastic in comparison to Neoplasticlesions.

To define the best cut off value of ADC value, receiver operating characteristics (ROC) curve was applied which was <1.2, with specificity of 100% positive predictive value of 100%, with sensitivity of 100% negative predictive value of 100% with area under the curve of 1.000 (Table 2).

Table (1): Comparison between nature of the lesions as regards radiological Findings

		Non neoplastic (No.=4)		Neoplastic (No.=45)		Chi square test/ one way ANOVA	
		No	**%**	**No**	**%**	**X^2/f***	**P value**
DWI	No diffusion restriction	4	100.00%	0	0.00%	100.00	<0.001
	Restricted diffusion	0	0.00%	46	100.00%		
ADC	Mean SD	1.70 ± 0.00		0.83 ±0.13		160.49**	<0.001

Table (2): Diagnostic Performance of ADC value in Discrimination of neoplastic lesion from non neoplastic lesion

Neoplastic	Cut-off	Sen.	Spe.	PPV	NPV	Accuracy
Non neoplastic vs. Neoplastic	**<1.2**	100%	100%	100%	100%	1.000

Table (3): Comparison between T2WI staging as regards histopathology stage

		Histopathology Stage				total	χ2 test	p- value
		T1	**T2**	**T3**	**T4**			
T2WI Staging	**T1**	2	0	0	0	2	127.267	<0.001
		100.0%	0.00%	0.00%	0.00%	4.8%		
	T2	0	4	0	0	4		
		0.00%	50.0%	0.00%	0.00%	9.5%		
	T3	0	4	16	0	20		
		0.00%	50.0%	88.9%	0.00%	47.6%		
	T4	0	0	0	14	14		
		0.00%	0.00%	0.00%	100.0%	33.3%		
	Total	2	8	16	14	40		
		100.0%	100.0%	100.0%	100.0%	100.0%		

Accuracy of T2WI for proper tumor staging was 100%, 50%, 88.9%, and 100 % for stages T1, T2, T3 and T4 respectively. (P ≤0.001) is highly significant.

Table (4): Comparison between DWI staging as regards histopathology stage

		Histopathology Stage						
		T1	**T2**	**T3**	**T4**	**total**	**χ^2 test**	**p- value**
DWI Stage	**T1**	2	0	0	0	2		
		100.0%	0.00%	0.00%	0.00%	4.8%		
	T2	0	6	0	0	6		
		0.00%	75.0%	0.00%	0.00%	14.3%		
	T3	0	2	18	0	20		
		0.00%	25.0%	100.0%	0.00%	47.6%		
	T4	0	0	0	14	14	215.05	<0.001
		0.00%	0.00%	0.00%	100.0%	33.3%		
	Total	2	8	18	14	42		
		100.0%	100.0%	100.0%	100.0%	100.0%		

Accuracy of DWI for proper tumor staging was100%, 75%, 100%, and 100% for stages T1, T2, T3 and T4 respectively. (P ≤0.001) is highly significant.

Table (5): Cut of point, sensitivity and specificity of DW image in differentiating between superficial cancer (T1 or less) and invasive cancer (T2 or more)

AUC	**Sensitivity**	**Specificity**	**-PV**	**+PV**
1.000	100.00	100.00	100.0	100.0

This table shows that in histopathology STAGE: Its sensitivity and Its specificity was100%.

The positive predictive value is100% The negative predictive value is100%.

4. Discussion:

Pathologic conditions of the bladder can manifest as a focal bladder mass or diffuse wall thickening. In both men and women, tumor of the urinary bladder is a common malignant tumor of the urinary system ***(Jade et al, 2006).*** The suitable management of urinary bladder cancer can be achieved through a precise preoperative staging ***(McLaughlin, et al, 2007).*** Hence, an important diagnostic role can be played by performing preoperative imaging studies which are capable for differentiating among the two main items of bladder cancer exactly. MRI (magnetic resonance imaging) is a vital complementary diagnostic device in the diagnosis, staging, and follow up of bladder cancer. Purposes: The main target of the present work was to explore the diagnostic effectiveness of pelvic MRI including ADC (apparent diffusion coefficient) and DWI (diffusion weighted imaging) in the assessment of bladder cancer grade and thus helping in patients' management ***(Khaled et al., 2017).***

Hence, the main target from this investigation was to explore the diagnostic effectiveness of pelvic MRI including ADC (apparent diffusion coefficient) and DWI (diffusion weighted imaging) in differentiating bladder masses and assessment of bladder cancer grade and stage and thus helping in patients' management.

According to the role of DW-MR imaging in differentiating between neoplastic and non-neoplastic lesion in our study, the sensitivity of DW in differentiating between neoplastic and non-neoplastic lesion was 100% which matched with ***Matsuki et al, 2007.*** Similar findings were reported by ***El-Assmy et al., 2008,*** the sensitivity and positive predictive values of DW- MRI were 100% in terms of correctly detecting the bladder carcinomas on 43 patients.

In a study carried out by ***Abou-El-Ghar et al, 2009,*** on 130 patients with hematuria, the cystoscopy was considered as a standard reference. The sensitivity, specificity, positive predictive value (PPV), negative predictive value and accuracy of DW-MRI were found respectively, 98.5%, 93.3%, 100%, 92.3% and 97%. The authors found excellent agreement between the DW-MR imaging and the conventional cystoscopy.

In a study carried out by Soichiro ***Yoshida et al, 2017,*** Bladder cancers mostly display a homogeneous hyper intense signal by using DWI of 800–1000 s/mm^2. The main parameters of DWI during examination of urinary bladder cancer regarding the sensitivity, specificity, and accuracy were ranged from 91–100%, 77–91%, and 81–96%, respectively.

Other study published by ***Nadine Barsoum et al., 2017,*** on 50 patients As regards the detection of urinary bladder carcinoma, DW-MRI demonstrated an overall sensitivity and specificity of 100%, and 75%, respectively. Whereas, the positive-and negative predictive value was reached 98% and 100%, respectively. Also, the accuracy detected was 98%.

In concordance with the results of the previous studies, all concerned about detection of the bladder tumors we have assessed were clearly measurable with DWI. In our study the aim is to differentiate between neoplastic and non-neoplastic lesions, 50 patients were examined by MR examination and the cystoscopy was taken as a standard reference method. The following parameters of DW-MRI for differentiating between neoplastic and non neoplastic lesion: The specificity, sensitivity, positive and negative predictive and finally the accuracy were found respectively, 100%, with statistically significant increase in ADC value in non neoplastic in comparison to Neoplastic, the mean ADC value in non neoplastic lesion 1.7 and in neoplastic lesion 0.8 -/+0.13 & the cut off value was 1.2.

The results of our and previously published studies suggest a high reliability of DW-MR imaging for differentiating between neoplastic and non neoplasticlesions.

In study published by ***El-Assmy et al., 2012*** studied the feasibility of using DW-MRI in diagnosis of bladder cancer follow-up after TUR. The results revealed that DW-MRI for identifying bladder tumors, the sensitivity was 91.6% (22/24), specificity was 91.3% (21/23), accuracy was 91.5% (43/47), positive and negative predictive values were averaged 91.6% (22/24) and 91.3% (21/23), respectively. The authors concluded that there was no significant variation was observed between DW-MRI and cystoscopy; therefore, DW-MRI has a high consistency in discerning post-TUR inflammatory alterations from bladder tumors, like that shown b cystoscopy. In addition, DW-MRI could be a first-tool in diagnosis of urinary bladder cancer in follow-up after TUR in patients. As we found in our study that the post-TUR inflammatory changes are of the same signal intensity of bladder wall on DW image.

In spite of cystoscopy is still a standard technique used in the follow-up of cases with a bladder cancer ***(Walker et al., 1993)*** and possessing a sensitivity of 90%, yet, cystoscopy is an aggressive technique and may need anesthetic agents, leading to worsen patient compatibility and prolonged periods of application ***(Wright and Jones, 2000; Tinzl and Marberger, 2003).*** DW-MRI seems to be a substitute to cystoscopy due to many benefits such as a non-invasive method, it has no any requirements for a contrast and enables uncomplicated patient compatibility offers a close association of diagnostic value for cystoscopy, necessitates a short time to scan (151 seconds).

In our knowledge, many of the previously mentioned published studies had common limitation that the value of DW against T2-weighted MR imaging for staging of bladder cancers was not evaluated.

As regard to the role of DW-MR imaging in staging of urinary bladder carcinoma, Some authors ***(Padhani et al., 2009)***, reported that DWI signal is measured by quantitative ADC value analysis and incomes of visual image interpretation**.** Local staging is performed according to the difference in the signal intensity between bladder cancer and the surrounding tissue due to DW images are functional images and the spatial resolution is intrinsically limited (typical voxel size is around 4 × 3.5 × 3.5 mm^3). At high b values, the muscle and submucosal layers show intermediate and low signal intensity**,** respectively ***(Takeuchi et al., 2009)***. The presence of low submucosal signal during imaging of bladder cancer can be used as a diagnostic base during bladder cancer staging criteria In addition; the pedunculated tumor stalk of composed of a mixture of fibrous tissue, capillaries and edematous submucosa which are characterized by a non-muscle-invasive bladder cancer, and inducing low signal intensity, in contract with a typical pedunculated papillary bladder tumors which induced a C-shaped high-signal-intensity area with a low-signal-intensity submucosal stalk or a thickened submucosa ***(Takeuchi et al., 2009),*** moreover, the diagnostic accuracy for differentiating non-muscle-invasive from muscle-invasive bladder cancer was enhanced from 79% to 96% when DWI was added to T2-weightedimaging in spite of conventional morphologic MRI is better than DWI for soft-tissue delineation.

In a study carried out by Soichiro ***Yoshida et al., 2017,*** they confirmed this diagnostic precision to be 66–71% sensitivity, 83–91% a specificity and 79–82%. an accuracy rate.

In our study there is improvement in detection of T2 stage when we use DW image after T2 - weighted imaging from 50% - 75 % & improvement in detection T3 stage from 88.9% -100%.

Many investigations dealing with the efficacy of the ADC value as an imaging biomarker in controlling bladder tumor ***(Yoshida et al., 2014).*** Intratumoral distribution of ADC values tends to be homogeneous on the ADC map, and the histogram for the distribution of the ADC of each pixel within the tumor demonstrated a single noticeable peak in 83% of bladder which attributed to the homogeneous diffusion nature within bladder cancer ***(Yoshida et al., 2012).***

The adding of ADC amounts to visual DWI valuation additional amended the local staging precision. The under staging rate of the inchworm sign for muscle- invasive bladder tumor enhanced from 27–25% to 4.5–4.0% by incorporating high ADC values (using a cutoff of 0.80 × 10−3 mm^2/s) to the inchworm sign (***Soichiro Yoshida et al, 2017).***

Other study carried by ***Eman et al, 2018.*** pathologic staging regarding Tis and T1 (superficial) was found to be 28% of cancers, whereas, the cutoff ADC value was averaged 1.275 × 10–3 as a valuable marker ($P < 0.005$) for distinguishing stages Tis to T1 from T2 to T4.

In our study, the cut off value for differentiating superficial cancer from invasive cancer is 1 with sensitivity 90%, positive predictive value is 95%.

Many investigations were dealing with the correlation among ADC values and histological grade of urinary bladder tumor ***(Avcu et al., 2011; Kobayashi et al., 2011; Sevcenco et al., 2011 and Takeuchi et al., 2009).*** These researches always demonstrated a significant decline in ADC values in case of high-grade bladder tumor than with low-grade cancer.

Tekes et al., 2005, hypothesized that the development in image resolution might improved in the revealing of perivesical situation, which commonly in the form of inflammatory or reactive disorders, more than perivesical extend of cancers. The investigators in addition, thinking that cancer surroundings could be determined more precisely by using DW scanning due to the reactive tissue or micro-vessels neighboring to the cancer could be improved to be seen as a tumor content by using contrast-enhanced images but could be differentiated from cancers with the contrast of DW images.

Regarding ADC values concluded by ***Ceylan et al, 2010,*** The average ADC values in a bladder cancer patients was ($1.05\pm0.22 \times 10^{-3}$ mm²/s), whereas, it averaged ($1.830 \pm0.18 \times 10^{-3}$mm²/s) from normal bladder wall In our study:

Receiver operating characteristics (ROC) curve was used to define the best cut off value of ADC value:

Grade I vs. III: which was <0.79, with 77.8% specificity, 88.9% sensitivity, 80%, positive predictive value, 87.5% negative predictive value and 0.827 an area under the curve.

Grade I vs. II: which was <0.86, with 77.8% specificity, 80% sensitivity, 66.7% and 87.5% positive and negative predictive values, respectively and 0.827 an area under the curve.

Based on our and prior studies, the ADC could forecast the histological grade of urinary bladder tumor.

The limitations of the present study include the following: First, we included a larger number of advanced stage tumors and large sized lesions (mean 5.39 cm), and this could explain the high sensitivity, specificity and accuracy of DW-MR imaging for distinguishing Tis to T2 from T3 to T4 cancers. Second, diffusion-weighted imaging is recognized to be more sensitive regarding bone and lymph node metastases: In the current study we didn't found its diagnostic presentation for N or M staging. though, another research is requisite to evaluate whether the use of diffusion weighted imaging enhances such diagnoses.

On the other hand, DW-MRI has many benefits like non-invasive technique, short acquisition time, and does not contain ionized radiation.

Conclusion:

From these results, it is concluded that MR scanning has high dependability for urinary bladder cancers diagnosis and differentiation between neoplastic and non neoplastic lesions owing to a non-invasive technique, rapid and does not need administration of contrast substances. DWI is a valuable and safe technique for the distinguishing between benign and malignant urinary bladder lesions and giving a valuable data concerning the grade of cancer and stage of urinary bladder carcinomas.

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