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Diffusion Weighted Magnetic Resonance Imaging in Evaluation of Non Muscle Invasive Bladder Cancer Correlated to the Second Cystoscopy

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ABSTRACT

Background: Proper management of the urinary bladder cancer depends on the stage of the lesions. The aim of this work was to correlate between the outcomes of DW-MRI results and biopsy results of 2nd look TURBT in NMIBC and to correlate between DW-MRI and conventional MRI in NMIBC.

Patients and methods: It was a prospective study included twenty four patients with NMIBC underwent 2nd look TURBT with preoperative imaging with DW-MRI on pelvis. Bladder mapping was done on 1.5 T Philips Achieva system class II MRI device is used. T1andT2 weighted is used for anatomical and morphological evaluation. Diffusion-weighted images were obtained by using single shot echo-planar imaging with a pair of rectangular gradient pulses along three orthogonal axes. Second look cystoscopy and biopsy was performed under spinal anesthesia. Resection of lateral wall bladder tumors was performed under general anesthetic with a paralytic agent to avoid inadvertent bladder wall perforation from an obturator nerve reflex .Biopsy was taken from the tumor base or residual of the mass if present for histopathological examination

Results: Sensitivity of DW-MRI was 100%, specificity was 92.8% and accuracy was 96.8% in prediction of malignancy, while Sensitivity of DW-MRI was 83.33%, specificity was 80% and accuracy was 81.25% in prediction of muscle invasion tumors. 14 of the 32 lesions analyzed in the second TURB were diagnosed as MIBC. There was a significant correlation between clinical staging by DW-MRI and pathological staging

Conclusion: This study show the superiority of DWMRI to T1W- and T2W-MRI in differentiating residual bladder cancer from postoperative changes after an initial TURB. DW-MRI showed reasonable high sensitivity, specificity, accuracy and agreement compared to the results of the gold standard pathological examination of urinary bladder tumors. DW-MRI can be a useful adjunct for

optimal selection of patients for a second TURB. It can replace the diagnostic part of second look cystoscopy

Keywords: Diffusion Weighted Magnetic Resonance; the Second Cystoscopy; Non Muscle Invasive Bladder Cancer

.**Introduction:**

Urinary bladder cancer is the second most common neoplasm of the urinary tract after cancer prostate. (1). In Egypt, carcinoma of the bladder is the most prevalent cancer, Bladder cancer has the highest recurrence rate of any malignancy. (2)

Bladder cancer is a heterogeneous disease, with 70% of patients presenting with superficial tumors, including stages Ta, Tis, and T1 (3). However, bladder cancer is multifocal, with a high recurrence rate further, in patients undergoing initial TURBT, the recurrence rate remains high, at 50–70%, with a progression rate of 15–30%. (4)

Several factors influence the outcome of the initial TURBT, such as multiple tumors, a large tumor or a location with an unidentifiable margin, and effortless bleeding that can obstruct the surgeon's vision, the surgeon's experience and skill, the quality of the specimens, and the pathologist's evaluation. Consequently, the pathological stage of the tumor is underestimated in 9–49% of patients with NMIBC after the first TURBT. (5)

Therefore, second-look TURBT has an important role in confirming or restaging to help clinicians make decisions regarding further disease management. In general, second-look TURBT is performed 2–6 weeks after the initial resection, which includes resection of the primary tumor site. (6)

For the radiological evaluation of the urinary bladder and prostate gland, MRI is a valuable imaging modality due to high tissue contrast, multiplanar imaging capabilities, and the possibility of tissue characterization. (7,8)

In recent times, diffusion-weighted imaging (DWI) has emerged as a diagnostic technique in the evaluation of various abdominal lesions. DWI reveals micromolecular diffusion, which is the Brownian motion of the spins in biologic tissues. This technique can delineate pathologic lesions with high tissue contrast against generally suppressed background signal. (9)

The aim of this work was to correlate between the outcomes of DW-MRI results and biopsy results of 2nd look TURBT in NMIBC and to correlate between DW-MRI and conventional MRI in NMIBC.

Patients and Method:

It was a prospective study included twenty four patients with NMIBC underwent 2nd look TURBT with preoperative imaging with DW-MRI on pelvis in

urology& Radiology department at Zagazig university hospitals from December 2018 till December 2019.

Patients with Non Muscle Invasive Bladder Cancer (Transitional cell carcinoma) were included in this study if they were indicated for 2nd look cystoscopy for incomplete initial resection, High grade or T1 tumor, or when specimen contains no detrusal muscle

Patients with muscle invasive bladder cancer, Patients with other non-urothelial tumors (e.g., squamous cell carcinoma or adenocarcinoma), Patients received previous treatment for bladder cancer, History of upper tract urothelial tumors and Patients has contraindications for MRI (like metallic implant and claustrophobia) were excluded from this study. Every patient was consented after detailed information about the procedure.

Bladder mapping was done during diagnostic cystoscopy for every case to add informations to region of interest should be measured later on1.5 T Philips Achieva system class II MRI device is used.T1andT2 weighted is used for anatomical and morphological evaluation

Thirty minutes before the MRI study, all patients were asked for drinking water and presented by full bladder. MR imaging was performed by using a pelvic phased-array coil with the patient in supine position. MR imaging examination included T2WI, DWI and T1WI without contrast.

T1-weighted fast field-echo images with and without fat suppression technique; TR/TE =500/20; matrix, 224 x 214; section thickness, 3 mm; gapless; field of view, 35 cm; were obtained.

After localizer images, T2-weighted spin-echo MR images were obtained from the aortic bifurcation to the symphysis pubis with the following parameters: repetition time msec/echo time msec, 4400/120, section thickness, 4 mm; intersection gap, 0.4 mm; field of view, 23 cm; matrix, 256 x 190. T2-weighted images were done in the axial and sagittal planes. Diffusion-weighted images were obtained by using single shot echo-planar imaging with a pair of rectangular gradient pulses along three orthogonal axes. The imaging parameters were as follows: TR/TE = 2800/74; field of view 25 cm, section thickness, 3 mm; intersection gap, 1 mm. Images were zero-filled to a 256 x 256 matrix. The orientation and location of these images were prescribed identically to the axial T2-weighted images. The b values were 0, 500 and 1000 s/mm. To gain better signal-to-noise ratios, a larger field of view was used for DW imaging than for T2-weighted imaging, and a thicker section was used for T2-weighted and DW imaging than for T1-weighted fast field echo imaging. DW images were obtained in the axial and sagittal planes

Second look cystoscopy and biopsywas performed under spinal anesthesia .Resection of lateral wall bladder tumors was performed under general anesthetic with a paralytic agent to avoid inadvertent bladder wall perforation from an obturator nerve reflex.

Biopsy was taken from the tumor base or residual of the mass if present .The biopsy was submitted in separate packets: (1) superficial biopsy from tumor base or residual, (2) deep biopsy containing muscle layer.

Primary bladder tumors were histologically evaluated. Multiple sections were obtained from the harvested biopsy for histological examination. Pathologic staging was done using TNM 2009 classification

Results:

We evaluated 24 patients with non-muscle invasive TCC and indicated for 2nd look cystoscopy. Number of masses in studied patients was 32. Eighteen masses were single and 14 masses were multiple. In our study, MRI examination was performed (22-40) days after the intial TURB, and (3-19) days before the second look TURB .Demographic data were collected in details as sgowen in table 1

DW-MRI has higher sensitivity, specificity, accuracy than conventional MRI, which are (100%, 66.6%) sensitivity, (92.8%, 50%) specificity and (96.8%, 56.25%) accuracy for DW-MRI and conventional MRI respectively. (table 2,3)

14 of the 32 lesions analyzed in the second TURB were diagnosed as MIBC. There was a significant correlation between clinical staging by DW-MRI and pathological staging. (Table 4)

Table (1): Demographic data of the studied masses (N=32).

Categorical data	**No.**	**%**
Sex		
Male	16	66.7%
Female	8	33.3%
Age (years)	61.25 ± 4.86	60.50 (55 – 70)
BMI (kg/m^2)	28 ± 3.62	27.50 (23 – 36)

Table (2): Validity of DW-MRI clinical staging in prediction of malignancy (pT1+pT2) in second look TURB.

	Estimate	(95%Confidence Interval)
Sensitivity (%)	100%	(85.47 – 100)
Specificity (%)	92.8%	(78.83 – 96.47)
Positive Likelihood Ratio	13.8	
Negative Likelihood Ratio.	0	
Positive Predictive Value (%)	94.7%	
Negative Predictive Value (%)	100%	
Accuracy (%)	96.8%	(89.11 – 98.32)
Area Under Curve	0.91	(0.79 – 0.95)

Table (3): Validity of conventional MRI clinical staging in prediction of muscle invasion (pT2) in second look TURB.

	Estimate	(95%Confidence Interval)
Sensitivity (%)	66.66%	(34.88 – 90.07)
Specificity (%)	50%	(27.19 – 72.80)
Positive Likelihood Ratio	1.32	(0.39 – 0.75)
Negative Likelihood Ratio.	0.68	(0.26 – 1.66)
Positive Predictive Value (%)	44.44%	(30.64 – 59.15)

Negative Predictive Value (%)	71.42%	(50.01 – 86.16)
Accuracy (%)	56.25%	(37.66 – 73.63)
Area Under Curve	0.583	(0.396 – 0.754)

Table (4): Agreement between DW-MRI clinical staging and pathological staging of second look TURB regarding detection of muscle invasion.

		Pathological staging of second look TURB		Total
		pT0+pT1	pT2	
DW-MRI clinical staging	cT0+cT1	16 (50%)	2 (6.2%)	18 (56.2%)
	cT2	4 (12.5%)	10 (31.2%)	14 (43.8%)
Total		20 (62.5%)	12 (37.5%)	32 (100%)

Concordant	Discordant	McNemar's test p-value (Sig.)	Cohen's kappa coefficient	
			Estimate (95%CI)	p-value (Sig.)
26 (81.2%)	6 (18.8%)	0.687 (NS)	0.813 (0.537 – 0.989)	<0.001 (HS)

95%CI: 95% Confidence Interval.p< 0.05 is significant.Sig.: Significance.

3- Discussion:

Tumor staging and regional disease spread are the strongest predictors of treatment outcome in urinary bladder cancer. (10) The management and prognosis of bladder cancer are based on T staging, pathologic grading of the tumor, and the presence or absence of metastatic disease. (11)

Surveillance strategies for urinary bladder carcinoma recurrence have historically relied on cystoscopy, but this procedure has drawbacks, including its high cost, invasiveness and the fact that it may lead to iatrogenic bladder injury and urinary sepsis. (12) TURB is considered invasive technique which may be risky particularly in patients with bleeding disorders. (13)

Diffusion weighted imaging (DWI) is an advanced, functional non-invasive radiological modality. It is highly sensitive in the detection of the random motion (Brownian motion) of water molecules and their collision against barriers like cell membrane. Thus, in cases of cellular overcrowding such as in malignancies, this motion well be restricted. DWI visualizes this motion; the more restricted the molecular motion inside the tissue, the higher the signal intensity on imaging will appear. (14)

Magnetic resonance imaging (MRI) is currently the best imaging technique for loco-regional staging for several malignancies because of its superior soft tissue contrast resolution with the advantage of avoiding exposure to ionizing radiation .(15)

In our study, DW-MRI has higher sensitivity, specificity, accuracy than conventional MRI, which are (100%, 66.6%) sensitivity, (92.8%, 50%) specificity and (96.8% , 56.25%) accuracy for DW-MRI and conventional MRI respectively.

One year follow-up after TURB. El-Assmy et al. (16) reported 91.6% ,sensitivity, 91.3% specificity and accuracy 91.5% , Wang et al. 17) reported 100%

sensitivity, 81.8% specificity and 92.6% accuracy and Nakamura et al. (18) reported 92% sensitivity, 82% specificity and 67% accuracy of DW-MRI for detecting bladder cancer recurrence during follow up after TURB.

Our results showed 100% sensitivity, 92.8% specificity and 96.8% accuracy of DW-MRI for detecting bladder cancer recurrence after 1ryTURB.

The differentiation of residual tumor from postoperative changes, which remains challenging in spite of technological advancements in morphological imaging and contrast-agent-based imaging, is another potential use of DW-MRI. (19)

Generally, a second TURB is performed shortly after an initial TURB, and the initial TURB-induced morphological change and neo-vascularization still remain at the time of the MRI examination prior to the second TURB. These post-therapeutic changes have significant effects on the appearance of T2W and DCE-MRI findings, manifesting as bladder wall thickening and early contrast enhancement; this lowers both modalities' specificity for detection of residual bladder cancer. (20, 21)

It is worth noting that these inflammatory changes are known to persist for many years after the operation. (18)

El-Assmy et al. (16) reported 2 false-positive lesions on DW-MRI confirmed as non-specific cystitis, consisted of two small bright superficial nodules confined to the bladder wall with no muscle invasion, Wang et al. (17) reported no false-positive lesions on DW-MRI and Nakamura et al.(18) reported 3 false-positive lesions on DW-MRI were histologically diagnosed as granulomatous tissue with inflammation.

Our study showed 4 false-negative lesions on DW-MRI .Nakamura et al. (18) reported 4 of the 30 lesions analyzed in the second TURB were diagnosed as MIBC. All these residual MIBCs were non-papillary on the second TURB and positive on DW-MRI, while no MIBC was detected from scars, edematous lesions, or DW-MRI negative lesions. These results suggest that deep resection involving muscle sampling should be performed for DW-MRI positive lesions with a non-papillary appearance. A series of studies exploring multi-sequence MRI have consistently shown the difficulty in detecting CIS lesions of the bladder. (11)

In the current study cohort, 14 of the 32 lesions analyzed in the second TURB were diagnosed as MIBC. Our study showed significant correlation between clinical staging by DW-MRI and pathological staging. In our study, the accuracy of detecting recurrent tumors was significantly ($P < 0.001$) high on DWI with areas under the ROC curves of 0.948.

Wang et al. (17) the accuracy of detecting recurrent tumors was significantly ($P < 0.05$) higher on DWI than DCE MRI with areas under the ROC curves of 0.909 and 0.517, respectively. DWI had excellent consistency with histopathology ($j = 0.85$, $P = 0$), whereas the consistency was fair for DCE MRI ($j = 0.38$, $P = 0.03$).

Limitations of the study include its small sample size and lack of evaluation of distant metastases, so a prospective study in a larger cohort is needed to confirm the current findings. Another limitation is that not all patients received MRI before initial TURB.

This study show the superiority of DWMRI to T1W- and T2W-MRI in differentiating residual bladder cancer from postoperative changes after an initial TURB. DW-MRI showed reasonable high sensitivity, specificity, accuracy and agreement compared to the results of the gold standard pathological examination of urinary bladder tumors. DW-MRI can be a useful adjunct for optimal selection of patients for a second TURB. It can replace the diagnostic part of second look cystoscopy

Conflict of Interest: No conflict of interest.

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