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ORGINAL ARTICLE

Comparison between Diffusion-Weighted Magnetic Resonance Images and Second-Look Cystoscopy Results of Superficial Bladder Cancer

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ABSTRACT

Background: Transurethral resection of bladder tumor (TURBT) is the common technique used in the management of non-muscle-invasive bladder cancer (NMIBC). Diffusion-weighted magnetic resonance imaging (DWI) is used to assess several urinary tract pathologies. This work aimed to correlate between the findings of DWI results and biopsy results of second-look TURBT in NMIBC and to correlate between DWI and conventional MRI in NMIBC before second-look cystoscopy.

Methods: A cross-sectional study was conducted at the department of Urology, Zagazig university hospitals during the period from December 2018 to December 2019. The study included 24 patients with NMIBC who underwent second-look TURBT with preoperative imaging with conventional and DWI on the pelvis. All studied subjects were preoperatively clinically evaluated by gathering history and doing the examination, pelvi-abdominal sonography, MRI including DWI, and routine pre-operative laboratory investigations. Second-look cystoscopy, biopsy, and pathologic evaluation were done.

Results: DWI had higher sensitivity, specificity, and accuracy than conventional MRI in pathologic correlation with the histological specimen, which were (100% VS 66.6%) sensitivity, (92.8% VS 50%) specificity, and (96.8% VS 56.25%) accuracy for DWI and conventional MRI, respectively in the detection of bladder carcinoma. Our results showed a high sensitivity of DWI for identifying the residual bladder cancer after 1ry TURBT. There was a significant correlation between clinical staging by DWI and pathological staging.

Conclusions: DWI could represent a beneficial tool for the best choice of patients before a second TURBT. Till now, it cannot replace the gold standard second-look cystoscopy with histopathology assessment.

Keywords: DWI; TURBT; NMIBC; Urology

INTRODUCTION

The cancer of the bladder is known to be the ninth most popular malignant tumor generally and also the 2nd most frequent urogenital cancer in the world. Nearly 75 percent of bladder cancer patients are found to be NMIBC involving Ta, Tis and T1[1].

In those groups of patients, TURBT is the common technique widely used in management of NMIBC. Even so, bladder cancer seems to be multifocal, with a great recurrence rate. In subjects who will undergo initial TURBT, the recurrence rate is still high, at 50–70 percent, with a progression rate of 15–30 percent [2].

Many factors impact the result of the initial TURBT as multiple tumors, large tumors or locations with an indistinct margin, effortless blood loss that can disrupt the vision of the surgeon, the experience and skill of the surgeon, the quality of the samples, and the assessment of the pathologist. As a result, the pathological stage of the tumor is misjudged in 9–49 percent of patients with NMIBC after the first TURBT [3].

As a result, second-look TURBT seems to have a major role to play in verifying or restaging to aid the physicians to make decisions on the further management of the disease. Generally, second-look TURBT is done two to six weeks after the first resection, involving resection of the primary site of the tumor [4].

At the primary transurethral resection, understaging of the tumor is a repeated finding and could retard definite management. So, a secondary TURBT is advisable within two to six weeks to guide the suitable management for highly risky patients and when the primary transurethral resection is unfinished or in those with large or multiple tumors, to repeat

transurethral resection of bladder tumor (TURBT) [5].

DWI is considered a non-invasive method of measuring the movement of water molecules. DWI is a common technique that can diagnose acute stroke. Recently, it had been used in the assessment of different diseases of the urinary tract such as different malignant tumors [6].

This work aimed to correlate between the outcomes of DWI results and biopsy results of second-look TURBT in NMIBC and to correlate between DWI and conventional MRI in NMIBC in the detection of residual bladder tumor after the 1st diagnostic TURB.

METHODS

A cross-sectional study was conducted at the department of Urology, Zagazig university hospitals during the period from December 2018 to December 2019. The study included 24 patients with NMIBC who underwent second-look TURBT with preoperative imaging with DWI on the pelvis. In our study, an MRI examination was performed (22-40) days after the initial TURBT, and (3-9) days before the second-look TURBT. Inclusion criteria involved patients who approved to share in the study and were diagnosed with NMIBC indicated for second-look cystoscopy as incomplete initial resection, high grade and/or T1 tumor, or when the specimen contained no detrusor muscle. On the other hand, exclusion criteria involved patients with muscle-invasive bladder cancer, other non-urothelial tumors, had taken treatment for bladder cancer in the past, history of upper tract urothelial tumor, or had contraindications for MRI as the presence of metallic implant or claustrophobia.

Methods: All patients were subjected to the preoperative clinical evaluation using standard physical examination and complete urological evaluation preoperatively with emphasis on the routine clinical assessment (history and examination), pelvi-abdominal sonography, and MRI (1.5 T Philips Achieva system class II MRI device is used). Thirty minutes before the MRI study, all patients were asked for drinking water and presented with a full bladder. MR imaging was performed by using a pelvic phased-array coil with the patient in the supine position. MR imaging examination included T1W without contrast, T2WI, DWI, and ADC map. 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. T2-weighted spin-echo 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 spin-echo imaging. DW images were obtained in the axial and sagittal planes. Routine pre-operative lab investigations such as urinalysis, serum creatinine, liver function tests, complete blood count, bleeding profile, and random blood sugar. Second-look cystoscopy, biopsy, and pathologic evaluation were done.

Administrative considerations: Written informed consent was obtained from all participants and the study was approved by the research ethics committee of the Faculty of Medicine, Zagazig University (Institutional Research Board IRB). The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

All data were collected, tabulated, and statistically analyzed using SPSS 20.0 for windows (SPSS Inc., Chicago, IL, USA). Quantitative data were expressed as the mean ± SD & median (range), and qualitative data were expressed as absolute frequencies (number) & relative frequencies (percentage). Continuous variables were checked for normality by using the Shapiro Walk test. Mann-Whitney U test was used to compare two groups of non-normally distributed variables. Kruskal Wallis H test was used to compare more than two groups of non-normally distributed variables. The validity of conventional MRI and DWI clinical staging in the detection of residual bladder cancer after 1st diagnostic TURB were calculated using diagnostic performance depending on sample 2x2 contingency tables generation using pathological staging as the gold standard reference. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated.

Inter-rater agreement in the prediction of residual disease or muscle invasion between MRI and pathological staging was analyzed using McNemar, and Kappa (K) statistics. The agreement was obtained if the McNemar was insignificant and the Kappa statistic was significant, criteria to qualify for the strength of agreement were as follows: = 0 indicating no agreement and 0–0.20 slight, 0.21–0.40 fair, 0.41–0.60 Moderate, 0.61–0.80 substantial, and 0.81–1 almost perfect agreement. All tests were two-tailed. p-value < 0.05 was considered statistically significant (S), p-value < 0.001 was considered highly statistically significant (HS), and p-value > 0.05 was considered statistically insignificant (NS).

RESULTS

Table (1) shows the demographic data of patients and the characteristics of the studied masses. Table (2) shows the validity of DWI clinical staging in the prediction of malignancy (pT1+pT2) in the second-look TURB. We found that it had a hundred percent sensitivity, 92.8 percent specificity, and 96.8% accuracy. Table (3) clears the validity of DWI clinical staging in the prediction of muscle invasion (pT2) in second-look TURBT (which was excluded from the study if proved to be muscle invasive by biopsy). We found that it had 83.33% sensitivity, 80% specificity, and 81.25% accuracy. Table (4) demonstrates the agreement between DWI clinical staging and pathological staging of second-look TURBT. The concordance represents 81.2% while the discordance represents 18.8%. Table (5) clears the agreement between DWI clinical staging and pathological staging of second-look TURB regarding the detection of muscle invasion. The concordance represents 81.2% while the discordance represents 18.8%.

Figure (1) showed a case of a 50-year-old male patient presented with a history of recurrent hematuria, T1WI showed a residual soft tissue mass of the urinary bladder. This lesion was seen at the dome of the urinary bladder, T2WI showed no interruption of the underlying muscle layer., DWI showed restricted diffusion of the lesion, ADC value of 1.05.

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

Basic characteristics	The studied masses (N=32)	
Categorical data	**No.**	**%**
Sex		
Male	16	66.7%
Female	8	33.3%
Site of tumor		
Trigone	4	12.5%
Right lateral wall	4	12.5%
Left lateral wall	8	25%
Dome	8	25%
Base	8	25%
Longest diameter		
<1cm	22	68.8%
≥1cm	10	31.2%
Mass shape		
Papillary	20	62.5%
Wide base	12	37.5%
Grade		
Grade II	14	43.8%
Grade III	18	56.2%
pT		
pTa	4	12.5%
pT1	28	87.5%
Indication of second-look TURB		
No muscle	6	18.8%
T1	18	56.2%
Grade III	14	43.8%
Incomplete resection	8	25%
Continuous quantitative data	**Mean±SD**	**Median (Range)**
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 the prediction of malignancy (pT1+pT2) in second-look TURB:

		Pathological staging of second-look TURB		Total
		Tumor (pT1+pT2)	**No Tumor (pT0)**	
DW-MRI clinical staging	**Tumor (cT1+cT2)**	18	1	19
	No Tumor (cT0)	0	13	13
Total		18	14	32

	Estimate	(95%CI)
SN (%)	100%	(85.47 – 100)
SP (%)	92.8%	(78.83 – 96.47)
+LR	13.8	
-LR	0	
PPV (%)	94.7%	
NPV (%)	100%	
Acc (%)	96.8%	(89.11 – 98.32)
AUC	0.91	(0.79 – 0.95)

SN: Sensitivity SP: Specificity.
+LR: Positive Likelihood Ratio -LR: negative Likelihood Ratio.
PPV: Positive Predictive Value NPV: Negative Predictive Value.
Acc: Accuracy AUC: Area Under Curve.
95%CI: 95% Confidence Interval.

Table 3: Validity of DW-MRI clinical staging in the prediction of muscle invasion (pT2) in second-look TURB:

		Pathological staging of second-look TURB		Total
		Tumor (pT2)	**No Tumor (pT0+T1)**	
DW-MRI clinical staging	**Tumor (cT2)**	10	4	14
	No Tumor (cT0+T1)	2	16	18
Total		12	20	32

	Estimate	(95%CI)
SN (%)	83.33%	(51.58 – 97.91)
SP (%)	80%	(56.33 – 94.26)
+LR	4.16	(1.67 – 10.37)
-LR	0.20	(0.05 – 0.75)
PPV (%)	71.42%	(50.01 – 86.16)
NPV (%)	88.88%	(68.90 – 96.65)
Acc (%)	81.25%	(63.56 – 92.79)
AUC	0.817	(0.640 – 0.931)

SN: Sensitivity SP: Specificity.
+LR: Positive Likelihood Ratio -LR: negative Likelihood Ratio.
PPV: Positive Predictive Value NPV: Negative Predictive Value.
Acc: Accuracy AUC: Area Under Curve.
95%CI: 95% Confidence Interval.

Table 4: Agreement between DW-MRI clinical staging and pathological staging of second-look TURB:

		Pathological staging of second-look TURB			Total
		pT0	pT1	pT2	
DW-MRI clinical staging	cT0	13 (40.6%)	0 (0%)	0 (0%)	13 (40.6%)
	cT1	1 (0%)	2 (6.2%)	2 (6.2%)	5 (15.6%)
	cT2	0 (0%)	4 (12.5%)	10 (31.2%)	14 (43.8%)
Total		14 (43.8%)	6 (21.9%)	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%)	0.414 (NS)	0.698	(0.496 – 0.899)	<0.001 (HS)

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

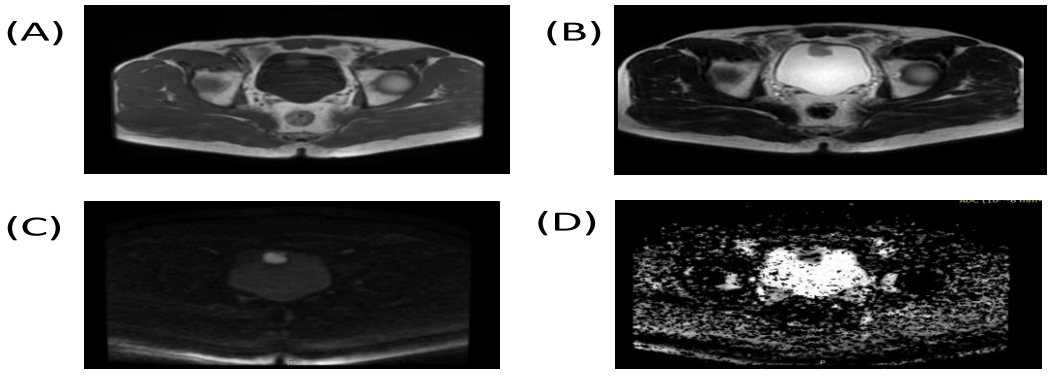
Sig.: Significance.

Table 5: 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.

Figure 1: A 50-year-old male patient presented with a history of recurrent hematuria:
(A) T1WI showed a residual soft tissue mass of the urinary bladder. This lesion was seen at the dome of the urinary bladder expressing intermediate signal intensity. (B) T2WI showed no interruption of the underlying muscle layer. (C) DW-MRI showed restricted diffusion of the mass with an intact underlying muscle layer. (D) ADC value of the urinary bladder mass with mean 1.05
The cystoscopic finding was a small lesion about 1cm at the dome of the bladder.
Histopathology was T1.

DISCUSSION

In the treatment of cancer of the bladder, understaging and uncompleted TURBT of NMIBC represent a major challenge. The guidelines recommended a secondary TURB after the primary uncompleted one for all cases with T1 or grade III cancers. The disadvantages of the repeated TURB were non-existent involving that it is considered invasive and elevated costs [7].

MRI is valuable in bladder cancer diagnosis as it offers a superior soft tissue delineation in comparison with other procedures of imaging [8].

Neovascularization is an inflammatory reaction and might remain for long period and can lead to false-positive residual cancer identified on MRI. Therefore, scientists sought new techniques that may be more accurate than conventional MRI and less invasive than cystoscopy [9].

Our results showed 100% sensitivity, 92.8% specificity, and 96.8% accuracy of DWI for detecting bladder cancer. On the other hand, El-Assmy et al. [14] reported 91.6% sensitivity, 91.3% specificity, and accuracy 91.5%, and Wang et al. [15] reported 100% sensitivity, 81.8% specificity, and 92.6% accuracy. Nakamura and colleagues reported (92 percent sensitivity), (82 percent specificity) and (67 percent accuracy) of DWI for identifying the recurrence of the cancer of the bladder after TURB [10].

In the current study, 2 false positive lesions on DWI were pathologically proven to be granulomatous scars. Image readers should be aware that the presence of these benign lesions can often lead to false-positive diagnoses. Correct staging is an essential part of managing bladder cancer. On the other hand, El-Assmy et al. [14] reported 2 false-positive lesions on DWI confirmed as non-specific cystitis, consisting of two small bright superficial nodules confined to the bladder wall with no muscle invasion, Wang et al. [15] reported no false-positive lesions on DWI and Nakamura and colleagues reported 3 false-positive lesions on DWI were histologically diagnosed as granulomatous tissue with inflammation.

Our study showed 4 false-negative lesions in DWI. On the other hand, El-Assmy et al. [14] reported 2 false-negative lesions were not detected on DWI. these two false-negative lesions were confirmed as transitional cell carcinomas, consisting of two polypoid lesions with diameters of 2 mm and 3 mm., Wang et al. [15] reported no false-negative lesions on DWI and Nakamura et al. [10] reported 1 false-negative lesion on DWI were not detected on DWI.

Our results showed a hundred percent sensitivity of DWI for detecting bladder cancer recurrence after 1ry TURB. DWI is proven to be more beneficial than T2W in the follow-up of several malignancies involving cancer of the bladder [11]. In addition, DWI needs a shorter period only when it is added to the MRI without contrast. The intensity of the signal on DWI is not particular to the malignant tissue, because the reactions to the inflammation may lead to equal observations [12]. The changes due to inflammation also reveal a signal of high intensity due to the infiltration via inflammatory cells chemotaxis, granulomas composition, and narrowing of the extracellular space [13].

El-Assmy and colleagues reported two false positive findings on DWI confirmed as cystitis [14]. Wang and colleagues reported no false-positive finding on DWI [15].

CONCLUSION

Our study indicates the preference of DWMRI to T1W- and T2W-MRI in identifying residual bladder cancer after the first TURB. DWI demonstrated suitable high sensitivity, specificity, accuracy, and agreement when compared to the results of the gold standard pathological examination of urinary bladder tumors. DWI could represent a beneficial tool for the best choice of patients before a second TURB. Till now it cannot replace the gold standard second-look cystoscopy with histopathology assessment.

Conflict of Interest: None

Financial Disclosures: None

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