

Diagnostic Accuracy of Diffusion Weighted Magnetic Resonance Imaging in Diagnosing Muscle Invasion in Urinary Bladder Cancer Taking Histopathology as Gold Standard

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ABSTRACT

Background: MRI is the most common investigation to diagnose bladder cancer. The efficacy of Diffusion weighted MRI in diagnosing muscle invasion in bladder cancer is questionable. **Objective:** To determine the diagnostic accuracy of diffusion weighted magnetic resonance imaging in diagnosing muscle invasion in urinary bladder cancer, taking histopathology as gold standard. **Study Design:** Cross-sectional validation study. **Settings:** Department of Radiology, DHQ Teaching Hospital, Sargodha Pakistan. **Duration:** August 01, 2018 to February 28, 2019. **Methods:** A total of 105 patients presented with hematuria >100 RBCs on high power micro field and irregular soft tissue structure projecting into bladder lumen from a fixed mural site on ultrasonography and age 25-65 years of either gender were included. Patients with h/o radiotherapy, CRF, recurrent tumor, biopsy proven muscle invasive urinary bladder cancer and any contraindication to MRI were excluded. All the patients were then underwent DW-MRI of the pelvis. DW-MRI findings were interpreted for presence or absence of muscle invasion in urinary bladder cancer and compared with DW-MRI findings. **Results:** In DW-MRI positive patients, 64 (True Positive) had muscle invasion and 03 (False Positive) had no muscle invasion on histopathology. Among 38, DW-MRI negative patients, 03 (False Negative) had muscle invasion on histopathology whereas 35 (True Negative) had no muscle invasion on histopathology ($p=0.0001$). Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of diffusion weighted magnetic resonance imaging in diagnosing muscle invasion in urinary bladder cancer was 95.52%, 92.11%, 95.52%, 92.11% and 94.29% respectively. **Conclusion:** This study concluded that DW-MRI is a highly sensitive and accurate non-invasive modality for diagnosing muscle invasion in urinary bladder cancer.

Keywords: Magnetic resonance imaging, Muscle invasion, Urinary bladder cancer.

INTRODUCTION

Bladder cancer is any of several types of cancer arising from the epithelial lining (i.e., the urothelium) of the urinary bladder. Rarely the bladder is involved by non-epithelial cancers, such as lymphoma or sarcoma, but these are not ordinarily included in the colloquial term "bladder cancer". It is a disease in which abnormal cells multiply without control in the bladder.¹ The most

common type of bladder cancer recapitulates the normal histology of the urothelium and is known as transitional cell carcinoma or more properly urothelial cell carcinoma.² Five-year survival rates are around 77%/0.³

Bladder cancer is the second most common genitourinary cancer in the United States and some 55600 new cases and 15100 deaths from bladder cancer are estimated to have occurred in 2012.⁴ Ceylan K *et al*⁵ in his study has shown

the prevalence of urinary bladder cancer as 67.79%/0 patients. At the initial diagnosis, a third of all cases are diagnosed as muscle invasive bladder cancer (MIBC), and radical cystectomy has long been the treatment of choice for the treatment of localized MIBC. However, concern for patients quality of life has strengthened the trend toward bladder-sparing approaches with various treatment modalities.⁶ The initial evaluation of a patient who presents with hematuria is not uniform: Some institutions perform computed tomographic (CT) urography for triage prior to cystoscopy, whereas others use cystoscopy as the first line of investigation. Nevertheless, cystoscopy and CT are complementary and have a definite management role in patients who present with hematuria.^{7,8}

Today, ultrasonography (US), Contrast-enhanced CT and conventional MRI are the standard techniques that have been used for the radiological evaluation of urinary system tumors. While CT is generally used to screen for metastasis, MRI plays a pivotal role in the staging of bladder cancer because of its superior soft tissue delineation, especially in the context of muscle-invasion.⁸ Magnetic resonance (MR) imaging of the pelvis is usually performed for T (tumor) staging once bladder cancer has been diagnosed, although its use is not widespread.⁹

Diffusion-weighted magnetic resonance imaging (DW-MRI) and determination of the apparent diffusion coefficient values (ADC) are modern functional MR-imaging techniques. The ADC value describes the ability of water molecules to diffuse in tissue, which is impaired by increased cellular density as is the case in tumors.^{10,11} In a meta-analysis, the prevalence of muscle invasive urinary bladder cancer was found to be 33.46% and sensitivity and specificity of DW-MRI in differentiating muscle invasive from non-muscle invasive urinary bladder cancer as 85.0% and 90.0% respectively.¹²

In another study, the sensitivity, specificity and diagnostic accuracy of DW-MRI for differentiating muscle invasive from non-muscle invasive urinary bladder cancer were 88.0%, 85.0% and 87.0%, respectively.⁹

METHODS

It was cross-sectional study conducted at the Department of Radiology, DHQ Teaching Hospital, Sargodha Pakistan. The duration of the study was six months from August 01, 2018 to February 28, 2019. A total of 105 patients were selected by using consecutive sampling technique.

Patients of both genders between the age of 25-65 years who presented with one-month history of hematuria and having > 100 RBCs on high power micro field and

irregular soft tissue structure (Size of lesion >1cm) projecting into bladder lumen from a fixed mural site on ultrasonography were included.

Patients with history of radiotherapy (assessed on medical record), renal disease (assessed on history and medical record i.e. s/creatinine >1.5 mg/dl), already biopsy proven muscle invasive urinary bladder cancer, recurrent bladder tumor were excluded from the study. Patients with contraindication to MRI i.e. claustrophobia and cardiac pacemakers and pregnant females were also not involved in the study.

Approval from ethical review committee and informed written consent from each patient was taken. MR examination was performed with the patients in supine position using a 1.5-T Philips MRI unit and a body phased-array coil. All sequences were obtained with a non-breath hold technique. After scout scanning midline axial and sagittal T2W turbo spin-echo (T2W-TSE) images were obtained. The scan protocol was TR 3000-4000ms., TE 70-90ms, field of view (FOV) 28x32x28x32cm, matrix 276x384, slice thickness 5mm and gap 1 mm. Then in all patients, diffusion weighted imaging (DWI) MR sequences with b=0, b=500 and b=1000, followed by apparent diffusion coefficient (ADC) mapping was done. DW-MRI findings were interpreted for presence or absence of muscle invasion in urinary bladder cancer. T2WI will show a hypointense tumor, DW-MRI displays the tumor as a high-signal mass invading the muscles with an ADC value <1.00 mm²/s was taken as positive. Biopsy was done from histopath010U lab Jinnah hospital Lahore and histopathology report was compared with DW-MRI findings. Presence of cellular atypia, increased mitotic figures, >1:1 nuclear cytoplasmic ratio up to bladder muscles on histopathology was taken as positive This all data was (age, gender, occupation, BMI) was recorded.

Collected data was analyzed through computer software SPSS 20.0. Mean and standard deviation were calculated for age, BMI, duration of disease and size of lesion. Frequency and percentage were calculated for gender, place of living (rural/urban), occupation (office/field/factory/domestic) and muscle invasion in urinary bladder cancer on DW-MRI and histopathology. 2x2 contingency table was used to calculate the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of DW-MRI in diagnosing muscle invasion in urinary bladder cancer, taking histopathology as gold standard.

Stratification was done for age, gender, duration of disease, BMI, size of lesion, place of living (rural/urban) and occupation (office/field/factory/domestic). Post-stratification 2x2 contingency table was used to calculate

the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of DW-MRI in diagnosing muscle invasion in urinary bladder cancer. P-value <0.05 was taken as significant.

Muscle invasion in Urinary Bladder Cancer on DW-MRI	Muscle invasion in urinary bladder cancer on Histopathology		
		Yes	No
	Yes	True Positive (a)	False Positive (b)
No	False Negative (c)	True negative (d)	

Sensitivity: $a / a+c \times 100$, Specificity: $d / b+d \times 100$, Positive predictive value: $a / a+b \times 100$, Negative predictive value: $d / C+d \times 100$, Diagnostic accuracy: $a+d / a+b+c+d \times 100$

RESULTS

Age range in this study was from 25-65 years with mean age of 51.50 ± 9.29 years. Majority of the patients 73 (69.52%) were between 45 to 65 years of age as shown in Table 1.

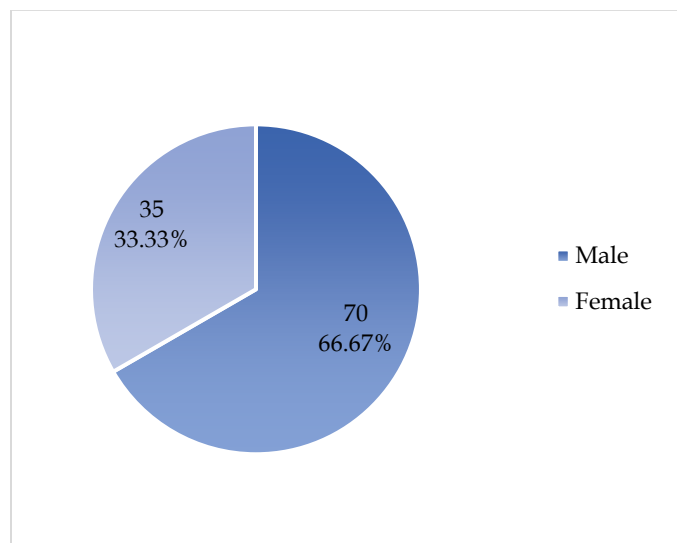
Table 1: Distribution of patients according to age

Age (years)	No. of Patients	Percentage
25-45	32	30.48%
46-65	73	69.52%
Total	105	100.0%

Mean \pm SD = 51.50 ± 9.29 years

Out of these 105 patients, 70 (66.67%) were male and 35 (33.33%) were females with male to female ratio of 2:1 (Figure 1).

Figure 1: Distribution of patients according to gender (n=105)



Mean duration of disease was 5.05 ± 1.87 months. Table 2

Table 2: Distribution of patients according to duration of disease (n=105)

Duration of disease	No. of Patients	Percentage
< 5 months	62	59.05%
> 5 months	43	40.95%

The mean size of lesion was 3.90 ± 1.21 cm (Table 3).

Table 3: Distribution of patients according to size of lesion

Size of lesion (cm)	No. of Patients	Percentage
≤ 3 cm	42	40.0%
≥ 3 cm	63	60.0%
Total	105	100.0%

Mean BMI was 29.14 ± 2.44 kg/m² (Table 4).

Table 4: Distribution of patients according to BMI

BMI (kg/m ²)	No. of Patients	Percentage
≤ 27	36	34.29%
≥ 27	69	65.71%
Total	105	100.0%

Distribution of patients according to place of living and occupation is shown in Table 5 & 6 respectively.

Table 5: Distribution of patients according to place of living

Place of living	No. of Patients	Percentage
Rural	48	45.71
Urban	57	54.29

Table 6: Distribution of patients according to occupation

Occupation	No. of Patients	Percentage
Office	19	18.10%
Field	39	37.14%
Factory	27	25.71%
Domestic	20	19.05%

All the patients were subjected to Diffusion weighted magnetic resonance imaging (DW-MRI). DW-MRI supported the diagnosis of muscle invasion in urinary bladder cancer in 67 (63.81 %) patients and non-muscle

invasion in 38 (36.19⁰/0) patients. Histopathology findings confirmed muscle invasion in urinary bladder cancer in 67 (63.81%) patients and non-muscle invasion in 38 (36.19%) patients. In DW-MRI positive patients, 64 (True Positive) had muscle invasion and 03 (False Positive) had no muscle invasion on histopathology. Among 38, DW-MRI negative patients, 03 (False Negative) had muscle invasion on histopathology whereas 35 (True Negative) had no muscle invasion on histopathology (p=0.0001) as shown in Table 7.

Table 7: Diagnostic accuracy of diffusion weighted magnetic resonance imaging in diagnosing muscle invasion in urinary bladder cancer, taking histopathology as gold standard

	Positive result on histopathology	Negative result on histopathology	P-value
Positive on DW-MRI	64	03	0.0001
Negative on DW-MRI	03	35 (TN)	

TP=True positive, FP=False positive, FN=False negative, TN=True negative
Sensitivity: 95.52%, Specificity: 92.11%, Positive Predictive Value (PPV): 95.52%,
Negative Predictive Value (NPV): 92.11%, Diagnostic Accuracy: 94.29%

Stratification of diagnostic accuracy with respect to age groups is shown in Table 8, 9.

Table 8: Stratification of age 25-45 years (n=32)

	Positive result on histopathology	Negative result on histopathology	P-Value
Positive on DW-MRI	18 (TP)	01 (FP)	0.001
Negative on DW-MRI	01 (FN)	12 (TN)	

Sensitivity: 94.74%, Specificity: 92.31%, Positive Predictive Value (PPV): 94.74%,
Negative Predictive Value (NPV): 92.31%, Diagnostic Accuracy: 95.75%

Table 9: Stratification of age 46-65 years (n=73)

	Positive result on histopathology	Negative result on histopathology	P-Value
Positive on DW-MRI	46	02 (FP)	0.001
Negative on DW-MRI	02 (FN)	23 (TN)	

Sensitivity: 95.83%, Specificity: 92.0%, Positive Predictive Value (PPV): 95.83%,
Negative Predictive Value (NPV): 92.0%, Diagnostic Accuracy: 94.52%

Gender stratification is shown in Table 10, 11.

Table 10: Stratification of Male Gender (n=70)

	Positive result on histopathology	Negative result on histopathology	P-Value
Positive	41 (TP)	02 (FP)	0.001
Negative on DW-MRI	01 (FN)	26 (TN)	

Sensitivity: 97.62%, Specificity: 92.86%, Positive Predictive Value (PPV): 95.35%,
Negative Predictive Value (NPV): 96.30%, Diagnostic Accuracy: 95.71%

Table 11: Stratification of Female Gender (n=35)

	Positive result on histopathology	Negative result on histopathology	P-Value
Positive on DW-MRI	23 (TP)	01 (FP)	0.001
Negative on DW-MRI	02 (FN)	09 (TN)	

Sensitivity: 92.90%, Specificity: 95.83%, Positive Predictive Value (PPV): 90.0%,
Negative Predictive Value (NPV): 81.82%, Diagnostic Accuracy: 91.43%

Stratification according to duration of disease. Table 12,13

Table 12: Stratification of duration of disease 55 months (n=62)

	Positive result on histopathology	Negative result on histopathology	P-Value
Positive on DW-MRI	37 (TP)	02 (FP)	0.001
Negative on DW-MRI	02 (FN)	21 (TN)	

Sensitivity: 94.87%, Specificity: 91.30%, Positive Predictive Value (PPV): 94.87%,
Negative Predictive Value (NPV): 91.30%, Diagnostic Accuracy: 93.55%

Table 13: Stratification of duration of disease >5 months (n=43)

	Positive result on histopathology	Negative result on histopathology	P-Value
Positive on DW-MRI	27 (TP)	01 (FP)	0.001
Negative on DW-MRI	01 (FN)	14 (TN)	

Sensitivity: 96.43%, Specificity: 93.33%, Positive Predictive Value (PPV): 96.43%,
Negative Predictive Value (NPV): 93.33%, Diagnostic Accuracy: 95.35%

Stratification of diagnostic accuracy with respect to size of lesion is shown in Table 14 & 15.

Table 14: Stratification of size of lesion 53 cm (n=42)

	Positive result on histopathology	Negative result on histopathology	P-Value
Positive on DW-MRI	26 (TP)	01 (FP)	0.001
Negative on DW-MRI	02 (FN)	13 (TN)	

Sensitivity: 92.86%, Specificity: 92.86%, Positive Predictive Value (PPV): 96.30%,
Negative Predictive Value (NPV): 86.67%, Diagnostic Accuracy: 92.86%

Table 15: Stratification of size of lesion >3 cm (u=63)

	Positive result on histopathology	Negative result on histopathology	P-Value
Positive on DW-MRI	38 (TP)	02 (FP)	0.001
Negative on DW-MRI	01 (FN)	22 (TN)	

Sensitivity: 97.44%, Specificity: 91.67%, Positive Predictive Value (PPV): 95.0%,
Negative Predictive Value (NPV): 95.65%, Diagnostic Accuracy: 95.24%

Stratification of diagnostic accuracy with respect to BMI is shown in Table 16, 17.

Table 16: Stratification of BMI \$27 kg/m' (n=36)

	Positive result on histopathology	Negative result on histopathology	P-Value
Positive on DW-MRI	26 (TP)	01 (FP)	0.001
Negative on DW-MRI	01 (FN)	08 (TN)	

Sensitivity: 96.30%, Specificity: 88.89%, Positive Predictive Value (PPV): 96.30%, Negative Predictive Value (NPV): 88.89%, Diagnostic Accuracy: 94.44%

Table 17: Stratification of BMI >27 kg/m' (n=69)

	Positive result on histopathology	Negative result on histopathology	P-Value
Positive on DW-MRI	38 (TP)	02 (FP)	0.001
Negative on DW-MRI	02 (FN)	27 (TN)	

Sensitivity: 95.0%, Specificity: 93.10%, Positive Predictive Value (PPV): 95.0%, Negative Predictive Value (NPV): 93.10%, Diagnostic Accuracy: 94.20%

Place of living stratification is shown in Table 18, 19.

Table 18: Stratification of rural area (n=48)

	Positive result on histopathology	Negative result on histopathology	P-Value
Positive on DW-MRI	26 (TP)	02 (FP)	0.001
Negative on DW-MRI	01 (FN)	19 (TN)	

Sensitivity: 96.30%, Specificity: 90.48%, Positive Predictive Value (PPV): 92.86%, Negative Predictive Value (NPV): 95.0%, Diagnostic Accuracy: 93.75%

Table 19: Stratification of urban area (n=57)

	Positive result on histopathology	Negative result on histopathology	P-Value
Positive on DW-MRI	38 (TP)	01 (FP)	0.001
Negative on DW-MRI	02 (FN)	16 (TN)	

Sensitivity: 95.0%, Specificity: 94.12%, Positive Predictive Value (PPV): 97.44%, Negative Predictive Value (NPV): 88.89%, Diagnostic Accuracy: 94.74%

Table 20 to 23 have shown the stratification according to occupation.

Table 20: Stratification of office workers (n=19)

	Positive result on histopathology	Negative result on histopathology	P-Value
Positive on DW-MRI	10 (TP)	00 (FP)	0.001
Negative on DW-MRI	01 (FN)	08 (TN)	

Sensitivity: 90.91%, Specificity: 100.0%, Positive Predictive Value (PPV): 100.0%, Negative Predictive Value (NPV): 88.81%, Diagnostic Accuracy: 94.74%

Table 21: Stratification of field workers (n=39)

	Positive result on histopathology	Negative result on histopathology	P-Value
Positive on DW-MRI	22 (TP)	02 (FP)	0.001
Negative on DW-MRI	01 (FN)	14 (TN)	

Sensitivity: 95.65%, Specificity: 87.50%, Positive Predictive Value (PPV): 91.67%, Negative Predictive Value (NPV): 93.33%, Diagnostic Accuracy: 92.31%

Table 22: Stratification of factory workers (n=27)

	Positive result on histopathology	Negative result on histopathology	P-Value
Positive on DW-MRI	18 (TP)	00 (FP)	0.001
Negative on DW-MRI	01 (FN)	08 (TN)	

Sensitivity: 94.74%, Specificity: 100.0%, Positive Predictive Value (PPV): 100.0%, Negative Predictive Value (NPV): 88.89%, Diagnostic Accuracy: 96.30%

Table 23: Stratification of domestic workers (NTL)

	Positive result on histopathology	Negative result on histopathology	P-Value
Positive on DW-MRI	14 (W)	01 (FP)	0.001
Negative on DW-MRI	00 (FN)	05 (TN)	

Sensitivity: 100.0%, Specificity: 83.33%, Positive Predictive Value (PPV): 93.33%, Negative Predictive Value (NPV): 100.0%, Diagnostic Accuracy: 95.0%

DISCUSSION

The DW-MRI technique was initially devised by Stejskal and Tanner in 1965. Since 1985, DW-MRI has been mainly used for neuroimaging, especially for diagnosis of acute cerebral infarction and intracranial tumors.¹³ With the recent advent of echo planar imaging, high gradient amplitudes, multichannel coils, and parallel imaging, DW-MRI of the abdomen and pelvis has become possible, and a growing number of studies have demonstrated the usefulness of this imaging technique in the diagnosis of malignant tumors of the abdomen.^{14,15} Because the signal of DW-MRI is derived from the inherent tissue contrast, this imaging technique requires no contrast agent and is applicable to patients with allergies to contrast agents or those with renal insufficiency. Furthermore, the addition of DW-MRI to a routine MRI examination requires only a few additional minutes and can be adopted for most current clinical MRI scanners.

DW-MRI is a functional imaging technique, the contrast of which results from quantifying the microscopic mobility of water molecules in tissue.^{14,15} In biological tissues, the diffusion of water molecule is inversely correlated to the tissue cellularity and the integrity of cell membranes. In the area of tumor tissues, which have a high cellular density with intact cell membranes, water

molecule diffusion is restricted, while the diffusion of water molecule is less restricted in areas of low cellular density. Areas where the diffusion is restricted generally show high signal intensity on DW-MRI, and malignant lesions typically show high signal intensity because of their higher cellularity, tissue disorganization, and decreased extracellular space, all of which restrict water diffusion. In recent years, an increasing number of studies have shown the usefulness of visual assessment of DW-MRI for detecting malignant tumors, and DW-MRI has quickly become a suitable adjunct for assessing various kinds of tumors including bladder cancer.^{9,16-18}

Age range in study was from 25-65 years with mean age of 51.50 ± 9.29 years. Majority of the patients 73 (69.52%) were between 45 to 65 years of age. Out of these 105 patients, 70 (66.67%) were male and 35 (33.33%) were females with male to female ratio of 2: 1. DW-MRI supported the diagnosis of muscle invasion in urinary bladder cancer in 67 (63.81%) patients and non-muscle invasion in 38 (36.19%) patients. Histopathology findings established muscle invasion in urinary bladder cancer in 67 (63.81%) patients and non-muscle invasion in 38 (36.19%) patients. In DW-MRI positive patients, 64 (True Positive) had muscle invasion and 03 (False Positive) had no muscle invasion on histopathology. Among 38, DW-MRI negative patients, 03 (False Negative) had muscle invasion on histopathology whereas 35 (True Negative) had no muscle invasion on histopathology ($p=0.0001$). Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of diffusion weighted magnetic resonance imaging in diagnosing muscle invasion in urinary bladder cancer was 95.52%, 92.11%, 95.52%, 92.11% and 94.29% respectively.

In a meta-analysis, the prevalence of muscle invasive urinary bladder cancer was found to be 33.46% and sensitivity and specificity of DW-MRI in differentiating muscle invasive from non-muscle invasive urinary bladder cancer as 85.0% and 90.0% respectively.¹² In another study, the sensitivity, specificity and diagnostic accuracy of DW-MRI for differentiating muscle invasive from non-muscle invasive urinary bladder cancer were 88.0%, 85.0% and 87.0%, respectively.⁹

Since the first report by Matsuki *et al*¹⁸ showing the utility of DW-MRI for detecting bladder cancer, a number of studies have shown the usefulness of DW-MRI for the diagnosis of bladder cancer.⁷⁻¹⁸ On DW-MRI with a high b-value, bladder cancers generally show a hyperintense signal, while the signals of the surrounding tissues, including urine, are much less intense.¹⁸ This good signal contrast is obtained between bladder cancer and the surrounding tissue. The sensitivity, specificity and accuracy for detecting bladder cancer were reported to be

90%-98%, 92%-93% and 91%-97%, respectively.^{9,17} In several studies, quantitative analysis consistently showed restricted diffusion and lower ADC values in bladder cancer compared with the surrounding structures.¹⁸

MIBC has the potential to metastasize to lymph nodes and distant organs, and detecting metastatic lesion is another problem in managing MIBC. At the time of surgery, 25% of the patients who undergo radical cystectomy have a lymph node metastasis. Lymph node staging has been generally performed by CT or conventional MRI based on size criteria and morphological appearance, and the accuracy for staging nodal disease ranges from 73% to 90%.¹⁹ On DW-MRI, benign lymph nodes show high signal intensity due to their highly cellular structures composed of lymphoid elements. The utility of DW-MRI has been shown in lymph node staging in various cancers.²⁰⁻²⁴ Papalia *et al*²⁵ showed that malignant lymph nodes have a significantly lower ADC value than benign lymph nodes with sensitivity of 76.4% and specificity of 89.4% in a study that included 36 patients with bladder cancer undergoing radical cystectomy. However, there is a substantial overlap in ADC values between malignant and benign lymph nodes, and discriminating malignant nodes from benign nodes on DW-MRI is still challenging.²⁶ Recently, Thoeny *et al*²⁷ reported an excellent diagnostic accuracy of 90% in detecting pelvic lymph nodal involvement by the combined use of ultra-small super paramagnetic iron oxide (USPIO) and DW-MRI. This agent is taken up by macrophages resulting signal loss in normal lymph nodes, while the signal of metastatic lymph nodes is not influenced.²⁷⁻³¹

El-Assmy *et al*³² reported the ability to discriminate MIBC from NMIBC with an accuracy of 63.6% in a study that included 106 patients. Takeuchi *et al*³³ reported that bladder cancer staging accuracy improved from 67 to 88% when DW-MRI was added to T2WI. Takeuchi *et al*³³ reported that the ADC value of grade 3 tumors was significantly lower than that of grade 1 and 2 tumors in a prospective study that included 40 patients. Avcu *et al*³⁴ also reported similar results showing an inverse correlation between the ADC value and the histological grade. The existence of a substantial overlap between the histological grades or stages poses a limit to qualitative analysis and the clinical application of this technique. However, these studies indicated that advanced and aggressive bladder cancers tend to have a low ADC values. Actually, Kobayashi *et al*⁹ found that clinically aggressive tumors, including MIBC and high-grade T1 tumors, had a significantly lower ADC value than the other less aggressive tumors. A threshold ADC value differentiated these two entities with 87% accuracy in a series of 121 patients. The underlying mechanisms whereby the ADC value reflects these tumor characters

are thought to be the tumor cell morphological characters such as dense cellularity and large cellular size.^{14,15} Recent studies have shown an inverse correlation between ADC value and the Ki-67 labeling index, a marker of cell proliferation, in bladder cancer.^{9,35,36}

CONCLUSION

This study concludes that DW-MRI is a highly sensitive and accurate non-invasive cost-effective modality for diagnosing muscle invasion in urinary bladder cancer, and has improved patient care by early screening, timely and proper treatment and avoiding unnecessary diagnostic biopsies, which consequently reduces patients' morbidity and mortality.

LIMITATIONS

The study was limited to cases of Sargodha Division. Nationwide sample collection can change the outcome.

SUGGESTIONS / RECOMMENDATIONS

We recommend that diffusion weighted MRI should be used routinely as a prime modality for the assessment of pre-operative assessment of muscle invasion in urinary bladder cancer for selecting proper treatment option and post-operative management plan.

CONFLICT OF INTEREST / DISCLOSURE

No personal, financial and institutional interest.

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