Role of Magnetic Resonance Imaging Techniques and Protocols in Diagnosis and Staging of the Urinary Bladder Carcinoma in Comparison with Histopathological Findings

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Abstract

Background: Bladder cancer is the second most common type of cancer of the urinary system in the world, after prostate cancer. Thus, we use a combination of the best imaging technology in the diagnosis and treatment of bladder cancer, because of its accuracy in local staging and grading .

Aim of The Study: To determine the accuracy and effectivity of MRI in early detection and diagnosis of bladder carcinoma by using different protocols and to Compare the sensitivity of MRI in staging of urinary bladder carcinoma with histopathological findings.

Patients and Method: : A prospective case control study was conducted in an oncology teaching hospital /the complex of Baghdad medical city. This study involved 41 suspected patient (35male &6 female). The participants ranged from (31–83 years) throughout the period of from September 2020 to January 2021. Patients who were referred for examination and diagnosis due to pelvic pain and hematuria, or who had been suspected of having bladder cancer by ultrasound were included in the study and were evaluated by the MRI performed with an MRI scanner (1.5 Tesla ,Siemens).

Results: : the study included 41 patients with bladder cancer, mean age was 64.8 years ranging from (31-83 years), about 31.7% was in 61 – 70 years, and about 24.4 was in 71–80 years, 85.4% were males, and 97.6% were smokers.82.9% with chronic renal disease(UTI),56.1% with heterogeneous enhancement & 39% with homogenous enhancement ,4.9% non-enhanced. 38 patients with symptom of hematuria, the lesion location according to the its site in the bladder wall was 34.1% in the lateral wall,24.4% in the posterior wall. The stages of T-primary tumor in MRI common protocols was(Tis=12% ,Tia=10% ,T1=17% ,T2=18% ,T3=28% ,T4=15%) .the accuracy and sensitivity for early stages (Tis,Ta,T1.&T2) in conventional MRI protocols) T1WI,T2WI) was Inconclusive in the diagnosis of bladder carcinoma accuracy ranging (44% – 57%) & sensitivity ranging (50% – 75%),while in both advance MRI modalities) DCE &DWI) had specificity for diagnosing stage bladder CA with DWI offering slightly higher sensitivity (SN) , negative predictive values (NPV), positive predictive value (PPV) , and accuracy (SN: 100% vs. 100%, SP: 50% for DCE &100% for DWI, accuracy: 97.6% vs 100%, PPV: 97.5% vs. 100%, and NPV: 100% vs.100%).

Keywords: *MRI, Pelvic Pain, Diffusion-weighted MRI , Apparent diffusion coefficient value, Bladder cancer, Hematuria.*

Introduction

The second most common tumor that may occur in the reproductive and urinary tract is bladder tumors (a prostate tumor is the most common) (1). It is the fifth most prevalent cancer in the USA and is highly treatable when diagnosed in the early stages (2). It accounts for up to 6-8 percent of overall malignancy in men and 2-3 percent in women, with the highest incidences rates in North America and Europe , as well as in areas with

endemic schistosomiasis (Africa and the Middle East). It is more prevalent in men than in women (3:1) and is common in patients over 50 years of age. (1) They are widely categorized as tumors that are either epithelial or nonepithelial (mesenchymal). On an average 90-95% of bladder cancers derive from the epithelium, the most common form is transitional cell carcinoma (90 percent) (1) Urothelial tumors are categorized as invading or non-invading muscle tumors (superficial or papillary). (3). About 80% to 85% of urothelial cell carcinomas are nonmuscle invasive. These are low-grade lesions that arise from a hyperplastic epithelium and may be multifocal. Those typically have a strong prognosis and seldom grow to invasive cancers, although there are about 50 percent urothelial recurrence rates, about 20 to 25% of the bladder cancer cases are muscle-invasive, emerge from in situ carcinoma or severe dysplasia, and have a higher histologic grade. Non muscular urothelial invasive tumors have a higher recurrence rate in comparison to muscle-invasive species. They are a precursor to invasive muscle tumors if left untreated. Almost every case of squamous carcinoma and bladder adenocarcinoma is invasive on diagnosis. Both bladder cancers can be worse off than urothelial tumors with intensive surgical therapy and chemotherapy.(3) Mesenchymal tumors comprise the remaining 5% of bladder tumors, with adult rhabdomyosarcomas, and leiomyosarcomas being the most prevalent subtypes.(4)

The clinical diagnoses and correct treatments of the bladder tumor cases are typically dependent upon detections and accurate staging of intravesical lesions. (5–7)

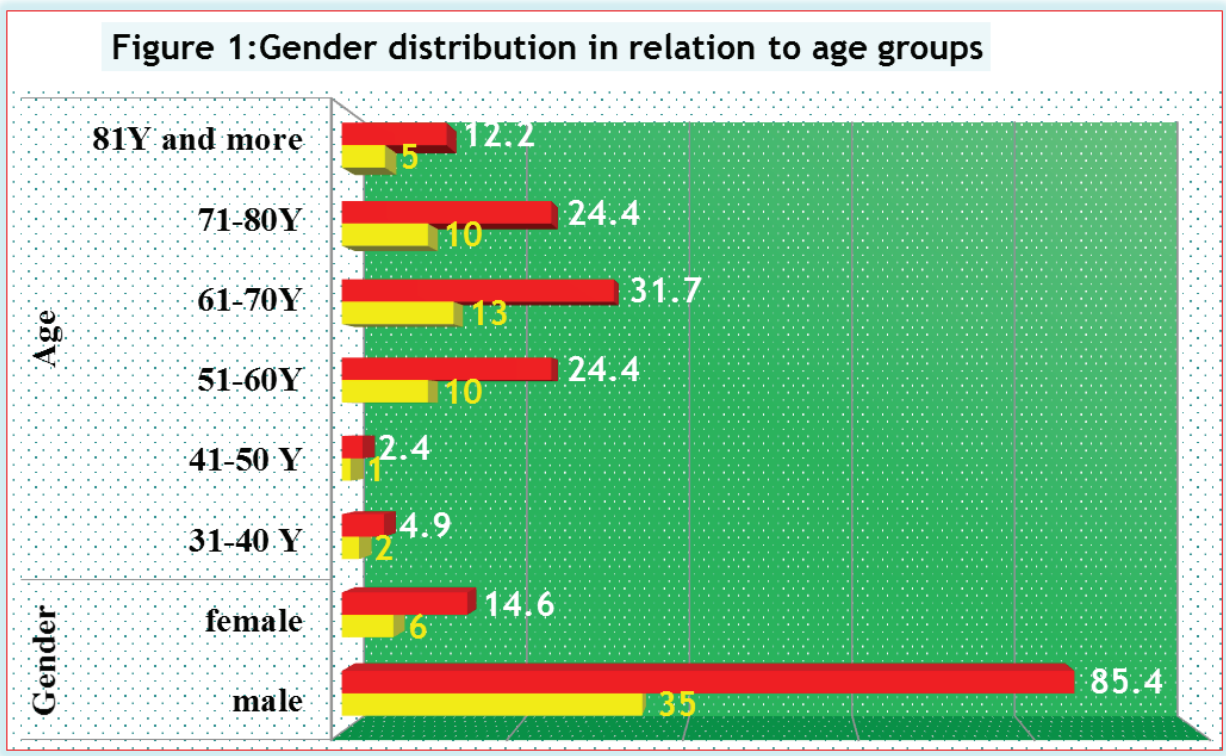
Random, multi-surface imaging capabilities of contrast-enhanced dynamic MRI (CONTRAST-enhanced DYNAMIC MRI) are particularly helpful in showing superficial bladder carcinomas and tumor invasion of the neighboring tissues. [6, 9, 10]. With data precision ranging from 88 to 97.6 percent, the analysis of dynamic gadolinium-enhanced MRI is much more beneficial for the staging/diagnosing of the bladder cancer. Diffusion-Weighted MR Imaging. Recently Weighted diffusion imaging (DWI) can be defined as a type of the MR imaging based on measuring the random Brownian movement of water molecules within a tissue voxel and is useful for tumor characterization (15) Diffusion-weighted MRI is a highly dependable technique for detecting and its can also be used in the identification of several forms of malignancy in different types of organs and the urinary bladder. [11] . There is a small number of the studies on the role of that new diagnostic approach in diagnosing and staging bladder tumor in literature. [8, 11–14] . This study aimed at assessing the role of the ADC and the DWMRI as a quantitative parameter for the diagnosis, staging of pathologies of bladder tumors and the pathological classification The usual bladder wall has been difficult to recognize on the DW images, we tended to paste the regions of interest (i.e. the ROIs) on ADC map following copying and finding the ROIs on T2-weighted images at the standard bladder wall. Using histopathological findings, the normal bladder wall situation at which the measurement of the ADC is conducted has been confirmed.

In the circular region of interests, values of the ADC have been calculated as mm2/s and the average ROI values were reported in b 100, b600 and b1000. The ADC, MRI, and DWMRI findings have been correlated with histopathology results.

Patients and Methods

MRI is a very preferred method for imaging bladder cancer due to both advanced protocols, for which (DWI) diffusion weighted MR imaging and dynamic contrast enhanced MRI (DCE) are excellent agreement for T staging of bladder cancer with DWI without the use of contrast media, so it may be utilized in the patients who Have renal impairment or sensitivity to the contrast media. All patients were examined initially with routine MRI protocol for the pelvis that included T2 weighted images , T1 weighted images, then diffusion , and post contrast T1WI. all patients were examined in the supine position throughout the examination in axial plane.

This study included 41 patients (35 male &6 female, according to the distribution of ages in (figure 1) .All patients in this study were referred to the radiology department of the Oncology and Abdominal Diseases Clinic. Who underwent magnetic resonance imaging at the Medical City Complex in Baghdad / Teaching Oncology Hospital from September 2020 to January 2021, due to pelvic pain and hematuria.



Standard MRI protocol(A) was included in the following sequences, T1-weighted turbo spin-echo in axial and sagittal planes, T2-weighted turbo spin-echo in axial , sagittal and coronal planes, Diffusion weighted MRI, Apparent diffusion coefficient(ADC) maps, Dynamic contrast-enhanced MRI: Contrast-enhanced MRI was performed in the axial plane using two-dimensional T1 fast field echo (FFE) sequence with fat suppression

Table(1): Imaging of urinary bladder MR sequences and parameters (1.5 T)

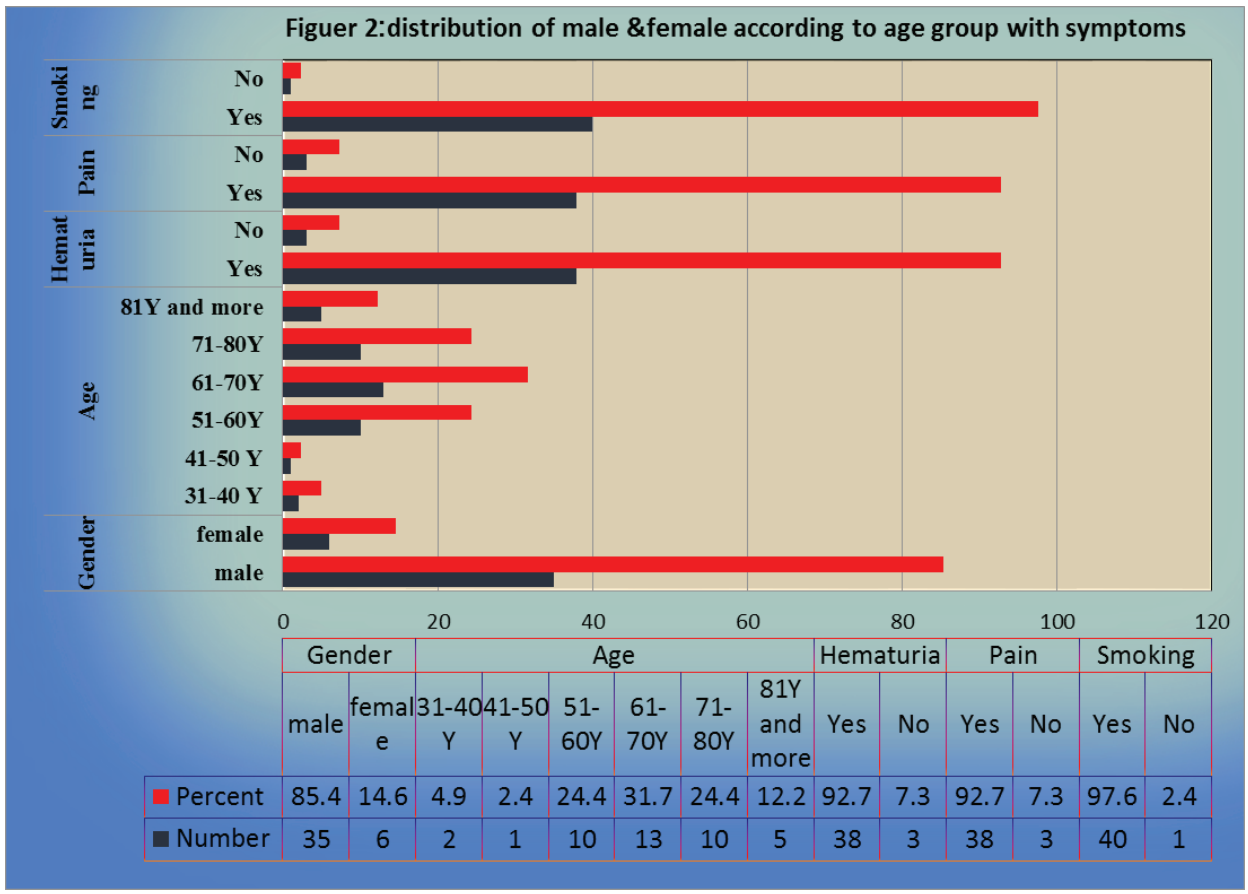
Sequence of pulses	T1	T2	DWI b-value(0 ,600.1000)	DCE
TR(Repetition Time)	550ms	4000-5500 ms	8000 ms	5.41 ms
TE (Echo Time)	9 ms	80-120 ms	61.2 ms	1.93 ms
Matrix(Frequency&phase- encoding stepes	512 x192	256 x256	256 x256	256x265
Number of slices	45	40	15	40
Fov	20 cm	24 cm	35 cm	22 cm
Slice Thickness	6 mm	6 mm	5mm	4 mm
Signal Acquired	4	4		
Intersection Gap	2 mm	2 mm	2 mm	2mm
Band Width(Hz/pixel)	140	161	142 KHZ	260
Acquisition Time	1.5 Min	2.3 Min	1.6 Min	2.3 min
Average /NEX	1	2	8	1

2.1.Examination technique:-

Anesthesia was not required for the MRI study, the bladder was distended to aid in accurate diagnosis. The lack of bladder dissidence, chemical shift artefact, motion artefact or include important artifacts in bladder imagery, The failure to detect small tumors can restrict the secondary detection in the bladder to muscular detrusor. On the other hand, the bladder distention can produce patient movement and decrease plaque sensitivity, such as lesions. The most optimal bladder size for MRI scanning is achieved by instructing the patient to begin to drink water 30min prior to the scan and arriving at examination with full bladder. In the case of the patients that have a urethral catheter, 250ml - 400ml of the sterile saline has been utilized for the purpose of increasing the volume of the bladder, throughout the procedure of the imaging, bladder fullness has been checked at the localizer images and the imaging process delay has been triggered in the case where the bladder wasn't entirely full.

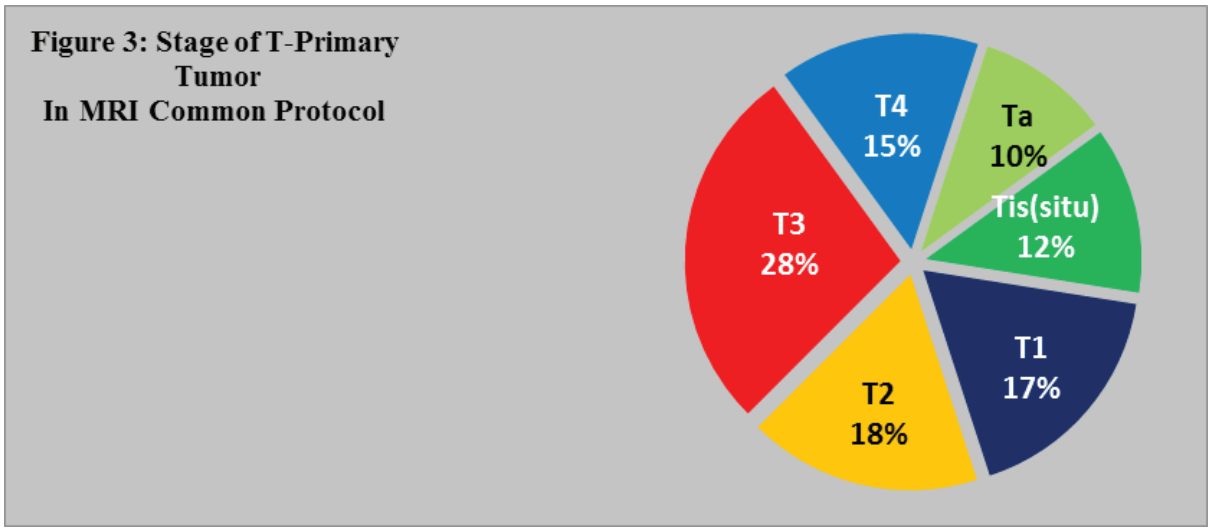
The object of bowel peristalsis may be decreased through the administration of an intra-muscular anti-peristaltic agent which can spread out from the abdomen in the pelvis. MRI testing was done using a body surface coil with 1.5 tesla MRI machine (Magnetom Aera, Siemens medical system, Germany) (26-28 cm).

3.Result:- In this study 41 patients have been included, Thirty five men as well as six women ,with age range from(31 - 83 years),38 patients presented with hematuria and pelvic pain while 3 patients presented without hematuria & pelvic pain , as shown in figure below.



	Gender		Age						Hematuria		Pain		Smoking	
	male	female	31-40 Y	41-50 Y	51-60Y	61-70Y	71-80Y	81Y and more	Yes	No	Yes	No	Yes	No
Percent	85.4	14.6	4.9	2.4	24.4	31.7	24.4	12.2	92.7	7.3	92.7	7.3	97.6	2.4
Number	35	6	2	1	10	13	10	5	38	3	38	3	40	1

Figure (1) Show The Distribution Of The Patients According To Their Age, Gender, Smoking Habit And Clinical Feature, Approximately 85 %Of The Age Classes Fall Between 50 To 80 Years . It Seems That The Majority Of The Patients Are Male (85.4 %), Smokers (97.6 %), And Had A Clinical Symptom Of Hematuria (92.7%).

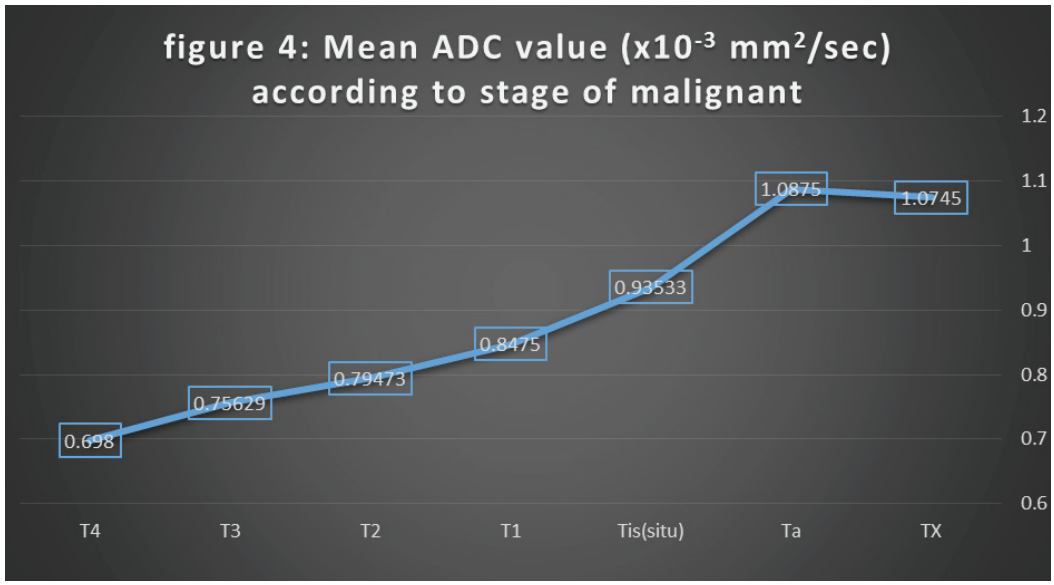


Figure(3): Shows The The Percentage Of Patients Present In Each Stage Of Bladder Carcinoma.

Table 2. Efficiency For Each Protocols

Efficiency For Each Protocols		Actual Diagnosis						Sensitivity	Specificity	PPV	NPV	Accuracy
		Malignant		Benign		Total						
		N	C%	N	C%	N	C%					
Histo_ Predictive	Malignant	39	100	0	0	39	95.1	100	100	100	100	100
	Benign	0	0	2	100	2	4.9					
Total		39	100	2	100	41	100					
MRI_Predictive by Conventional protocols	Malignant	38	97.4	1	50	39	95.1	0.974	0.5	0.974	0.5	0.951
	Benign	1	2.6	1	50	2	4.9					
Total		39	100	2	100	41	100					
MRI_Predictive by DCE Protocols	Malignant	39	100	1	50	40	97.6	100	0.5	0.975	100	0.976
	Benign	0	0	1	50	1	2.4					
Total		39	100	2	100	41	100					
MRI_Predictive by DWI Protocols	Malignant	39	100	0	0	39	95.1	100	100	100	100	100
	Benign	0	0	2	100	2	4.9					
Total		39	100	2	100	41	100					

Table (2) Shows The Efficiency For Each Protocols As well as explaining the Sensitivity, Specificity, PPV, NPV & the Accuracy. The table shows that the accuracy of the MRI device using the DWI protocol (100%)is the closest to the accuracy of the golden rule on which we relied on diagnosis. In general, the accuracy of the MRI device using the DCE protocol(97.6%) is close to or similar to the DWI MRI, However, accuracy of DCE decreases in the early stages of cancer invasion(in Tis stage 88.9%, T1=90.9%



Correlation between stage of carcinoma and ADC value		
	r	p.value
Actual stage	-0.917	.000

Correlation is significant at the 0.01 level

Table 3: ANOVA

ADC value according to stages	Mean	Std. Deviation	F	Sig.	Sig. level
TX	1.07450	.000707	57.205	.000	Very high sig
Ta	1.08750	.006455			
Tis(situ)	.93533	.084180			
T1	.84750	.009354			
T2	.79473	.024904			
T3	.75629	.048808			
T4	.69800	.015811			

Figure (4)&table (3): Shows The Relationship Between Cancer Stage And ADC Value Is Very High Significant, As The ADC Value In Early Stages Of Bladder Cancer(Tis,Ta, T1) Was High (1.875 × 10^{-3} mm^2/s), While On The Contrary, ADC Value Was Low(0.698 ×10^{-3} mm^2/s) In Advanced Stages(Fromt2b To T4 Stages) Of Bladder Cancer. At The Same Time, The ADC Value Was High In The Low Grade Malignancy And Low In High Grade Malignancy.

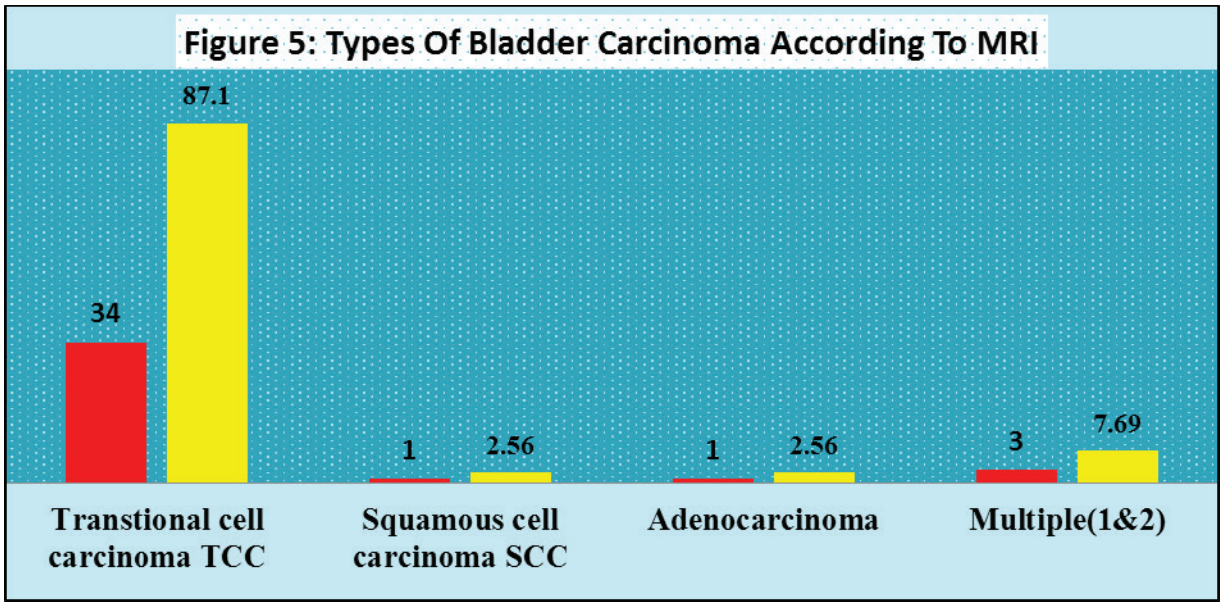


Figure (6): shows types of bladder carcinoma, Most common type were TCC, about 85.1%.That is, 34 patients, while SCC and adenocarcinoma were about 2.56%, with only one patient for each, and finally about 7.69%, multiple between TCC and SCC.

Discussion

In this paper, approximately 93.50% of patients aged > 50, with an average age of diagnosis 64.80 years that ranged between 31 and 83 years that has been was similar to some of the other researches (1,16) the findings of this study have been consistent with the cancer statics of the year 2010 that showed most cases happen past the age of 50 (17) in this research, the ratio of males to females has been 5.80:1 and it has been a little higher compared to that of the cancer statistics of the year 2010 that showed a 3:1 males to females ratio (17) and in addition to that higher than Gupta etal with 4:1 (1) those findings have indicated that the age (> 50) has been considered as one of the risk factors to develop bladder cancer (due to the fact that most cases have been higher than 50 years old) and that male higher predisposition in comparison with the female for acquiring that cancer type.

In this research, 60.9% of the patients had high grade tumor, 34.1% of patient had low grade tumor, this elevated ratio of high grade and invasive muscle disease can be attributed to Iraqi patients presented to physician only after the disease reaching advance stages, as shown in previous Iraqi study in which they found 63.27% having muscle invasive and 42.9% had grade II disease and 44.9% had grade III disease.

In this paper, 34.1% of cases that have been presented with the low grade bladder cancer and 60.9% with high grade bladder cancer based upon the histopathological examinations, our findings have not been in agreement with the findings of Gupta et al, where 41.70% had low grade and 25% presented with high grade (15) in addition to that, Takeucji et al have shown that 27% had high grade and 73% had low grade (14)

Whereas other researches have been in agreement with the findings of this study, S, fakianos et al have shown that 75.30% had high grade tumor (18) Divrik etal have shown 78.70% had high grade tumor (18). Such disagreements amongst the researches may be a result of the differences in the environmental, genetic and social predisposing in a variety of the populations that are evaluated in those researches.

DWMRI results in our study show that bladder tumor nature is well linked to histopathologic results. DWMRI results We managed to find tumors in the patients with 100% sensitivity, 100% specificity, but also 100% accuracy. However, this percentage may decrease because the number of patients is less than what was taken in other studies &These high diagnostic accuracy values were higher or close to other similar studies. (19, 20) , DWMRI do not discriminate benign and malignant

bladder, due to the fact that the two types of the lesion result in the restriction of the water diffusion and have a high signal intensity. (19)

However, the results using DCE MRI were slightly lower than those of using DWI. . We have identified 100% sensitivity to the bladder tumors , 50% specificity and 97.6% accuracy. But results are less in the early stages of bladder cancer, especially in Tis, Ta, T1, and T2 Where it decreases the earlier the stage of carcinoma , as well as We identified the bladder tumors with that the 83.3% sensitivity,100% specificity and 88.9% accuracy. our findings was in disagreement with Gupta et al in which 90% sensitivity , 80% specificity, 86.7% accuracy. (15) DWI studies (Bladder masses) related to bladder tumors tend to be more intensively conducted on recent years. The ADC level in tumor tissue has been considerably lower than ADC level in the surrounding tissue. Matsuki et al (23) 17 tumour weights were examined in 15 bladder carcinogens. These researchers therefore stressed the need for further studies.

The ADC levels of 41 patients referred to our clinic were assessed in our sample with a predisposition of the bladder tumor, Of the 41 patients, 39 had histopathological carcinomas. Diffusion restrictions were observed for all 39 mass lesions in the malignant group. Of the two benign case groups.

The mean ADC value in our study according to stages was ranging from (1.08750 in Ta stage to 0.69800 in T4 stages) × 10-3mm2/s. In the patients with advanced stages, the value of the ADC is found to be significantly lower. (T2b-T4 ,High grade) of bladder cancer compared to early stage (Ta,T1) low grade, as illustrated in table 3 and figure 4.

When compare our study with others studies , Our study is consistent with his study Avcu, S., Koseoglu et al (22), 41 malignant tumor patients average ADC levels (1.0689 ± 0.26× 10-3 mm2/s).

In our study the histopathological types of bladder carcinoma as illustrated in figure 5 Transitional cell carcinoma number was 34 patient 87.1% , Squamous cell carcinoma & Adenocarcinoma (No = 1) 2.56% for each one and multiple(TCC &SCC) types about (NO=3) 7.69%,our finding disagreement with the study of (Al Johi, R. S., Seifeldein) Which was TCC=72%, SCC=23.6% and adenocarcinoma 4.3%.

In our study the as shown in figure(3) the Percentage Of Patients Present In Each Stage Of Bladder Carcinoma was (,TIS=12%,Ta=10% ,T1=17% ,T2=18% ,T3=28% ,T4=15%) . but when compare our result with Al Johi, R. S., Seifeldein et al(23) they reported (T1=9.8% ,T2=19.6% ,T3=15.7% ,T4=7.8%) , but(Tis,Ta) they was excluded from T stage analysis.

Conclusion

Our results demonstrate that diffusion weighted MRI (DWMRI) with ADC has been defined as a fast and reliable means of diagnosing and classifying the bladder masses. Additionally, more studies are necessary for the purpose of verifying the effectiveness of this kind of technique, and its application to other problems. Diffusion-weighted MRI and dynamically contrast-enhanced MRI have also been of great support for Bladder Cancer T-staging.

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Conflict of Interest: None to declare.

Ethical Clearance: "All experimental protocols were approved under the Department of Radiology Technologies and all experiments were carried out in accordance with approved guidelines".

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