Role of Magnetic Resonance Imaging Protocols in Detecting 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 /Baghdad medical city complex. 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 magnetic resonance imaging 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**) , positive predictive value (**PPV**) , negative predictive values (NPV) 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%).

Conclusion: Both Diffusion weighted MR imaging and dynamic contrast enhanced MRI offer excellent agreement for T-staging of bladder cancer, Diffusion weighted MR imaging (DWI) and dynamic contrast enhanced MRI (DCE) at 1.5 tesla are a good imaging modalities for early detection and staging of bladder carcinoma, , with DWI is preferred without use of contrast media, so it can be used in patient with renal impairment or contrast media allergy.

1. 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 non-muscle invasive. These are low-grade lesions that arise from a hyperplastic epithelium and may be multifocal. They usually have a strong prognosis and rarely grow into an invasive cancer, although there are about 50 percent urothelial recurrence rates, Approximately 20%-25% of bladder cancers are muscle-invasive, emerge from severe dysplasia or in situ carcinoma, and have a higher histologic grade. Non muscular urothelial invasive tumors have a higher recurrence rate than the 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)

Clinical diagnosis and appropriate treatment of bladder tumors almost always depend on the detection and correct staging of the intravesical lesion. (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 surrounding tissues. [6, 9, 10]. With data precision ranging from 88 to 97.6 percent, the analysis of dynamic gadolinium-enhanced MRI is much more advantageous for staging/diagnosing bladder cancer. Diffusion-Weighted MR Imaging. Recently Weighted diffusion imaging (DWI) is a type of 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 as well as urinary bladder. [11] .

There are limited studies on the role of this new diagnostic technique in the diagnosis and stage of bladder tumors in the literature. [8, 11–14] . This study aimed at assessing the role of the DWMRI and ADC as a quantitative parameter for the diagnosis, staging of pathologies of bladder tumors and the pathological classification The usual bladder wall was difficult to see on DW images, we tended to paste regions of interest (ROIs) on the ADC map after finding and copying ROIs on T 2-weighted images at the standard bladder wall. Using histopathological findings, the normal situation of the bladder walls at which ADC measurement is performed has been confirmed. In the circular region of interests, ADC values were calculated as mm 2/s and the average ROI values were reported in b 100, b 600 and b 1000. The findings of MRI,

DWMRI and ADC were correlated with histopathology results.

2. Patients and methods

MRI is a very preferred method for imaging bladder cancer due to both advanced protocols, for which (DWI)diffusion weighted magnetic resonance imaging and dynamic contrast enhanced magnetic resonance imaging(DCE) are excellent agreement for T staging of bladder cancer with DWI without the use of contrast media, so it can be used in patients who Have renal impairment or sensitivity to 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.

Figure 1:Gender distribution in relation to age groups
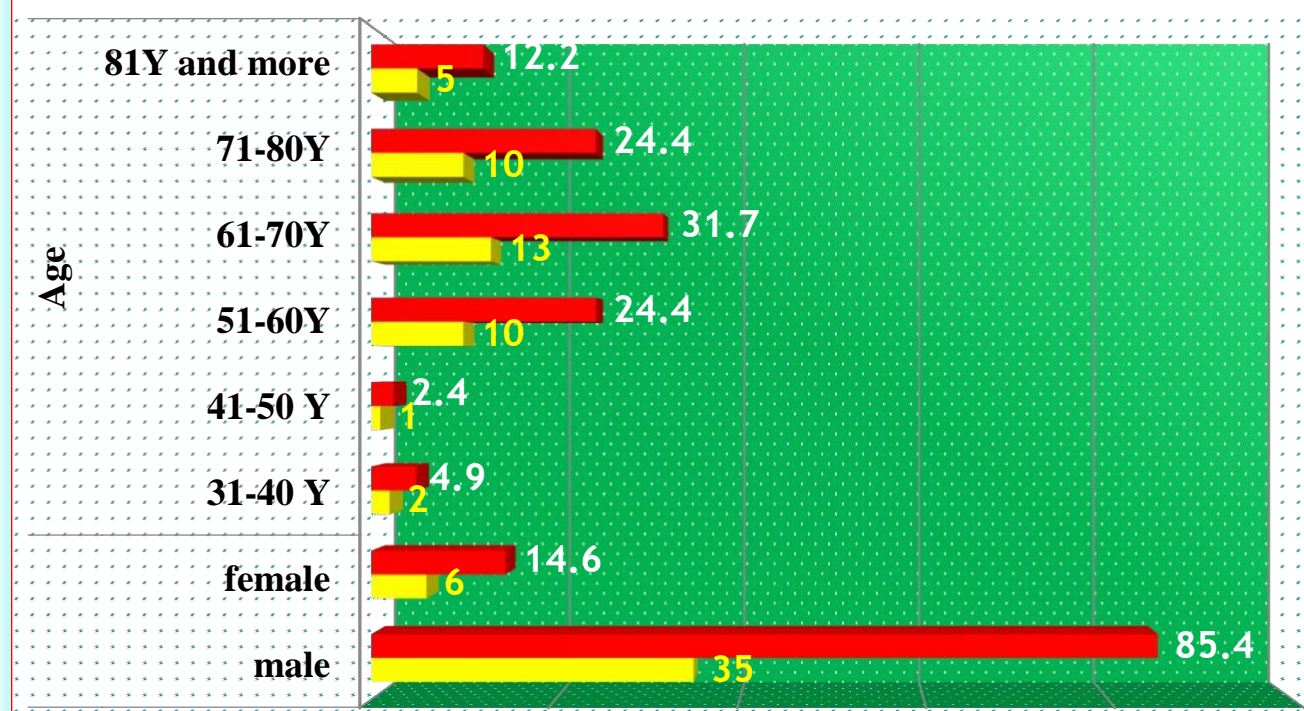
Standard MRI protocol(A) was included in the following sequences, T1-weighted turbo spin-echo in axial and sagittal planes, T2-weighted turbo spin-echo in axial , sagittal and coronal planes, Diffusion weighted MRI, Apparent diffusion coefficient(ADC) maps, Dynamic contrast-enhanced MRI: Contrast-enhanced 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

Examination technique:-
Anesthesia was not required for the MRI study, the bladder was distended to aid in accurate diagnosis. The lack of bladder dissidence, motion artifact and chemical shift artifact 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 start drinking water 30 minutes before the scan and arriving at the examination with a full bladder. In patients with a urethral catheter, 250 - 400 ml of sterile saline was used to increase bladder volume, during the imaging procedure, fullness of the bladder was checked at localizer images and the delay of imaging procedure was triggered if the bladder was not full.
The object of bowel peristalsis can be reduced by administering an intramuscular antiperistaltic 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

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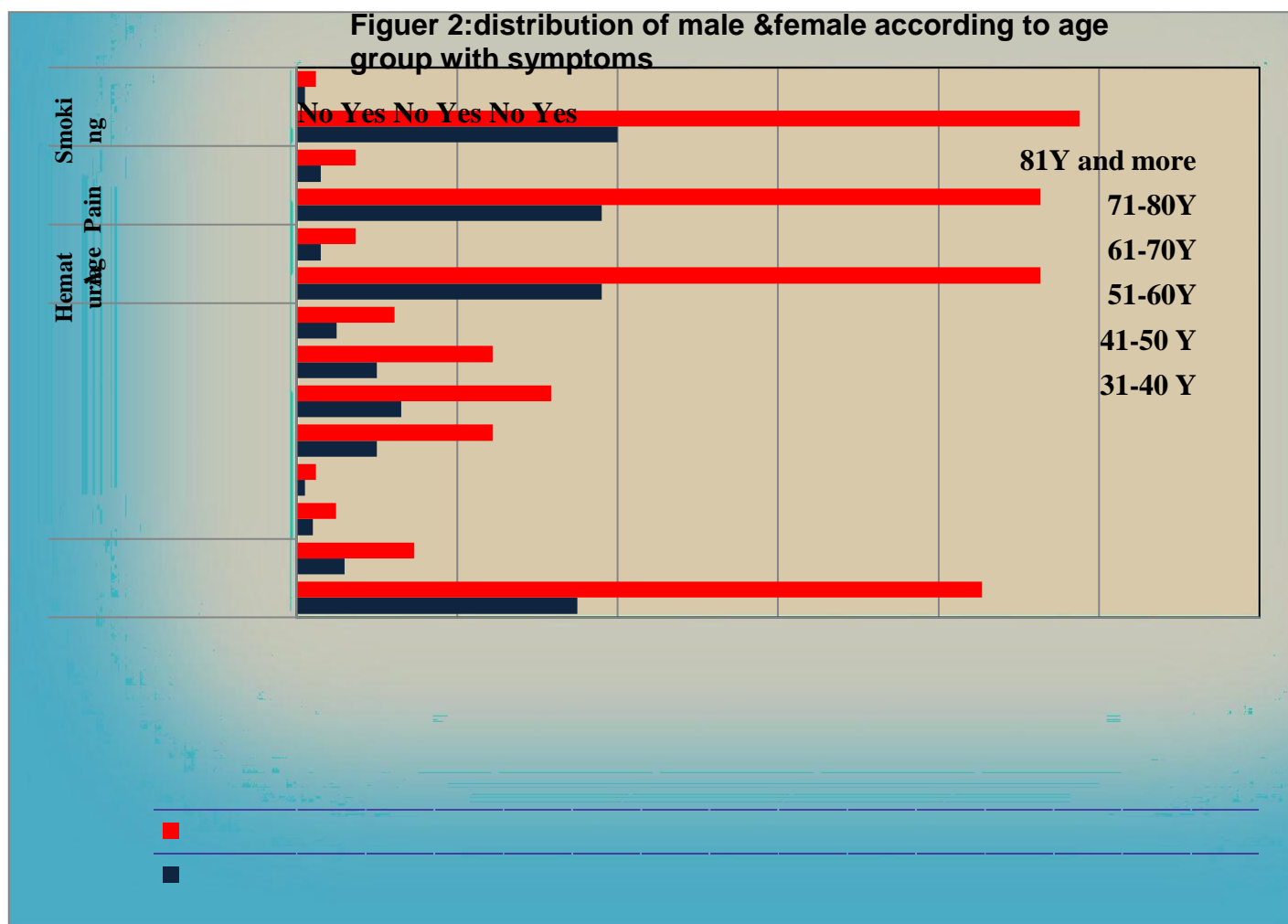
	Gender		Age						Hematuria		Pain		Smoking	
	male	female	31-40 Y	41-50 Y	51-60 Y	61-70 Y	71-80 Y	81 Y and more	Yes	No	Yes	No	Yes	No
Percent	85.4	14.6	4.9	2.4	24.4	31.7	24.4	12.2	92.7	7.3	92.7	7.3	97.6	2.4
Number	35	6	2	1	10	13	10	5	38	3	38	3	40	1

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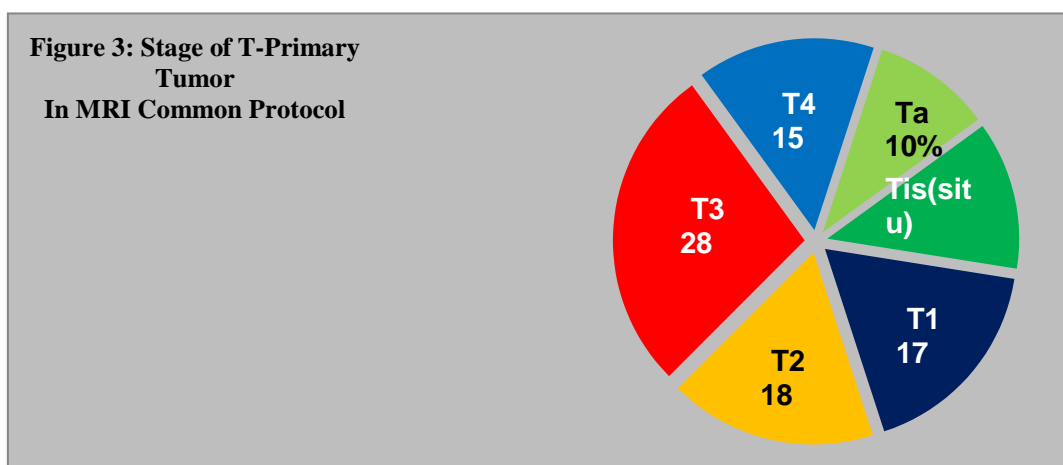
Figure(3): Shows The The Percentage Of Patients Present In Each Stage Of Bladder Carcinoma.

Table 2: Efficiency For Each Protocols		Actual Diagnosis						Sensiti vity	Specifi city	PP V	NP V	Accur acy
		Maligna nt		Benign		Total						
		N	C %	N	C %	N	C%					
Histo_ Predictive	**Maligna nt**	39	100	0	0	**39**	**95.1**	**100**	**100**	**10 0**	**100**	**100**
	Benign	0	0	2	100	**2**	**4.9**					
Total		**39**	**100**	**2**	**100**	**41**	**100**					
MRI_Predictiv e by Conventional protocols	**Maligna nt**	38	97. 4	1	50	**39**	**95.1**	**0.974**	**0.5**	**0.9 74**	**0.5**	**0.951**
	Benign	1	2.6	1	50	**2**	**4.9**					
Total		**39**	**100**	**2**	**100**	**41**	**100**					
MRI_Predicti ve by DCE Protocols	**Maligna nt**	39	100	1	50	**40**	**97.6**	**100**	**0.5**	**0.9 75**	**100**	**0.976**
	Benign	0	0	1	50	**1**	**2.4**					
Total		**39**	**100**	**2**	**100**	**41**	**100**					
MRI_Predicti	**Maligna nt**	39	100	0	0	**39**	**95.1**					

ve by DWI Protocols	Benign	0	0	2	100	2	4.9	100	100	100	100	100
	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%

figure 4: Mean ADC value (x10^{-3} mm^2/sec) according to stage of malignant
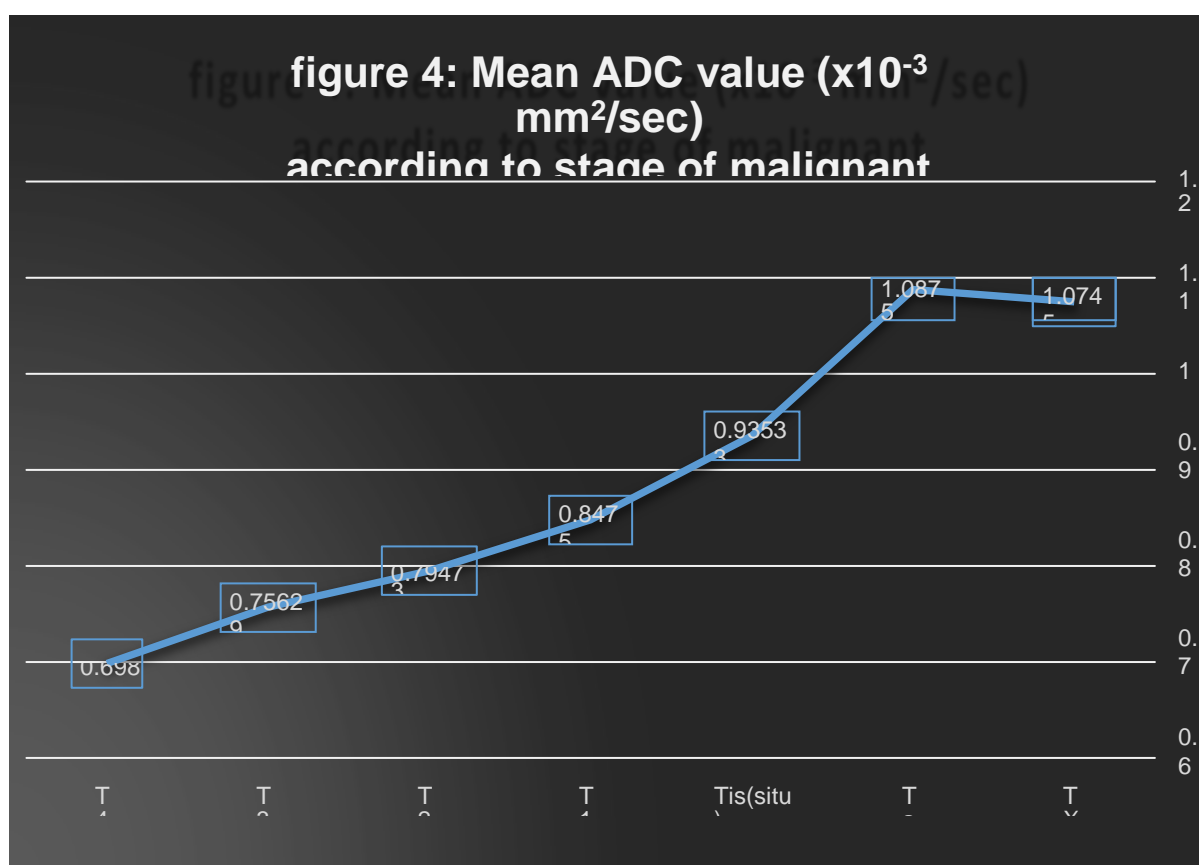
Correlation between stage of carcinoma and ADC value		
	r	p.value
Actual stage	-0.917	.000

Correlation is significant at the 0.01 level

Table 3: ANOVA table					
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 $(1.875 \times 10^{-3}$ mm^2/s), While On The Contrary, ADC Value Was Low$(0.698 \times 10^{-3}$ 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.
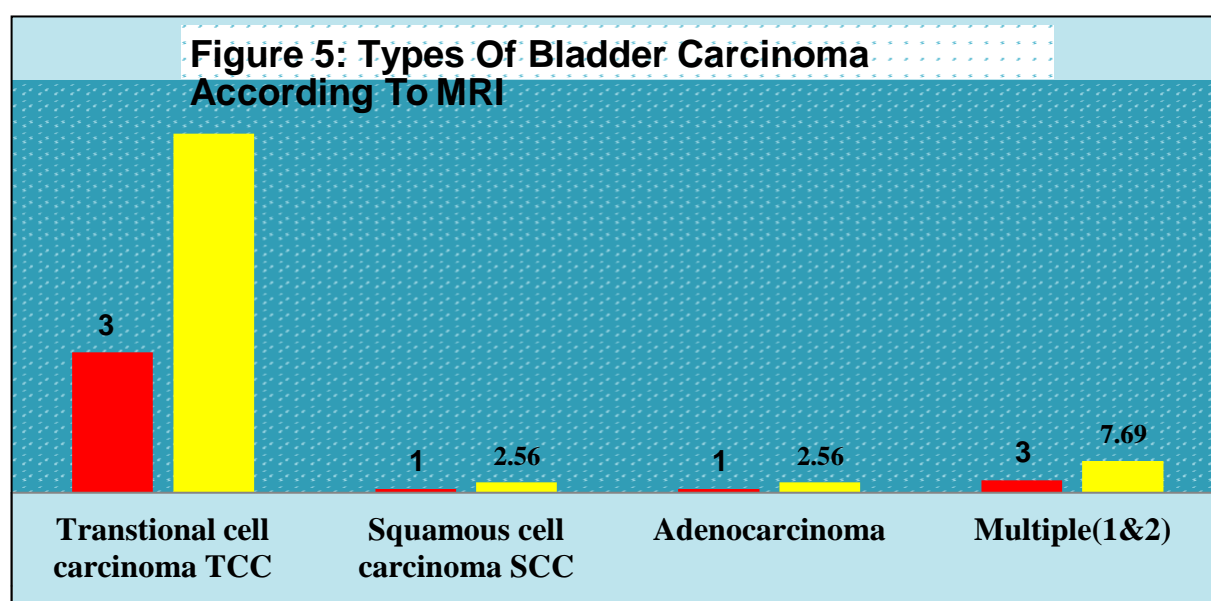

Figure 5: Types Of Bladder Carcinoma According To MRI

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.
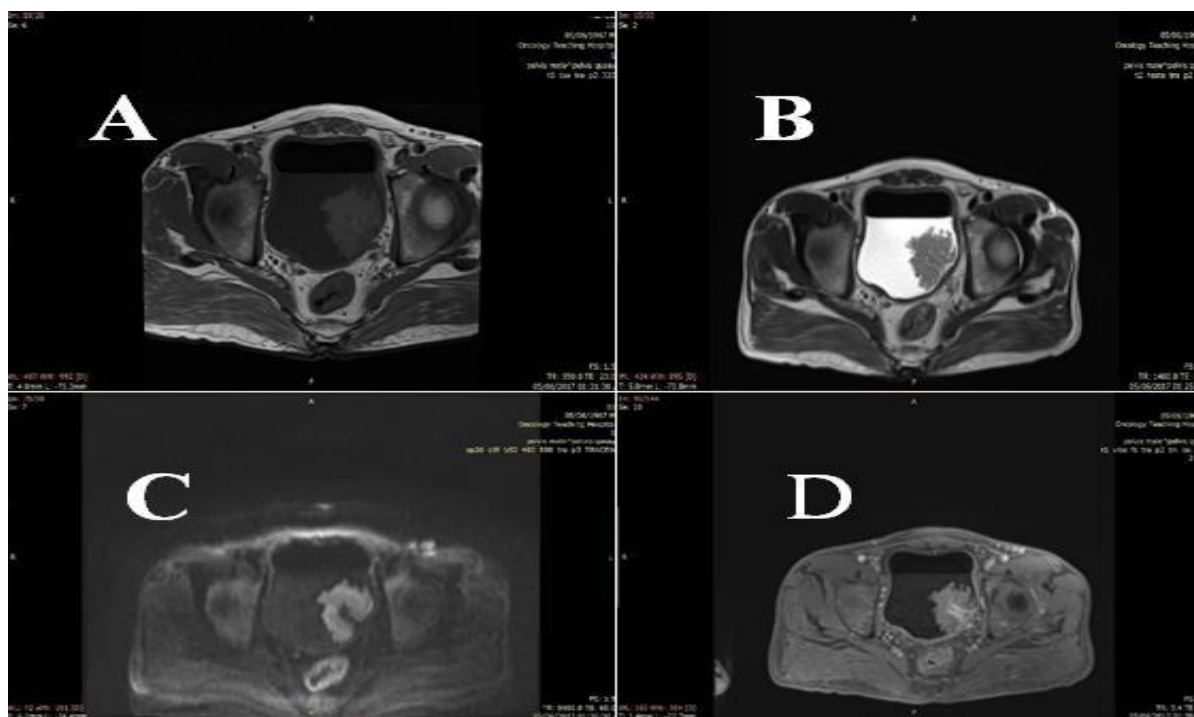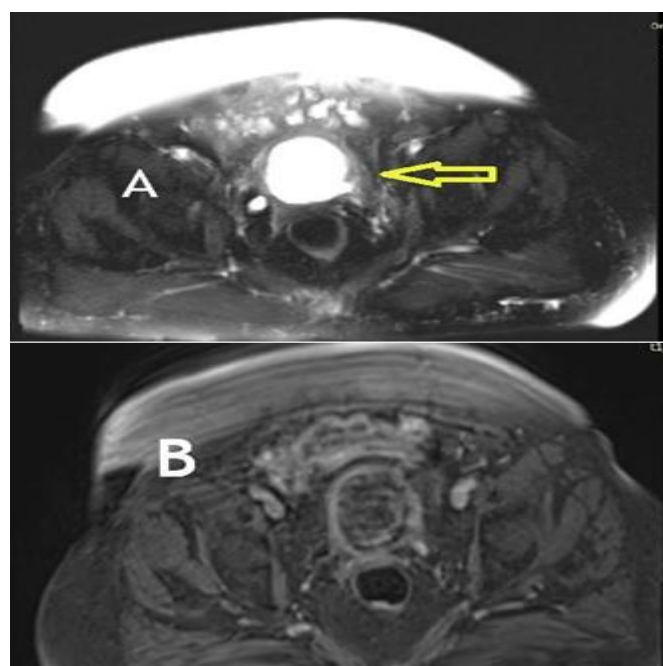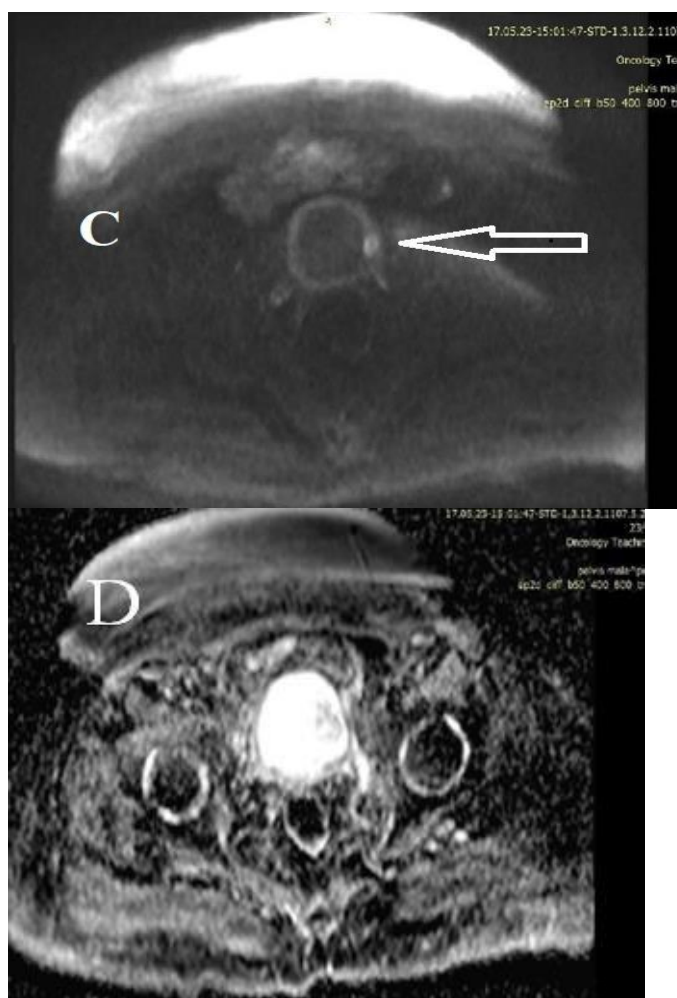
Figure (7): MRI of the pelvis for male patient 55 years old, presented with painless hematuria. **(A&B):** axial T1WI & T2 ,show that the tumor with intermediate **SI** seen in LT posterior lateral wall of the bladder. **(C):** axial DWI show that the tumor restricted in diffusion.**(D):** immediate sequence of DCE T1 axial fat suppression show that the moderately enhancing tumor in this case staging by DWI the tumor stage I bladder cancer and pathological report proved also that the tumor is stage I.

Figure(8): MRI of the pelvis for female patient 78 years old, presented with painless hematuria.(**A**)axial T2WI,show that the tumor with intermediate signal intensity seen in LT lateral wall of the bladder. (**b**)axial post contrast dynamic enhanced T1 show that the eraly enhancing tumor. (**C**) Axial DWI show that the tumor restricted in diffusion ,DWI clearly show that the tumor invasion to the superficial muscle consistent with stage II bladder CA. (**d**)ADC confirmed that the mass restricted in diffusion with ADC value 1.1x10_3mm2/s, in this case staging by DWI the tumor stage II bladder cancer and pathological report proved also that the tumor is stage II.

4. Discussion: In the current study about 93.5% of the patients their age above 50 years, with mean age at diagnosis 64.8 years ranging from 31 – 83 years which was similar to other studies [1,16] our findings was agreement with cancer statics in 2010 showing that the majority of the cases occur after the age of 50 years [17] in the current study male to female ratio was 5.8:1 which was slightly higher than that of cancer statistics 2010 showing 3:1 ratio of male to female[17] and also higher than Gupta et al with 4:1 [1] these finding indicate that age (above 50 years) is risk factor for development of bladder cancer (since the majority of the cases were above 50 years) and that male higher predisposition compared to female to acquire this type of cancer.

In the current study 60.9% of patient 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 the current study 34.1% of the cases presented with low grade bladder cancer and 60.9% with high grade bladder cancer based on histopathological examination, our findings was in disagreement with Gupta et al in which 41.7% had low grade and 25% presented with high grade [15] also Takeucji et al demonstrated that 73% had low grade and 27% had high grade [14]

While other studies was in agreement with our findings, S, fakianos et al showed that 75.3% had high grade tumor [18] Divrik et al revealed 78.7% had high grade tumor [18]. This disagreement between studies can be attributed to difference in social, environmental and genetic predisposing in the different population begin evaluated in these studies.

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, since both lesion types restrict water diffusion and have 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 the tumour tissue was significantly lower than the 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) × 10-3 mm2/s. In patients with advanced stages, the apparent diffusion coefficient (ADC) value 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.

5. Conclusion: Our results demonstrate that diffusion weighted MRI (DWMRI) with ADC is a fast and reliable means of diagnosing and classifying bladder masses. Additionally, Further studies are necessary to verify 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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