The Value of Diffusion Weighted Magnetic Resonance Imaging 3 Tesla in Detection and Staging of Bladder Carcinoma

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ABSTRACT:

BACK GROUND:

To evaluate the value of diffusion weighted magnetic resonance imaging (DWMRI) in detection and T- staging of bladder carcinoma and correlation with histopathological staging.

PATIENTS AND METHODS:

An analytic prospective study was conducted at the MRI units of Al-yarmook teaching hospital in the period from January of 2015 to December 2015, 42patients (36male and 6 female) presented with hematuria (40 patients) and 2 patients presented with pelvic pain were enrolled prospectively ,they underwent conventional magnetic imaging(MRI) and diffusion weighted MRI using 3 tesla MR units (Achieva ; Philips medical systems, the Netherlands).

Diffusion weighted images were obtained using a single shot echo planar imaging sequence EPI with b value 0,500sec/mm$^{2.}$ADC value map was reconstructed and mean ADC value were measured in 42 patients .and histological examination was done to all patients.

RESULTS:

Correlation between standard MR staging of bladder carcinoma and histopathological results revealed that 17 patients (40%) had the same T -staging while 17 patients(40%) over staged. DWI and ADC values were able to declare the cause of overstating by discrimination between tumoral tissue and peritumoral inflammation. Statistically significant difference is found between ADC value of bladder tumor and those of urine.

CONCLUSION:

Diffusion weighted MR imaging at 3 tesla is new and good imaging modalities for detection and staging of bladder carcinoma, , without using contrast media, so can used in patient with renal impairment or contrast media allergy.

KEYWORDS : bladder cancer ,diffusion _weighted MRI.

INTRODUCTION:

1.1. Overview

Bladder cancer is the ninth most commonly diagnosed cancer worldwide, with more than 380,000 new cases each year and more than 150,000 deaths per year, and an estimated male-female ratio of 3.8:1.0. [1]

More than 90% of bladder carcinoma are transitional cell carcinoma derived from urothilium, About 6% to8% are squamous cell carcinoma and 2% adenocarcinoma which is either urachal or non urachal origin, the latter type is generally thought to arise from metaplasia of chronically irritated transitional epithelium.[2.]

The most common presenting features is hematuria either gross or microscopic in 85_95% of patients[3,]and smaller percentage of patient ,its accompanied by symptoms of vesical irritability ,frequency ,urgency and dysuria[.4].

1.2. Anatomy of the urinary bladder

The urinary bladder is musculomembranous sac, predominantly extra peritoneal, its position and relation varying according to the amount of fluid it contains. Peritoneum covers the superior surface or the dome of the bladder. The bladder receives both ureter posteriolaterally, whereas inferiorly, bladder neck is continuous with the urethra .the orifice of the ureters at the ureterovesical junction are joined by an elevated ridge covered by mucosa (interureteric ridge).the trig one describe a triangular region on the internal face of the bladder on the inferior wall, marked at its corners by the ureterovesical junction and the urethra. [1]

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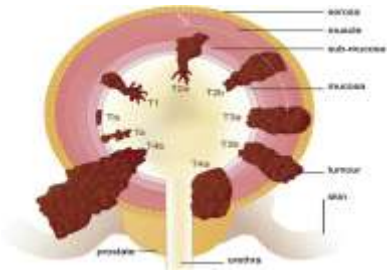

Figure 1: Diagram illustrating the layers of the bladder wall and the tumor staging based on the depth of invasion. [3].

1.3. Investigation

In clinical management of urinary bladder cancer ,non-muscle invasive tumors(stageI)are usually treated by transurethral resection(TUR),whereas muscle invasive tumors(stage II or higher) are treated by radical cystectomy or by palliative chemotherapy or radiation therapy[1].

Thus ,preoperative imaging studies that could precisely differentiate the two types of the tumor could play an important diagnostic roles[5],and avoiding radical surgery in incurable patients.[6]

Contrast enhanced CT and MRI are the standard techniques that have been used for the radiological evaluation of urinary bladder carcinoma. While CT is generally used to screen for metastasis, MRI plays pivotal role in the staging of bladder cancer because its superior soft tissue delination,especially in the context of muscle invasion.[7] .

MRI has excellent soft tissue resolution and multiplanar capabilities, which has made it an important staging modality for bladder cancer. Fundamental to its importance in local staging is the ability to manipulate image contrast by using different sequences. The tumor appear intermediate signal intensity on T1 and T2. [8]

On T2-weighted images the bladder tumor is usually more conspicuous. The signal from perivesical fat can be suppressed using short tau inversion recovery (STIR) sequences, allowing signal from the tumor to be highlighted by suppressing signal from adjacent surrounding normal tissue[9]. In conjunction with gadolinium-containing contrast, MRI has an accuracy of 85% in differentiating NMIBC from MIBC and 82% accuracy in distinguishing organ confined disease from non-organ confined disease [10]. However, Gad- Contract should be avoided in those with renal impairment (estimated glomerular filtration rate (GFR) <60 ml/minute), as there is an increased risk of developing nephrogenic systemic fibrosis[4] . also the inherent sensitivity to motion still creates problems in the study of the abdomen due to artifacts caused by the heartbeat and intestinal peristalsis Therefore, to reduce respiratory motion, the patient must hold his/her breath during the examination, Such an approach limits the acquisition time, and both the signal-to-noise ratio and the spatial resolution must be compromised as a result[11]. To resolve those problems(breathing and contrast enhanced T1), Takahara et al.[reported a procedure of body DW MRI under free breathing, which enables a longer scan time.. However, the use of DW MRI under free breathing gives more thin-slice images, with multiple signal averaging, and provides high-quality multiplanar display.[12]

PATIENTS AND METHODS:

2.1. Patients and data collection

This prospective study was conducted at the MRI units of Al-yarmook teaching hospital in the period from January 2015 to December 2015.

A total 42 patients with bladder tumor were included in this study.

The patients were referred to the MRI unit. Inclusion criteria all or any of the following (a)clinical features of hematuria (b) u/s findings of bladder mass and (c) patient had recent cystoscopy revealing urinary bladder carcinoma .exclusion criteria were the common contraindication to MRI (pace maker ,metallic foreign body ,and impaired renal function or claustrophobia) also excluded were patients who received radio or chemotherapy for uterine or prostate cancer, and excluded patients who refusing consent for the study.

These 42 patients examined by MRI study and subsequently conventional cystoscopy and biopsy done for all.

2.2. Examination technique:

No anesthesia was required for MRI study, bladder distention is of fundamental importance for accurate diagnosis. Over distention can result in flat or plaque like lesions being missed, and under distention can result in smaller lesions being missed because of detrusor muscle thickening so patient were instructed to start

drinking water 30 mint's. Before MRI study and arrive for their examination with full bladder .
In patients with a urethral catheter ,250-400 ml sterile saline was used to distended bladder ,during the imaging procedure fullness of the bladder was checked at the localizer images and the examination was delayed if the bladder was not full.
MRI was performed with 3 tesla system(achieva,.Philips medical system ,the Netherlands)using phased array body coil .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 T1 weighted images. all patients were examined in the supine position throughout the examination in axial plane.

RESULTS:

Forty two patients were included in this study; 36male and 6 female ,with age range from(47 - 86 years),40 patients presented with hematuria while 2 patients presented with pelvic pain , as shown in table below:

Table 1: The observed frequencies and percentages of patients group according to age ,gender ,smoking habit and clinical features.

Groups		Frequency (total 42)	Percentage (%)
Age (years)	47-56	14	33.33
	57-66	13	30.95
	67-76	10	23.81
	77-86	5	11.91
Gender	Male	36	85.71
	Female	6	14.29
Clinical Feature	Hematuria	40	95.24
	Pelvic Pain	2	4.76
Smoking habit	Yes	29	69.05
	NO	13	30.95

This Table (1) show the distribution of the patients according to their age, gender, smoking habit and clinical feature . Approximately 89 % of the age classes fall between 47 to 76 years . It seems that the majority of the patients are male (85.71 %), smokers (69.05 %), and had a clinical symptom of hematuria (95.24 %) . Regarding MRI staging of 42 patients (using T2WI,post contrast T1,DWI) and correlated with staging done by histopathological findings as shown in table (2,3,4) and figures(2):

Table 2 : The frequencies and percentages of correct staged, over staged and under staged patients diagnosed by T2-wieghted imaging in comparison to histopathological staging.

Staging	Frequency (total 42)	Percentage (%)
Correct Staging	17	40.47
Over staging	17	40.47
Under staging	8	19.06

Table 3: The frequencies and percentages of correct staged, over staged and under staged patients diagnosed by Post contrast T1-Weighted imaging in comparison to histopathological staging.

Staging	Frequency (total 42)	Percentage (%)
Correct Staging	17	40.47
Over staging	19	47.24
Under staging	6	14.29

Table 4 : The frequencies and percentages of correct staged, over staged and under staged patients diagnosed by DW imaging in comparison to histopathological staging.

Staging	Frequency (total 42)	Percentage (%)
Correct Staging	41	97.62
Over staging	0	0
Under staging	1	2.38

According to the tables (2,3,4) , the highest percentage of correct staged patients (97.62%) was seen by DW imaging when it is compared to histopathological staging . The results obtained by T2 and post contrast T1 were equal (40.47 %).

The numbers of over staged patients were 17 (40.47 %), 19 (40.47 %) and 0 (0 %) by using T2W, post contrast T1 and DW imaging respectively; while the numbers of under staged patients were 8 (19.06 %), 6 (14.29 %) and 1 (2.38%) that were diagnosed by T2W, post contrast T1 and DW imaging respectively .

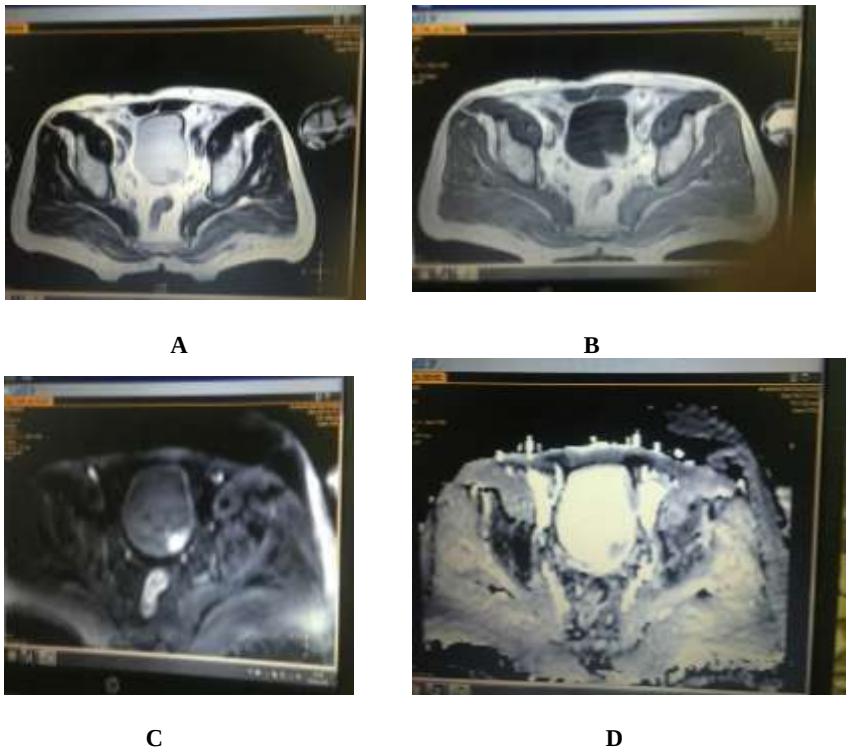

Figure 2:MRI of the pelvis for male patient 71 years old, presented with painless hematuria.(A) axial T2WI,show that the tumor with intermediate signal intensity seen in LT posterior lateral wall of the bladder(but not easy to say that is stage I or II),(b)axial post contrast T1 show that the moderately 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 I bladder CA ,(d) ADC confirmed that the mass restricted in diffusion with ADC value 1.2x $10^{-3}$$mm^2$/s, in this case staging by DWI the tumor stage I bladder cancer and pathological report proved also that the tumor is stage I.

DISCUSSION:

DWI is a recently introduced technique that depicts differences in molecular diffusion caused by the random and microscopic motion of molecules which is known as Brownian motion , Restriction to the molecular diffusion of water in neoplastic tissues[2], can be related both to the greater cellular density in the tissues, generated by the high index of neoplastic replication with a consequent reduction in the width of intercellular spaces, and to the ultra-structural alteration of the normal tissues[13]. T staging of bladder cancer has an important role in the appropriate choice of

therapy ,DWI is convenient and safe technique that does not require along examination time or contrast agent which may cause adverse effect such as nephrogenic systemic fibrosis[14], the accuracy of T staging with DWI exceeds that of conventional methods[15], correlation between standard MRI staging of bladder carcinoma and diffusion weighted MRI with histopathological results was done ,regarding pathological comparison we found that 17/42 correct staging while 17/42 over staging , watanabe et al was agree with our study that over staging is the most frequent error in MRI staging of bladder carcinoma due to peritumoral inflammatory changes which mimic tumor on T2 MRI [16]. Also these study were in agreement with EL Assmy et al. who did their study on 43 patients and reveled that all carcinoma in these 43 patients were clearly shown as high signal intensity(SI) relative to the surroundings structures so proper staging was obtained .there were no false positive cases and results were quite similar to those of our study[17]. Takeuchi et al. also reported that an inflammatory changes or fibrosis surroundings the tumor mimics the invasion of bladder cancer on T2 weighted imaging or enhanced MRI and could lead to over staging ,but DWI could differentiate between them Cleary because these benign changes do not show high SI on DWI[18].

Kim et al. showed that gadolinium enhanced MRI more accurate than other MR techniques in staging of bladder cancer ,although over staging is the most frequent error[19].,Takes et al that the accuracy was low as 62%and over staging is the most frequent error 32% and compatible to our results which show the accuracy 66% and over staging 47%.[20]. Our results show that the frequency of over staging was significantly reduced when adding diffusion weighted MRI (47% of tumors over staged with gadolinium enhanced MRI versus 0% with diffusion weighted images).

Retrospective study published by watanabe at al[16].compared DWI with T2 and gadolinium enhanced techniques for tumor staging and compare these findings with histopathology ,tumor T stage was correct with DWI 68%,58% with contrast enhanced and 53% with T2 weighted imaging ,and another study done by Hossam M Adel rah man[19], that the results of tumor T stage compared also with histopathology was correct in 75% regarding DWI,45% with T2 and 45% with contrast enhanced T1 WI, our results was slightly higher than these two results regarding the DWI possibly due to higher field strength used in our study (3 tesla versus 1.5 tesla) used from these studies, which found the tumor T stage correct with DWI 97%,40% with T2 and 40% with contrast enhanced T1WI, also agree with another study by alassmy [21]. who found the accuracy of DWI for tumor staging is more accurate than T2MRI.

CONCLUSION:

In conclusion DWI at 3T can provide accurate information for evaluating the T- stage of bladder cancer.

DWI is more sensitive than T2 in differentiating staged T1 tumor from those staged T2 tumor or higher, it is noninvasive, fast and does not require contrast administration so it can used in patient with renal insufficiency or contrast material allergy. Also can be used as complementary method for detection and staging of bladder cancer with cystoscope and histopath

Recommendation

1. We recommend adding DWI as routine sequence in patient with urinary bladder carcinoma which would help guide for therapeutic planning .
2. Further study is required to differentiate between post TUR inflammatory changes from tumor recurrence.

REFERENCES:

1. J.AWitjes(chair),E. Comperat, N.C. Cowan, M. De santis, G.Gakis, N.James, T.Lebret, A.Sherif,A.G.van der heijden, M.J.Ribal, giudlines associates: M.Bruins, V.Hernandez, E.Veskimae. guidelines on - muscle-invasive and metastatic bladder cancer, European association of urology 2015.avialable from :https://www.uroweb.org./guidline/online-guidline.
2. Moin M. Hoosein ,Arum gam Rajesh . MR Imaging of the urinary bladder,2014. Available from :http://dx.doi.org..
3. Emil A. Tanagho .Jack .W. McAninch. SMITH,S GENERAL UROLOGY 17th ed.new york:MacGraw_Hill;2008:321-33.
4. Alan J. Wein . CAMPBELL –WALSH. volume 1.10th ed.USA;2012:1517-28.
5. Peter J. Bostrom ,Bas W.G. Van Rhijin ,Neil Fleshner ,Antonio Finelli, Michael Jewet, John Thoms,Sally Hanna, Cynthia KUK, Alexandre R.Zlotta. Staging and Staging Errors in Bladder Cancer ,2010.Avialable from:www.scincedirect.com.

6. Josephon D, Pasin E, Stein JP. Superficial bladder cancer management .Expert Rev Anticancer Ther 2007;7:567-81.
7. kirstan Bouchelouche ,Baris Turkbey and peter L Choyke . PET/CT and MRI in bladder cancer,2012.Avialable from: http://dx.doi.org/10.4172/1948-5956.s14-001.
8. David M.Albala, Allen F.Morey, Leonard G.Gomella, John P.Stein. oxford American hand book of urology.New York:New York;2011:246-93.
9. Halial ARSLAN,Fatih Mehmet TEZCAN,Oktay ALGIN. urothelial cancers: clinical and imaging evaluation, 2012.Avilable from: http:/doi:10.3906/sag-1111-9.
10. Shaista Hafeez and Robert Huddart, advances in bladder cancer imaging ,2013.Avialable from: http:/www.biomedcentral.com/1741-7015/11/104.
11. National center instituite.comprehensive cancer information. pretreatment staging invasive bladder cancer.,accesed 1 august 2012.Avialable from:http:/www.cancer.gov/cancertopics/types/bladder.
12. Michael P. Federle, R.Brooke Jeffrey, Paula J.Woodward ,Amir A.Borhani.diagnostic imaging of abdomen.2nd ed.Canada;2010:1204-11.
13. Ozgur Kilickesmez, Tan Cimilli, Ercan Inci, Arda Kayhan, Sibel Bayramoglu, Neslihan Tasdelen, Nevzat Gurman.Diffusion weighted MRI of urinary bladder and prostate cancers,2009;15:104-10.
14. Kadir Ceylan, Kerem Taken, IIhan Gecit,Necip Pirincci, Mustafa Gunes,Serhat Tanik, Ihsan Karaman.Comparison of Cystoscopy with Diffusion –Weighted Magnetic Resonance Images Used in the Diagnosis and Follow Up of Patients with Bladder Tumors,2010,Asian pacific J cancer prev,11,1001-4.
15. Yasushi Yamada, Shigeki Kobayashi, Shiho Isoshima,Kiminobu Arima, Hajime Sakuma, Yoshiki Sugimura.The uselfulness of diffusion- weighted magnetic resonance imaging in bladder cancer staging and functional analysis,2014.Avialable from:www.cancerjournal..net,DOI:10.4103/0973-1482.138225.
16. Watanabe H, Masayuki K, Hiroshi K.Preoperative T staging of urinary bladder cancer: does diffusion –weighted MRI have suuplementary value?AJR 2009;192:1361-66.
17. Matsuki M,Inada Y, Tatsugami F.Diffusion-weighted MR imaging for urinary bladder carcinoma: initial result.Eur Radiol 2007;17:201-4.
18. Takeuchi M, Sasaki S,Ito M, Okada S, Takahashi S, Kawai T, et al.Urinary bladder cancer:diffusion –weighted MR imaging-accuracy for diagnosing T stage and estimating histologic grade.Radilogy 2009;251:112-21.
19. Kim B, Semelka RC, Ascher SM,Chalpin DB, Carroll PR, Hricak H.Bladder tumor staging :comparision of contrat –enhanced CT,T1-and T2-weighted MR imaging, dynamic gadolinium-enhanced imaging,and late gadolinium -enhanced imaging. Radiology 1994;193:239-254.Link.
20. Takes A, Kamel I, Imam K. Dynamic MRI of bladder cancer: evaluation of staging accuracy.AJR Am J Roentgenol 2005;184:121-27.
21. El-Assmy A,Abou-El-Ghar ME,Mosbah A,El-Nahas AR,Refaie HE,Hekal IA,et al..Bladder tumor staging :comparision of diffusion_and T2-weighted MR imaging .Eur Radiol 2009;19:1575- 81.