ORIGINAL ARTICLE

DIAGNOSTIC ACCURACY OF MRI IN DETECTION OF INVASIVE BLADDER CARCINOMA

Asma Zafar,[1] Ameet Jesrani,[2] Waseem Mehmood Nizamani,[3] Mustansir Zaidi[4]

[1] Department of Radiology, Sindh Institute of Urology & Transplant (SIUT), Karachi, Pakistan
[2] Department of Radiology, Liaquat National Hospital, Karachi, Pakistan
[3] Department of Radiology, Ziauddin Hospital, Karachi, Pakistan
[4] Statistics Department, Liaquat National Hospital, Karachi, Pakistan

PJR October - December 2015; 25(4): 136-141

ABSTRACT

BACKGROUND: MRI and clinical staging are considered essential for evaluation of urinary bladder carcinoma. Though clinical staging allows for immediate biopsy, but it can't accurately distinguish superficial from invasive tumors and is not capable of detecting extent of extravesical disease. **OBJECTIVE:** To determine diagnostic accuracy of MRI in differentiating non-muscle invasive from muscle invasive bladder carcinoma taking Histopathological staging as a gold standard. **METHODS:** Total 58 patients of either gender having age 25 to 85 years, cystoscopically proven bladder carcinoma were included and underwent MRI. Patient with radiologically negative tumor was assigned stage T0. When multiple tumors are present, highest T Stage was represent tumor stage. Data was regrouped to evaluate accuracy of MRI in distinguishing superficial (≤ T1) from invasive (≥ T2). Histopathological grading served as standard of reference. **RESULTS:** There were 49 males and 9 female with age ranged from 25 to 85 years. Total 52 patients showed presence of bladder tumor. On final histopathological staging 20 patients have Ta-T1, 8 patients have stage T2b, 18 patients have stage T3a-b, 4 patients have stage T4a and 2 patients have stage T4b. Tumor size range was 0.4-7.5 cm. 10 patients had more than one tumor detected by MRI. The sensitivity, specificity, and diagnostic accuracy of MRI for detection of invasive tumors were 88%, 81%, and 77% respectively. **CONCLUSION:** MR imaging has vast advantages and great accuracy is possible in detection of deeply invaded bladder tumor.

Key Words: Diagnostic Accuracy; MRI; Non-muscle invasive bladder carcinoma; Muscle invasive bladder carcinoma

Introduction

Bladder Cancer (BCa) is a heterogeneous disease, with 70% of patient's presenting with superficial tumors and 30% presenting as muscle invasive disease associated with a high risk of death from distant metastases.[1,2] Bladder cancer accounts for 6-8% of overall malignancy in men and 2-3% in women.[3] Most often BCa present with painless haematuria.[4] The principal clinical findings of muscle invasive disease consist of gross or microscopic hematuria and, to a much lesser extent, voiding dysfunction or pelvic pain.[5]

Clinical and imaging assessments are important for bladder cancer staging; however, imaging assessment forms a vital part of the management protocol.[6,7] Cystoscopy with biopsy is still the gold standard tool for bladder cancer staging due to its high sensitivity in detecting lesions and the possibilities of tumor resections,[8] invasiveness, limitation in detection of flat lesions, and lack of the assessment of extravesical tumor invasion represent the main drawbacks.[9] Proper

Correspondence : Dr. Waseem Mehmood Nizamani
Department of Radiology,
Dr. Ziauddun Hospital,
Karachi, Pakistan
Mobile: 0333-2341941
Email: dr_waseemayub@hotmail.com

Submitted 3 June 2015, Accepted 29 June 2015

staging and grading of bladder tumor are crucial for management.[10] Under staging subjects patients to suboptimal treatment while over staging subjects patients to unwarranted treatment related morbidity.[11] Patients with No Muscle Invasion (NMI) have much better prognosis than patients with Muscle Invasion (MI).[12] Radiological evaluation is a significant part of diagnosis and staging of bladder cancer. Grey scale sonography is initial modality to confirm the presence of the lesion, evaluate morphology of tumor, perivesical extension, lateral pelvic wall involvement, lymph node status, to exclude metastasis and to look for back pressure changes in kidneys.[13]

Diffusion weighted MRI has been introduced in clinical MRI protocols because of its higher contrast resolution and ability to detect and reflect molecular diffusion restriction in malignant tissue.[14,15] Microscopic extravesical spread (T3a disease) cannot be reliably identified, but MRI readily shows macroscopic extravesical extension (T3b disease). Magnetic resonance imaging is the modality of choice in imaging bladder tumor and its accuracy ranges from 73% to 96%.[7,16] According to Tekes et al., gadolinium-enhanced MRI has accuracy of 85% in differentiating non invasive versus invasive disease and of 82% in differentiating organ confined from non organ confined disease.[17]

Material & Method

A cross sectional study was conducted to evaluate total 58 patients of both genders with age between 25 to 85 years who had cystoscopically proven bladder carcinoma. Patients who had an initial TURBT (transurethral resection of bladder tumor) after biopsy and had localized disease were also included for staging by MRI at time of imaging. Patients were referred to the Radiology department for MRI of pelvis from Oncology department, Sind Institute of Urology and Transplantation. Informed written consent was taken from all the patients. History was taken in each case regarding the duration of symptoms, presenting complaints, smoking, exposure to chemical carcinogens, and prior medical or surgical treatments. MRI was performed with a 1.5-T MR unit (Signa Horizon, General Electric Medical Systems) with body phased array coil. Each patient underwent imaging with three MR pelvis techniques: (1) T1 weighted SE sequence TR (400-800 ms), TE (15-30 ms), (2) T2 weighted SE sequence TR (1600-2500 ms), TE (80-120 ms), and (3) A short-TI inversion recovery (STIR) sequence TR (2000), TE 60-75, T1 150-275. Unenhanced and enhanced (0.1 mmol/kg) fast spoiled gradient echo images with fat suppression were also obtained. Enhanced images were acquired in arterial phase (20 sec) followed by venous phase. MR images were interpreted independently by senior MR radiologists without prior knowledge of the final staging obtained at transurethral resection, cystectomy, or clinical follow-up. On basis of imaging findings a radiologic stage was assigned.

An intact, hypointense line (muscle layer) at the base of the tumor was classified as stage T1; an irregular inner margin of hypointense line, stage T2a; a disrupted hypo intense line without perivesical fat infiltration, stage T2b; a lesion with an irregular, shaggy outer border and streaky areas of the same signal intensity of the tumor in perivesical fat, stage T3b; and a lesion extending into an adjacent organ or abdominal and pelvic side walls with the same signal intensity of the primary tumor, stage T4a or T4b. Lymph nodes were considered abnormal if the long axis was 10 mm or more.

Data compilation and analysis was done on SPSS version 21. Descriptive statistics were calculated. Quantitative variables were expressed as mean ± SD and qualitative variables were presented in terms of frequency and percentages. Sensitivity, specificity, positive predictive value, and negative predictive values were calculated using 2 by 2 tables. Patient with radiologically negative tumor was assigned stage T0 and when multiple tumor were present, highest T Stage was represented tumor stage. In addition, data were regrouped to evaluate accuracy of MRI in distinguishing superficial ($\leq$ T1) from invasive ($\geq$ T2).

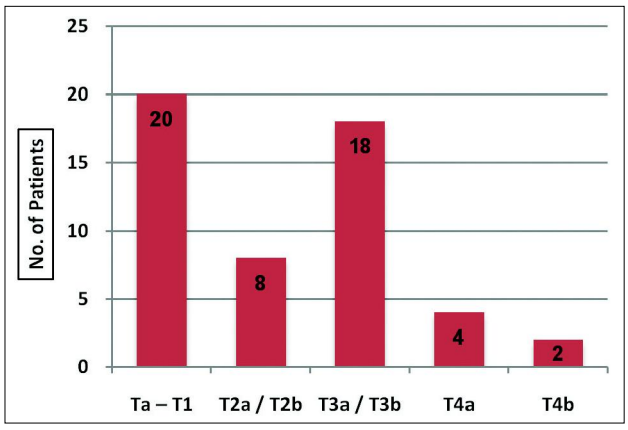
Results

There were 49 (84.5%) males and 9 (15.5%) female with male to female ratio was 5:1. Mean age of the

study subjects was 55 ± 1 year. Hematuria was present in 45 cases. Out of the 58 patients with urinary bladder carcinoma 52 showed presence of bladder tumor at time of staging and 6 were assigned stage T0. These patients have initially received chemotherapy after cystoscopy and transurethral resection and have been referred for MRI for staging of local disease.Tumor was correctly detected in 52 among them 35 were true positive and 17 were true negative (Tab. 1). Out of correctly diagnosed patients, on final histopathological staging 20 patients have Ta-T1 disease (superficial disease), 8 patients have stage T2b, 18 patients have stage T3a-b, 4 patients have stage T4a and 2 patients have stage T4b (Graph 1). When compared with the results submitted from the histopathology unit 49 of these patients had transitional cell carcinoma, one patient had squamous cell carcinoma and adenocarcinoma was detected in one patient. On MRI of correctly detected 52 patients with bladder tumor, 37 had mass lesion and 14 patients had diffuse wall thickening.

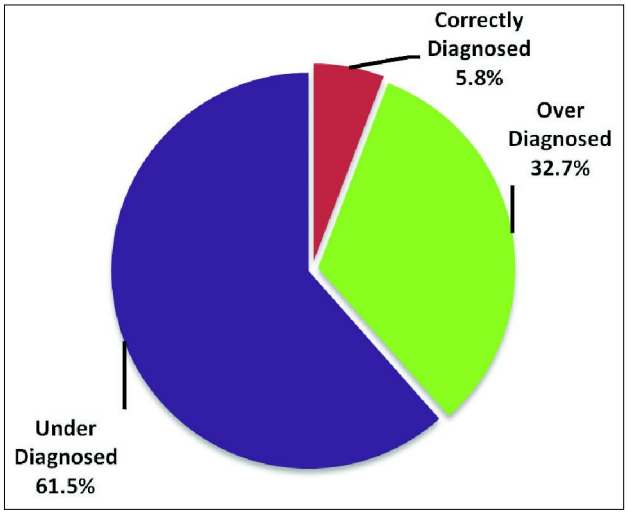
True Positive	True Negative	False Positive	False Negative
35	17	4	3

Table 1: Diagnostic values of MRI for muscle non-invasive v/s muscle invasive bladder carcinoma



Graph 1: Frequency of histopathological findings of stages

Tumor size range detected on MRI was (0.4-7.5 cm mean 2.5 cm). Ten patients had more than one tumor detected by MRI. On reviewing stages obtained by MRI it was found that of 52 patients 32 (62%) were correctly staged by MRI, over staging was done in 17 patients (32%), and under staging was done by MRI in 3 patients (6%) (Graph-2). The stages found in both procedures are presented in (Tab. 2). Using more detailed TNM classification, the sensitivity, specificity, and percent accuracy of MRI for detection of invasive tumors was 88%, 81%, 77% respectively (Tab. 3).



Graph 2: Percentage of MRI findings of stages

MRI STAGES	HISTOPATHOLOGICAL STAGES						
	T0	Ta-T1	T2a / T2b	T3a / T3b	T4a	T4b	Total
T 0	**6**						**6**
Ta – T1		**17**	2	2			**21**
T2a / T2b		2	**5**	1			**8**
T3a / T3b		1		**14**	2		**17**
T4a					**3**	**1**	**4**
T4b						**2**	**2**
TOTAL	**6**	**20**	**7**	**17**	**5**	**3**	**58**

Note: Correctly stage tumors by MRI are mentioned in bold

Table 2: Frequency of staging frequency of 58 patients diagnosed by MRI and Histopathology.

Sensitivity	Specificity	Diagnostic Accuracy	Positive Predictive Value	Negative Predictive Value
89%	81%	79%	86%	85%

Table 3: Sensitivity of MRI formuscle non-invasive v/s muscle invasive bladder carcinoma.

Discussion

MR imaging and clinical staging both are considered essential for the evaluation of urinary bladder carcinoma. The treatment and prognosis of urinary bladder carcinoma is largely established by the depth of the tumor growth and its extent at the time of diagnosis.[18] One of the most important significance for performing preoperative imaging is distinction of superficial tumors from muscle invasive tumors as well as identification of organ confined disease from tumor that has spread outside the bladder. This distinction is impor-tant because patients with non organ confined disease have higher recurrence rates and worse survival rates than patients with organ confined superficial disease.[19] Conventional clinical staging-including bimanual examination under anesthesia, urography, cystoscopy, and transurethral resection are not consi-dered enough for this distinction. Most studies have showed that the error of clinical staging increases as the tumor becomes more invasive.[20]

Limitation of the clinical staging for the diagnosis of bladder tumor is the determination of extent of tumor growth in the muscle layer of the bladder wall (stages T2 and >T2), however the role of MR in bladder tumor is continue to evolve.[21] MRI has its own limitations. There are number of factors which can be patient related or MRI related. The most important are motion artifacts and the degree of bladder distension. Voluntary motion artifacts can be reduced by making the patient feel ease in case of claustrophobic patients, sedatives may be effective. Involuntary motion artifacts are caused by respiration, intestinal peristalsis and bladder motion.

Another limitation of clinical staging is the inadequate staging resulting from the superficial resection of the tumor during the biopsy which limits the diagnostic criteria and differentiation remains impossible. Clinical staging which includes deep fractionated resection appeared to have a low accuracy in infiltrating tumors (stages T2 and higher) especially when using clinical staging as a gold standard.

The accuracy of the clinical staging which includes deep fractionated transurethral resection is sufficient for superficial tumors. However, the accuracy of clinical staging for stage T2-T4b tumors is poor. For staging deeply infiltrating tumors (stages > T3a), MRI is superior. For differentiation between muscular invasion (stage T3a) and invasion into the perivesical fat (stage T3b), MR imaging is better. In deeply infiltrative tumors (stages 3b, T4a, and T4b), MR imaging is generally agreed to be the most accurate staging technique. In lower stage tumors stages Ta, T1, and T2, MR imaging has limitations. Common error that was established in our study was over staging of tumors by MRI. Our staging accuracy for detection of invasive bladder carcinoma was 79% that was found to be slightly lower than previous studies, Tekes reported accuracy of 82%.[21] This could be attributed to fact that almost all of our patients have undergone superficial biopsy before MRI.

The possibility of using MR imaging to differentiate between superficial (stage T2) and deep invasion of the muscle layer of the bladder wall (stage T3a) has received a lot of attention. This distinction cannot be made with clinical staging. In our study group only 2 patients had non transitional cell carcinoma including 1 squamous cell carcinoma and 1 adenocarcinoma. Though these tumors are less common and generally more aggressive and extending beyond bladder wall at time of diagnosis but no significant difference was determined in accuracy of staging these tumors by MRI.

Conclusion

MR imaging is the most accurate technique for differentiating the various stages or deeply invasive tumors (stages T2 and higher) whereas, clinical staging is the best technique for various stages of superficial tumors (stages T2 and lower), the accuracy of clinical staging for stage T2-T4b is poor. MR has vast advantages and great accuracy is possible in detection of deeply invaded tumor.

MR imaging and clinical evaluation both are complementary for staging the urinary bladder carcinoma. The early detection of invasive bladder carcinoma by MRI can improve overall prognosis, diagnosis and treatment of patients. Thus due to increased diagnostic accuracy, staging should be started with non-invasive MR imaging and followed by the resection and clinical staging.

References

1. Bouchelouche K, Turkbey B, Choyke PL. PET/CT and MRI in Bladder Cancer. J Cancer SciTher S. 2012; **14:** 1-8.

2. Kaufman DS, Shipley WU, Feldman AS. Bladder cancer. Lancet. 2009; **374:** 239-49.

3. Gupta N, Sureka B, Kumar MM, Malik A, Bhushan TB, Mohanty NK. Comparison of dynamic contrast enhanced and diffusion weighted magnetic resonance image in staging and grading of carcinoma bladder with histopathological correlation. Urol Ann. Apr-Jun 2015; **7(2):** 199-204.

4. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010 CA. Cancer J Clin. 2010; **60:** 277-300.

5. Malkowiczsb, van Poppel H, Mickisch G, Pansadoro V, Thüroff J, Soloway MS. Muscle Invasive Urothelial Carcinoma of the Bladder. Urol. 2007; **69(1):** 3-16.

6. Abdel-Rahman HM, El Fiki IM, Desoky EAE, Elsayed ER,Samad KMA. The role of diffusion-weighted magnetic resonance imaging in T staging and grading of urinary bladder cancer, Egypt J RadiolNucl Med (2015).

7. Bostrom PJ, Rhijn BWG, Fleshner N. Staging and staging errors in bladder cancer. Eur Urol Suppl. 2010; **9:** 2-9.

8. Teama AH, El-monem DAN, Hasan AAE, Rasha AT. Role of multidetector computed tomography virtual cystoscopy in evaluation of urinary bladder carcinoma. Eur J Rdiol Necu Med. 2014; **45:** 543-54.

9. Amin MF, Abd El Hamid AM. The diagnostic accuracy of multidetector computed tomography with multiplanar reformatted imaging and virtual cystoscopy in the early detection and evaluation of bladder carcinoma: comparison with conventional cystoscopy. Abdom Imaging. 2013; **38(1):** 184-92.

10. Sylvester R, van der Meijden APM, Oosterlinck W. Predicting recurrence and progression in individual patients with stage Ta T1 bladder cancer using EORTC risk tables: a combined analysis of 2596 patients from seven EORTC trials. Eur Urol. 2006; **49:** 466-77.

11. Omar MA, El-Mallah AS. The role of transabdominal, transrectal and transurethral ultrasonography in staging of carcinoma of the urinary bladder. Egypt J Radiol Nucl Med. 2003; **34(2):** 997-1004.

12. Stenzl A, Cowan NC, De Santis M, Kuczyk MA, Merseburger AS. Treatment of muscle-invasive and metastatic bladder cancer: update of the EAU guidelines. Eur Urol. 2011; **59:** 1009-18.

13. Bachor R, Kotzerke J, Reske SN, Hautmann R. Lymph node staging of bladder neck carcinoma with positron emission tomography. Urologe A. 1999; **38:** 46-50.

14. Kibel AS, Dehdashti F, Katz MD, Klim AP, Grubb RL. Prospective study of [18F]fluorodeoxyglucose positron emission tomography/computed tomography for staging of muscle-invasive bladder carcinoma. J Clin Oncol. 2009; **27:** 4314-20.

15. Apolo AB, Riches J, Schöder H, Akin O, Trout A. Clinical value of fluorine-18 2-fluoro-2-deoxy-D-glucose positron emission tomography/ computed tomography in bladder cancer. J ClinOncol. 2010; **28:** 3973-78.

16. El-Assmy A, Abou-El-Ghar ME, Refaie HF. Diffusion weighted MR imaging in diagnosis of superficial and invasive urinary bladder carcinoma: a preliminary prospective study. Sci World J. 2008; **8:** 364-70.

17. Jadvar H, Quan V, Henderson RW, Conti PS. Fluorodeoxyglucose PET and PET-CT in diagnostic imaging evaluation of locally recurrent and metastatic bladder transitional cell carcinoma. Int J ClinOncol. 2008; **13:** 42-7.

18. Sherif A, Jonsson MN,Wiklund NP. Treatment of muscle invasive bladder cancer. Expert Rev Anti-cancer Ther. 2007; **7:** 1279-83.

19. Mussurakis S, Buckley DL, Horsman A. Dynamic MR imaging of invasive bladder cancer: correlation with tumor grade and other histological factors. Br J Radiol. 1997; **70:** 446-51.

20. Dinney CP, Babkowski RC, Antelo M. Relationship among cystectomy,microvessel density and prognosis in stage T1 transitional cell carcinoma of the bladder. J Urol. 1998; **160:** 1285-90.

21. Tekes A, Kamel IR, Chan TY, Schoenberg MP, Bluemke DA. MR imaging feature of Transitional cell carcinoma of urinary bladder. Am J Radiol. 2003; **180:** 771-77.