ORIGINAL ARTICLE

Diagnostic Accuracy of High Resolution MR Imaging in Local Staging of Bladder Tumors

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ABSTRACT

Objective: To determine the diagnostic accuracy of high-resolution MR imaging done at 1.5T in distinguishing bladder-restricted tumor from non-bladder-restricted tumor and compare the mean short axis dimension of metastatic pelvic lymph nodes with benign pelvic lymph nodes.

Study Design: Analytical study.

Place and Duration of Study: Shaukat Khanum Memorial Cancer Hospital, Lahore, Pakistan, from March 2008 to July 2011.

Methodology: Patients with bladder cancer were enrolled. Based on pathologic T-staging following radical cystectomy, patients were assigned to one of two groups. Patients with stage T1 and T2 disease were assigned to the bladder-restricted tumor (BRT) group and those with stage T3 and T4 disease to the non-bladder-restricted tumor (NBRT). High-resolution unenhanced MR imaging done prior to cystectomy was reviewed retrospectively (1.5 T MRI unit; GE Healthcare). Results from MR imaging-based categorization were compared with pathology reports to fulfill the objective. Mean short-axis diameter of largest visible lymph nodes in patients with nodal metastasis was compared with mean short-axis diameter of largest visible lymph nodes in patients with benign lymph nodes.

Results: The accuracy of MRI in differentiating distinguishing bladder-restricted tumor from non-bladder-restricted tumor was 67.72%. The mean short axis diameter of metastatic lymph nodes was greater than that of non-metastatic lymph nodes, i.e., 7.4 mm and 5.4 mm respectively.

Conclusion: Conventional high resolution 1.5T MRI does not appear to offer advantage over imaging done at low field strength scanners.

Key Words: *Staging. Magnetic resonance imaging (MRI). Urinary bladder neoplasms. Sensitivity. Specificity.*

INTRODUCTION

Bladder cancer accounts for 6% of all male and 2% of all female malignant urothelial tumors, being the most common urological malignancy in Pakistan and the fourth most common malignancy overall.[1-3] Treatment depends on accurate local staging; the depth of tumor invasion has a more significant bearing on overall survival than histologic tumor grade.[4] Whilst early stage (T1) disease can be treated with endoscopic ablation, evidence of detrusor muscle involvement (T2 and above) necessitates cystectomy, usually in combination with chemotherapy and radiotherapy.[5] As a result, making the distinction between bladder restricted and non-bladder-restricted disease is the main objective of initial staging in bladder cancer patients.[6] Out of clinical examination, CT and MRI, MRI has been shown to be the most superior staging modality.[4,6,7]

Until recently, majority of the studies reporting accuracy of MRI in local staging of bladder cancer were performed on low field strength scanners and employed thick slices.[8-11]

The purpose of this study was to evaluate the diagnostic accuracy of short FOV, thin slice imaging done at 1.5 T in distinguishing bladder restricted tumor from non-bladder-restricted tumor and to find a difference between benign and pathologic lymph nodes in terms of short axis diameter to aid accurate classification.

METHODOLOGY

The institutional review board waived the requirement for informed written consent. All patients who had urinary bladder cancer underwent pre-operative staging MRI followed by radical cystectomy between March 2008 and July 2011 were included. Patients with T1 disease did not undergo cystectomy and were thus excluded. Patients who had received neo-adjuvant radiotherapy were also excluded as this could mislead MR interpretation due to treatment-related changes.

MRI was done on a 1.5T GE Sigma Unit (GE Medical Systems, Milwaukee, USA), using a torso coil. The high-resolution sequences included axial T1-weighted and

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Received: September 17, 2012; Accepted: December 10, 2013.

T2-weighted spin-echo sequences (TR/TE/NEX of 450 ms/13 ms/1 and 5000 ms/130 ms/1 respectively) obtained using acquisition matrix of 512 x 512, slice thickness of 3 mm, and short field of view (FOV) of 18 cm centered over the urinary bladder. Standard (non-high resolution) coronal (T1-weighted) and sagittal images (T2-weighted) were additionally obtained using slice thickness of 4 mm, acquisition matrix of 256 x 256, and FOV of 22 cm (coronal images) and 32 cm (sagittal images). The purpose of acquiring coronal and sagittal slices at larger FOV was to allow detection of lymph nodes in the common iliac territory not covered on the short FOV axial slices.

All patients underwent total cystectomy involving removal of the bladder and the prostate and seminal vesicles in men, and the uterus in women. Twenty three patients also underwent bilateral pelvic lymph node dissection. The specimens were routinely stained with hematoxylin-eosin stain and reported by the staff histopathologists in accordance with the American Joint Committee on Cancer (AJCC) TNM staging system.[12] Online histopathology reports were accessed retrospectively to determine the tumor and nodal stage. The histologic outcome was recorded for each patient and patients were assigned to one of the two categories, i.e., those with local stage T1 or T2 tumor were categorized as bladder-restricted tumor (BRT) and those with stage T3 or T4 tumor were categorized as non-bladder-restricted tumor (NBRT). Pathologic nodal stage was recorded and patients were grouped as either 'metastatic' or 'benign' in terms of nodal status.

Interpretation of MRI studies was done by radiologist having more than 10 years' experience in oncology imaging (ND) who was blinded to pathologic stage. Well established MRI imaging criteria were used for tumor evaluation.[9,13] When the tumor was not visible, it was assigned T0 category. Tumor appearing as a focal elevation visible separately from the intact low-T2 signal bladder wall was categorized as T1. Any focal or diffuse replacement of the low-T2 signal bladder wall in the region of the tumor was deemed necessary to make a diagnosis of stage T2. Spread of tumor into the peri-vesical fat only (T3) was considered in two situation; either when there was gross spread of tumor signal outside the bladder wall, or when the peri-vesical fat appeared indistinct adjacent to tumor as compared with disease-free bladder wall regions (referred to commonly as 'peri-vesical fat stranding' in radiology literature). Gross invasion of adjacent viscera or encroachment of tumor to within 3 mm of pelvic sidewall muscles was denoted as T4 disease. Based on these parameters, a comprehensive T-stage was assigned to each tumor and later tumors were sub-grouped into BRT and NBRT categories in a manner similar to that adopted for histopathologic categorization. In cases of T3 tumors, further information was recorded as to whether the assignment was based on peri-vesical fat stranding alone or on gross extension into peri-vesical fat. Both T1- and T2-weighted images were reviewed together to assign a stage.

Nodal evaluation was performed by recording the maximum short-axis diameter (MSAD) of the largest visible pelvic lymph node for each patient who had undergone lymph node dissection. Results from lymph node dissection were reviewed to determine pathology nodal staging.

Data were analyzed using statistical software (SPSS 17 for Windows; SPSS Japan). Diagnostic accuracy of MRI interpretation was compared with histopathology for the two categories, i.e., BRT and NBRT by creating a 2 x 2 contingency table. Two-tailed Fisher's exact test was used to determine statistical significance. P-value of < 0.05 was taken as standard. Comparison of MSAD of visible pelvic lymph nodes was done between 'metastatic' and 'benign' nodal groups by comparing the mean values. For statistical significance, independent samples t-test was utilized.

RESULTS

A total of 31 patients fulfilled the inclusion criteria. Twenty seven out of 31 patients (87.1%) were male with an age range from 3 years to 79 years (median age: 57 years). Histopathologic breakdown was such that one patient each had sarcomatoid cancer and adeno-

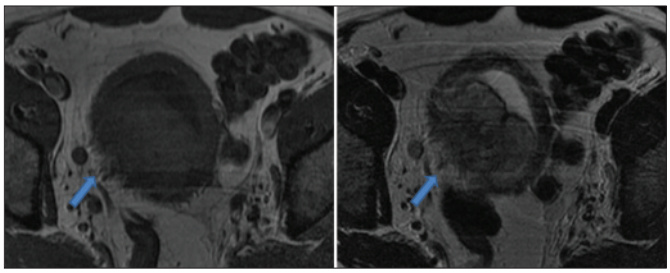

Figure 1: False positive NBRT: High-resolution T1-weighted imaging (left) and T2-weighted imaging (right) shows peri-tumoral fat stranding (arrows) on the basis of which the patient was classified as having NBRT (stage T3 on MRI). However, on radical cystectomy, the tumor was BRT. The peri-vesical changes were retrospectively believed to be inflammatory in nature.

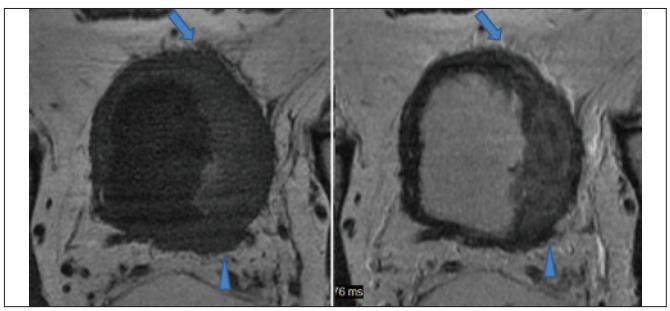

Figure 2: True positive NBRT: High-resolution T1-weighted imaging (left) and T2-weighted imaging (right) shows a semi-annular tumor involving the left wall of the bladder. There is peri-tumoral fat stranding anteriorly (arrows) and bulge of the bladder contour posteriorly (arrowheads) - both features indicative of NBRT (stage T3) on MRI. Histopathologic analysis following radical cystectomy confirmed the MRI staging.

carcinoma, 2 patients had rhabdomyosarcoma, and the rest (n=28) had transitional cell carcinoma (TCCA) of the bladder.

In summary, tumors were correctly staged in 21 cases, overstaged in 7 cases and understaged in 3 cases. In distinguishing non bladder-restricted tumors from bladder-restricted tumors, MRI had a sensitivity of 80%, specificity 56.3%, positive predictive value (PPV) of 63.2%, negative predictive value (NPV) of 75% and accuracy 67.72% (Figure 1 and 2).

MRI analysis of pelvic lymph nodes showed that lymph nodes were visible in all patients except one, ranging in short axis diameter from 3 to 13 mm. The mean MSAD for metastatic lymph nodes was larger, i.e., 7.4 ± 3.65 mm as opposed to mean MSAD for benign lymph nodes which was 5.4 ± 2.23 mm; the difference was not statistically significant (p:0.3).

DISCUSSION

In this study, the overall accuracy of un-enhanced high-resolution MRI in discriminating bladder restricted tumor from non-bladder-restricted tumor is modest at 67.7%. This is most likely due to inflammatory and desmoplastic peri-vesicle changes in T2 cancers mimicking early T3 disease on MRI - a well-described phenomenon which limits the accuracy of MRI in local bladder cancer staging.[6,14] A significant majority of stage T2 tumors (7 out of 11) were thus overstaged in this study. These results reflect this over-staging of T2 tumors to be the main limitation of conventional MRI of bladder cancer.

Previous authors have reported a wide range of accuracy for MRI in local bladder cancer staging (50-96%). These findings support the conclusions drawn from previous studies on un-enhanced conventional MRI in terms of limited accuracy of MRI in accurate staging of T2 disease. Furthermore, as shown by present and previous authors' results, it appears that adding high-resolution short FOV sequences does not confer any advantage to the staging protocol. For example, Barentsz *et al*. directly compared bladder tumor staging performed at 0.5T and 1.5T magnets.[15] The authors concluded that 1.5T imaging does not add advantage to local staging of bladder cancer over imaging done at 0.5T. Similarly, Buy *et al*. staged bladder tumors on 0.5T using 8 mm thick slices reported an overall staging accuracy of 60% for MRI which is also close to these results.[9] A more recent study by Leidberg *et al*. utilizing 3T MRI on a cohort of 53 patients showed that MRI overestimated tumor stage in almost half of the patients.[16] A likely explanation of similar results between high-resolution high field strength imaging protocol such as ours and that used by Liedberg *et al*. and imaging done on low field strength (< 1.5T) scanners with thick slices is that there is increased detection of peri-tumoral fat stranding on thinner slices and thus more frequent over-staging of T2 disease, which outweighs any advantage over low-field strength scanning at increased slice thickness.

More recent studies report the use of dynamic sequences with contrast enhanced MRI, 3D MRI, and diffusion weighted imaging (DWI), which have gained popularity in recent years.[6,17-22] Compared with the presently employed protocol which employed conventional un-enhanced T2-weighted imaging as the primary staging sequence, these newer techniques have inherent advantages in tumor staging. Tanimoto *et al*. compared dynamic MRI with conventional unenhanced MRI and CT;[10] they found a significantly higher staging accuracy for dynamic MRI as compared to the latter two techniques. Moreover, the authors reported that the addition of DWI did not contribute significantly toward accurate distinction between bladder restricted and non-bladder restricted tumors. Similarly, Takeuchi *et al*. reported a combined accuracy of 92% when all three sequences were used together, i.e., dynamic contrast-enhanced, T2-weighted, and DW images, compared with 67% accuracy for T2-weighted imaging alone.[5]

The secondary goal of this study was to compare nodal size in pathologic vs. benign lymph nodes on MRI. It was found that small lymph nodes were visible in all patients save one. While mean short axis diameter was slightly greater for individuals with metastatic lymph nodes, results were not conclusive. Hence, the authors were unable to define a morphologic cut-off to allow reliable detection of nodal metastasis. Results from several meta-analyses put the sensitivity and specificity of MRI at 72% and 87% respectively.

To-date, although 8 mm is a generally accepted cut-off to determine nodal involvement in pelvic malignancy, size criteria to determine nodal involvement remain unreliable.[23]

This study has several limitations. The sample size was small, especially with regards to our secondary objective of comparison of MSAD for which our results remain inconclusive. Secondly, there was a selection bias with a relatively high number of bladders with T2-stage disease in this study, since patients with T1 stage do not undergo radical cystectomy hence were not incorporated into the study. As mentioned earlier, this would affect the reported staging accuracy of MRI, which suffers limitations in distinguishing stage T2 tumor from early stage T3 disease. A further shortcoming was that unenhanced MRI was used for staging. Due to the reported superiority of newer MRI techniques such as DWI, 3D imaging, and dynamic contrast-enhanced MRI, these additional sequences are part of the routine staging protocol in many regions of the world. However, while these techniques may allow earlier detection of bladder cancer and improved differentiation between stage T2 and T3 tumors, both stages are treated with

radical cystectomy and the advantage is mainly of prognostic value.[4,24] To justify the use of additional expensive imaging protocols, further studies from the region would be needed to determine their economic feasibility and additional survival benefit conferred to patients.

CONCLUSION

Unenhanced high-resolution MRI is a good triage tool to identify patients who are likely to benefit from radical cystectomy and rule out patients with advanced disease who are then referred for palliation. However, its tendency to overstage tumors limits its value in bladder-restricted cancer. Use of high-resolution imaging does not appear to confer significant advantage over imaging done on low field-strength scanners in improving staging accuracy of MRI.

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