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Vigor of bi-parametric MRI with MR segmentation unity in valuation of UB neoplasm mural invasion

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Abstract

Background The urinary bladder neoplasm is considered the second most frequent kind of neoplasm globally, after prostate cancer. Bladder neoplasm clinical management strategies and prognosis depend on the extent of loco-regional disease. MRI is increasingly being employed for preoperative, local staging of BC. The aim of this study was to expose the mastery of bi-parametric MRI (MRDWI and T2WI conjunction) with signal intensity-based MR segmentation in evaluation of UB neoplasm mural invasion if unaccompanied by contrast-enhanced MRI with special concern to Vesical Imaging Reporting and Data System (VIRADS) score taking the histopathological diagnosis as a reference.

Results This prospective study was conducted on 99 patients (with 100 UB lesions), who were referred from the urology department with bladder neoplasm suspicion. The mean age of the patients was 64.8 years. About 66.6% of the cases were smokers. The most common pathology of the UB neoplastic lesions was urothelial carcinoma. ADC in muscle-invasive bladder cancer (MIBC) was significantly lower than in non-invasive bladder cancer (NMIBC), with the minimum to maximum value of the ADC in all cases about 0.01–2.0. Also, we have done DWI at different b values, where b 1000 turned out to be the most accurate in detection of muscle invasion. Sensitivity, specificity, PPV, NPV and accuracy were calculated for T2WI only VIRADS, DWI only VIRADS, bi-parametric MR (T2WI and DWI)-based VIRADS, signal intensity-based MR segmentation VIRADS and for bi-parametric and MR segmentation conjunction-based VIRADS. The diagnostic performance for the combination of the bi-parametric MRI and signal intensity-based MR segmentations attained the highest values in sensitivity, specificity, PPV and NPV as well as accuracy.

Conclusions Bi-parametric MRI (MRDWI with T2WI) and signal intensity MR segmentation conjunction have proven to be efficacious in accurately determining the UB neoplasm mural invasion allowing for the dispensability of CE-MRI in the event of contrast contraindications, unavailability or even its high cost.

Keywords Bladder cancer/neoplasm (BCa), Diffusion-weighted images (DWI), Apparent diffusion coefficient (ADC), Vesical imaging reporting and data system (VIRADS)

A prospective study to expose the mastery of bi-parametric MRI (MRDWI and T2WI conjunction) with MR segmentation in evaluation of UB neoplasm mural invasion if unaccompanied by contrast-enhanced MRI with special concern to Vesical Imaging Reporting and Data System (VIRADS) score taking the histopathological diagnosis as a reference.

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Introduction

Background

The urinary bladder neoplasm is considered the second most frequent kind of neoplasm globally, after prostate cancer. In 2018, there were more than 550,00 bladder neoplasm cases reported globally [1]. Bladder neoplasm clinical management strategies and prognosis depend on the extent of loco-regional disease and on the discrimination between superficial (\leq T1 stage) and muscle-invasive disease (\geq T2 stage). Depending on the stage of the lesions, urinary bladder neoplasm must be treated appropriately [2, 3]. Because of its high soft tissue contrast resolution and ability to measure the depth of bladder wall invasion, MRI is increasingly being employed for preoperative, local staging of BC [4].

Objectives

The aim of this study was to expose the mastery of bi-parametric MRI (MRDWI and T2WI conjunction) with signal intensity-based MR segmentation in evaluation of extent of UB neoplasm mural invasion if unaccompanied by contrast-enhanced MRI with special concern to Vesical Imaging Reporting and Data System (VIRADS) score taking the histopathological diagnosis as a reference.

Methods

This study was a prospective, observational study, conducted on 99 patients (with 100 UB lesions). The study conducted between January 2022 and February 2024. The 99 patients were referred from the urology department with bladder neoplasm suspicion. The study was approved by the ethical committee (Approval No. 701:7/2022).

Inclusion criteria

1. All patients with UB mass.

Exclusion criteria

1. Persons who have MRI contraindications, such as claustrophobia, implants that cannot be read by MRIs, or persons who often utilize artificial devices.
2. If MRI revealed no evidence of malignancy

Patients and methods

- Full history taking with an emphasis on: age, smoking and previous bladder operations for previous masses.

Patient preparation

Patients were required to fast for 4–6 h before undergoing the MRI examination (for the prevention of motion and susceptibility artifacts from bowel peristalsis), with appropriate bladder distension, by drinking a large amount of water and avoiding urination for at least 1 h before the procedure.

MRI scan protocol: performed prior to transurethral resection.

MRI examinations were carried on 1.5 T MRI scanner (Ingenia, Philips Healthcare, Netherlands) at the MRI unit at Minia radiology department using multichannel phased-array external surface coil. The coil was placed with the arms sideways above the coils' level with the patient in the supine position with head pointing toward the magnet. The center of the coil was placed about 10 cm below the iliac crest level. Scanning of the whole pelvis was performed from the bifurcation of the aorta to the inferior margin of the symphysis pubis. A 3D fast spin echo with variable flip angle (CUBE) will be used for high-resolution T2WI, and an arbitrary plane perpendicular to tumor base was modified. The suggested parameters for 2D-FSE are slice thickness of 3–4 mm, field of view of 160–180 and matrix of 285; 3D spin-echo collection may also be used; in axial 2D, TSE or FSE.

The protocol included T2-weighted high-resolution (T2WI) imaging in axial, coronal and sagittal planes; diffusion-weighted imaging (DWI) in axial planes was also done for all patients. The b values applied to DWI were as follows: b=0, 500, 1000 and 1500 s/mm², and the ADC values were calculated (ADC). Free breathing was used to perform DWI using an axial and sagittal water-excited single-shot spin-echo echo-planar sequence. Contrast was not given to any patients.

Image analysis and interpretation

Qualitative analysis: Examining the location, size, heterogeneity, tumor margins and SI of lymph nodes (LNs) was done using T2WI, DWI, T2WI plus DWI and the

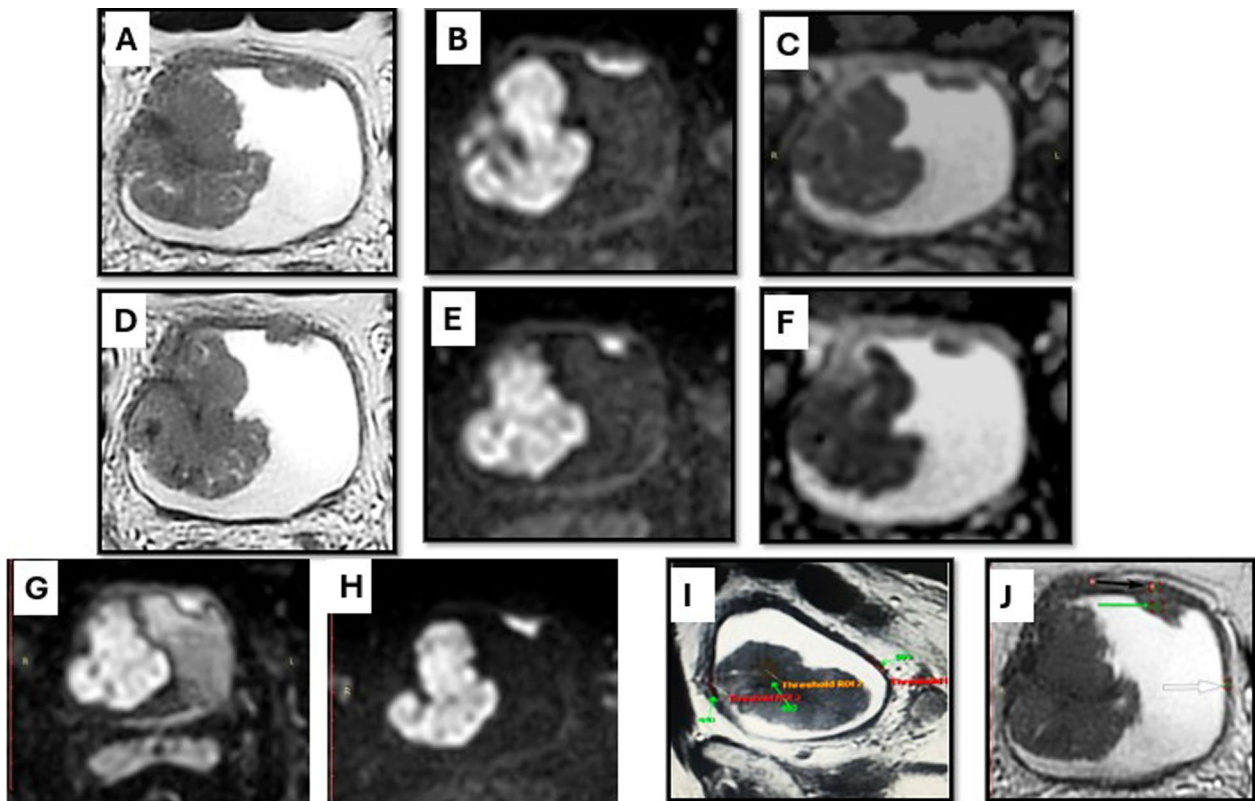


Fig. 1 Case number 1: Clinically, a 72-year-old man, smoker, complaining of gross hematuria (A) and (D) T2WI axial images showing two UB mass lesions, the larger one is related to the right anterolateral wall of the urinary bladder, measuring $4.6 \times 3.9 \times 5$ cm, with interruption of the low SI (signal intensity) of the underlying UB wall, while the smaller one is noted at the anterior wall, more inclined to the left side, measuring $1.8 \times 0.5 \times 2$ cm, with suspicious interruption of the underlying low signal UB wall, more notably at (D). Based on T2WI alone; the larger lesion was given VIRADS IV, while the smaller one was given VIRADS III. (B), (C) and (E), (F) DWI at b value 1000 with their corresponding ADC values. The larger UB lesion shows restricted diffusion where interruption of the underlying UB muscle wall is noted, with corresponding ADC values about 0.6×10^{-3} mm^2/s , while the smaller lesion shows restricted diffusion with corresponding ADC values about 0.9×10^{-3} mm^2/s , with clear underlying UB wall and no definite interruption. Based on DWI alone; the larger lesion was given VIRADS IV, while the smaller one was given VIRADS II. (G) and (H) DWI at b values 500 and 1500, respectively, the former one shows no clear discrimination of the lesion from the underlying UB layer, while the latter one shows no conspicuousness of the UB walls underlying the lesion. (I) and (J) MR segmentation of both UB lesions: The large one shows that: the signal of the tumor = 480, the signal of the wall adjacent to tumor = 440, while the signal of the normal UB wall away from the lesion site = 593. The smaller lesion shows that: the signal of the tumor = 480 (green arrow), the signal of the wall adjacent to the tumor = 580 (black arrow), while the signal of the normal UB wall away from the lesion site = 593 (white arrow). Based on MR segmentation alone, the larger lesion was given VIRADS IV, while the smaller one was given VIRADS II. After combination of bi-parametric MRI (T2WI and DWI) with MR segmentation in VIRADS Assessment: VIRADS IV was given for the larger lesion while VIRADS II was given for the smaller lesion. The pathology of the larger lesion was invasive papillary transitional cancer (T2b stage), and for the smaller lesion was non-invasive papillary transitional cancer (Ta stage)

ADC map. On T2WI, the muscle layer of the bladder wall appeared as a low SI layer. While on DWI, it is visualized as intermediate SI. In bladder cancer, the SI is higher than the SI of the muscle layer in T2WI and DWI. Therefore, T2WI and DWI data were used together to identify the locations of the tumor and detect its extent.

Quantitative analysis

ADC maps: measured to estimate the degree of diffusion. It was measured by drawing a region of interest (ROI)—with an area of 2 cm^2 —at the visually determined prominently restricted areas (the area with the most

hypointensity in ADC map). Malignancy is suggested at ADC value of 1×10^{-3} mm^2/s at b value between 1000 s/ mm^2 .

Muscle invasion was evaluated according to VIRADS [5] as follows

The VIRADS classifies the probability of bladder cancer invasion to muscle by using a 5-point scoring system:

VIRADS 1; muscle invasion is highly unlikely, tumors with a diameter of < 10.0 mm and flat lesions were reported to be almost all non-muscle invasive.

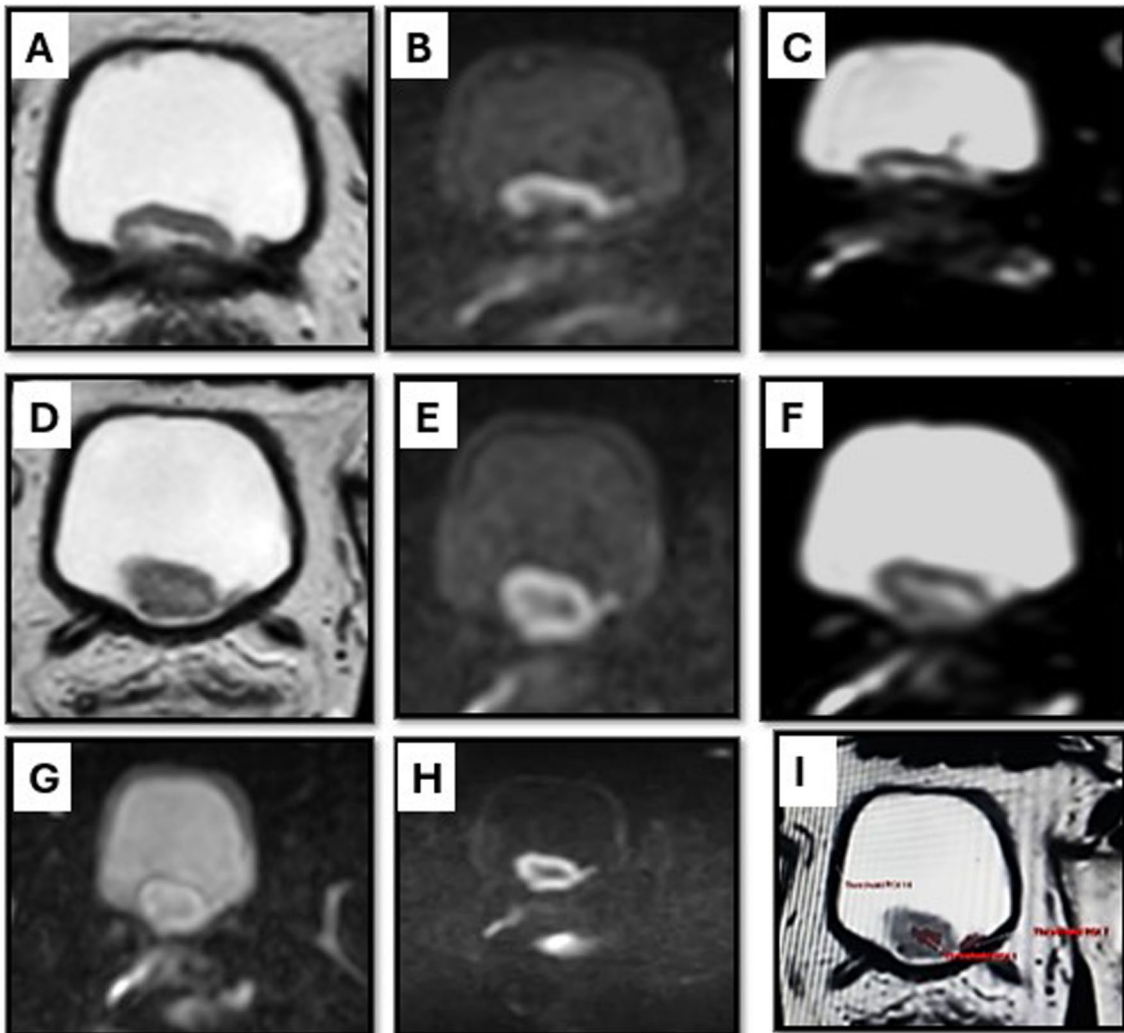


Fig. 2 Case number 2: Clinically, a 65-year-old man, smoker, complaining of gross hematuria and discomfort (A) and (D) T2WI axial images showing UB mass in the posterior wall of the UB with no interruption of the low SI (signal intensity) of the underlying UB muscle wall or encroachment upon the ureteric orifices. ...Based on T2WI only, the lesion was given VIRADS II. (B), (C) and (E), (F) DWI at b value 1000 with its corresponding ADC values, showing restricted diffusion with ADC value about $0.8 \times 10^{-3} \text{ mm}^2/\text{s}$, where no evidence of interruption or invasion of the underlying UB muscle walls. Based on DWI only, the lesion was given VIRADS II. (G) and (H) DWI at b values 500 and 1500, respectively, the former one shows no clear discrimination of the lesion from the underlying UB layer, while the latter one shows no conspicuousness of the UB walls underlying the lesion. (I) MR segmentation of the lesion shows that: the signal of the lesion = 237, the signal of the adjacent UB wall to the lesion = 350, while the signal of the normal UB wall away from the lesion = 420.... Based on MR segmentation only, the lesion was given VIRADS II. -After combination of bi-parametric MRI (T2WI and DWI) with MR segmentation in VIRADS Assessment: VIRADS II was given for the UB lesion. -Pathology of the lesion was urothelial carcinoma just infiltrating the lamina propria (stage T1)

VIRADS 2; muscle invasion is unlikely, tumors with a diameter ≥ 1 cm and a thickened inner layer.

VIRADS 3; muscle invasion is equivocal, disappearance of Category 2 findings, but no clear disruption of a low SI muscle layer.

VIRADS 4; muscle invasion is likely, interruption of a low SI line suggesting a muscle layer.

VIRADS 5; muscle invasion is very likely, an extension of an intermediate SI tumor to extra vesical fat.

Signal intensity-based MR segmentation: additional to using high-resolution T2 and diffusion, we tried out using the signal intensity-based MRI segmentation as an additive tool to determine muscle wall invasion. We measured the signal of the tumor, the signal of the wall adjacent to the tumor and compared it with the signal of normal bladder wall, we took the mean value of the signal intensity of the tumor and the normal bladder wall as a cutoff value to determine invasiveness for each case.

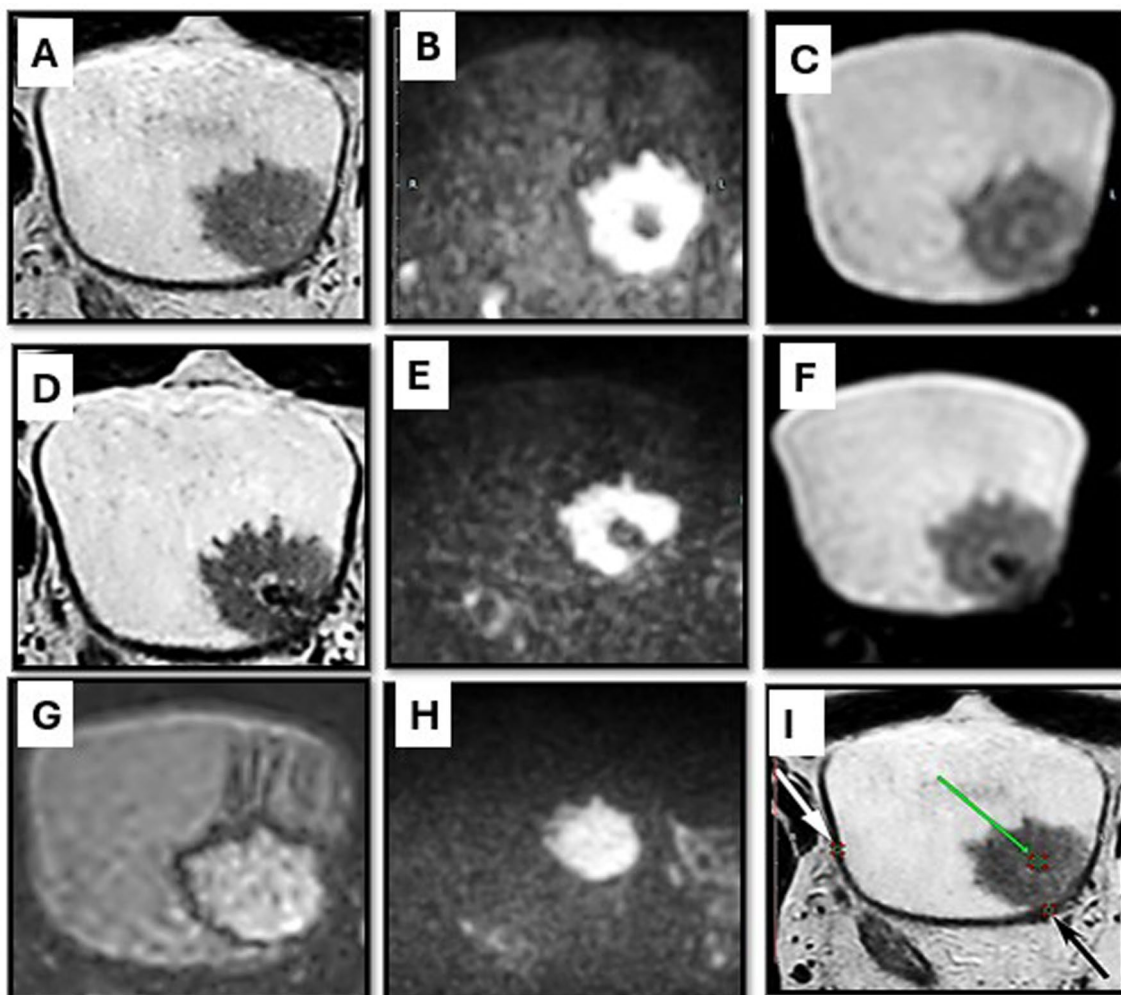


Fig. 3 Case number 3: Clinically, a 65-year-old man, non-smoker, complaining of gross hematuria and discomfort. **(A), (D)** T2WI axial images showing UB mass in the left posterolateral wall of the urinary bladder, measuring 3.4×3.8×4 cm in its largest dimensions. It has a hypointense stalk and irregular outlines, suspicious minimal interruption of the underlying low SI of the UB muscle wall is noted.Based on T2WI alone, the lesion was given VIRADS III. **(B) (C), (E), (F)** DWI at b value 1000 and corresponding ADC values, showing restricted diffusion of the UB lesion with hypointense stalk and ADC value of $1.1 \times 10^{-3} \text{ mm}^2/\text{s}$. No definite interruption of the underlying UB wall noted. Based on DWI alone, VIRADS II is proposed. **(G)** and **(H)** DWI at b values 500 and 1500, respectively, the former one shows no clear discrimination of the lesion from the underlying UB layer, while the latter one shows no conspicuousness of the UB walls underlying the lesion. **(I)** MR segmentation of the lesion showing that the signal of the lesion = 303 (green arrow), the signal of the adjacent UB wall to the lesion = 430 (black arrow), while the signal of the normal UB wall away from the lesion = 521 (white arrow)....Based on MR segmentation, the lesion attains VIRADS II. –After combination of bi-parametric MRI (T2WI and DWI) with MR segmentation in VIRADS Assessment: VIRADS II was given for the UB lesion. –Pathology revealed: non-invasive urothelial carcinoma (stage Ta)

Muscle invasion was considered to be likely if the measured signal intensity of the wall adjacent to the tumor was less than the mean value—near that of the tumor and far away from the number of the normal bladder wall-.

Urological & histopathological assessment: After doing bi-parametric MRI, all patients underwent conventional cystoscopy and transurethral resection of the bladder tumor in the same institution within a week of the MR examination, including the description of the lesion, number, size, morphology, location and local staging of

the tumor. Histopathology data were correlated to the preoperative VIRADS score in order to evaluate the diagnostic efficacy of bp-MRI with histological reports.

Statistical analysis

For statistical analysis, the SPSS application for Windows v. 20 (SPSS Inc., Chicago, IL) was utilized. The data have been statistically represented using the required frequencies (number of occurrences), means, standard deviations (SD) and percentages. The researched diagnostic test's

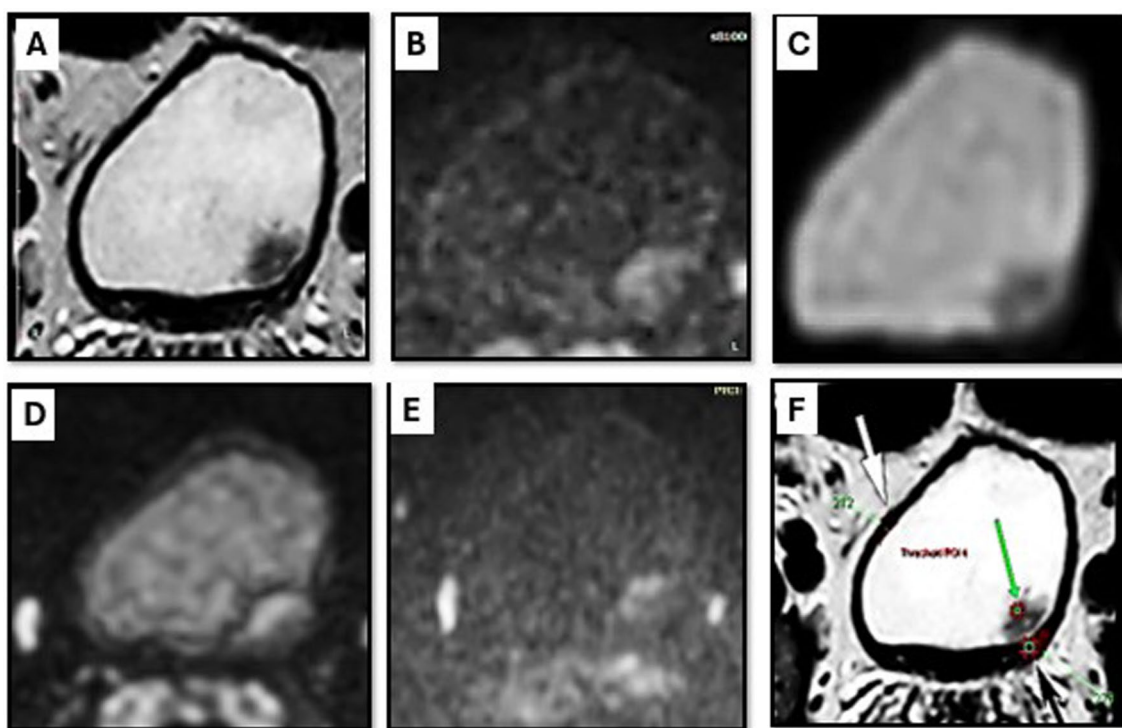


Fig. 4 Case number 4: Clinically, a 68-year-old man, smoker, complaining of gross hematuria and discomfort (A) T2WI axial image showing UB mass in the left posterolateral wall of the UB with no interruption of the low SI (signal intensity) of the underlying UB muscle wall or encroachment upon the ureteric orifices. ...Based on T2WI only, the lesion was given VIRADS II. (B) and (C) DWI at b value 1000 with its corresponding ADC values, showing restricted diffusion with corresponding low ADC values about $1 \times 10^{-3} \text{ mm}^2/\text{s}$ and no evidence of interruption or invasion of the underlying UB muscle walls.Based on DWI only, the lesion was given VIRADS II. (D) and (E) DWI at b values 500 and 1500, respectively, the former one shows no clear discrimination of the lesion from the underlying UB layer, while the latter one shows no clear conspicuousness of the lesion or the UB walls underlying the lesion. (F) MR segmentation of the lesion shows that: the signal of the lesion = 392 (green arrow), the signal of the adjacent UB wall to the lesion = 520 (black arrow), while the signal of the normal UB wall away from the lesion = 610 (white arrow).... Based on MR segmentation only, the lesion was given VIRADS II. -After combination of bi-parametric MRI (T2WI and DWI) with MR segmentation in VIRADS Assessment: VIRADS II was given for the UB lesion. -The pathology of the lesion was non-invasive urothelial carcinoma (stage Ta)

overall accuracy in predicting malignancy was evaluated using its sensitivity, specificity and reliability. With the use of a probability value, the statistical significance was assessed ($p=0.05$). The receiver operating characteristic (ROC) curve was accustomed to calculate the cutoff values for the semi-quantitative features.

Results

This prospective study included 99 patients (with 100 UB lesions). The patients were complaining of gross hematuria (Figs. 1, 2, 3, 4, 5, 6, 7 and 8).

Table 1 shows distribution of the studied cases according to demographic data. Their age ranged from 47 to 74 years with mean (64.8) years \pm standard deviation (7.49) years. The study included 82 males (82.8%) and 17 females (17%).

Table 2 shows classification of the studied cases according to smoking, where 66.6% of the cases were smokers.

The different pathology types included in the study are summarized in Table 3, where the most common pathology of the UB neoplastic lesions was urothelial carcinoma (transitional cell carcinoma) accounting for 75% of the included cases.

Table 4 summarizes the descriptive analysis of the studied cases according to signal-based MRI segmentation variable values of the included lesions.

Descriptive analysis of the studied cases in relation to ADC tumor is shown in Table 5 where ADC in muscle-invasive bladder cancer (MIBC) is significantly lower than in non-invasive bladder cancer (NMIBC), with the minimum to maximum value of the ADC in all cases about 0.01–2.0.

Table 6 discloses different b values of the studied cases utilized in VIRADS. The most accurate one in detection of muscle invasion was b 1000 (48 cases were truly invasive while 20 cases were equivocal). However, b values

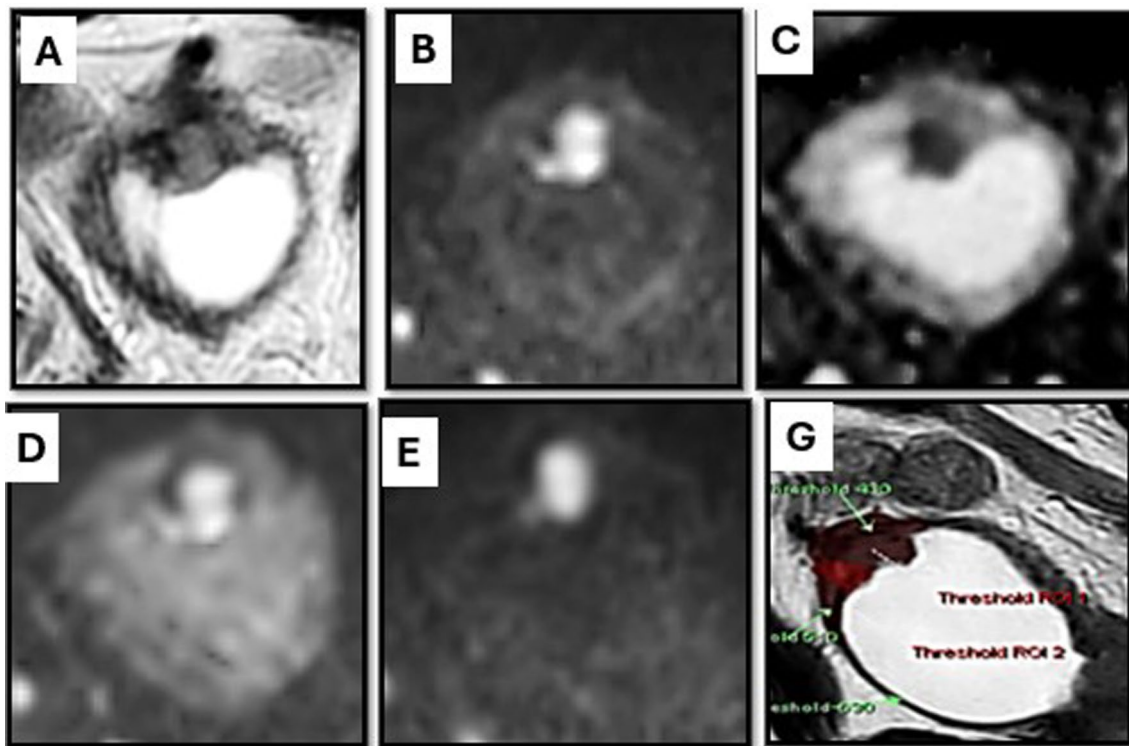


Fig. 5 Case number 5: Clinically, a 74-year-old man, smoker, complaining of gross hematuria (A) T2WI axial image showing a UB mass lesion, measuring about $1.5 \times 2.3 \times 2$ cm, related to the anterosuperior wall of the urinary bladder, with high probability of interruption of the low SI (signal intensity) of the underlying UB wall. Based on T2WI alone; the lesion was given VIRADS IV. (B), (C) the DWI at b value 1000 with their corresponding ADC values, the UB lesion shows restricted diffusion with corresponding ADC values about $0.7 \times 10^{-3} \text{ mm}^2/\text{s}$ where interruption of the underlying UB muscle wall is noted, in the DWI and corresponding ADC values. Based on DWI alone; the lesion was given VIRADS IV. (D) and (E) DWI at b values 500 and 1500, respectively, the former one shows no clear discrimination of the lesion from the underlying UB layer, while the latter one shows no conspicuousness of the UB walls underlying the lesion. (G) MR segmentation of the UB lesion shows that: the signal of the tumor = 410, the signal of the wall adjacent to tumor = 510, while the signal of the normal UB wall away from the lesion site = 630. Based on MR segmentation alone, the larger lesion was given VIRADS IV. –After combination of bi-parametric MRI (T2WI and DWI) with MR segmentation in VIRADS Assessment: VIRADS IV was given for the UB lesion. –The pathology of the lesion was invasive urothelial carcinoma with squamous differentiation (stage T2a)

500 and 1500 showed equivocal values about 64 and 36 cases, respectively.

Table 7 elaborates the sensitivity, specificity, PPV, NPV and accuracy of T2WI only VIRADS, DWI only VIRADS, combined T2WI and DWI VIRADS (bi-parametric MRI), signal-based MR segmentation VIRADS and of combination of T2WI, DWI, MR segmentation VIRADS, the diagnostic performance for the combination of the bp-MRI and MR segmentations attain the highest values in sensitivity, specificity, PPV and NPV as well as accuracy.

Two radiologists, who have 10- and 20-year experience in urogenital MRI, independently interpreted all images, they were blinded to the pathological results of the biopsy specimens. The cases of disagreement and discrepancies were resolved by consensus. The percent agreement was excellent between interpreters of bi-parametric MRI (T2WI and DWI) as well as MR segmentation; the inter-reader reliability was calculated at 96% and 95%, respectively (Table 8).

Discussion

Urinary bladder cancer is the ninth most common malignant disease and the thirteenth most common cause of cancer death worldwide [6].

The aim of this study was to expose the mastery of bi-parametric MRI (MRDWI and T2WI conjunction) with MR segmentation in evaluation of extent of UB neoplasm mural invasion if unaccompanied by contrast-enhanced MRI with special concern to Vesical Imaging Reporting and Data System (VIRADS) score taking the histopathological diagnosis as a reference.

The mean age of patients affected by urinary bladder neoplasm in our study was 64.08 ± 7.49 SD, 66.6% of them were smokers, that was in concordance with the study conducted by Ahmed et al. [7] who evaluated the influence of DCE MRI and DWI in assessment of pathologic complete response following neoadjuvant chemotherapy (NAC) in patients with muscle-invasive bladder cancer (MIBC); in their study, the mean age of affected

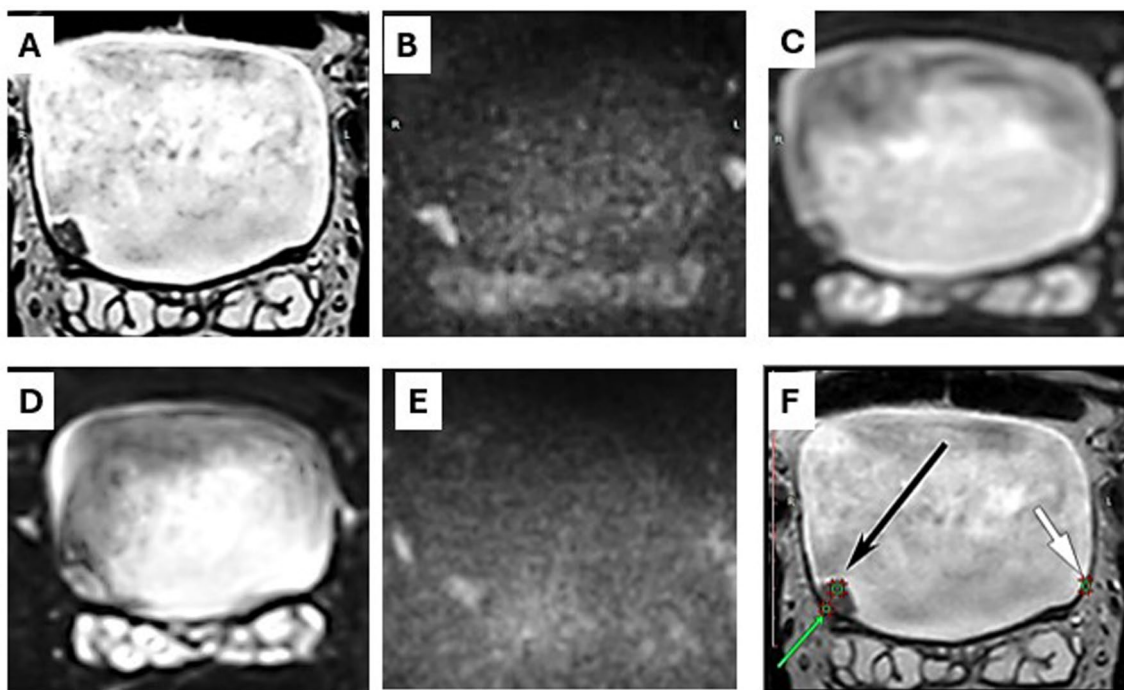


Fig. 6 Case number 6: Clinically, a 59-year-old man, smoker, complaining of hematuria (A) T2WI axial image showing UB mass in the right posterolateral wall of the UB with no interruption of the low SI (signal intensity) of the underlying UB muscle wall or encroachment upon the ureteric orifices. ...Based on T2WI only, the lesion was given VIRADS II. (B) and (C) DWI at b value 1000 with its corresponding ADC values, showing restricted diffusion with corresponding low ADC values about $1.1 \times 10^{-3} \text{ mm}^2/\text{s}$ and no evidence of interruption or invasion of the underlying UB muscle walls. Based on DWI only, the lesion was given VIRADS II. (D) and (E) DWI at b values 500 and 1500, respectively, the former one shows no clear discrimination of the lesion from the underlying UB layer, while the latter one shows no conspicuousness of the UB walls underlying the lesion. (F) MR segmentation of the lesion shows that: the signal of the lesion = 443 (green arrow), the signal of the adjacent UB wall to the lesion = 630 (black arrow), while the signal of the normal UB wall away from the lesion = 670 (white arrow).... Based on MR segmentation only, the lesion was given VIRADS II. –After combination of bi-parametric MRI (T2WI and DWI) with MR segmentation in VIRADS Assessment: VIRADS II was given for the UB lesion. –The pathology of the lesion was non-invasive urothelial carcinoma (stage Ta)

patients was 52.4 ± 6.3 years, 71% of the studied patients were smokers. Likewise, the study conducted by Delli Pizzi et al. [8], where patients with bladder neoplasm, mean age was 72.5 years, 36.8% of the them had smoking history.

The most common pathology of the UB neoplasm encountered in the current study was the urothelial cell carcinomas which accounted for 75% of the included cases. About 60% of the included cases were invasive while 40% were non-invasive according to the pathology. This was in agreement with Gmeiner et al. [9] study, where the majority of their patients (89.5%) were urothelial carcinomas, 51% were classified as high grade while 27.5% as muscle-invasive urothelial carcinomas.

Based on the fact that the management is modified according to the invasiveness of the UB neoplasm — whether muscle-invasive bladder cancer (MIBC) or non-muscle-invasive bladder cancer (NMIBC)—, where it is proved that the first line of treatment for NMIBC has included cystectomy or systemic chemotherapy, while those for MIBC have included intravesical chemotherapy,

immunotherapy or transurethral excision of the bladder tumor [5]. We distinguished between NMIBC and MIBC using the Vesical Imaging Reporting and Data System (VIRADS) by means of the bp-MRI (bi-parametric MRI) and the MR segmentation. This was in rapprochement to the study of Barchetti et al. [10] and Ghanshyam et al. [11] who reported that VIRADS score is a good and effective preoperative radiological technique for the forecast of muscle invasion in bladder neoplasm. Likewise, the study of Gomez-Gonzalez et al. [12], who claimed that the VIRADS is important for early staging to avoid the need for follow-up biopsies and for monitoring the efficacy of therapy to avoid needless complete cystectomy. Also it could lower the total lifetime medical costs related to bladder cancer.

When descriptive analysis of the studied cases in relation to ADC values of the included lesions was done, ADC values in muscle-invasive bladder cancer (MIBC) were significantly less than in non-invasive bladder cancer (NMIBC) with a mean ADC value about $0.6 + _{0.37}\text{SD}$ in MIBC and $1.31 + _{0.43}\text{SD}$ in NMIBC

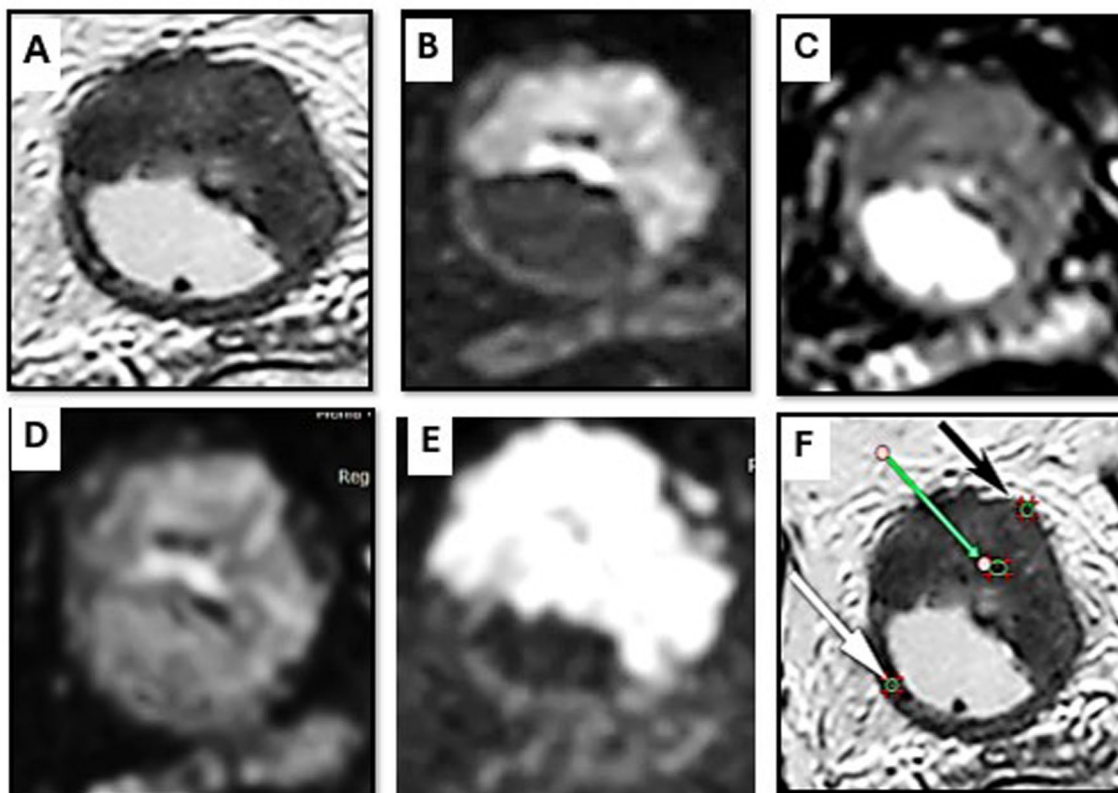


Fig. 7 Case number 7: Clinically, a 61-year-old man, smoker, complaining of gross hematuria (A) T2WI axial images showing a large UB mass lesion, seen occupying the left anterolateral aspect of the UB, measuring $5.7 \times 2.9 \times 5.9$ cm in its largest dimensions. It is seen interrupting the low SI (signal intensity) of the underlying UB wall. Based on T2WI alone; the lesion was given VIRADS IV. (B) and (C) DWI at b value 1000 with their corresponding ADC values, the UB lesion shows restricted diffusion where interruption of the underlying UB muscle wall is noted, in the DWI with the corresponding ADC values about 0.8×10^{-3} mm²/s. Based on DWI alone; the lesion was given VIRADS IV. (D) and (E) DWI at b values 500 and 1500, respectively, the former one shows no clear discrimination of the lesion from the underlying UB layer, while the latter one shows no conspicuousness of the UB walls underlying the lesion. (F) MR segmentation of the UB lesion shows that: the signal of the tumor = 510 (green arrow), the signal of the wall adjacent to tumor = 540 (black arrow), while the signal of the normal UB wall away from the lesion site = 643 (white arrow). Based on MR segmentation alone, the larger lesion was given VIRADS IV, while the smaller one was given VIRADS IV. –After combination of bi-parametric MRI (T2WI and DWI) with MR segmentation in VIRADS Assessment: VIRADS IV was given for the UB lesion. –The pathology of the lesion was invasive urothelial cancer (stage T3a)

with sensitivity of 93% and specificity of 85%. That tailed the study of Ahn et al. [13] who stated that quantitative assessment of the ADC values aided in determination of the extent of muscle invasion. In like manner is the study that was done by Wei Zhang et al. [14] where they found out that ADC values reflect the muscular invasion of bladder neoplasm. It is especially suitable for bladder neoplasm patients with renal insufficiency or tumor recurrence.

Indubitably, selection of appropriate b values is crucial for accurate evaluation of diffusion environment in bladder neoplasm tissues surrounded by urine.

Despite we utilized three b values for the DWI, yet we came to a conclusion that the b value 1000 was the most accurate one for the detection of muscle invasion and determining the ADC value meticulously. The b value 500 s/mm² produced T2 shine-through effect while

generating the DW-MRI signal of bladder neoplasm with lack of perfect discrimination of the lesion from the UB wall. On the other hand; the ultra-high b value 1500 performed poorer signal-to-noise ratios, so was inappropriate for accurate measurement of the ADC values and the UB wall was inconspicuous. That considerably matched the study conducted by Yoshida et al. [15], where their results stated that the optimum b value to be used for bladder neoplasm was b value 1000, for it actually mitigates the DW-MRI signal of urine and strengthens that of bladder neoplasm, for measuring ADC values.

These results were yielded upon our calculations of the sensitivity and specificity of using the b value 1000 compared to b values 500 and 1500, where those of b value 1000 were 80% and 65%, respectively, which were much higher than those of the other ones. These findings were in agreement with the results in a study done by Delli

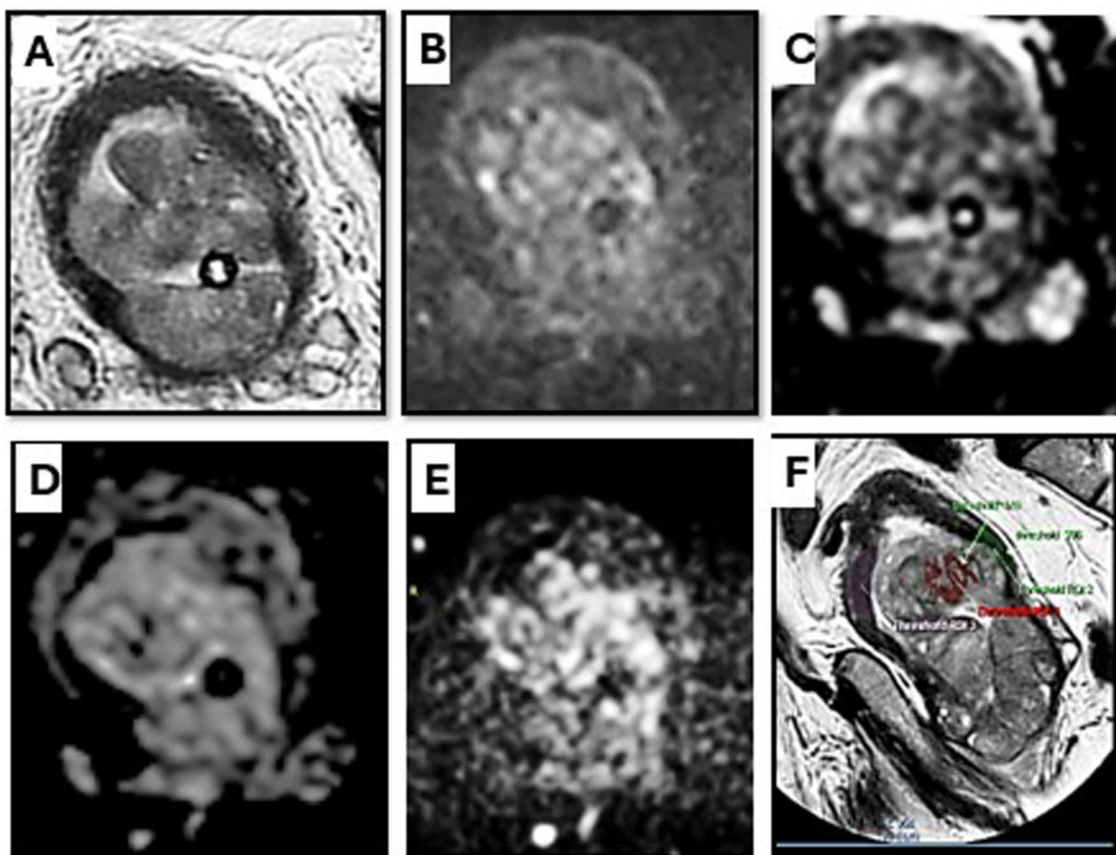


Fig. 8 Case number 8: Clinically, a 72-year-old man, smoker, complaining of gross hematuria and obstructive uropathy (A) T2WI axial images showing a large UB mass lesion, seen occupying the whole UB cavity, measuring 6.1 × 8 × 6 cm in its largest dimensions. Interruption of the low SI (signal intensity) of the posterior UB wall is suspected as it is seen thinned out and partially decreased signal than the remaining UB walls. Based on T2WI alone; the lesion was given VIRADS III. (B) and (C) the DWI at b value 1000 with the corresponding ADC values, the UB lesion shows T2 blackout effect with no definite discernment of the lesion in the DWI; hence, this hinders proper evaluation of the lesion infiltration of the underlying UB wall. The lesion attains patchy low ADC values, maximal about $0.9 \times 10^{-3} \text{ mm}^2/\text{s}$. Based on DWI alone; the lesion was given VIRADS III. (D) and (E) DWI at b values 500 and 1500, respectively, the former one shows no clear discrimination of the lesion from the underlying UB layer, while the latter one shows no conspicuousness of the UB walls from underlying the lesion. (F) MR segmentation of the UB lesion shows that: the signal of the tumor = 376, the signal of the wall adjacent to tumor = 396, while the signal of the normal UB wall away from the lesion site = 530. Based on MR segmentation alone, the lesion was given VIRADS IV. –After combination of bi-parametric MRI (T2WI and DWI) with MR segmentation in VIRADS Assessment: VIRADS IV was given for the UB lesion. –The pathology of the lesion was invasive urothelial cancer (stage T2b)

Table 1 Demographic data of the included studied cases

	No	%
<i>Gender</i>		
Male	82	82.8
Female	17	17.0
<i>Age (years)</i>		
Min.–Max	47.0 – 74.0	
Mean ± SD	64.08 ± 7.49	
Median (IQR)	65.0 (59.0–70.0)	

IQR: Interquartile range and SD: Standard deviation

Table 2 Classification of the studied cases according to smoking

	No	%
<i>Smoking</i>		
Non-smoker	33	33.3
Smoker	66	66.6

Pizzi, Andrea, et al. [16], where they revealed that b value 1000 s/mm² allowed for more accurate tumor–wall interface measurement with increased sensitivity and specificity. A very high b value (b = 2000s/mm²) was related with decreased conspicuity and an increase in false-negative

Table 3 Distribution of the studied cases according to pathology type

Pathology	No	%
<i>Pathology type</i>		
Transitional (urothelial)	75	75.0
Papillary urothelial carcinoma with bilharziasis	4	4.0
Papillary urothelial with squamous differentiation	11	11.0
Hyperplastic transitional	4	4.0
Squamous	6	6.0
MIBC	60	60.0
NMIBC	40	40.0

Table 4 Descriptive analysis of the studied cases according to signal-based MRI segmentation

	Min.–Max.	Mean ± SD.	Median (IQR)
<i>Signal-based MRI segmentation</i>			
Signal of tumor	207.0–560.0	394.9 ± 102.5	450.0 (370.0–463.0)
Signal of the wall adjacent	211.0–520.0	361.9 ± 94.68	395.0 (290.0–420.0)
Signal of the normal wall	262.0–692.0	435.8 ± 135.2	410.0 (321.0–511.0)

IQR: Interquartile range and SD: Standard deviation

Table 5 Descriptive analysis of the studied cases in relation to ADC tumor

	ADC values			
	Mean values	Min–Max	Sensitivity	Specificity
MIBC	0.6 + _{0.37} SD	0.01–2.0	93%	85%
NMIBC	1.31 + _{0.43} SD			

SD: Standard deviation

Table 6 Distribution of the studied cases in relation to different b values of DWI

	No	Pathology	Sensitivity (%)	Specificity (%)
<i>DWI b 500</i>				
Truly no invasive	12	40	33.3	30
Equivocal	64			
Truly invasive	20	60		
<i>DWI b 1000</i>				
Truly no invasive	26	40	80	65
Equivocal	26			
Truly invasive	48	60		
<i>DWI b 1500</i>				
Truly non-invasive	22	40	66.7	55
Equivocal	36			
Truly invasive	40	60		

cases, particularly in small (5 mm) lesions, subsequently decreased sensitivity.

Something to be considered, that this is the first study to examine the efficacy of measuring the signal intensity in MR segmentation of the urinary bladder neoplasm. We measured the signal intensity of the neoplasm, the UB wall underneath and the normal UB wall away from the tumor. We have determined the mean value between the signal intensity of the neoplasm and that of the normal UB wall as a cutoff value to detect UB neoplasm invasiveness according to each case. The results in the study proved that the signal intensity-based MR segmentation is of noteworthy significance for the diagnosis and detection of invasiveness of bladder tumors when compared to the pathological results. Regarding its sensitivity, specificity, PPV, NPV and accuracy of the signal intensity-based MR segmentation, they were reported as 86.7%, 75% and 83.8%, 75% and 82%, respectively. Yet, MR segmentation based on the tumor interface was used in many studies before, like the study conducted by Ahn et al. [13], who reported that dependence on the MRI sequence and tumor–wall interface showed AUROCs of 0.90–0.92 and accuracy of 0.84–0.90 at suggested thresholds (3 ± 0.3 cm).

Besides, we paralleled the sensitivity, specificity, PPV, NPV and accuracy of each parameter alone and in combination with each other in VIRADS classification of the included cases. We yielded that the highest sensitivity, specificity, PPV, NPV and accuracy were accomplished by combination of bi-parametric MRI—T2WI and DWI—, with the signal-based MR segmentation-based VIRADS, as they were 93.3, 95, 96, 95 and 94, respectively. That was much higher than those of T2WI-based VIRADS alone, or DWI-based VIRADS alone or signal-based MR segmentation-based VIRADS alone, and also higher than combination of T2WI and DWI VIRADS only. In case of unavailability of MR segmentation, then combination of T2WI and DWI for VIRADS classification would be preferred than leaning on T2WI only or DWI only. These results were in line with those of the study conducted by Settein et al. [17], who reported that the sensitivity, specificity and accuracy of utilizing T2WI and DWI together were higher (95%, 100% and 98%, respectively) than using T2WI alone to distinguish the T1 stage from later stages. Furthermore, that also tailed the study done by Lian Ming Wu et al. [18] who reported that for differentiating Tis to T1 tumors from T2 to T4 tumors, the AUCs for T2WI and DWI (0.97 for observer 1 and 0.96 for observer 2) were greater than those for the DWI alone (0.92 for observer 1 and 0.90 for observer 2) ($P < 0.05$). So, T2WI combined with DWI can be a reliable sequence for preoperative

Table 7 Diagnostic performance for each parameter alone and in combinations in detecting invasive tumors

	Non-invasive	Invasive	Sensitivity	Specificity	PPV	NPV	Accuracy
VIRADS T2WI alone	20/40	44/60	73.3	50.0	68.8	55.5	64.0
VIRADS DWI alone	26/40	48/60	80	65.0	77.4	68.4	74.0
VIRADS T2 &DWI (> 3)	32/40	56/60	93.33	80.0	87.5	80.0	88.0
Signal-based MRI segmentation	30/40	52/60	86.67	75.0	83.8	75.0	82.0
Combined VIRADS T2/DWI and MRI segmentation	38/40	56/60	93.33	95.0	96.5	95.0	94.0

evaluation of T stage urinary bladder cancer, and it is particularly more useful in differentiating T1 or lower tumors from T2 or higher tumors compared to DWI alone. Likewise, the study of Delli Pizzi et al. [8], where they showed that for the detection of MIBC, a contrast-free MR imaging technique comprising T2W and DWI provides equivalent diagnostic accuracy to a normal mp-MR imaging technique. This is in addition to the study conducted by Abd El Salam et al. [19], who stated that the use of DW-MRI is a safe and non-invasive method in early detection and T staging of urinary bladder carcinoma, and it showed higher accuracy than T2WI in detection of the degree of muscle invasion so it can be added to the routine protocol of MRI examination especially in patients with renal impairment. Over and above that was the study carried out by Aslan et al. [20], where they reported that a bi-parametric MRI protocol has a diagnostic accuracy comparable to a multi-parametric MRI protocol for the detection of muscle-invasive BC using the VIRADS criteria.

Limitations of our study were the high cost of the MRI with the recommendations in the future is to include more cases with usage of combination of bi-parametric MRI with MR segmentations for evaluation of the local spread of the UB cancer beyond the UB wall confines (infiltration of surrounding organs and local LNs).

Conclusion

Bi-parametric MRI (MRDWI with T2WI) and signal intensity-based MR segmentation conjunction have proven to be efficacious in accurately determining the UB

neoplasm mural invasion allowing for the dispensability of CE-MRI in the event of contrast contraindications, unavailability or even its high cost.

Abbreviations

ADC	Apparent diffusion coefficient
AUC	Area under curve
BCa	Bladder cancer
Bp-MRI	Bi-parametric MRI
DWI	Diffusion-weighted imaging
MIBC	Muscle-invasive bladder cancer
NAC	Neoadjuvant chemotherapy
NMIBC	Non-muscle-invasive bladder cancer
NPV	Negative predictive value
PPV	Positive predictive value
UCC	Urothelial carcinoma
T2WI	T2-weighted imaging
Tis	Tumor in situ
VIRADS	Vesical Imaging Reporting and Data System

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Author contributions

SMR and FRT carried out the manuscript preparation and editing, study concepts as well as the experimental studies and data analysis, design and literature research, EAA and MMA were responsible for the clinical studies and also shared in the statistical analysis. While SSS and GMB are the guarantor of integrity of the entire study and carried out the statistical analysis. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and analyzed during the study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Research Ethics Committee (REC), approval number (701:7/2022), Faculty of Medicine, Minia University. Written and informed consent was obtained for all participants.

Consent for publication

All patients included in this research gave written informed consent to publish the data contained within this study according to our institution rules for ethics committee.

Table 8 Inter-rater reliability

	Agreement (%)	Kappa (95% CI)	P value
Bi-parametric MRI (T2WI and DWI)	96	0.12–0.97	0.0001
Signal-based MR segmentation	95	0.89–0.97	0.0001

Competing interests

The authors declare that there is no conflict of interest.

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