Role of 3-dimensional ultrasonography and virtual cystoscopy in detection of bladder lesions in patients with hematuria

Naglaa H. Shebrya a,*, Hazem F. Abu El Hamayeda, Samer M. Botros a, Mohamed S. Shoebb

a Radiology Department, Faculty of Medicine, Ain Shams University, Egypt
b Urology Department, Faculty of Medicine, Ain Shams University, Egypt

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Abstract
Objective: To study the accuracy of three-dimensional (3D) sonography and sonographic cystoscopy in diagnosing bladder tumors in patients with hematuria in comparison with two-dimensional (2D) sonography.

Patients and methods: Twenty-seven patients with hematuria underwent a trans-abdominal US for kidney and bladder. Patients with hematuria and free upper urinary tract at ultrasound underwent a 3D US and conventional cystoscopy (CS). The results of 3D US were compared with those of conventional cystoscopy.

Results: Conventional cystoscopy revealed 22 tumors in 15 patients, while 12 patients showed no bladder tumors. Overall, 3D US gave a correct diagnosis in 21 of 22 lesions (95.5%) in the 15 patients and effectively diagnosed all the 12 negative cases as being negative. Three dimensional sonography had a sensitivity of 95.5%, specificity of 100%, positive predictive value of 100% and negative predictive value of 92.3% in comparison to 81.8%, 66.7%, 81.8% and 66.7% respectively by 2D US.

Conclusion: 3D US was more sensitive than 2D US in diagnosing bladder tumors in patients with hematuria.

1. Introduction

Bladder tumors are among the most common neoplasms of the urinary tract, accounting for 6% of all malignancies in men and 2% of those in women (1). Almost all patients with bladder cancer present with painless hematuria with or without irritative voiding symptoms (2). The role of cross-sectional imaging in the initial evaluation of bladder cancer is limited, and computed tomography (CT) and magnetic resonance imaging are used to stage the disease.
(MR) imaging are usually performed to evaluate extravesical extension or to stage the tumor (2,3). Although conventional cystoscopy is considered the gold standard for urinary bladder evaluation providing diagnostic and therapeutic advantages of biopsy and transurethral resection, it is invasive, time consuming with limitation of bladder neck evaluation. Moreover it is of high cost with risks of urinary sepsis and iatrogenic bladder injury (4).

Trans-abdominal two-dimensional ultrasonography (2D-US) is a good screening modality for bladder tumors, being non-invasive, easy to perform and safe (5). It is often used when a bladder tumor is suspected. Most exophytic tumors can be detected, but especially small papillary tumors, flat tumors and those at the bladder dome are hardly detectable and difficult to differentiate from benign lesions (6).

Three-dimension US imaging has recently become a widely available feature in most ultrasound machines. This technology permits the acquisition and storage of a data set collected from a specific region of interest. This data set is further analyzed by multiplanar display, surface rendering or volume calculation. As there is considerable contrast gradient between the bladder wall and its lumen, the surface rendering algorithm can allow displaying sufficient detail for the surface of the bladder, giving a cystoscopic-like image, enhancing the characterization of the bladder wall abnormalities (7).

The purpose of this study is to evaluate the potential value of 3D sonography and virtual sonographic cystoscopy in detection of bladder tumors, in patients with hematuria in comparison with 2D sonography.

2. Patients and methods

Patients admitted to the urology clinic at the Ain Shams University Hospital with painless hematuria and without history of trauma or evidence of urinary tract infection were prospectively enrolled in our study in the period from October 2012 to November 2013. All patients underwent conventional trans-abdominal 2D US for bladder and kidney in the emergency department by a radiologist. Patients diagnosed with kidney disease, or calculi causing the hematuria were excluded. Patients with hematuria and free upper urinary tract at ultrasound were scheduled for a 3D US examination, usually the next day, followed by flexible or rigid cystoscopy. Written informed consent was obtained from each patient, and the study was approved by our local Ethics Committee.

Sonographic examinations were performed in a private clinic with Voluson E8 GE USA, and a 2–5 MHz multifrequency broadband convex probe. For optimizing scanning, the bladder must be filled to the maximum capacity that could be tolerated by the patient (>200 mL).

Initially routine gray-scale sonography of the pelvis was performed. The device parameter settings were optimized to ensure high-quality 2D images. 2D US was done in the transverse and sagittal plane, and the bladder was carefully evaluated for the presence of abnormalities. 2D US was used to assess the inner surface of the bladder wall, and intravesical pathologies such as bladder tumors. For any lesion seen on the gray scale examination, the size, location and number were recorded.

Subsequently, 3D US of the bladder was done using a free-hand technique. The examiner moved the transducer with a steady, smooth motion and only the angle of the transducer was changed. After scanning, the software automatically created 3D volume data sets. To examine the bladder surface, volume-rendered, surface-rendered, maximum intensity projection, and minimum-intensity projection algorithms were used. The whole surface of the bladder was examined from anterior to posterior at different angles while displayed on the monitor of the machine. Pathologic findings were recorded as single images. After the examination, multiplanar reconstruction (MPR) with different planes was performed manually and reviewed. For each patient, the 3D sonographic examination and image reconstruction procedures were completed within 10–15 min. The number, location size and morphological features of the lesions were evaluated on 3D virtual and MPR images. The lesions were recorded as polypoid, sessile, or wall thickening. A lesion that was taller than its width was considered polypoid, and a lesion that was wider at the base was defined as sessile. A lesion was characterized as wall thickening when there was elevation of the bladder wall without a discrete mass.

All patients underwent conventional cystoscopy under general anesthesia in the urology department by a urologist who was unaware of the prior sonographic examination results. Bladder biopsy or transurethral resection of bladder tumor, and the histopathological results were then reviewed. The cystoscopy was taken as the reference standard. Comparative analysis was carried out between the imaging findings collected by 2D and 3D US to those of the cystoscopy.

2.1. Statistical methods

Continuous variables are expressed as mean and Standard Deviation. Categorical variables are expressed as frequencies and percents. The McNemar test was used for comparing 2D and 3D results. A significance level of $P < 0.05$ was used in all tests. All statistical procedures were carried out using SPSS version 15 for Windows (SPSS Inc., Chicago, IL, USA).

3. Results

Twenty-seven patients were enrolled in the study, the mean age was 62.8 ± 10.8 years ranging between 29 and 77 years; males represented the majority of cases (77.8%) (Table 1).

Conventional cystoscopy revealed urinary bladder tumors (UBTs) in 15 (55.5%) of 27 patients. The total number of lesions detected by conventional cystoscopy was calculated as 22 in 15 patients. Ten (66.6%) patients had solitary and 5 (33.3%) had multiple tumors. Morphologically, the most frequent type of tumor was polypoid in 14 (63.6%) of 22 tumors, while sessile tumors were 8 (36.3%).

Two dimensional (2D) gray scale images showed sessile tumors in 2 patients while 3D US and cystoscopic images revealed these lesions to be a middle lobe prostate. One patient appeared to have a suspicion of a polypoid tumor on 2D US which proved to be a polypoid tumor on 3D US and conventional cystoscopy. Two small sessile tumors were detected by 3D US and conventional cystoscopy that were not shown on corresponding 2D images in one patient (Fig. 5). Conventional cystoscopy revealed a 10 mm polypoid tumor in a patient with normal 3D and 2D sonographic findings. Moreover, 2D US failed to detect a second tumor in 3 patients with double
tumors that were shown by 3D US and conventional cystoscopy (Fig. 1).

Our findings showed that 2D US has a true positive (TP) of 18 out of 22 tumors (truly diagnosed as bladder tumors by CS); true negative (TN) of 8 out of 12 (truly diagnosed without mass by CS) as for 3D US TP of 21 out of 22 and TN of 12 out of 12. Thus, specificity (SP) (ability to detect those without mass as CS) for 2D US = 66.7% vs 100% of 3D US, also, sensitivity (SN) 81.8% for 2D US vs 95.5% for 3D US. The ability to predict positive findings (P+) for 2D US = 81.8% vs 100% for 3D US, while the negative predictive value (P-) for 2D US is 66.7% vs 92.3% for 3D US. The accuracy for 2D US was 76.4% vs 97% for 3D US (Tables 2 and 3). Using the McNemar test, we could not find a statistically significant difference between these observations (for 2D and 3D sonography $P > 0.05 = $ non significant) (Tables 4 and 5).

### Table 1  Description of personal data.

<table>
<thead>
<tr>
<th></th>
<th>Mean ±SD</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Median</th>
</tr>
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<tbody>
<tr>
<td>Age</td>
<td>62.89 ±10.18</td>
<td>29.00</td>
<td>77.00</td>
<td>63.00</td>
</tr>
<tr>
<td>Sex</td>
<td>Male (n %)</td>
<td>21</td>
<td>77.8%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female (n %)</td>
<td>6</td>
<td>22.2%</td>
<td></td>
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</tbody>
</table>

### Table 2  Diagnostic criteria of 2D US.

<table>
<thead>
<tr>
<th>Lesions diagnosis 2D</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>Lesions diagnosis 2D</td>
<td>18(TP) 81.8</td>
<td>4(FP) 33.3</td>
</tr>
<tr>
<td>Positive</td>
<td>18(TP) 81.8</td>
<td>4(FP) 33.3</td>
</tr>
<tr>
<td>Negative</td>
<td>4(FN) 18.2</td>
<td>8(TN) 66.7</td>
</tr>
</tbody>
</table>

The sensitivity of 2D US in detecting tumor was 81.8%, as it was able to detect 18 lesions from 22 lesions diagnosed by cystoscope, with a PPV of 81.8%. On the other hand the specificity of 2D US was 66.7% as it was able to determine 8 negative lesions from 12 detected by cystoscope, with a NPV of 66.7%. The accuracy of 2D US was 76.4%.

Fig. 1  65 year old man with two bladder masses. (A) 2D ultrasound image showing one polyp infiltrating the right ureteric orifice, (B) volume rendered 3D image showing two bladder polypoid masses, the second polyp is arrowed, (C) volume rendered image showing the missed polyp in 2D, (D) and (E) surface rendered 3D image showing the surface of the larger polyp, (F) multiplanar 3D reconstruction images of the polyp confirming its ureteric invasion.
The location, size, morphologic features of the lesions detected by 3D US agreed well with the findings of conventional cystoscopy (Figs. 1–5) except in few cases. Regarding the site; 3 lesions were found to be in the posterior wall by CS rather than base and the left lateral wall by 3D US images. As regards the size of the lesions; 4 lesions were of larger dimensions by 3D US images than CS images and 2 more lesions were shown to be smaller on 3D US than on CS images.

All 15 patients with bladder tumors on cystoscopy underwent a transurethral resection, 13 had transitional cell carcinomas (TCCs) 1 had an adenocarcinoma, and the remaining patient (that was missed by 3D US) was revealed to have polypoid cystitis. Lesion diameter ranged from 1 to 6 cm (mean 2.4 cm).

### Table 3  Diagnostic criteria of 3D US.

<table>
<thead>
<tr>
<th>Lesions diagnosis 3D</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Lesions diagnosis 3D</td>
<td>21 (TP)</td>
<td>95.5</td>
</tr>
</tbody>
</table>

The sensitivity of 3D US in detecting tumor was 95.5%, as it was able to detect the 21 lesions diagnosed by cystoscope, with a PPV of 100%. On the other hand the specificity of 3D US was 100% as it was able to determine 12 negative lesions detected by cystoscope, with a NPV of 92.3%. The accuracy of 3D US was 97%.

### Table 4  Comparison between 2D and 3D as regards their sensitivity of diagnosis.

<table>
<thead>
<tr>
<th>2D Positive</th>
<th>2D Negative</th>
<th>3D Positive</th>
<th>3D Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>18</td>
<td>81.8</td>
<td>4</td>
<td>18.2</td>
</tr>
</tbody>
</table>

There was no significant difference between 2D and 3D as regards their sensitivity of diagnosis among positive lesions, as 2D sensitivity was 81.8% compared to a 95.5% for 3D.

### Table 5  Comparison between 2D and 3D as regards their specificity of diagnosis.

<table>
<thead>
<tr>
<th>2D Positive</th>
<th>2D Negative</th>
<th>3D Positive</th>
<th>3D Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>4</td>
<td>33.3</td>
<td>8</td>
<td>66.7</td>
</tr>
</tbody>
</table>

There was no significant difference between 2D and 3D as regards their specificity of diagnosis regarding positive lesion, as 2D specificity was 66.7% compared to a sensitivity of 100% for 3D.

The location, size, morphologic features of the lesions detected by 3D US agreed well with the findings of conventional cystoscopy (Figs. 1–5) except in few cases. Regarding the site; 3 lesions were found to be in the posterior wall by CS rather than base and the left lateral wall by 3D US images. As regards the size of the lesions; 4 lesions were of larger dimensions by 3D US images than CS images and 2 more lesions were shown to be smaller on 3D US than on CS images.

### 4. Discussion

When evaluating patients with painless hematuria it is crucial to exclude the existence of tumors of the urinary tract. US imaging is one of the initial examinations since it is widely available, non-invasive, easy and a safe technique to perform. Many abnormalities can be detected with conventional 2D US and hence transurethral resection is subsequently performed; however, when the US examination is normal or inconclusive, a diagnostic cystoscopy becomes mandatory (6,7).

Conventional cystoscopy is the gold standard for urinary bladder evaluation and is useful for direct visualization of the inside of the bladder. However this modality has some

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**Fig. 2**  60 year old man with hematuria, (A) 2D ultrasound image showing mass in the right superior bladder wall, (B) volume rendered 3D image showing the same mass (arrows), (C) surface rendered image showing the irregular surface of the bladder mass similar to its appearance in conventional cystoscopy.
limitations; being invasive, can cause iatrogenic bladder on urethral perforation, infection, hematuria or a urethral stricture (8–10). Three-dimensional ultrasound is now an established imaging tool in several specialties, and has been recently used in the evaluation of bladder tumors (7). Three dimensional ultrasonography has been shown to be more reliable and repeatable than gray-scale ultrasonography in evaluating anatomical structures (11,12).

In our study, we examined the feasibility of 3D sonography and virtual sonographic cystoscopy in detection of bladder lesions in patients with hematuria and we found greater sensitivity (95.5%) for 3D virtual cystoscopy than 2D US (81.8%). Our results for 3D US are comparable with those obtained by Kocakoc et al. (13), whose findings showed that 3D virtual sonography has sensitivity of 96.2% for tumor detection versus 93% for 2D US, in a study of 31 patients with suspected or known bladder tumor.

Mitterberger et al. (2) studied 42 patients with plainless hematuria, all of whom had an abnormal 2D US. They found that 3D US yielded overall correct diagnosis in 86% (36 of 42) of the patients whereas 2D US diagnosis was correct only in half of them. In their study, 3D US provided better diagnostic

![Fig. 3](image1) 59 year old male with hematuria, (A) 2D ultrasound image revealing right lateral wall bladder mass, (B) surface rendering 3D image demonstrating the mass surface and residual bladder lumen.

![Fig. 4](image2) Fungating bladder polypoid mass seen by 3D multiplanar reconstructed images, volume rendered and surface rendered images clearly demonstrating the morphology of the lesion.
diagnosed by 3D US. So, we think that this technology is of great value when used in the diagnostic work-up of patients with hematuria of unknown cause, being more sensitive in detecting bladder tumors.

5. Conclusion

Three-dimensional bladder US has superior sensitivity than 2D US in diagnosing bladder tumors in patients with hematuria. Although cystoscopy is still the gold standard examination, 3D US is a promising tool in diagnosing bladder tumors and might reduce the number of cystoscopies needed to assess these patients.

Conflict of interest

We have no conflict of interest to declare.

References