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The role of 3-dimensional sonography and virtual sonographic cystscopy in detection of bladder tumors

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Abstract
Introduction: Bladder cancer is the second most common genitourinary malignancy. Recent technological advances have led to the development of virtual endoluminal internal views similar to those obtained with conventional endoscopy (virtual cystoscopy).
Objectives: To evaluate the potential value of virtual cystoscopy in the detection and follow up of bladder tumors.
Patients and methods: A total of 50 patients from Ain Shams University Hospital were studied between August 2012 and April 2014 at Ain Shams' Radiology Department and Sonoscan Radiology Center. All patients underwent 2D-US, 3D virtual sonographic cystoscopy and conventional cystoscopy, with results compared for sensitivity and specificity in correlation with the site, size and shape of the tumor.
Results: 3D virtual cystoscopy showed a sensitivity of 96.5%; while its specificity in identifying lesions was 85.7%; positive predictive values were 96.5%; negative predictive value were 85.7%. The sensitivity of the 2D ultrasound was 77.2%; while its specificity in identifying lesions was 57.1%; positive predictive values came at 88%; negative predictive value were 38.1%. Calculations were made taking into consideration the conventional cystoscopy "gold standard".
Conclusion: Additional to lower costs and no radiation exposure, 3D sonography appears comparable to the use of CT scans and MRI in providing virtual cystoscopy in investigating bladder cancer. Virtual sonographic cystoscopy may therefore be a useful alternative for screening and follow up of tumors, particularly if conventional cystoscopy cannot be performed. However, 3D sonography cannot replace pathological

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staging, and there is still a need to further improve this technology for enhanced assessment of mucosal abnormalities.

Introduction

Bladder cancer is the 9th most common form of cancer worldwide; with 13.1 cases per 100,000, Egypt ranks in 10th position by country in terms of bladder cancer incidence [1].

The current evaluator method for initial diagnosis traditionally involves IVU with two-dimensional ultrasonography (2D-US), CT, MRI and cystoscopy with eventual biopsy, of which the latter is an invasive and relatively expensive procedure. Trans-abdominal 2D-US is often used for examining patients when a bladder tumor is suspected. Although the majority of exophytic tumors can be detected, small papillary tumors, flat 'lawn-like' tumors and those on the dome of the bladder, in particular, present low detectablility or cannot be differentiated from benign lesions [2,3].

The sensitivity of US in detecting bladder tumors depends on operator experience, and is variably reported to range between 26% and over 80% [4,5]. However, this rate is much lower in patients with tumors smaller than 5 mm or for tumors located on the bladder dome or anterior wall [5].

Recent advances in computer technology and display techniques (including spiral and multi-detector CT imaging and MRI with rapid image acquisition and 3-dimensional [3D] rendering) have led to the development of virtual endoluminal views of hollow organs, similar to those obtained with conventional endoscopy. Virtual cystoscopy performed via computed tomography or magnetic resonance imaging has been developed with promising results [6–9]. These techniques appear more sensitive than US, despite their being significantly more time consuming, expensive, and frequently inaccessible for clinicians (Fig. 1).

Three-dimensional ultrasound is now an established imaging tool in several specialties, and is available as part of most medium and upscale equipment. In urology, it has been used in planning and guiding treatment for prostate cancer [10], to accurately measure bladder volume [11], and in imaging the urethral sphincter in pelvic floor disorders [12]. Vining et al. [13] were the first to apply this technique in the detection of bladder cancers, after several studies, including CT or MR virtual endoscopy of the bladder, were published [14–19].

Three-dimension US imaging has recently become a widely available feature as part of many ultrasound machines. This technology permits the acquisition and storage of a dataset selected from a specific region of interest, which can be further analyzed, either by multiplanar display, surface rendering, or volume calculation. As there is a considerable contrast gradient between the bladder lumen and its wall, the surface rendering algorithm can usually display, with sufficient detail, the surface of the bladder, revealing a cystoscopy-like image, enhancing the characterisation of bladder wall abnormalities [20].

In our study we aimed to evaluate the potential value of virtual cystoscopy in the detection and follow up of bladder tumors (Fig. 2).

Patients and methods

A total of 50 patients fitting the inclusion criteria were selected from the Urology Clinic at the Ain Shams University Hospital at El-Demerdash, and were prospectively enrolled in our study in the period between August 2012 and April 2014.

Inclusion criteria for patients taking part included: presentation of total gross painless hematuria without a history of trauma or evidence of urinary tract injury or infection; suspicious lesions or inconclusive readings by 2D ultrasonography and scheduled for cystoscopy; patients scheduled for follow up cystoscopy after previous superficial bladder tumor resection. Patients presenting with hematuria due to systemic etiology, patients who were diagnosed with CIS from previous cystoscopy, patients with kidney disease, or calculi causing the hematuria and patients unfit for surgical intervention were excluded from the study (Table 1).

All patients underwent trans-abdominal 2D US focusing on the bladder and kidneys. Patients were subsequently scheduled for a 3D US examination the following day and conventional cystoscopy with a rigid cystoscope within 14 days. Written informed consent was obtained from each patient, and the study was approved by the Ethics Committee at Ain Shams University. Sonographic examinations were undertaken through a single experienced radiologist using a SonoAce X8 system (MEDISON Co.,Ltd.), with a 4–7 MHz volume trans-abdominal transducer used to create images. The radiologist was unaware of the 2D US results.

Examination protocol

Approximately 1 h before the US examination, 500 ml of water was orally given to each patient. The examination was performed with the bladder filled up to 350 ml, or up to each patient's tolerance.

2D ultrasonography

An initial routine gray-scale sonography of the bladder was performed. The device parameter settings were optimised to ensure high-quality 2D images, with the size, location, morphology and number of the tumors recorded.

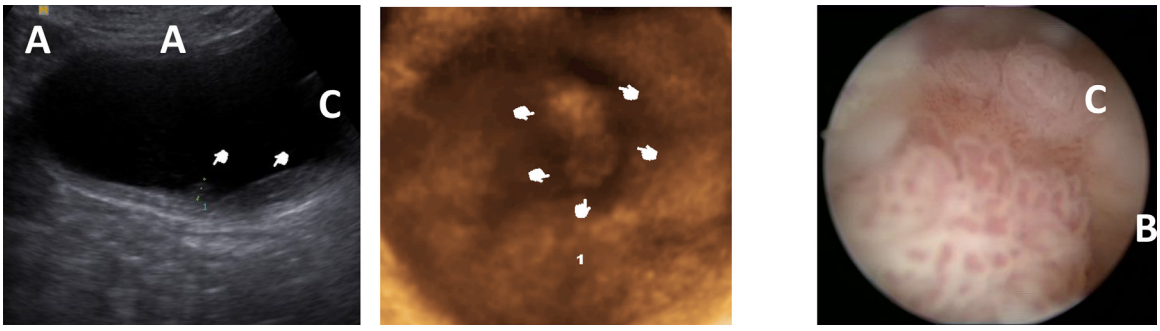

Figure 1 Ultrasonographic examination before the second conventional cystoscopy (6 month follow up) in a 74 years old man with a history of bladder cancer treated by transurethral resection. (A) Transverse grey scale ultrasonography showing thickening of the posterior wall of the urinary bladder with small papillary projections (white pointers) into the lumen. (B) Real-time three dimensional ultrasonography based virtual cystoscopy showing a broad-based elevated lesion (pointers) at the posterior wall. (C) Conventional cystoscopic appearance of the same lesion. Transurethral resection and biopsy revealed low grade superficial transitional cell carcinoma.

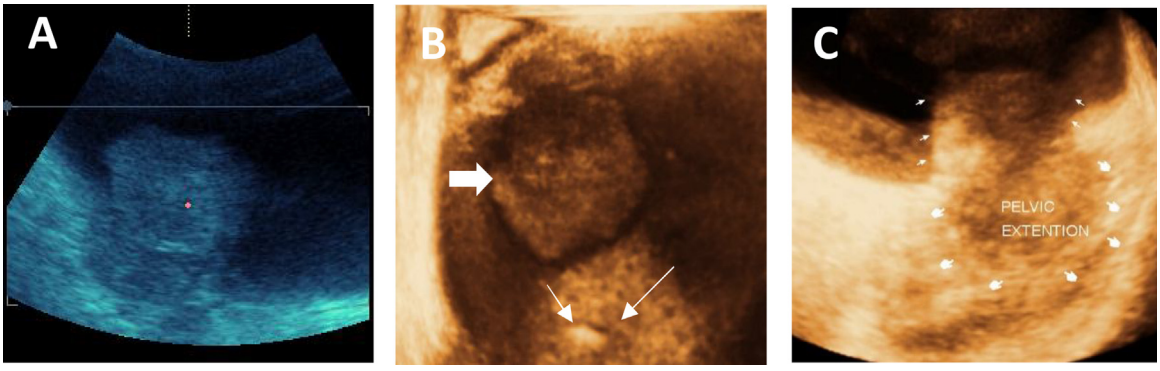

Figure 2 Male patient 67 years old presented with hematuria and elevated kidney functions . (A) Transverse grey-scale ultrasonography revealed a hyperechoic lesion 6 cm on the posterior wall of the bladder.(B) Surface rendered 3D sonography from a different angle shows an additional small polypoid mass (small arrow) on trigone of the bladder and the same polypoid mass (large arrow) on the posterior wall of the bladder.(C) cut section of reconstructed 3D images showing extra vesical extension (white pointers).

Table 1 Comparison of the number and shapes of the lesion detected between 3D US and conventional cystoscopy.

			CS shape			Total
			Free	Polyp	Sessile	
3D shape	Free	Count	12	2	0	14
		% within 3D shape	85.7%	14.3%	0.0%	100.0%
		% within CS shape	85.7%	5.6%	0.0%	19.7%
	Polyp	Count	1	34	0	35
		% within 3D shape	2.9%	97.1%	0.0%	100.0%
		% within CS shape	7.1%	94.4%	0.0%	49.3%
	Sessile	Count	1	0	21	22
		% within 3D shape	4.5%	0.0%	95.5%	100.0%
		% within CS shape	7.1%	0.0%	100.0%	31.0%
Total		Count	14	36	21	71
		% within 3D shape	19.7%	50.7%	29.6%	100.0%
		% within CS shape	100.0%	100.0%	100.0%	100.0%

		CS			Total
		Free	Polyp	Sessile	
3D	Free	12 (85.7%)	2 (5.6%)	0 (0%)	14
	Polyp	1 (7.1%)	34 (94.4%)	0 (0%)	35
	Sessile	1 (7.1%)	0 (0%)	21 (100%)	22
Total		14 (100%)	36 (100%)	21 (100%)	71

Table 2 Comparison of the number and shapes of the lesion detected between 2D US and conventional cystoscopy.

			CS shape			Total
			Free	Polyp	Sessile	
2D shape	Free	Count	8	9	4	21
		% within 2D shape	38.1%	42.9%	19.0%	100.0%
		% within CS shape	57.1%	25.0%	19.0%	29.6%
	Polyp	Count	0	25	12	37
		% within 2D shape	0.0%	67.6%	32.4%	100.0%
		% within CS shape	0.0%	69.4%	57.1%	52.1%
	Sessile + wall thickening	Count	6 (3 + 3)	2	5	13
		% within 2D shape	46.2%	15.4%	38.5%	100.0%
		% within CS shape	42.9%	5.6%	23.8%	18.3%
Total		Count	14	36	21	71
		% within 2D shape	19.7%	50.7%	29.6%	100.0%
		% within CS shape	100.0%	100.0%	100.0%	100.0%

		CS			Total
		Free	Polyp	Sessile	
2D	Free	8 (57.1%)	9 (25%)	4 (19%)	21
	Polyp	0 (0%)	25 (69.4%)	12 (57.1%)	35
	Sessile + wall thickening	6 (3 + 3) (42.9%)	2 (5.6%)	5 (23.8%)	22
Total		14 (100%)	36 (100%)	21 (100%)	71

3D ultrasonography

A 3D US of the bladder was undertaken following the 2D Ultrasound using a freehand technique. The examiner moved the transducer with a steady, smooth motion and only the transducer's angle was changed. The bladder's surface was examined from anterior to posterior at different angles while displaying on the machine's monitor. Pathologic findings were recorded as single images. The 3D sonographic examination and image reconstruction procedures were completed within 10–15 min.

Conventional cystoscopy

Cystoscopy procedures were performed in the Ain Shams University Urology Department's OR. Regional anesthesia was usually applied in the procedures. The surgeon performing the cystoscopy was unaware of the prior sonographic examination results.

Statistical methods

A significance level of $P < 0.05$ was used in all tests. All statistical procedures were carried out using SPSS version 17 for Windows (SPSS Inc., Chicago, IL, USA). Results were subdivided into three groups based on the diagnostic modality used (conventional, 2d ultrsonography, 3d ultrasonogrphic virtual cystoscopy), with comparative statistics completed using Chi-square and Mann–Whitney tests for qualitative and quantitative data respectively. The diagnostic value of 3D virtual cystoscopy was analysed in relation to the gold standard test (conventional cystoscopy) by cross tabulation with an estimation of sensitivity, specificity, PPV, and NPV.

Results

Among the 50 patients included in this study, 38 were males (76%), 12 were females (24%) with the male to female ratio 3:1. Patient ages ranged from 25 years to 77 years with a mean of 57.72 ± 11.05. A total of 32 patients had a single lesion, while 18 patients had multiple lesions.

Two lesions thought to be present with 3D US (1 polypoid and 1 sessile) were proven to be a false positive, and were absent in the conventional cystoscopy. Of those two lesions, one patient appeared to have a polypoid tumor in the 3D virtual cystoscopy, which, in a conventional cystoscopy, was diagnosed as a bladder hematoma. A further basal sessile mass was found to be median lobe of the prostate.

The size of lesions detected by 2D US was significantly larger than the size of lesions detected only by conventional cystoscopy (P value: 0.021). There was no significant size difference between lesions detected by 3D virtual cystoscopy and lesions detected by conventional cystoscopy only (P value: 0.607).

By comparing the sites of missed lesions from 2D US with lesions sites by conventional cystoscopy, data illustrates that 2D ultrasound is clearly defective in the detection of anterior wall lesions (amounting to 54% of missed lesions) and domal lesions (23% of missed lesions). The 3D virtual cystoscopy was able to detect lesions at all sites of the bladder, but missed 2 lesions: 1 on the posterior wall; and 1 on the right lateral wall.

Regarding the number of the lesions detected, the sensitivity of the 2D ultrasound was 77.2%; while its specificity in identifying lesions was 57.1%; the positive predictive values were 88%; the negative predictive value was 38.1%. The 3D virtual cystoscopy had a sensitivity of 96.5%; while its specificity in identifying lesions was

Table 3 Correlation between the results of published studies and current thesis regarding sensitivity of 2D ultrasonography, 3D virtual sonographic cystoscopy and conventional cystoscopy for bladder tumors detection.

Reference	Number of patients	Number of tumors detected		
		2D	3D	Cystoscopy
Mitterberger et al.	42	29	37	37
Kocakoc et al. [25]	28	39	41	47
Park et al. [27]	14	19	22	28
Silva-Ramos et al. [26]	21	0	5	7
Current study	50	44	55	57
Total	155	131	160	176
Sensitivity[a] %		74.4	90.9	100

[a] Calculations were made considering cystoscopy as the "gold standard".

85.7%; positive predictive values was 96.5%; and negative predictive value: 85.7%.

Discussion

Different radiologic techniques have been used to detect and evaluate bladder cancer, for example, ultrasonography, excretory urography, computed tomography, magnetic resonant imaging. However, none have been found to be dominant in reliability in the detection of bladder tumors, and the ideal and most cost-effective imaging method is yet to be determined [21]. Therefore, using conventional cystoscopy remains the gold standard in detecting bladder tumors and their evaluation [15].

Cystoscopy, however, has some limitations, notably: it is invasive, time consuming, and expensive; requires sedation or anaesthesia; carries a 5%–15% risk of urinary tract infection; and sometimes leads to iatrogenic injury. In addition, the evaluation of lesions located in the base or neck of the bladder, or in the diverticulum, is difficult because of the cystoscope's limited field of view. Examination is also unsuitable in patients with severe urethral strictures, or in the presence of active bleeding [22,15].

Reports regarding the efficacy of virtual imaging techniques have already been undertaken, and the feasibility of virtual cystoscopy for bladder tumor detection has already been proven [23].

CT virtual cystoscopy was initially used in generating 3D images from volumetric data obtained with helical CT or MR imaging. Vining et al. insufflated carbon dioxide via a Foley catheter into the bladders of 3 patients (2 of whom had bladder tumors), obtaining views of tumors similar to those provided by conventional cystoscopy [13].

Recently, the use of 3D US in the evaluation of bladder tumors has been reported, with results showing a moderate-to-perfect inter-observer agreement. This technology has unlimited viewing perspectives and planes, and different viewing algorithms allow the data to be displayed with a variety of techniques, such as surface rendering, volume rendering, and multi-planner reconstruction (MPR). Additionally, this technique illustrates greater reliability, and consistency in end results, than gray scale sonography in evaluating anatomic structures and disease entities [24].

In this study, we examined the 50 study patients with suspected bladder lesions with 2D ultrasonography, 3D virtual cystoscopy, using conventional cystoscopy as the reference point. 3D virtual cystoscopy had a sensitivity of 96.5%; specificity was 85.7%; positive predictive values were 96.5%; and the negative predictive value was 85.7%.

There was a statistically significant difference between 2D ultrasonography and 3D virtual cystoscopy in diagnostic performance. The sensitivity of the 2D ultrasound was 77.2%; its specificity was 57.1%, positive predictive values: 88%, negative predictive value: 38.1% (Table 2).

These results for 3D US are comparable with those obtained by Kocakoc et al., whose findings showed that 3D virtual cystoscopy has a sensitivity of 96.2% in tumor detection, versus 93% for 2D US, in a study of 31 patients with suspected or known bladder tumors [25].

Another study by Park et al. compared the accuracy of 2D and 3D US in 14 patients with proven bladder tumors, finding 3D US to have a superior sensitivity of 78.6% against 67.9% for 2D US. A similarly greater sensitivity (83.3%) of 3D US in the detection of bladder tumors was found in a study by Silva-Ramos et al., who evaluated only patients with an undetermined cause of hematuria after 2D US [26,27].

In comparison with 2D US, 3D US illustrated a superior sensitivity and specificity in tumor detection. The visualisation and selective examination of the suspected lesions in surface and volume rendered mode was helpful in the diagnosis. It was also useful in areas of the bladder that are difficult to assess, for example the bladder dome and anterior wall (Table 3).

Three-dimensional ultrasonography with virtual sonographic cystoscopy has some advantages over other virtual techniques. Insufflation of air or carbon dioxide into the bladder requires catheterisation and presents some limitations, including patient discomfort and failure of the procedure in severe urethral stenosis. However, in 3D US, catheterisation is unnecessary, with no risk of catheter-related trauma or infection [19].

Virtual cystoscopy presents some limitations, the most important of which is its inability to show flat or intramural lesions (carcinoma in situ), which appear as subtle mucosal colour changes on a conventional cystoscopy [15].

A further limitation of virtual cystoscopy is its ineffectiveness in providing tissue samples for histologic evaluation, which is possible with conventional cystoscopy and biopsy.

A further drawback we encountered in our study is that virtual images alone cannot confirm the nature of the mass [19]. This entails that the neoplastic or inflammatory or the origin of the mass vesical or extravesical like enlarged median lobe of the prostate gland which simulated an intravesical lesion in a study done by Song et al., and we encountered the same drawback with a case in our study [19].

As a screening tool, it has been established that 3D US has superior sensitivity in tumor detection compared to regular 2D sonography. It also demonstrated a diagnostic performance comparable to other virtual imaging techniques (CT and MRI). In clinical practice, the use of 3D US has been established as valuable in diagnosing additional cases that cannot be diagnosed with 2D [25].

Conclusion

3D virtual sonographic cystoscopy is a non-invasive, innovative new technique in detecting bladder tumors. This technology's results also appear comparable with CT and MR imaging in providing virtual cystoscopy for investigation of bladder cancer with lower costs and no radiation exposure. Therefore, virtual sonographic cystoscopy may be a useful alternative for screening and follow up. However, this technology cannot replace pathological staging, and there remains a need for further improvement of 3D US technology in its use to diagnose of mucosal abnormalities.

Conflict of interests

The authors certify no conflict of interest.

Ethical Committee Approval

This study was approved by the Ethics Committee of Ain Shams University.

Authors' contributions

Tawfeek A.M., Abd El Fattah D.M., Mahmoud A., Shorbagy A.A., Mousa W.E., Hamza, I.H.: patients collection, study design, performing cystoscopies and biopsy.

Radwan A.: performing ultrasonography.

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