Original Article

Virtual cystoscopy (pneumo-cystoscopy)—Its utility in the prospective evaluation of bladder tumor

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ABSTRACT

Aim:To evaluate the role of virtual cystoscopy (VC) comparing it with cystopanendoscopy (CPE) for detecting bladder tumor(s).

Material and Methods: Ethical clearance was obtained from the Institutional ethics committee. After an informed consent 30 patients fulfilling the inclusion criteria were enrolled in the prospective non-randomized clinical study and were evaluated as per protocol with VC performed by a qualified radiologist who was blinded to the findings of CPE performed by a qualified urologist. The results so obtained were analyzed using appropriate statistical tools.

Results:The mean age of the patients was 56 years. Sensitivity of VC in detecting bladder lesions was 92%. However, when axial images were also interpreted along with VC, the sensitivity increased to 96% for detecting bladder lesions. The specificity of VC with axial CT was 40% in respect of detecting bladder lesions.VC with axial CT was 85.7% sensitive in identifying multiple bladder tumors. There were no complications on account of performing VC. Minor problems were encountered with VC and CPE in 16.7% and 13.3% patients respectively.

Conclusions: VC with axial CT is 96% sensitive in detecting bladder lesions and 85.7% sensitive in detecting the multiplicity of the tumors. VC may be a useful complementary diagnostic tool for the workup of select patients with suspected bladder lesions. However, larger randomized controlled studies are needed to better define the precise clinical and diagnostic role of VC in routine practice.

Settings and Design: Prospective Clinical Comparative Non Randomized Clinical Study

Key words: Bladder tumor, cystopanendoscopy, pneumocystoscopy, virtual cystoscopy

INTRODUCTION

With the availability of three-dimensional (3D) computer volume-rendering techniques or virtual-reality imaging it is now possible to perform accurate intra-luminal imaging. Intra-luminal navigation through several hollow viscera like the colon, bronchus, stomach and the urinary bladder[1-10] has been reported in the literature. Urinary bladder may be an ideal intra-abdominal organ for performing VC. Some studies have compared the relative accuracy of VC and CPE.[1,3,11] The accuracy of VC in detecting bladder lesions (≤1 cm) has been variously reported by some researchers as 60-100%.[1,3] Bladder lesions <5 mm have also been reportedly detected by others by VC.[4,5,6] While some authors[2]have found the visualization of such lesions to be difficult, others[12]have reported to the contrary. There exists lack of consensus on the precise utility and type of contrast needed for VC[13]as some authors have used air while others have used intravenous contrast with their attendant merits and demerits. Failure of the intravenous contrast and urine to mix homogenously may lead to scanning artefacts during VC.[10] The literature regarding the accuracy of VC in detecting sessile intravesical lesions is also scarce and equivocal. This study aims to answer these concerns on VC by prospectively evaluating the utility of VC versus CPE in detecting bladder tumor(s).

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MATERIALS AND METHODS

After obtaining ethics committee approval and an informed

consent, 30 patients with history or investigations suggestive of urothelial cancer were evaluated. Thirty patients aged 19-85 years (mean age 56.83±12.80 years) including 28 males and two females were enrolled in the current study. CPE was taken as reference gold standard. A focused history-examination, urine analysis/culture/cytology for malignant cells, renal function tests and ultrasonography (USG) of kidney, ureter and bladder (KUB) region was performed in all the patients.

For this study all our patients underwent VC+CT instead of the usual computed tomography (CT) of whole abdomen with oral/IV contrast and CPE. Thus they were not exposed to additional radiation dose for the sake of this study. VC+CT was performed as per protocol by a qualified radiologist who was blinded to the findings of CPE. Helical CT scanning was performed using the CT scanner (Somatome-Vol-4- zoom, Siemens AGR) with the following settings: collimation 5 mm, pitch 1.3, 140 Kvp and 120-140 mA, and table increment 6.5 mm with reconstruction done at 2 mm. Axial images were taken in the supine and prone positions. Multiplanar reconstruction and 3D volume rendering was done using the Virtuos O Work StationR™. A 12-Fr Foley's catheter was inserted under aseptic precautions and 200-300 cc of room air was insufflated into the bladder. During VC, the endoscope was placed in the centre and all areas of the bladder were looked upon from the centre. In case any lesion was detected, zooming in was done to obtain close-up details of that lesion. Parameters recorded on axial images were site, size, character, vascularity, number of lesions, thickness of bladder wall, extension into adjacent structures, lymphadenopathy, hydroureter and hydronephrosis. Panel Figure 1a and c depicting the virtual cystoscopy reconstructed images in a patient with bladder tumor.

Diagnostic CPE was performed with strict asepsis under local anesthesia and with a rigid cystoscope. CPE findings were used as the reference standard to evaluate the sensitivity and specificity of VC+CT. The data was analyzed to compare the findings of VC+CT and CPE with regard to their specificity, sensitivity and predictivity. Taking finding of CPE as gold standard and a confidence interval of 95% the comparison between sensitivity and specificity for calculating significance was evaluated using McNemar's test.

RESULTS

Transitional cell carcinoma (TCC), vesical leiomyoma and cystitis were diagnosed in 24, 2 and 4 patients respectively based on CPE and urine cytology. Sixty-eight percent of the tumors were located at the left bladder lateral wall. Urine cytology was positive for malignant cells in 19 patients (63.4%), of which 18 patients had proven TCC of the bladder, while in one patient with positive cytology no lesion could be detected on CPE. In the remaining 11 patients (36.7%) with a negative cytology 5, 2 and 4 patients had TCC of the bladder, leiomyoma and cystitis respectively.

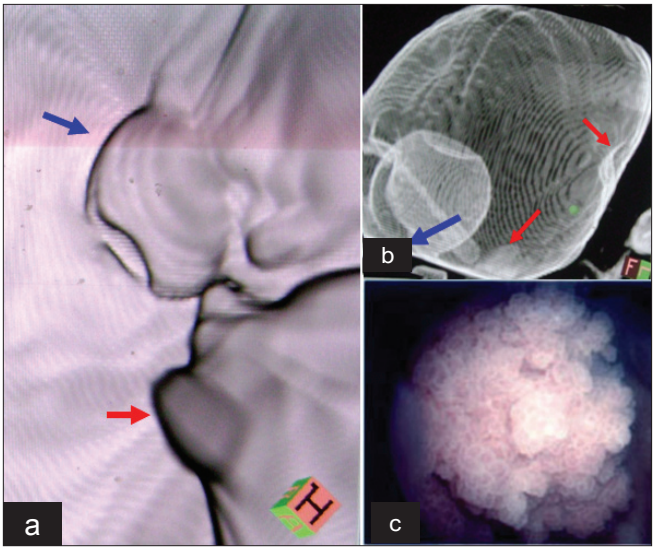

Figure 1: (a) Virtual cystoscopy showing the tumor adjacent to the bladder neck (red arrow); with Foley's catheter at bladder neck region (blue arrow);(b) Global view of virtual cystoscopy in the patient showing one tumor adjacent to the bladder neck and another sessile tumor in the left lateral bladder wall (red arrows), blue arrow shows the Foley's bulb at the bladder neck; (c) Cystoscopic view of the bladder tumor in the patient

Table 1:Depicting the status of CT & VC for Bladder Tumors

Table-1a :Depicting the sensitivity & specificity of CT versus VC for bladder tumor detection

Parameter	Tumor detected (N)	Tumor not detected (N)	True positives (N)	True negatives (N)	False positives (n)	False negatives (n)
CPE*	25	5	25	5	0	0
AXIAL CT	27	3	24	2	3	1
VC	26	4	23	2	3	2

*CPE –Cystopanendoscopic examination was taken as the reference standard. N=Number of patients, VC-Virtual cystoscopy

Table-1b: Depicting the sensitivity & specificity of CT combined with VC in detecting multiple bladder lesions

Parameter	Sensitivity (95% ci)	Specificity (95% ci)	Ppv	Npv
AXIAL CT	96 (80.5-99.3)	40 (11.8-76.9)	88.9	66.7
VC	92 (75.0-97.8)	40 (18.8-81.2)	88.5	50

PPV- Positive predictive value, NPV- Negative predictive value, VC- Virtual cystoscopy

VC detected 23 of the 25 patients with bladder tumor/s correctly [Table1a]. Two patients were falsely detected as negative on VC. One patient was found to be having a sessile tumor 2x2 cm on the left lateral wall on CPE but VC diagnosed it as only thickening of the left lateral wall. It turned out to be TCC. Another patient with a 0.5 cm tumor detected on the left lateral wall by CPE, could not be detected by VC. However, when the axial images were interpreted along with VC this tumor could be detected. The combined sensitivity of CT+VC thus turned out to be 96% [Table1b].

Three patients were found to be falsely positive on VC. In one patient in whom a 0.6 cm tumor was detected on the posterior wall of the bladder by axial CT+VC, no lesion was found on CPE. The patient was eventually diagnosed as a case of chronic cystitis. In two patients who were labeled as bladder tumor at bladder neck by axial CT and VC, only prostatomegaly could be detected on CPE. One of these patients was eventually diagnosed as benign prostatic hyperplasia. The second patient turned out to be TCC (based on urine cytology) but no tumor could be detected even on CPE. This patient was lost to follow-up, and workup to rule out a probable upper urinary tract TCC could not be done. Thus, the combined specificity of CT+VC was 40% as compared to CPE [Table 2a].

Patients having more than one lesion were labeled as having multiple lesions and sensitivity and specificity of CT+VC were calculated taking CPE as the reference standard. Axial CT and VC were equally sensitive in detecting multiple tumors. CPE failed to detect two lesions on the anterior wall of the bladder in two patients that were detected by VC, which were rather interpreted as false positives for VC as CPE was taken as the reference standard. The sensitivity, specificity, positive and negative predictive value for this character of the tumor is depicted in Table 2b.

The smallest size of tumor detected on axial CT+VC was 2 mm and for conventional CPE was 5 mm. In detecting prostatic involvement by the bladder tumor, CT+VC detected 4 out of 5 patients correctly. There were 2 false positives and 1 false negative. Thus, axial CT+VC had a sensitivity of 80% when compared against CPE. CT+VC correctly detected all 8 cases in which there was involvement of internal urethral orifice, bladder neck and trigone. Two false positives were also detected on CT+VC. In 1 of these 2 patients, the intravesical protrusion of the median lobe was misinterpreted as extension of the tumor to the bladder neck. In the second false-positive patient, the extension of a lateral wall tumor to the bladder neck was labeled as positive on axial CT+VC. Three and four patients developed UTI following cystoscopy and VC respectively (treated with oral antibiotics) while two patients had mild self-limiting bleeding per urethra.

DISCUSSION

Although several imaging techniques like intravenous urography, USG, CT and magnetic resonance imaging (MRI) have been used for detecting bladder tumors, none of them may be completely sensitive in all aspects. Conventional CPE has traditionally served as the reference standard for detecting intravesical lesions.[1,10] However, it is invasive, time-consuming, often requires sedation and carries the risk of iatrogenic urethral and bladder injuries. While overall CT may be a useful radiological tool, it's sensitivity appears to be low particularly in so far as the detection of small bladder lesions is concerned, more over negative findings on CT may warrant further evaluation with CPE.[6,8,10] VC does not appear to be a sensitive tool to detect ureteric orifices.[11,14,15] It is uncertain whether varied approaches may improve the diagnostic accuracy of detecting perivesical disease.[1] A recent meta-analysis of 26 studies done by Xinhua Qu et al., has reported the pooled sensitivity and specificity of VC to be 93.9% and 98.1% respectively.[16]

VC is a relatively non-invasive emerging tool in the diagnostic armamentarium of bladder pathology. Table 3 depicts a comparative assessment of the overall sensitivity/specificity of global series of VC as reported in the literature till date. The reported sensitivity of urine cytology in detecting bladder cancers has been 20.2-64%,[17,18] while in the present study this was 72.6%. The mean age of the patients included in the study was 56.83±12.80 (mean±S.D) years with a range of 20-85 years.

Table2: Sensitivity and specificity of CT-VC in detecting multiple bladder lesions

Table2 a: Tumor detection in patients with multiple bladder lesions (>1 Lesion)

Parameter	No. of patients (N)	True positives (N)	True negatives (N)	False positives (n)	False negatives (n)
CT+VC	13	6	16	7	1
CPE	7	7	23	0	0

Table 2b: Sensitivity and specificity in detecting patients with multiple lesions

Parameter	Sensitivity (95% CI)	Specificity (95% CI)	PPV	NPV
CT+VC	85.7 (48.7-97.4)	69.56 (49.1-84.4)	46.2	94.1

CI=Confidence interval, PPV=Positive predictive value, NPV=Negative predictive value

The VC data in this study was obtained by the combined use of supine and prone images, as reported by others,[2,3,4,19] that was calculated patient-wise.[10,13,16,19]Other authors have calculated these results lesion-wise and not patient-wise.[1,3,4] We calculated the data patient-wise and not lesion-wise because in patients with multiple small lesions aggregated over an area it is very difficult to calculate the exact number of lesions. The sensitivity of VC and axial CT in our study was 92% and 96% respectively. When the virtual and axial images were read together (as is usually the case in clinical practice) the sensitivity increased to 96% [Table 2b].

Various authors have reported sensitivity of VC ranging from 60% [1] for tumors ≤5 mm in size to 100%[3] for lesions ≤1 cm in size with others reporting overall VC sensitivity as high as 83-94%.[2,12] A study from Chennai, India reported 90% sensitivity for VC, although their study design was different as they used contrast medium for filling the urinary bladder. In a study by Rajiv *et al.*,[13] sensitivity for lesion detection by bladder site was significantly greater with VC (90-95%) than with multiplanar reconstruction (60-78%), followed by source CT images (65-68%), and the specificity for all the three modalities and the sensitivity (patient-wise) did not differ. The overall sensitivity and specificity (1-mm slices) in their study after taking all the three components together was 96% and 98%.[13]

Table 3 :Depicting the Comparative Assessment & Review of Global Series of Virtual Cystoscopy (VC) For Bladder Tumor Detection As Reported in The Literature

Author	No.	Salient conclusions
Koplay *et al.*, 2010	27	Sensitivity (91%) , Specificity (92%) for CT cystography with VC
Panebianco *et al.*, 2009	38	Sensitivity and specificity of combined CT and VC (93-100% and 92.3-100%)
Kivrak *et al.*, 2009	33	Sensitivity (94%), specificity (90%), PPV (87%), NPV(93%), accuracy 93% with VC
Tsampoulas *et al.*, 2008	50	Sensitivity 96%(VC)
Kishore *et al.*, 2006	11	Sensitivity 85.7% (VC)
Kim *et al.*, 2005	47	Sensitivity 90-95% (VC)
Fu *et al.*, 2005	40	Sensitivity 98%, (VC)
Prando *et al.*, 2002	49	Sensitivity 78% (VC)
Nambirajan *et al.*, 2004	18	Sensitivity 94% (VC)
Tsili *et al.*, 2004	24	Sensitivity 100% (VC)
Yazgan *et al.*, 2004	39	Sensitivity 89-96%(VC)
Wang *et al.*, 2004	42	Sensitivity 95.4% (VC)
Regine *et al.*, 2003	21	Sensitivity 77% (VC)
Bernhardt *et al.*, 2003	28	Sensitivity 97.2 % (VC)
Marini *et al.*, 2003	15	Sensitivity 89 %(VC)
Wang *et al.*, 2003	28	Sensitivity 96.2% (VC)
Kim *et al.*, 2002	43	Sensitivity 95%, Specificity 87% (VC)
Song *et al.*, 2001	26	Sensitivity 90% (VC)
Gualdi *et al.*,1999	12	Sensitivity 90% (VC)
Present series	30	Sensitivity 92%(VC) vs. 96%(Axial CT)

VC detected three patients with bladder tumor which were undetected by CPE (VC specificity of 40%), implying that tumors detected by VC, that went undetected on CPE were labeled as false positives of VC [Table 1]. However, if these three patients were to be re-evaluated by a repeat CPE, these lesions may have been detected and counted as true positives of VC. In the current study this retrospective assessment (repeat CPE/biopsy/surgery) was inadvertently omitted due to the blinding methodology inherent to our protocol. Our situation was somewhat analogous to a study by Fielding and colleagues[2]in which the workers had used color coding for wall thickness on VC to diagnose malignancy, and the cases which were positive on color coding but negative on conventional CPE, too were not subjected to biopsies or surgery. Though the authentication of VC is still not well established in the literature, nevertheless we believe that in future studies, such limitations could be overcome by incorporating the retrospective assessment of tumors by a repeat CPE and VC (VC may subsequently be used as a reference standard in place of CPE).

As the multiplicity of bladder tumors may change the treatment plan, we analyzed the sensitivity and specificity of VC in detecting patients with multiple lesions. A patient with more than one bladder lesion was labeled as having multiple lesions. It was found that VC was 85.7% sensitive in detecting patients with multiple lesions. The low specificity of axial CT+VC (69.56%) may possibly be because the patients labeled as false positives (n=7) by VC were actually undetected by CPE [Table 2]. As described above, such limitations could be overcome by incorporating, in the future studies, the retrospective assessment of patients by repeat CPE.

The smallest lesion that was detected on CPE was 5 mm. Others have detected tumors of 2-3 mm in size[3,10] by VC. In our study the smallest lesion detected was 2 mm on VC. CPE failed to detect 2 lesions (false positives of VC) in the anterior wall of the urinary bladder which were detected by VC. As discussed earlier, it is possible that these were actually the false negatives of CPE rather than false positives of VC. This again emphasizes the fact that rigid CPE may rarely miss some blind areas, like the anterior wall and bladder neck.[12]

As reported by others,[11,14,20] in our study VC alone too failed to identify the ureteric orifices in all our patients. None of the 6 patients with diverticulae detected on axial CT were detected on CPE. Contrary to reports by Arslan and colleagues[13]diverticulae were not seen on VC without axial CT images, possibly due to the small size of the diverticulae in this study. Although the urinary bladder was emptied

before scanning and we insufflated additional air before prone imaging, nevertheless insignificant residual urine remained in all patients. However, as reported by others[3] this does not impair the image quality or their interpretation.

Four (13.3%) patients developed UTI while one patient had mild bleeding per urethra after VC. Others have reported a complication rate of 0-4%[1,3,14]following VC. The UTIs may have been catheter-induced or could be related to the use of unsterile (room) air while inflating the bladder. Following CPE three (10%) and one had UTI and per urethral bleeding respectively. The reported incidence of UTI following CPE has been 7.5-21%.[21,22] The radiation dose per patient in this study was 7.19 mSV which was comparable with the figure of 8-14.4 mSV reported by others.[23,24] Thus no additional radiation exposure was involved as a consequence of this study.

Apart form the small sample size here were certain other limitations too in the present study. These included: (i) lack of a randomized group, (ii) Excluding patients with negative urine cytology for TCC and (iii) a possible undetermined surreptitious increase in the number of positive VC cases. The latter two limitations [(ii) and (iii)] were due to the inclusion criteria inherent in our study protocol.

CONCLUSIONS

Axial CT and VC may offer comparable detection of bladder tumor characteristics as compared to CPE. Despite certain benefits of VC (less invasive, minimal discomfort, low incidence of complications, comparable sensitivity with Cystoscopy), due to its limitations in detecting small mucosal lesions/ pseudo-lesions (due to altered bladder wall anatomy), we believe that in select cases VC may serve as a useful diagnostic adjunct to conventional CPE. VC may be a viewed as a complementary diagnostic utility for the workup of select patients with suspected vesical lesions. However, larger randomized controlled studies are the need of the day in order to better define the precise role of VC in routine practice.

REFERENCES

1. Song JH, Francis IR, Platt JF, Cohan RH, Mohsin J, Kielb SJ,*et al*. Bladder tumor detection at virtual cystoscopy. Radiology 2001;218:95-100.
2. Fielding JR, Hoyte LX, Okon SA, Schreyer A, Lee J, Zou KH,*et al*. Tumor detection by VC with color mapping of bladder wall thickness. J Urol 2002;167:559-62.
3. Fenlon HM, Bell TV, Ahari HK,Hussain S. Virtual cystoscopy: Early clinical experience. Radiology 1997;205:272-5.
4. Bernhardt TM, Schmidl H, Philipp C, Allhoff EP, Rapp-Bernhardt U. Diagnostic potential of VC of the bladder:MRI vs CT. Preliminary report. Eur Radiol 2003;13:305-12.
5. Hara AK, Johnson CD, Reed JE, Ahlquist DA, Nelson H, MacCarty RL,*et al*. Detection of colorectal polyps with CT colography: Initial assessment of sensitivity and specificity. Radiology 1997;205:59-65.
6. Bernhardt TM, Rapp-Bernhardt U. Virtual cystoscopy of the bladder based on CT and MRI data. Abdom Imaging 2001;26:325-32.
7. Rubin GD, Beaulieu CF, Argiro V, Ringl H, Norbash AM, Feller JF, *et al*. Perspective volume rendering of CT and MR images: Applications for endoscopic imaging. Radiology 1996;199:321-30.
8. Vining DJ, Zagoria RJ, Liu K,Stelts D. CT cystoscopy: An innovation in bladder imaging. AJR Am J Roentgenol 1996;166:409-10.
9. Tavernaraki AA, Stasinopoulou M, Deliveliotis C, Thanos AI, Stasis A, Pavlopoulos SA ,. Virtual cystoscopy: Early clinical experience. Radiology 1998;209:592.
10. Kim JK, Ahn JH, Park T, Ahn HJ, Kim CS, Cho KS.Virtual cystoscopy of the contrast material filled bladder in patients with gross hematuria. AJR Am J Roentgenol 2002;179:763-8.
11. Regine G, Atzori M, Buffa V, Miele V, Ialongo P, Adami L. Virtual CT-pneumocystoscopy: indications, advantages and limitations:Our experience. Radiol Med 2003;106:154-9.
12. sili ACh, Tsampoulas C, Chatziparaskevas N, Silakos A, Kalef-Ezra J, Sofikitis N, *et al*. Computed tomographic VC for the detection of urinary bladder neoplasms. Eur Urol 2004;46:579-85.
13. Arslan H, Ceylan K, Harman M, Yilmaz Y, Temizoz O, Can S. Virtual computed tomography cystoscopy in bladder pathologies. Int Braz J Urol 2006;32:147-54.
14. Anand C, Sudhakar L, Sivasankaran G, Jayaganesh R, Ilangovan M, Muthulatha N, Rajamanickam MG, Emmanuel R. Virtual cystoscopy–a promising diagnostic technique. Indian J Urol 2003;20:18-22.
15. Merkle EM, Wunderlich A, Aschoff AJ, Rilinger N, Görich J, Bachor R,*et al*. Virtual cystoscopy based on helical CT scan data sets: Perspectives and limitations. Br J Radiol 1998;71:262-7.
16. Qu X, Huang X, Wu L, Huang G, Ping X, Yan W. Comparison of Virtual cystoscopy and ultrasonography for bladder cancer detection: A meta-analysis. Eur J Radiol2010 Epub ahead of print.
17. Roy MK, Islam MF, Kibria SA. Role of ultrasonography and urinary cytology in diagnosing recurrence of superficial urinary bladder cancer compared to cystoscopy. Bangladesh Med Res Counc Bull 2001;27:23-32.
18. Degtyar P, Neulander E, Zirkin H. Fluorescence in situ hybridization performed on exfoliated urothelial cells in patients with transitional cell carcinoma of the bladder. Urology 2004;63:398-401.
19. Yadav R, Kumar R. Virtual versus real cystoscopy. Indian J Urol 2007;23:85-6.
20. Giuliani L, Carmignani G, Belgrano E. Computed tomography for staging bladder tumors. In: Schulmah CC, editor. Advances in Diagnostic Urology. New York: Springer-Verlag; 1981.p. 197-201.
21. Clark KR, Higgs MJ. Urinary infection following out-patient flexible cystoscopy. Br J Urol 1990;66:503-5.
22. Rané A, Cahill D, Saleemi A, Montgomery B, Palfrey E. The issue of prophylactic antibiotics prior to flexible cystoscopy. Eur Urol 2001;39:212-4.
23. Tsampoulas C, Tsili AC, Giannakis D, Alamanos Y, Sofikitis N, Efremidis SC.16-MDCT cystoscopy in the evaluation of neoplasms of the urinary bladder. AJR Am J Roentgenol 2008;190:729-35.
24. Khanna PC, Kukreja KU, Merchant SA, Farooq M.Virtual cystoscopy: Reality in imaging of bladder tuberculosis. J Postgrad Med 2006;52:35-7.

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