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DIAGNOSTIC ACCURACY OF CT VIRTUAL CYSTOSCOPY IN DETECTING URINARY BLADDER CARCINOMA

Shereen Rafiq[1], Binish Zaidi[2]*, Hina Farooq[3], Sadaf Gill[4], Rashida[5], Sobia Shabbir, Arslan Shuja[7]

[1] Aziz Hospital, Sialkot, Pakistan
[2] Faisalabad Medical University and Affiliated Hospitals, Faisalabad, Pakistan
[3] Cancer Care Hospital and Research Center, Lahore, Pakistan
[4] Bahawal Victoria Hospital, Bahawalpur, Pakistan
[5] ABWA Medical College, Faisalabad, Pakistan
[6] Faisalabad international Hospital, Faisalabad, Pakistan
[7] Institute of Molecular Biology and Biotechnology (IMBB), CRiMM, The University of Lahore, Lahore Pakistan.

***Corresponding Author:** Dr. Binish Zaidi
*Email: biniahzaidi@gmail.com Cell: +92 300 7311244

ABSTRACT

Background: Urinary bladder carcinoma is a prevalent malignancy worldwide, requiring early and accurate detection for effective management. Conventional cystoscopy is the gold standard for diagnosis but is invasive, associated with discomfort, and carries procedural risks. CT Virtual Cystoscopy (CTVC) has emerged as a promising, non-invasive imaging technique for detecting bladder carcinoma.

Objectives: The aim of current study was to evaluate the diagnostic accuracy of CTVC in detecting urinary bladder carcinoma using conventional cystoscopy as the gold standard.

Methods: This cross-sectional validation study was conducted at Faisalabad Medical University and Allied Hospital, enrolling n=95 patients aged 25–70 years presenting with gross painless hematuria. All patients underwent CTVC followed by conventional cystoscopy for comparison. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy were calculated using a 2×2 contingency table. Stratification was performed based on age and gender, and a p-value ≤ 0.05 was considered statistically significant.

Results: CTVC demonstrated a sensitivity of 86.49%, specificity of 93.10%, PPV of 88.89%, and NPV of 91.53%, with an overall accuracy of 90.53%. Stratified analysis revealed 100% accuracy in patients aged 25–55 years and 90.62% accuracy in those aged 56–70 years. Gender-based stratification showed slightly higher accuracy in female patients (94.12%) than in males (89.74%).

Conclusion: CT Virtual Cystoscopy is a highly accurate, non-invasive diagnostic modality for detecting urinary bladder carcinoma, offering a viable alternative to conventional cystoscopy. Given its high sensitivity, specificity, and diagnostic accuracy, CTVC can be integrated into routine clinical practice for early detection and follow-up of bladder cancer patients. Future research should focus on multi-center trials, AI-assisted imaging, and biomarker integration to further enhance diagnostic efficiency.

Keywords: Bladder Cancer, CT Virtual Cystoscopy, Conventional Cystoscopy, Diagnostic Accuracy, Non-Invasive Imaging, Sensitivity and Specificity, Urinary Tract Neoplasms

INTRODUCTION

The urinary bladder carcinoma is a significant health problem worldwide, being the ninth most common cancer and the seventh most common in men. Global incidence rates are 10.1 per 100,000 for men and 2.5 per 100,000 for women, where the incidence is affected by geographical, environmental, and occupational exposures [1]. Bladder cancer is increasingly being recognized as a public health problem in Pakistan, and national registries are still lacking in providing precise epidemiologic data. Given an aging population, rising tobacco use, and industrial expansion increasing exposure of workers to chemical carcinogens, the burden of bladder cancer in Pakistan is also likely to be underreported and increasing. Additionally, late-stage diagnoses are due to inadequate cancer awareness, lack of healthcare-seeking behaviour, and poor prognosis with high mortality [2].

Bladder carcinoma is a multifactorial disease, and the pathogenesis of its disease is well established. In Pakistan, where cigarette consumption is on the increase, accounting for more than half of all bladder cancer cases worldwide, tobacco smoking is a growing concern, and alternative tobacco products such as gutka, naswar, and betel quid have their carcinogenic compounds. Occupational exposure to hazardous chemicals such as aromatic amines, benzidine derivatives, and heavy metals is also an important risk, especially in Pakistan's dye, rubber, leather, and textile industries [3]. Out of poor occupational safety measures and weak regulatory enforcement in the country's industrial sector, low-income labourers are increasingly exposed to bladder carcinogens. Pelvic irradiation, chronic cystitis, Schistosomiasis, genetic predisposition, and human papillomavirus (HPV) infection are also other factors that may contribute to the development of cervical cancer, and the impact of these risk factors is different in different populations because of disparities in lifestyle, environmental pollutants, and healthcare accessibility [4].

In the majority of patients, the classical clinical presentation of bladder carcinoma is gross, painless hematuria. Nevertheless, hematuria is a nonspecific symptom with a wide differential diagnosis, including urinary tract infections, nephrolithiasis, benign prostatic hyperplasia, and glomerulonephritis, and therefore precise diagnostic evaluation is necessary [5]. Imaging modalities such as Excretory Urography (EU), ultrasonography, computed tomography (CT), retrograde ureterography, conventional cystoscopy, and ureteroscopy have been used for diagnostic purposes. Nevertheless, direct visualization and biopsy sampling capabilities of conventional cystoscopy continue to be the gold standard for bladder cancer detection. However, conventional cystoscopy is an invasive, expensive, and painful procedure with a risk of urinary tract infection, urethral stricture, and postprocedural bleeding [6].

In resource-limited settings like Pakistan, access to specialized urological services is constrained, especially in rural areas, which results in delays in diagnosis and treatment. Additionally, many patients are discouraged from seeking timely medical evaluation because of financial barriers and lack of insurance coverage. The challenges presented above underscore the requirement for an inexpensive, non-invasive, and widely accessible method of bladder cancer detection [7].

Compared with conventional cystoscopy, Computed Tomography Virtual Cystoscopy (CTVC) has become a promising non-invasive alternative based on the advancement of cross-sectional imaging techniques. Multidetector CT scanners are used by CTVC to generate three-dimensional endoluminal reconstructions of the bladder to perform a precise evaluation of bladder wall lesions. Sensitivity and specificity values reported in the literature vary from 60—to 100% and are highly concordant with findings of conventional cystoscopy. In addition, rigid cystoscopy is limited in its visualization of such anatomical regions as the bladder, neck, and diverticula, where CTVC offers better visualization. Being important, it eliminates the risk of infection, discomfort, and complications related to invasive cystoscopic procedures [8, 9].

Nevertheless, CTVC has some drawbacks: it has lower sensitivity for detecting carcinoma in situ (CIS) and does not distinguish benign inflammatory changes from early carcinomas. However, there have been several studies that suggest that CTVC is as good as conventional cystoscopy, especially for detecting papillary bladder tumors, and one study reported a sensitivity and specificity of 92% each. As bladder cancer is on the rise, healthcare infrastructure is not developed and is also very expensive. CTVC is a good alternative that could help in early detection and improve clinical outcomes of the patients, particularly in the areas where there is no progress [10].

Although CTVC is increasingly shown to be of use in bladder cancer detection internationally, there is little local data as to its diagnostic accuracy. No large-scale studies have been done in Pakistan to assess its effectiveness, feasibility, and potential for integration into routine clinical practice. As bladder cancer is a high-burden disease and there are limited skilled urologists and financial constraints of invasive procedures, it is important to assess the diagnostic accuracy of CTVC in a local population. If CTVC has high sensitivity and specificity, it could thus be an inexpensive, non-invasive alternative that could be used particularly for patients with painless hematuria, thereby reducing diagnostic delays, improving cancer surveillance, and lowering healthcare costs [11, 12].

The purpose of this study was to assess the CTVC in the diagnosis of urinary bladder carcinoma using conventional cystoscopy as the gold standard. The establishment of CTVC as a reliable diagnostic alternative could have a role in reducing patient discomfort, reducing financial burden, and facilitating early diagnosis, which would improve morbidity and mortality outcomes of bladder cancer in Pakistan [13].

MATERIALS AND METHODS

Study Design and Setting:

A Cross-sectional validation of this study was done at the Department of Diagnostic Radiology, Faisalabad Medical University and Allied Hospital, Faisalabad, from October 1, 2018, to July 29, 2022. The study's purpose was to evaluate the diagnostic accuracy of CT Virtual Cystoscopy (CTVC) for detecting urinary bladder carcinoma vs. conventional cystoscopy. A total of 95 patients were recruited by a nonprobability consecutive sampling technique. Sensitivity of 92%, specificity of 92%, and expected bladder carcinoma prevalence of 33.3% were used to calculate sample size with a 95% confidence level and 8% absolute precision to obtain a statistically significant sample.

Patient Selection:

The patients considered for the study were between 25 and 70 years old, with gross painless hematuria confirmed by urine analysis. Patients of both sexes were eligible. Pregnant women were excluded, as one could be exposed to potential radiation exposure risks from CT scanning, and patients who were claustrophobic and unable to tolerate the enclosed space of a CT scanner were also excluded. The Institutional Ethical Review Committee approved the study, and written informed consent was obtained from all patients before inclusion. All procedures were carried out according to the ethical guidelines for human research, and patient confidentiality was strictly maintained.

Procedure:

CT Virtual Cystoscopy (CTVC) was followed 1 day later by conventional cystoscopy. A CTVC procedure started with the drainage of residual urine with a 12 Fr Foley catheter; the bladder was insufflated with 300-400 mL of room air with a 60cc syringe and clamp to ensure maximal bladder distention. To ensure adequate bladder filling, a scout CT scan was done. After that, the single breath-hold Multidetector CT scan (BrightSpeed, GE Healthcare) was done with 1 mm collimation, 120 kV tube voltage, 250 mA tube current, and a table speed of 7–10 mm/sec, and images reconstructed at 1.25 mm intervals were used to obtain high-resolution intraluminal views of the bladder. To better visualize the scan, identical CT parameters were used, and the scan was repeated in the prone position. Specialized software for interactive intraluminal navigation with volume rendering algorithms was used to analyze the obtained CT images. An Independent review of the CTVC images by a radiologist and urologist was carried out, which was blinded to conventional cystoscopy findings. Discrepancies were resolved by consensus of their interpretations.

The morphological characteristics of the lesions seen on CTVC were then classified. Those that appeared taller than wide were defined as polypoidal lesions, whereas those with broad bases were called sessile lesions. A discrete mass was also noted, and the bladder was found to be thickened without a mass. Each lesion was documented for comparison with conventional cystoscopy findings regarding the number, size, location, and morphology. All patients were then subjected to conventional cystoscopy by a consultant urologist using rigid wide-angle telescopes following CTVC. Systemic examination of the bladder mucosa was carried out, and any suspicious lesions were biopsied for histopathological confirmation. Diagrams or video documentation were used to record findings for accuracy.

Data Analysis:

SPSS version 25.0 was used to analyze all the collected data. The quantitative variables (patient age) were expressed as mean±SD, and the categorical variables (gender distribution, presence of bladder carcinoma) were described as frequencies and percentages. The diagnostic accuracy was assessed by a 2×2 contingency table in which sensitivity is calculated as (True Positives / (True Positives + False Negatives)) × 100 and specificity as (True Negatives / (True Negatives + False Positives)) × 100. The positive predictive value (PPV) was calculated as (True Positives / (True Positives + False Positives)) * 100 and the negative predictive value (NPV) as (True Negatives / (True Negatives + False Negatives)) * 100. Overall diagnostic accuracy was calculated as (True Positives + True Negatives) / Total Patients × 100, and the likelihood ratio was analyzed to evaluate the diagnostic strength of CTVC vs. conventional cystoscopy.

To avoid the introduction of confounding factors, stratification was performed by age and gender to minimize the variability of diagnostic accuracy across patient demographics. A p-value ≤ 0.05 was used for statistical validation of the study results, and post-stratification diagnostic accuracy was analyzed.

RESULTS

The accuracy of CT Virtual Cystoscopy (CTVC) in the diagnosis of urinary bladder carcinoma was determined compared to conventional cystoscopy as the gold standard in 95 cases fulfilling the selection criteria.

The age distribution of the study population was 21.05% (n=20) of patients were between 25 and 55 years, and 78.95% (n=75) were between 56 and 70 years. The majority of the participants were in the older age group with a mean ± SD of 58.04 ± 5.34 years. The predominance of bladder carcinoma in older individuals is well-established in the literature, as age-related changes in bladder epithelium and prolonged exposure to carcinogens contribute to disease progression (Table No. 1).

TABLE No. 1: AGE DISTRIBUTION
(n=95)

Age (in years)	No. of Patients	%
25-55	20	21.05
56-70	75	78.95
Total	**95**	**100**
Mean ± SD	**58.04 ± 5.34**	

The gender distribution showed that the number of participants was mostly male (82.11%, n:78), and 17.89% (n:17) were female. Global epidemiological trends of bladder carcinoma cases, as well as the male predominance, are consistent with the increased exposure to carcinogenic substances, such as tobacco smoke and industrial chemicals (Table No. 2), and thus the male predominance of bladder carcinoma cases.

TABLE No. 2: GENDER DISTRIBUTION
(n=95)

Gender	No. of Patients	%
Male	78	82.11
Female	17	17.89
Total	**95**	**100**

The frequency of morbidity by conventional cystoscopy was recorded as 38.95% (n=37), and 61.05% (n=58) had no findings of morbidity. The detection rate of this study is consistent with the detection rates expected for hematuria in high-risk populations (Table No. 3), which further supports the need for efficient diagnostic tools such as CTVC for early detection and treatment of bladder carcinoma.

TABLE No. 3: FREQUENCY OF BLADDER CARCINOMA (n=95)

Bladder Carcinoma	No. of Patients	%
Yes	37	38.95
No	58	61.05
Total	**95**	**100**

To evaluate the frequency and accuracy of CT Virtual Cystoscopy in diagnosing urinary bladder carcinoma as compared with conventional cystoscopy as the gold standard. The accuracy of the findings was 90.53%, sensitivity 86.49%, specificity 93.10%, positive predictive value (PPV) 88.89%, and negative predictive value (NPV) 91.53%. The value of 12.53 indicated that the CTVC is highly effective in distinguishing malignant lesions from benign findings. These results are consistent with previous research suggesting that CTVC is a useful noninvasive diagnostic tool for bladder carcinoma in situations in which conventional cystoscopy is either contraindicated or unfeasible (Table No. 4).

TABLE No. 4: DIAGNOSTIC ACCURACY OF CT VIRTUAL CYSTOSCOPY (n=95)

CT Virtual Cystoscopy	Bladder Carcinoma (Positive)	Bladder Carcinoma (Negative)	Total
Positive	True Positive (32)	False Positive (4)	36
Negative	False Negative (5)	True Negative (54)	59
Total	37	58	95

**Sensitivity = 86.49%*
**Specificity = 93.10%*
**Positive Predictive Value (PPV) = 88.89%*
**Negative Predictive Value (NPV) = 91.53%*
**Overall Accuracy = 90.53%*
**Likelihood Ratio = 12.53*

To control for possible confounding variables, stratification by age and gender was achieved. The sensitivity, specificity, PPV, NPV, and accuracy were all at 100% among patients aged 25-55 years, indicating that CTVC is a good method for detecting bladder carcinoma in younger individuals. The sensitivity, specificity, PPV, NPV, and overall accuracy of the method for patients aged 56-70 years were 83.87%, 93.02%, 86.67%, 88.89%, and 90.62%, respectively (Table No 5), which was high for different age groups.

TABLE No. 5: STRATIFICATION FOR AGE

Age Group	Sensitivity	Specificity	PPV	NPV	Accuracy	P-value
25-55 yrs	100%	100%	100%	100%	100%	<0.0001
56-70 yrs	83.87%	93.02%	86.67%	88.89%	90.62%	<0.0001

Stratified by gender, male patients had a sensitivity of 86.67%, a specificity of 91.67%, and an accuracy of 89.74%. In the female subjects, CTVC proved to be sensitive (85.71%), specific (100%), and accurate overall (94.12%), indicating that CTVC is accurate in both sexes (Table No. 6).

TABLE No. 6: STRATIFICATION FOR GENDER

Gender	Sensitivity	Specificity	PPV	NPV	Accuracy	P-value
Male	86.67%	91.67%	86.67%	91.67%	89.74%	<0.0001
Female	85.71%	100%	100%	90.91%	94.12%	0.0003

This study strongly supports the use of CT Virtual Cystoscopy as a noninvasive diagnostic modality with high sensitivity, specificity, and predictive values. As an alternative to conventional cystoscopy, its ability to detect bladder carcinoma with minimal discomfort to the patient makes this a good alternative for patients in resource-limited settings or those who cannot tolerate invasive procedures.

DISCUSSION

Early detection is important for patient prognosis of urinary bladder carcinoma, which is one of the most prevalent malignancies around the world. Although conventional cystoscopy remains the gold standard for bladder cancer diagnosis, its invasiveness, associated complications, and patient discomfort demand alternative means of diagnosis [14]. This study finding indicates that CT Virtual Cystoscopy (CTVC) is a reliable, noninvasive diagnostic tool for urinary bladder carcinoma. The sensitivity and specificity of CTVC compared with conventional cystoscopy were high, and CTVC is a promising alternative, especially in patients who cannot be exposed to invasive procedures [15].

The sensitivity of CTVC in this study was 86.49%, close to previous studies that have reported sensitivity values for CTVC of 85–95% in the detection of bladder carcinoma. This confirms that CTVC can identify bladder tumors, especially those larger than 5 mm in size. The specificity of CTVC in this study was 93.10%, similar to previously published values of 89-96%. Further evidence of the reliability of CTVC in distinguishing benign from malignant bladder lesions includes a positive predictive value of 88.89% and a negative predictive value of 91.53%. This is in agreement with other studies that validated CTVC as a useful tool for bladder cancer detection with an overall diagnostic accuracy of 90.53% [16].

CTVC provides accurate three-dimensional intraluminal views of the bladder as well as multiplanar reconstructions, which further enhance its accuracy in evaluating tumor size, morphology, and anatomical location. Additionally, CTVC visualized tumors within the bladder neck, diverticula, and along the posterior bladder wall better than conventional cystoscopy. Nevertheless, a major disadvantage of CTVC is its decreased sensitivity for the detection of flat carcinoma in situ (CIS), as the absence of mass formation has been confirmed in previous studies[17, 18].

Stratification analysis according to age showed 100% accuracy in detecting bladder carcinoma in the age group < 56 years while 90.62% accuracy in > 56 years of age. This implies that CTVC may be especially effective in younger patients, who generally have focal tumors and well-defined tumors, as opposed to older patients who present with diffuse bladder wall thickening, bladder trabeculation, or mucosal inflammation, all of which can obscure tumor visualization on CTVC images. Also, we found that CTVC slightly outperformed in female patients (accuracy: 94.12%) than in male patients (accuracy: 89.74%). This discrepancy could be explained by anatomical variations; male patients having benign prostatic hyperplasia (BPH) or other lower urinary tract conditions may have irregular bladder wall thickening, which may make it difficult to differentiate from malignancy [19, 20].

CTVC offers several advantages over other imaging techniques, such as ultrasound and traditional CT urography. Since ultrasound is the first-line imaging modality for hematuria, it is not able to detect small bladder tumors (<1 cm) and thus has high false negative rates. CTVC has also been explored as a means for bladder cancer detection, using Magnetic Resonance (MR) Cystography, which showed promising results, but with its cost, longer scan time, and limited availability, it is not as practical as CTVC. Unlike conventional CT urography, CTVC is more effective in detecting intraluminal lesions and provides detailed mucosal imaging of the bladder [21].

CTVC offers one of the major advantages of a non-invasive, more comfortable, and less risky procedure compared to the conventional cystoscopy. Frequent follow-ups are often deterred by patients due to the discomfort and post-procedure urinary tract infections and hematuria that are

commonplace with conventional cystoscopy. However, CTVC does not require catheterization, thus the need for iatrogenic infection and rapid, high-resolution imaging [22].
However, this study has several limitations due to its promising role in bladder cancer diagnostics. The major limitation is that CTVC cannot detect carcinoma in situ (CIS) lesions, which are best identified by fluorescence cystoscopy or urinary biomarkers. A potential limitation is that bladder distension with air insufflation during CTVC may cause tumors to appear slightly larger than their actual size and overdiagnose. In addition, CTVC may result in false positive images in inflammatory bladder conditions such as chronic cystitis, tuberculosis, and radiation-induced bladder wall thickening mimicking malignancy [23]. Also, CTVC does not provide for direct tissue biopsy, so conventional cystoscopy is still required in suspected cases for confirmation of histopathology. A further limitation of CTVC is the potential for radiation exposure, which has been greatly lessened by modern low-dose CT protocols but can still be dangerous for those patients who need repeated imaging. Overall, the results of this study should be confirmed by larger multi-center cohorts [24].
Finally, several prospects and clinical applications of CTVC should be considered looking ahead. CTVC has the high sensitivity and specificity to be added to bladder cancer screening programs for high-risk populations, such as chronic smokers, industrial workers exposed to carcinogens, and patients with recurrent hematuria [25]. In addition, CTVC can be used as a noninvasive follow-up tool for bladder cancer patients, especially for patients with nonmuscle invasive bladder cancer (NMIBC), to decrease the number of invasive cystoscopies. Automated tumor detection with artificial intelligence and machine learning algorithms integrated into CTVC imaging has the potential to improve diagnostic accuracy and decrease inter-observer variability. In addition, combining CTVC with urinary biomarkers, including NMP22, UroVysion FISH, and microsatellite assays, can increase early detection rates and decrease false positives. Future research also includes the development of ultra-low dose CT protocols that would significantly reduce radiation exposure while maintaining high diagnostic accuracy [26].

Conclusion:

The results of this study support CT Virtual Cystoscopy as a highly accurate, non-invasive imaging modality for the detection of urinary bladder carcinoma. Reinforcing CTVC's diagnostic value, especially in patients who may not tolerate invasive cystoscopic procedures, the high sensitivity (86.49%) and specificity (93.10%) observed are also reported. Despite its limitations, CTVC offers significant advantages in terms of patient comfort, diagnostic efficiency, and clinical applicability. These findings are further validated in multi-center trials with larger sample sizes to validate these findings and to refine CTVC protocols for large-scale clinical implementation. CTVC holds promise for future advancements such as artificial intelligence-driven analysis as well as biomarker integration to further increase its diagnostic power to become a hallmark in bladder cancer diagnosis and surveillance.

Conflict of interest:

The authors declared no conflict of interest for the publication of the current study.

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Authors' Contributions:

SR: Conceptualization, study design, manuscript drafting
BZ: Data collection, methodology, statistical analysis
HF: Literature review, manuscript writing, results interpretation
SG: Supervision, critical revision, approval of the final manuscript
R: Data validation, manuscript editing, discussion writing
SS, AS: Manuscript formatting, reference management, proofreading
All authors have read and approved the final manuscript.

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Data Availability:
The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

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