Original Article

Diagnostic Accuracy of Retrograde Urethrogram in Determination of Urethral Stricture taking Cystoscopy as Gold Standard

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ABSTRACT

Objective: To assess the diagnostic accuracy of retrograde urethrogram in determination of urethral strictures taking cystoscopy as the gold standard.

Methodology: This cross-sectional study was conducted at the Department of Radiology, Sharif Medical & Dental College, Lahore from May to October 2024. After ethical approval and written informed consent, 189 patients meeting the inclusion criteria were recruited through non-probability convenience sampling technique. These patients underwent retrograde urethrogram (RUG) with contrast injection, followed by cystoscopy 4-5 days later. Demographic details and history of risk factors were recorded. Radiographic findings were assessed by a radiologist, and patients were classified as positive or negative for urethral strictures. Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 25. A 2x2 table was made and diagnostic accuracy was calculated. Chi-square test was used to compare categorical variables.

Results: Retrograde urethrogram detected urethral strictures in 24.3% of cases with a sensitivity of 75.56%, specificity of 91.67%, positive predictive value (PPV) of 73.91%, and negative predictive value (NPV) of 92.31%. The overall diagnostic accuracy of RUG was 87.83%. Age groups, history of urinary tract infections, and prostate surgeries had significant association with the presence/absence of strictures on RUG ($p < 0.05$).

Conclusion: The diagnostic accuracy of retrograde urethrogram was high in determination of urethral strictures taking cystoscopy as the gold standard. Urethral strictures were significantly more prevalent among older males with history of urinary tract infections and prostate surgeries.

Keywords: *Urethral stricture. Cystoscopy. Contrast media. Iohexol.*

INTRODUCTION

The male urethra is an essential part of the urinary system, measuring approximately 20 cm in length, and it is surrounded by the corpus spongiosum, a vascular tissue that plays a critical role in maintaining the structure and function of the urethra. The urethra itself is divided into two primary sections: the anterior urethra and the posterior urethra, which are separated by the membranous urethra.[1] Each part of the urethra serves a unique function in the passage of urine from the bladder to the outside of the body.[2]

Urethral stricture is a condition characterized by the narrowing of the urethra, which can have a significant impact on a patient's quality of life. This condition develops slowly over time and can result in a variety of symptoms, including dysuria, weak urinary stream, incomplete bladder emptying, and urinary tract infections (UTIs).[3] In recent years, the incidence of iatrogenic urethral strictures has been increasing, primarily due to the rise in minimally invasive, transurethral urological procedures like cystoscopy and transurethral resection of the prostate (TURP).[4] Chronic inflammatory conditions such as lichen sclerosis, urinary tract infections, prolonged catheterization, and the increased cases of urethral traumas resulting from traffic accidents and workplace injuries are among other contributing factors.[5] Many complications including acute urinary retention, prostatitis, epididymo-orchitis, hydronephrosis, chronic kidney disease, peri-urethral abscess, and kidney stones can arise if the disease remains untreated for a longer duration.[6]

Various diagnostic techniques like uroflowmetry, cystoscopy, RUG, voiding cysto-urethrography (VCUG) can be useful in making diagnosis of urethral strictures and describing key characteristics like position & length of stricture and severity of condition. Cystoscopy, usually performed under anesthesia, makes the definitive diagnosis of urethral stricture. However, it cannot assess the length of the stricture and does not provide information about the condition of the surrounding tissue.[4] Retrograde urethrogram technique offers several advantages including its ability to provide real-time imaging of the urethra as contrast material is injected, allowing for dynamic assessment of the stricture's characteristics. It also enables the clinician to measure its length, which is a crucial factor in

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planning further treatment, such as urethral dilation, urethrotomy, or urethroplasty.[7]

A recent high number of urethral strictures is being reported in Pakistan due to increased prevalence of sexually transmitted diseases and improper catheterization techniques. Retrograde urethrogram is comparatively inexpensive, and less invasive technique for its diagnosis. It was pertinent to compare the diagnostic accuracy of RUG against the gold standard (cystoscopy) in our local setting to develop locally relevant diagnostic guidelines and improve patient outcomes.

METHODOLOGY

After approval from the institutional review board (Letter No. SMDC/SMRC/337-24, 22-05-2024), this cross-sectional study was carried out at the Department of Radiology, Sharif Medical & Dental College, Lahore from May to October 2024. A sample size of 189 was estimated using 90% confidence level, 7% margin of error, 100% sensitivity of RUG, 66.7% specificity, and prevalence of urethral strictures at 28.5%.[8] The male patients aged 18-75 years, who presented with restricted urinary flow from the bladder, urinary tract infection, or inflammation of the bladder, incomplete voiding, and/or painful urination were enrolled by using non-probability convenience sampling technique. Patients who had suggestive symptoms of acute urethritis, malignancy or metastatic disease, and received renal implant were excluded.

After obtaining written informed consent, demographic and risk factors detail [name, age, body mass index (BMI), duration of symptoms, marital status, occupation, history of diabetes, hypertension, smoking, urinary tract infection, and previous prostate surgery] were recorded on a questionnaire. The patients then underwent retrograde urethrogram in the right oblique or semi-lateral position after emptying the bladder. The right leg was partially flexed, with the left leg stretched above it and the left hip just above the table. A Foley's catheter was placed in the external meatus after disinfecting the glans, and 10-15 ml of 15% (w/v) Iohexol was injected through catheter. The patients were told to relax their pelvic floor muscles during the injection. The penile tip was pressed tightly around the catheter during injection to prevent the escape of contrast medium. A single spot film was taken with a constant film focus distance of 1 meter maintained for all radiographs. All scans were performed and interpreted by two consultant radiologists with at least 4 years of experience in radiology to improve accuracy. Patients were labeled as positive for urethral strictures if annular or longitudinal narrowing of the urethra was seen on radiographs.[9] After 4-5 days, cystoscopy was performed through the suprapubic tract, and the cystoscope was advanced through the bladder neck to the level of the stricture. Findings were recorded, and patients were confirmed for presence or absence of urethral strictures. The cases that were positive on both RUG and cystoscopy were labelled as true positives (TP). Those who were positive on RUG but negative on cystoscopy were false positives (FP). False negatives (FN) were negative on RUG but positive on cystoscopy. Those who were negative on both the tests were true negatives (TN).

STATISTICAL ANALYSIS

Data was entered and analyzed using Statistical Package for the Social Sciences (SPSS) version 25. Descriptive statistics like mean±standard deviation and frequency (percentage) were used for numeric and categorical variables, respectively. A 2x2 table was made by taking cystoscopy as a gold standard. The sensitivity, specificity, PPV, NPV, and diagnostic accuracy of RUG were calculated. The categorical variables were compared using Chi-square test. A p-value of <0.05 was considered statistically significant.

RESULTS

The study included 189 male participants and the mean age of the participants was 46.87±16.74 years, indicating a wide range of ages (from 30.9 to 63.6 years). Most of the participants (56.6%) belonged to 18-50 years age group. Nearly half (48.1%) of them were married and only 45% were employed. The mean BMI was 27.31±4.87 kg/m^2, suggesting that the majority of the participants were in the overweight range. The mean duration of symptoms was 11.70±6.72 weeks, reflecting that some participants experienced longer duration of symptoms than others. The frequency of urethral stricture on RUG was 24.3%. The age groups showed significant association with urethral strictures on RUG. Most of the patients with urethral strictures were older than 50 years (Table 1).

The risk factors profile of 189 participants revealed 47.6% diabetics, 40.7% hypertensive and 49.7% smokers. None of these factors had any significant association with urethral strictures on RUG ($p \geq 0.05$). Urethral stricture was significantly more prevalent among those with UTIs (16.9%) and history of prostate surgery (15.9%) (Table 1).

The cross-tabulation of cystoscopy and RUG outcomes showed significant results (Table 2).

Retrograde urethrogram showed a sensitivity of 75.56%, specificity of 91.67%, PPV of 73.91%, NPV of 92.31%, and an overall diagnostic accuracy of 87.83%.

DISCUSSION

This study aimed to evaluate the diagnostic accuracy of retrograde urethrography for detecting urethral strictures keeping cystoscopy as gold standard. The frequency of urethral stricture on RUG was 24.3%. The mean age of the participants was 46.87±16.74 years and most of the patients with urethral strictures on RUG were older than 50 years age (p=0.00001). Similarly, de Farias RB et al. showed that urethral strictures were significantly more frequent (82.2%) among patients over 40 years of age (p <0.001).[10] However, a previous study didn't reported any significant association of age with the occurrence of urethral strictures among post-TURP patients (p=0.932).[11] The results of the current study showed that hypertension, diabetes mellitus, and smoking had no significant association with the occurrence of urethral stricture on RUG. Contrary to our findings, diabetes mellitus (p=0.038) and hypertension (p=0.012) were significant risk factors in recurrence of urethral strictures among patients who underwent internal urethrotomy.[12]

Our significant results also revealed that the majority of cases of urethral strictures diagnosed on RUG had a history of UTI and prostate surgeries. Another study also reported that TURP represented 41% of all iatrogenic causes of urethral strictures. Infections accounted for 26.6% of cases.[13] Sekar et al. found that 12.8% patients who underwent TURP developed urethral strictures. They also revealed that the use of larger size Foley's catheter during this procedure was significantly associated with post-operative urethral strictures.[14]

When compared with cystoscopy as gold standard in our study, RUG had a sensitivity of 75.56%, specificity of 91.67%, positive predictive value of 73.91%, negative predictive value of 92.31%, and an overall accuracy of 87.83%. In a previous study, when RUG was compared with intraoperative findings as gold standard, it showed 100% sensitivity, 66.7% specificity and an overall accuracy of 83.3% in detecting urethral strictures.[8] Patel et al. also documented in their review of literature that RUG was the best technique in making diagnosis of urethral structures following urethral traumas.[15]

Table 1: Association of Risk Factors with Urethral Strictures on RUG (n=189)

Risk Factors		Urethral Stricture on RUG		Total	p-value
		Present (n=46)	Absent (n=143)		
Age Groups (Years)	**16-50**	09(4.8%)	98(51.9%)	107(56.7%)	0.00001*
	51-70	37(19.5%)	45(23.8%)	82(43.3%)	
	Total	46(24.3%)	143(75.7%)	189(100%)	
Urinary Tract Infections	**Yes**	32(16.9%)	57(30.2%)	89(47.1%)	0.0004*
	No	14(7.4%)	86(45.5%)	100(52.9%)	
	Total	46(24.3%)	143 (75.7%)	189(100%)	
History of Prostate Surgery	**Yes**	30(15.9%)	58(30.7%)	88(46.6%)	0.003*
	No	16(8.4%)	85(45%)	101(53.4%)	
	Total	46(24.3%)	143(75.7%)	189(100%)	

**Significant p-value*

Table 2: Cross Tabulation for Determining Diagnostic Accuracy of RUG in Diagnosis of Urethral Strictures taking Cystoscopy as Gold Standard

Retrograde Urethrogram	Cystoscopy (Gold Standard)		Total	p-value
	Positive	Negative		
Positive	34(18%) (TP)	12(6.3%) (FP)	46(24.3%)	0.00001*
Negative	11(5.8%) (FN)	132(69.9%) (TN)	143(75.7%)	
Total	45(23.8%)	144(76.2%)	189(100%)	

**Significant p-value*

In contrast to our findings, a study reported that RUG was used in combination with VCUG for the evaluation of urethral strictures. They found that combined preoperative use of RUG and VCUG underestimated urethral stricture measurements, especially in the membranous and bulbar regions, when compared with intraoperative results ($p < 0.05$).[16] A high level of diagnostic accuracy is especially important as the precise location and length of the stricture are critical for planning surgical interventions like simple urethral dilation, an internal urethrotomy, or a more complex urethral reconstruction, i.e. urethroplasty. Misjudging the length or location of the stricture can lead to suboptimal outcomes, such as incomplete stricture excision or recurrence of the stricture postoperatively.[16,17]

Despite its high diagnostic accuracy reported in the literature, RUG had limitations, particularly in its ability to provide critical and detailed information regarding the fibrosis of soft tissues surrounding the stricture, such as spongiofibrosis or periurethral fibrosis. This condition required a more extensive reconstruction, and failing to detect it preoperatively could result in inadequate treatment.[18] To address this limitation, alternative imaging modalities such as sonourethrography (SUG) and magnetic resonance urethrography (MRU) have been explored. Bogdanov et al. found that stricture measurements on RUG were significantly different than those of intraoperative findings. However, MRU results were significantly similar to those of intraoperative findings.[19] A study documented that MRU was significantly most accurate in preoperative evaluation of strictures, followed by cystourethrography (RUG and VCUG) when compared to intraoperative measurements. The least accurate was SUG in this regard.[9] In contrast, a previous study showed that SUG was the most accurate method with a sensitivity of 60% and specificity 87.8% when compared with VCUG and cystoscopy for determining the length of strictures.[17] Jesrani et al. also highlighted that SUG had a higher diagnostic accuracy in determination of urethral strictures as compared to RUG.[20] With advancements in technologies, artificial intelligence and machine learning were more accurate in the detection and reconstruction of urethral strictures.[21]

Our findings reflected the broad utility of RUG in clinical practice, where it can be used for assessing urethral strictures providing crucial information about the location, length, and severity of the stricture.

CONCLUSION

When compared with cystoscopy as gold standard, retrograde urethrography had a good diagnostic accuracy in determination of urethral strictures among males. Urethral strictures were significantly more prevalent among older males with history of urinary tract infections and prostate surgeries.

LIMITATIONS & RECOMMENDATIONS

This study had a few limitations: cross-sectional design, single-centered study, non-probability convenience sampling technique limiting the generalizability of results. This study also lacked information on detailed characteristics of the stricture and post-operative follow-up. Further research is needed to explore the role of advanced imaging modalities and the integration of RUG with other techniques in the comprehensive evaluation of urethral strictures, particularly in complex cases where precise assessment of soft tissue involvement is necessary.

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Authors' Contributions:
R.I: Supervised the overall project, reviewed the final manuscript critically for important intellectual content, and approved it for publication.
A.Q: Contributed to study design, methodology development, and critical revision of the manuscript.
H.B: Performed data analysis, interpretation, and drafted the initial manuscript.
H.M: Conceived and designed the study, supervised data collection.

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