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Address of Correspondence :
Editor, Bangladesh Journal of Urology, Room No. 464, 3rd floor
National Institute of Kidney Diseases & Urology, Sher-E-Bangla Nagar, Dhaka-1207, Bangladesh.
E-mail: baus_1988@yahoo.com

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EDITORIAL

CHANGING PRACTICE IN THE MANAGEMENT OF SMALL RENAL MASS

Small renal masses are defined as solid renal tumors that enhance on computed tomography (CT) and magnetic resonance imaging (MRI) and are suspected of being renal cell carcinomas (RCC). They are generally low-stage and relatively small (< 4 cm in diameter) at presentation. Recently throughout the world, as well as in Bangladesh, management of small renal mass has been changing. This is not only due to increasing diagnosis, but also for their varied biological behaviors, interpretation of various imaging modalities, tissue sampling and varied treatment options.

We do not have any statistics in Bangladesh. However in the United States in the year 2010, as estimated 58,000 new cases of RCC were diagnosed[1]. The rate is increasing by 3% to 4% per year as the use of CT and MRI increases[2,3]. On the other hand we see stage migration in renal tumour diagnosis, i.e. more tumours are now being discovered in clinical stage T1[4]. Currently, clinical T1 renal tumors account for 48% to 66% of cases[5]. The clinical presentation of RCC has also changed. Previously, systemic manifestations or paraneoplastic syndromes such as hypercalcemia or hypertension were more common in patients with metastatic renal cell carcinoma, so they were called internist tumour. Now most are discovered incidentally on CT or MRI done for various abdominal symptoms, so they termed now as radiologist tumour.

Small renal masses vary in biologic aggressiveness. Despite early diagnosis &and treatment, mortality from RCC has not been declined. This Suggest that many of these small renal mass does not require aggressive surgical treatment[6]. Data from larger series indicates that 20% of small renal masses are benign, such as oncocytoma, atypical or fat-poor angiomyolipoma, metanephric adenoma, urothelial carcinoma, metastatic lesions, lymphoma, renal abscess, renal infarction, mixed epithelial or stromal tumor, pseudotumor, and vascular malformations. Fifty five percent to 60% of small renal mass are indolent renal cell carcinomas and 20% to 25% have potentially aggressive features, defined by high nuclear grade or locally invasive characteristics[7,8,9].

Predictor of aggressiveness for small renal mass has been defined by some observer. Size directly correlates with the risk of malignant pathology. When tumours are less the < 1.0 cm, 38% to 46% are benign, and when > 7.0 cm, 6.3% to 7.1% are benign. But Size at presentation did not predict the growth rate[7]. 1.0-cm increase in tumor diameter correlates with a 16% increase in the risk of malignancy[10]. There have been no documented reports of disease progression in the absence of demonstrable tumor growth[11]. Type 2 papillary RCCs, mostly high grade and have worse prognosis compared with type 1 papillary RCCs. Chromophobe RCCs found to have better prognosis compared with papillary and clear cell RCCs[12].

Ultrasound is the most commonly used diagnostic technique and may be used in subsequent surveillance without radiation burden. Ultrasound has particular utility in the characterization of cystic masses, including hyperdense cysts that may pose a diagnostic challenge to CT. The sensitivity of ultrasound decreases with tumor size. At 1 cm, ultrasound was only able to identify 20% of masses, compared with 76% identified by CT. The detection rate becomes equal when the lesions measured 3.5 cm[13]. Contrast-enhanced ultrasound with intravascular microbubble contrast agents can assess enhancement of vascular elements within tissue and a detection specificity of 96.4% and a sensitivity of 77.3%[14,15]. Triple-phase CT is ideal, >15 Hounsfield units (HU) of enhancement on CT imaging are considered suggestive of RCC, < 10 HU of enhancement are more likely to be benign. Enhancement in the range of 10 to 15 HU is considered equivocal[16]. In CT scan angiomyolipoma merits a special attention. With rare exceptions, dense fat within a renal mass reliably indicates benign angiomyolipoma. Beyond this, no clinical or radiological feature ensures that a small renal mass is benign. MRI normally done when patient allergic to IV contrast or have moderate renal dysfunction.

Renal mass sampling has been done with percutaneous needle biopsy or cytotogy. These were not routinely performed previously due to over 18% false-negative

rates and potential morbidity[17]. A negative biopsy could not be trusted and renal mass sampling would not ultimately change patient management. Needle biopsy traditionally had a restricted role to diagnose renal lymphoma, carcinoma that had metastasized to the kidney and primary renal abscess. After 2001 renal mass sampling has become safer and more accurate than thought. A meta-analysis of contemporary series indicate that its accuracy in differentiating benign from malignant tumors is actually greater than 95%[18]. In addition, false-negative rates are now consistently less than 1%. When biopsy results are noninformative (10% cases) then biopsy can be repeated, or the mass can be surgically excised, or the patient can undergo conservative management if he or she is unfit or unwilling to undergo surgery. Serious complications requiring clinical intervention or hospitalization occur in less than 1% of cases. The risk of tumor seeding is now estimated to be less than 0.01%[18]. Recent studies have also indicated that molecular profiling through gene expression analysis or proteomic analysis can further improve the accuracy of renal mass sampling[19].

Radical Nephrectomy, partial nephrectomy, minimal invasive surgery, thermal ablation therapy and active surveillance all has been tried for small renal mass from time to time. The reference standard treatment of RCC is radical nephrectomy as defined by Robson et al. In 1969[20]. The cancer-specific survival rate for pT1a tumors is 97%[21]. However when technically feasible, partial nephrectomy gives equal oncologic outcome for TI lesions. Partial nephrectomy is more technically difficult as it involves renal reconstruction but conserves renal tissue. Radical nephrectomy is now indicated for technically unfavorable lesions because of their location and comorbidity[22]. Over the last decade, various studies have highlighted the association between radical nephrectomy and the subsequent clinical onset of chronic kidney disease, and and cardiovascular events and elevated mortality rates[23]. The situation is quite different in renal transplant, where donors undergo stringent screening to ensure that their general health is good and that their renal function is robust, both of which are not true in many patients with small renal masses, particularly if they are elderly. The overuse of radical nephrectomy prompted the AUA to commission a panel to provide guidelines for the management of clinical stage T1 renal masses. After an extensive review and rigorous meta-analysis, the panel concluded that partial nephrectomy is the gold standard for most patients[23]. Complication rates for partial nephrectomy are slightly greater than those for radical nephrectomy. Laparoscopic partial nephrectomy is a highly challenging surgical procedure that demands specialized laparoscopic training[24]. There appear to be equivalent functional and early oncologic outcomes[24]. Robot assisted laparoscopic partial nephrectomy is making the thing easier but at increasing cost.

Thermal Ablation therapy with radiofrequency ablation and cryoablation has been used in selected cases. They can be used with percutaneous, open or laparoscopic approach. Radiofrequency ablation (RFA) using a needle probe with temperatures up to 105pÿC causes cell death and coagulation necrosis[25]. 5-year actuarial metastasis-free and cancer-specific survival rates is around 95% and 99%, respectively[26]. However, there are concerns about the use of radiologic criteria for the assessment of tumor viability. Cryoablation, introduced in 1995 decreases tissue temperature to -40º C, destroying the tumor by cellular damage resulting from freezing, apoptosis, coagulation necrosis, and immunologic action[27]. Experience is limited for ablation of renal masses with high-intensity focused ultrasound. There is also no standard protocol recommendation for frequency of follow-up imaging after the ablation[28]. The majority of local recurrences after ablation have been successfully retreated by subsequent ablation[29].

Active surveillance involves careful initial monitoring for progression, with treatment delayed. The new term small renal mass has become increasingly relevant for today's urological practice. Many small renal masses are benign. Active surveillance is a relatively new approach for the treatment of renal tumors and is particularly indicated for elderly and infirm patients. It is recommended to biopsy before making a treatment decision in the event that the tumor is benign. Cross-sectional imaging of the abdomen with CT scan is usually performed at 3, 6, and 12 months; then every 6 months for 2 years and yearly thereafter[30,31]. Ultrasound or MRI is acceptable for patients with contraindications to CT. Chest radiography are performed annually to detect asymptomatic metastasis.

So, management for small renal mass has changed. An initial CT-or ultrasound-guided percutaneous biopsy should be considered for any patient with a newly diagnosed small renal mass. The treatment decision should be made after assessment of age, comorbidities, tumor characteristics (i.e., location and size), imaging characteristics, and histologic diagnosis, if available. In

this scenario, I emphasize to develop the skill of our histopathology diagnosis. Where possible, partial nephrectomy showed be consider as gold standard for removing small renal mass. Radical nephrectomy should be considered for technically unfavorable lesions because of their location and comorbidity. It showed not be done for only cosmetic reason using laparoscope or robot assistance, as chance of chronic kidney disease is high after radical nephrectomy. Thermal Ablation Therapy with Radio frequency ablation and Ablation can be used in selected cases. Active surveillance is a treatment option for many patients, particularly elderly and infirm patients.

Small renal masses are a distinct entity, and the clinical approach should be different from those previously established for renal cell carcinomas.

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Md. Jahangir Kabir
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Abbreviations:

RCC : Renal cell carcinoma
CT : Computed tomography

ORIGINAL ARTICLES

ANTIBIOTIC PROPHYLAXIS IN PROSTATE BIOPSY: A COMPARATIVE STUDY BETWEEN SINGLE DOSE & MULTIPLE DOSES OF CIPROFLOXACIN

MD. SIRAJUL ISLAM[1], MA AWAL[2], SM MAHBUB ALAM[3]

[1]Department of Urology, Sadar Hospital, Jhenidah, [2]Department of Urology, Dhaka Medical College Hospital

Abstract:

Objective: *To compare the effect of single dose and multiple doses of ciprofloxacin as prophylaxis for prostate biopsy.*

Method and material: *This was a prospective quasi-experimental study carried in the department of Urology, Dhaka Medical College Hospital over seventy patients undergoing prostate biopsy. Half of the patients received single dose of ciprofloxacin and the rest half received three doses of the same drug as antibiotic prophylaxis.*

Result: *Two patients from single dose group and one patient from multiple dose group developed urinary tract infection without any statistical significance*

Conclusion: *Single dose of ciprofloxacin has equal clinical and bacteriological efficacy as that of multiple doses of the same drug for prophylaxis in prostate biopsy.*

Key word: *TNBP(Trans-rectal needle biopsy of prostate).*

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Introduction:

Biopsy from the prostate is taken for the suspicion of malignancy stipulated by abnormal findings on digital rectal examination (DRE) or by raised prostate specific antigen (PSA) or by both. The trans rectal route is preferred to trnsperineal and transurethral routes because of its convenience of its being out patient procedure. But this advantage is associated with some infectious and traumatic complications.

Gut micro-organisms including E.coli, Enterobacter, Proteus and Klebsiella get access to the prostate tissue as the biopsy needle pierces the rectal mucosa during the procedure. Some Gram positive aerobes including Enterococci and Staphylococcus saprophyticus have also been identified[1]. So prevention of infection during this procedure is an important issue of serious consideration for the urologist and this goal can be achieved with judiciously selected antimicrobial prophylaxis that has been observed to have reduced the incidence of infection[2]. Antibiotic prophylaxis should have the property to eliminate or at least to decrease the incidence of infection to an acceptable level[3].

Keeping in mind the microbiological population responsible for infection in prostate biopsy, fluoroquionolones having a broad spectrum antibacterial activity and good absorption from gut can be a good choice for this purpose. Both multiple doses and single dose of this agent have been used throughout the world as prophylaxis for prostate biopsy. But the efficacy in preventing the infection has not differed significantly between multiple and single dose[4]. Many investigators found single dose antibiotic prophylaxis encouraging as it reduces the chance of developing antimicrobial resistance and for patient compliance and cost saving effect.

This quasi experimental study was designed to compare the efficacy and safety of single dose and multiple doses of ciprofloxacin as prophylaxis for prostate biopsy.

Materials and method:

The study was a quasi experimental one, conducted in the department of urology, Dhaka Medical College

Correspondences: Md. Sirajul Islam, Mobile-01711316666, e-mail- sirajulislam1961@yahoo.com

Hospital form January, 2006 to December, 2007. Patients having serum PSA>4 ng/ml, abnormal digital rectal examination or both, were included in this study. All these patients

were numbered chronologically and randomly allocated into group-A and group –B.Group- A included patients with odd number and was intended for three doses of ciprofloxacin. Group B included patients with even numbers and was intended for single dose of the same drug. Exclusion criteria were diabetes mellitus, hypersensitivity to quinolone antibiotic, uraemia, steroid therapy, indwelling urethral catheter, bleeding disorder and painful rectal pathology& rectal stenosis.Patients were evaluated by history, physical examination and pre-operative investigations. Investigations done preoperatively included urinalysis, urine culture and sensitivity, total count of WBC, random blood sugar, serum creatinine, bleeding-, coagulation- and prothrombin time, USG of KUB and prostate and ECG. Group A patients received three doses of ciprofloxacin 500 mg orally_ first dose one hour before the biopsy, 2nd dose twelve hours after the procedure and 3rd dose 24 hours after biopsy. Group B patients received single dose of 500 mg ciprofloxacin orally one hour before biopsy. Patients of both groups received single dose of laxative the night before biopsy. Patients on aspirin and antiplatelet therapy were asked to stop the medication one week before biopsy. Patients with urinary tract infection were treated with antibiotic according to culture sensitivity and biopsy was deferred for one week after treatment.

All the potential complications including fever greater than 101^0F, gross haematuria, urinary retention, rectal bleeding, urinary symptoms e.g. frequency, urgency, dysuria, suprapubic pain and flank pain were also explained to the patients. Patients developing urinary retention, fever greater than 101^0F and flank pain were asked to attend urology department immediately for evaluation and management.

Both ultrasound and digital guided eight to twelve core biopsies were performed using the Bard biopty gun and 18 gauge needle. Patients were asked to come for follow up on third and seventh POD. During follow up patients were questioned about fever, chill, urinary frequency, urgency, dysuria, haematuria, suprapubic pain, flank pain and rectal bleeding and were requested to submit urine for urinalysis and culture sensitivity and blood for total and differential count of WBC.

Pyuria was defined as the presence of $\geq$ 5 WBC / HPF in urine.

Positive urine culture was defined as the bacterial growth $\geq 10^5$ CFU /ml of urine.

Urinary tract infection was defined as positive urine culture on 3rd POD or 7th POD or both.

Clinical success was defined as the absence of clinical manifestation of genito-urinary infection evidenced by the rise of temperature >101^0F with or without frequency, urgency and dysuria.

Bacteriological success was defined as the negative culture (<10^5 CFU/ml) of urine either on 3rd or 7th POD or on both.

Data were collected in a predesigned and pre-tested sheet and processed and analyzed using software SPSS (statistical package for social science). The test of statistical significance employed to analyze the data were Chi-square (c^2) or Fisher's exact probability test and student's't'-test. For all analytical tests, the level of significance was set at 0.05 and $p < 0.05$ was considered significant.

Results:

A total of 64 patients out of 70 were available for final data analysis. Six patients, 2 from group- A and 4 from group-B were not included in final data analysis for violation of study protocol. Of these 64 subjects, a total of 3, 1 from group- A and 2 from group- B, developed clinical as well as bacteriological evidence of urinary tract infection and were treated with antibiotic according to culture and sensitivity report. Three patients, 1 from group- A and 2 from group- B, who developed urinary retention, were managed by temporary catheterization. Four patients, 2 from each group, developed gross haematuria and were advised to take plenty of fluid by mouth. Three patients, 1 from group A and 2 from group-B developed per-rectal bleeding and resolved spontaneously. None having bleeding needed blood transfusion.

Mean age of the groups were 64 ± 6.3 and 64 ± 5.4 years respectively. No significant difference of mean age between groups was found by doing student's't' test. Prostate volume of the patients was also recorded and was found almost similar between groups (Fig-1).

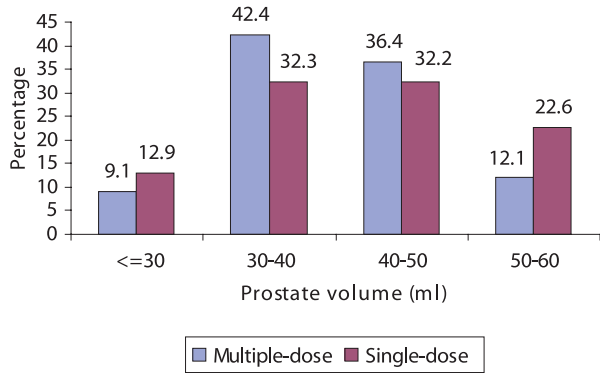

Fig. 1: *Comparison of prostate volume between groups (n = 64)*

Clinical findings of the patients including frequency, urgency, suprapubic pain, dysuria, chills, flank pain and fever (Temperature $\geq 101^0$F) were recorded on 3rd POD (Table- I) and were compared between groups. In group-A, observed findings were—frequency in 9 (27.3%), urgency in 5 (15.2%), suprapubic pain in none, dysuria in 3 (9.1%), chills in 2 (6.1%), flank pain in 1(3.0%) and fever in 1 (3.0%) patients. While in group-B, the observed findings were—frequency in 5 (16.1%), urgency in 2 (6.5%), suprapubic pain in 1 (3.2%), dyusuria in 5 (16.1%) fever in 2 (6.5%) and chills and flank pain were nil. These findings were compared between groups using Fisher's exact test and chi-square test and no significant difference was found

Table-I

Comparison of postoperative clinical findings between groups on 3rd POD

Postoperative variables	Regimen		p-value
	Multiple-dose (n = 33)	Single-dose (n = 31)	
Urinary frequency¶	9(27.3)	5(16.1)	0.281
Urgency#	5(15.2)	2(6.5)	0.240
Suprapubic pain#	00	1 (3.2)	0.484
Dysuria¶	3(9.1)	5(16.1)	0.319
Chills#	2(6.1)	00	0.262
Flank pain#	1(3.0)	00	0.516
Fever# (Temperature $\geq 101^0$ F)	1(3.0)	2(6.5)	0.484

Figures in the parenthesis denote corresponding percentage.
Data were analyzed using Fisher's Test; ¶Data were analyzed using Chi-square (χ^2) Test.

The same clinical characteristics were also observed on the 7th POD (Table-II) as were done on the 3rd POD. In both groups urinary frequency, urgency and dysuria decreased substantially while suprapubic pain, chills, flank pain and fever disappeared completely. The findings were also compared between groups using Fisher's exact test and no significant difference was observed between groups.

Table II

Comparison of postoperative findings between groups on 7th POD

Postoperative variables	Regimen		p-value
	Multiple-dose (n = 33)	Single-dose (n = 31)	
Urinary frequency¶	3(9.1)	2(6.5)	0.481
Urgency#	1(3.2)	1 (3.2)	0.955
Dysuria#	1(3.2)	2(6.5)	0.549

Figures in the parenthesis denote corresponding percentage.
Data were analyzed using Fisher's Test.

Table III

Comparison of laboratory findings on 3rd postoperative day

Variables	Regimen	
	Multiple-dose (n = 33)	Single-dose (n = 31)
Positive urine culture (Bacterial count $\geq 10^5$ colony forming unit/ml)	1(3.0)	1(3.5)
Pyuria (pus cell e" 5/HPF)	2(6.1)	3(9.7)
Leucocytosis (WBC $\geq 11000/mm^3$	1(3.0)	2(6.5)

Figures in the parenthesis denote corresponding percentage.

Investigations including urine-R/E &C/S and total count of WBC were done on 3rd and 7th POD.

On 3rd POD, in group- A, only 1 (3.0%) patient developed positive urine culture, 2 (6.1%) patients had pyuria and 1 (3%) developed leucocytosis while in group-B, out of 31 patients, 1(3.0%) developed positive urine culture, 3 (9.7%) had pyuria and 2 (6.5%) developed leucocytosis.The findings were compared between

groups using Fisher's test and no significant difference was observed (Table- III)

Table- IV
Comparison of laboratory findings on 7th postoperative day

Variables	Regimen	
	Multiple-dose (n = 33)	Single-dose (n = 31)
Positive urine culture (Bacterial count $\geq 10^5$ colony forming unit/ml)	0(0.0)	1(3.2)
Pyuria (pus cell e" 5/HPF)	1(3.0)	2(6.5)
Leucocytosis (WBC $\geq$ 11000/mm^3)	1(3.0)	1(3.2)

Figures in the parenthesis denote corresponding percentage.

On 7th POD, in group-A, none developed positive urine culture, 1 (3%) had pyuria and 1(3%) developed leucocytosis while in group-B, 1(3.2%) developed positive urine culture, 2 (6.5%) had pyuria and 1(3.2%) developed leucocytosis (Table-IV) and no significant difference was observed between groups in respect of these findings.

Table V
Comparison of clinical outcome between groups.

Clinical response#	Regimen		p-value
	Multiple-dose (n = 33)	Single-dose (n = 31)	
Success	32(97.0)	29(93.5)	0.476
Failure	1(3.0)	2(6.5)	

Figure in the parentheses denoted corresponding percentage

Data were analyzed using Chi-square (χ^2)Test.

In this study, remaining afebrile or temperature less than 101^0F was considered clinical success of the prophylaxis. In group- A, only 1 (3%) patient developed temperature 101^0F while in group-B, 2(6.5%) patients developed the same feature. Clinical success was compared between groups using Chi-square ($\div^2$) test and the difference between groups was insignificant (p=0.476) (Table- V)

In this study only 1(3%) patient in group-A and 2(6.5%) patients in group-B developed positive urine culture (e"10^5 cfu/ml) (Table-VI). On comparison using chi-square ($\div^2$) the observed difference between groups was insignificant (P=0.476).

Table VI
Comparison of bacteriological response between groups (n = 64)

Bacteriological response	Regimen		p-value
	Multiple-dose (n = 33)	Single-dose (n = 31)	
Growth of bacteria	1(3.0)	2(6.5)	0.476
No growth of bacteria	32(97.0)	29(93.5)	

Figure in the parentheses denoted corresponding percentage

Data were analyzed using Chi-square (χ^2) Test.

Regarding complication, in group-A, only 1(3.0%) patient developed acute urinary retention, 2 (6.1%) patients noticed gross haematuria and 1(3%) patient developed per rectal bleeding while in group- B, 2 (6.5%) patients developed urinary retention, 2 (6.5%) patients noticed gross haematuria and 2 (6.5%) patients developed per rectal bleeding. On comparison using Fisher's exact test the difference between groups was insignificant (Pe" 0.05) (Table-VII).

Table VII
Postoperative complications between groups

Complications	Regimen	
	Multiple-dose (n = 33)	Single-dose (n = 31)
Urinary retention	1(3.0)	2(6.5)
Gross haematuria	2(6.1)	2(6.5)
Per-rectal bleeding	1(3.0)	2(6.5)

Discussion:

Since the beginning of past the century, biopsy of the prostate has been used to diagnose prostate cancer. Astraldi[5]did the first prostate biopsy through trans-rectal route in 1937. In his original description he did not find any complication without any antibiotic. In 1971 Wendell and Evan et al[4] first described the danger of infection particularly the risk of infection with coli form organisms. In 1980, Johnson et al[6] showed incidence of

bacteraemia in 73% cases and that of UTI in 51% cases after trans-rectal needle biopsy of prostate (TNBP) with no antimicrobial prophylaxis. So clinicians attempted to reduce rate of infection with prophylactic antibiotic and reported considerable success. Different prophylactic regimen of antibiotic has been studied both in oral and intravenous form giving rise to a variable opinion as to the choice of agent and dose schedule to be used. In 1987 ciprofloxacin became available and was found to have higher concentration in the prostatic tissue than the serum level, a key factor in preventing infection. In 1998, Shandera KC et al[7] demonstrated effectiveness of simple and inexpensive pre-biopsy preparation using single dose of ofloxacin. In 1998, Kapoor DA et.al[2] demonstrated the efficacy of single dose of ciprofloxacin in preventing infection in prostate biopsy.

On the 7th POD, suprapubic pain, chills, flank pain and fever disappeared totally while urinary frequency, urgency and dysuria declined substantially in both groups (Table-II). Most of the complications occurred in the early post operative day. This impression was supported by the study of Shandera KC et al[7] in which complications were detected within 5th POD, the febrile one earlier than the others. In the study of Machado MT et al[8], the febrile episodes were detected within first 48 hours and positive urine culture was found on the 3rd POD.

No significant difference was observed between groups (P= 0.470) in respect of UTI on 3rd POD (Table- III). UTI as evidenced by bacterial colony count $\geq 10^5$ CFU/ml.UTI was found in 3.0% and 3.5% patients of multiple doses and single dose group respectively. In the study of Schaeffer at al[9], positive urine culture (colony count $\geq 10^5$ CF U/ml) was found in 2% of the multiple doses and 5.2% of the single dose patient. In the study of Lindstedta et al[10]the incidence positive urine culture ($\geq 10^5$ CFU/ml) was 4.3% in the single dose treated patients. The incidence of positive urine culture ($\geq 10^5$ CF/ml) in the above mentioned studies are almost closer to the present study. In the study of Kapoor DA et al[2] (1998) 3% of single dose ciprofloxacin treated patients undergoing prostate biopsy had significant bacteriuria ($>10^4$ CFU/ml) developed clinical feature of infection.

The number of cases with positive urine culture, pyuria and leucocytosis reduced on 7th POD (Table-IV) than those noted on 3rd POD (Table- III). This was also consistent with the clinical findings observed on the corresponding day (Table- I & II).

No statistically significant difference was observed between group (P=0.476) when clinical evidence of infection (defined as temperature $\geq 101^0$F) was compared between groups (Table- I &II). Three percent of multiple doses group and 6.5% of the single dose group of patients developed clinical evidence of infection.

In the study of Machado MT et al [8]3.1% of the patients developed fever (101^0F) in single dose but 2.1% of the patient developed fever in multiple doses. In the study of Kapoor DA et al[2], the incidence of fever (temp > 101^0F) was noted in 2% of single dose ciprofloxacin treated patients. The study of Shandera KC et al[7]. Showed only 0.67% clinical evidence of infection using single dose of fluoroquinolone. Febrile complication (temperature $\geq 101^0$F) was observed in 2.9% patients in the study of Enlund AL et al[11]

During follow up only 1 (3%) patient of group-A and 2 (6.5%) patients of group-B developed urinary retention and no significant difference was observed between groups by doing statistical test (Table- VII). These patients were managed with catheterization. In the study of Enlund et al [11] , 0.2% subject developed urinary retention and in the study of Isen K et al [3] retention was noted in 2.7% of the subjects. Acute urinary retention was found in 0.25% of the patient in the study of Griffith BC et al (2002). Gross haematuria was noted in 2 (6.1%) patients of group-A and in 2 (6.5%) patients of group-B (Table- VII). Haematuria was noted in about 14.3% of the patients in the study of Isen K et al [3.] Per-rectal bleeding was observed in 1(3%) patients of group-A and in 2(6.5%) of group-B (Table- VII). The problem was noted in 6.36% of the patients in the study of Isen K et al [3] which is consistent with the present study. Only 0.25% patient developed per-rectal bleeding in the study of Griffith BC et al [11] which is much lower than that of the present study. In the study conducted by Enlund et al [13] the incidence of per-rectal bleeding was observed in 21.7% of the patients which is higher than that of the present study

Conclusion:

Trans-rectal needle biopsy of prostate is now a common urological procedure. To prevent infection, antibiotic prophylaxis with proper agent in adequate dose is something of immense value. Antibiotic prophylaxis with single dose of ciprofloxacin has equal clinical and bacteriological efficacy as multiple doses of the same drug in preventing infection and has cost saving effect and increased patient compliance.

Conflict of Interest : None Declared

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Abbreviations:

DRE : Digital Rectal Examination
PSA : Prostate Specific Antigan
UTI : Urinary Tract Infections

IMPACT OF TRANSURETHRAL RESECTION OF PROSTATE ON INTERNATIONAL PROSTATE SYMPTOM SCORE AND PEAK URINARY FLOW RATE

MD. WALIUL ISLAM[1], MD. ABUL HOSSAIN[2], MD. NURUL HOODA[1], KAZI RAFIQUL ABEDIN[1], HUSNE ARA[3]

[1]Department of Urology, NIKDU, Dhaka, [2]Dept. of Urology, ShSMC, Dhaka, [3]Dept. of Radiology and Imaging, DMCH, Dhaka

Abstract:

Objectives: *To evaluate urinary symptoms and quality of life in patient with BPH before and after TURP. To determine the impact of TURP on the urinary symptoms (IPSS) and peak urinary flow rate.*

Methods: *This study is prospective study carried out between 2010 and 2011 in the department of Urology, National Institute of Kidney Diseases & Urology. Total 102 cases were selected purposively according to selection criteria. Each patient was observed and followed up at 8 weeks (1st visit), 16 weeks (2nd visit) 24 weeks (3rd visit) after transurethral resection of prostate (TURP). IPSS score, QOL score also recorded and uroflowmetry was done to see the peak urinary flow rate (Q_{max}) of urine and voiding time. USG was done to see post voidal residual urine volume and DRE also done in selected cases. Data was complied and statistical analysis were done using computer based software, Statistical Package for Social Science (SPSS), using paired 't' test. A P value <0.05 was taken as significance.*

Results: *Before TURP, IPSS range 17-25 and mean 21.61±2.43, after TURP, range 0-7 and mean 4.27±1.71). Hence a significant improvement of IPSS was found from 2 months to 6 months follow up after TURP. The change was tested using "paired student 't' test". Before TURP Q_{max} range 7-12.2 and mean was 9.96±1.69, which became range 18-25 and mean was 22.61±2.28 after TURP and therefore change of mean Q_{max} was 12.64±2.69. The change was tested using "paired student 't' test". The change was found significant (P<0.001).*

Conclusion: *Transurethral resection of prostate resolves obstructive symptoms, rapid improvement of urinary flow rate*

Key words: *Benign prostatic hyperplasia, IPSS, peak urinary flow rate, TURP.*

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Introduction

Benign Prostatic Hyperplasia (BPH) is a common condition in middle-aged and elderly men and its prevalence increases with age (Berry et al., 1984). Symptoms of BPH are caused by mechanical and dynamic obstruction of urine flow. The mechanical obstruction is due to compression or intrusion into the urethra by the enlarging nodule of the prostate or by protrusion of The median lobe of prostate into the bladder neck and leading to higher bladder outlet resistance. Dynamic obstruction is caused by increasing muscle tone of the bladder neck and prostate, which is regulated by a-adrenergic receptor (Caine et al., 1975). A reduction tone might be expected to reduce prostatic urethral pressure and to improve obstructive symptoms. Benign Prostatic Hyperplasia (BPH) is associated with obstructive symptoms (like hesitancy, decrease force and narrow stream, sensation of incomplete bladder emptying, double voiding, straining to urinate, post void

Correspondences: Md. Waliul Islam, Department of Urology, NIKDU, Dhaka, E-mail: manf401@ovi.com

dribbling) and irritative symptoms (like urgency, frequency, nocturia) which may be troublesome to an elderly men.

The self-administered questionnaire developed by the American Urological Association (AUA) is both valid and reliable in identifying the need to treat patients and in monitoring their response to therapy (Barry et. al 1992). The IPSS symptom score questionnaire is perhaps the single most important tool used in the evaluation of patients with BPH.

The International Prostate Symptoms Score (IPSS) initiated the guideline panel for diagnosis and management of benign prostatic hyperplasia. Patients with mild symptoms (having a score of 0 to 7) were assigned to watchful waiting, those with moderate (8 to 19) or sever (20 to 35) symptoms would undergo farther testing and/ or treatment. The IPSS-7 symptom index is not diseases specific.

Transurethral resection of prostate (TURP) aimed at reducing the symptoms experienced by patients and their effects on quality of life (QOL). Quality of life measures are important because the same symptoms are not equally bothersome for all patients: getting up three times a night patient may have a significant impact on quality of life, whereas another patient may not find this a problem. Hence patient- reported symptoms must be supplemented by measures of their perception on quality of life (Luckacs et al., 1993).

There are many options for treatment of symptomatic BPH like watchful waiting, medical therapy with a a-receptor blocker and 5a-reductase inhibitor, phytotherapy and surgical treatment including minimally invasive therapy. Symptoms are best assessed by IPSS and peak urine flow (Q_{max}) rate and quality of life Score (Chapple, 1995). Watchful waiting should be considered when a symptom in mild (0-7). Medical treatment is usually chosen, when there are moderate symptoms and no absolute indication for surgical intervention (Abrams et al., 1997). Medical treatment is cost effective, time consuming, sometimes patients forget to take medicine regularly, co-morbidity increased, unwanted adverse effect (like postural hypotension, headache, dizziness etc.), total symptoms free not possible, chance of progression of disease.

Indication for surgical intervention are: failed medical treatment of BPH. and complications of an obstructing prostate- such as acute or chronic urinary retention, recurrent urinary tract infection, haematuria, bladder stone and postrenal azotemia. The most common reasons that intervention is recommended in a patient with symptoms of bladder outlet obstruction and irritability are that symptoms are moderate to sever, bothersome and interfere with the patients quality of life. 90% of patients under going a TURP had symptoms of prostatism, but 70% had another indication as well (eg. acute urinary retention) occurring in 27% (Mebust et al., 1989).

A surgical approach when indicated may reduce urinary symptoms, thus restoring a good quality of life (Sagnier at al., 1995).

As life expectancy increase in Bangladesh so, lower urinary tract symptoms due to benign prostatic hyperplasia also increasing. Treansurethral resection of prostate (TURP) is still considered as a gold standard treatment option for benign prostatic hyperplasia (BPH). So it is important to determine the impact of TURP on symptoms related to BPH.

Study Methods : This study is prospective study carried out between 2010 and 2011 in the department of Urology, National Institute of Kidney Diseases & Urology. Total 102 cases were selected purposively according to selection criteria with prostatic volume of >50 mL from the patients attending urology out patient department with lower urinary tract symptoms due to BPH. Each of the patient was followed up at 8 weeks (1^{st} visit), 16 weeks (2^{nd} visit) 24 weeks (3^{rd} visit).

Before TURP for base line study of each patient was evaluated by history, physical examination, digital rectal examination (DRE), International Prostate Symptoms Scoring (IPSS), Quality of Life Scoring (QOL) Urinalysis, volume of the prostate and post voidal residual urine (PVR) were determined by ultrasonogram.

Digital rectal examination was done to determine the prostate size and to exclude carcinoma prostate. Perinal sensation, anal tone and bulbocavernosus reflux were observed to detect any neurological lesions.

Urinalysis, if needed culture and sensitivity. Prostate specific antigen, serum creatinine were done in the same laboratory of NIKDU and out side reliable pathological laboratories to exclude urinary tract infection, carcinoma prostate and renal failure respective. Transabominal USG was done by the sonologist (Radiology Department, NIKDU and reliable out side Laboratories) to detect any hydronephrotic change, Post voidal residual urine, prostate size, echotexture, any hypoechoic lesion in

the prostate. Uroflowmetry was done with a voided volume of >200 mL. Plain x-ray KUB region was done to exclude urinary stone diseases cases, neuropathic bladder was excluded from the study.

All history and examination followed a similar protocol. Informed consent was taken from all patients. A detail data sheet was completed and this included particulars of the patient- history, results of physical examinations and relevant base line investigations. From the supplied sheet IPSS Symptoms Score and QOL score were determined (Salam, 1999).

Each patient was observed and followed up at 8 weeks (1st visit), 16 weeks (2nd visit) 24 weeks (3rd visit) after transurethral resection of prostate (TURP). On each follow up visit, each patient was evaluated by history to find out incontinence, retrograde ejaculation (Dry Coitus). IPSS score, QOL score also recorded and uroflowmetry was done to see the peak urinary flow rate (Q_{max}) of urine and voiding time. USG was done to see post voidal residual urine volume and DRE also done in selected cases. Improvement of lower urinary tract symptoms and quality of life was determined using IPSS score.

Improvement was based on the changes from base line in symptoms, urinary flow rate, amount of post voidal residual urine and quality of life. Urine flow rate was measured by uroflowmetry as peak urinary flow rate (Q_{max}), voding time and voided volume and was considered valid only if the voided volume was >200 ml.

Symptoms were assessed urinary IPSS & consisting of seven symptoms (frequency, nocturia, urge in continence, urgency, hesitency, terminal dribbling and sense of incomplete evacuation) that were graded from 0-5. An overall symptoms score was calculated.

Data was collected in a pre-designed and pre-tested data collection sheet. Data was complied and statistical analysis were done using computer based software, Statistical Package for Social Science (SPSS), using paired 't' test. A P value <0.05 was taken as significance.

Results

A total 102 cases were selected consecutively according to selection and exclusion criteria from the patients attending urology out patient department of Dhaka Medical College Hospital, Dhaka with lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH). 102 cases were evaluated by history, physical examination, digital rectal examination (DRE), international prostate symptom scoring (IPSS), quality of life (QOL) scoring, uroflowmetry, post voided residual urine (PVR) and volume of prostate by USG and serum prostate specific antigen (PSA).

None of the patients had a prostatic nodule or solid lesion suspicious for prostatic cancer on the DRE, USG shows no hypo-hypercohoic lesions of the prostate.

The mean size >50ml and all specimens showed benign adenomutous tissue. The mean operative duration was 50 (40±75) minutes.

Cases were selected between 60-75 years. In group-A, among 42 cases (41.2%) ≤65 years and group-B, 60 cases (58.80%) > 65 years. Age of the patients of each group was compared with IPSS, PVR and Q_{max}.

Table-I

Changes in IPSS from base line to end point after TURP (n=102)

IPSS	Baseline (before TURP)	Endpoint (after TURP)	t	df	P value
Mean±SD	21.61±2.43	4.27±1.71	82.508	101	<0.001
Range	17-25	0-7			
Change Mean±SD		-17.33±2.12			

Paired Student 't' test.

Before TURP, IPSS range 17-25 and mean 21.61±2.43, after TURP, range 0-7 and mean 4.27±1.71). There was significant correlation between the IPSS obstructive scores and Qmax at base line (P=<0.001), while correlations at the 1st, 2nd and 3rd follow up significant. There was also a significant correlation between IPSS obstructive score and PVR, and quality of life.

After TURP, the IPSS Score showed significant improvements in urinary symptoms with the IPSS showing more significant change for obstructive symptoms.

Hence a significant improvement of IPSS was found from 2 months to 6 months follow up after TURP. The change was tested using "paired student 't' test".

Table –II

Change in peak urine flow (Q_{max} from base line to end point after TURP.

Q_{max} (ml/sec)	Baseline (before TURP)	Endpoint (after TURP)	t	df	P value
Mean±SD	9.96±1.69	22.61±2.28	-47.512	101	<0.001
Range	7 12.2	18 25			
Change Mean±SD		12.64±2.69			

Paired Student 't' test.

Before TURP Q_{max} range 7-12.2 and mean was 9.96±1.69, which became range 18-25 and mean was 22.61±2.28 after TURP and therefore change of mean Q_{max} was 12.64±2.69.

TURP caused a significant change in Q_{max} the mean Q_{max} being 12.64±2.69 ml/sec and mean PVR range >100 ml. The mean (SD) improvement in Q_{max} was 12.64±2.69 ml/sec and reduction in PVR, 60 patients having no detectable PVR at the 6 months follow up.

The change was tested using "paired student 't' test". The change was found significant (P<0.001).

Table-III

Changes in voiding time from base line to end point after TURP (n=102).

Voiding time (Sec)	Baseline (before TURP)	Endpoint (after TURP)	t	df	P value
Mean±SD	54.65±7.09	21.08±1.86	45.030	101	<0.001
Range	40-45	20-25			
Change		-33.57±7.53			

Mean±SD

Paired Student 't' test.

Mean voiding time was 54.65±7.09 sec at base line, which became 21.08±1.86 sec at end point and therefore change of mean voiding time was -33.57±7.53 sec.

Hence a significant improvement of voiding time was found after transurethral resection of prostate (TURP). The changes was tested using 'Paired student 't' test'. The change was found significant (P=<0.001).

Table- IV

Change in PVR from base line to end point after TURP (n=102).

PVR (ml))	Baseline (before TURP)	Endpoint (after TURP)	t	df	P value
Mean±SD	205.27±14.76	4.07±8.92	147.075	101	<0.001
Range	180-220	0-5			
Change		-201.21±13.82			
Mean±SD					

Paired Student 't' test.

Mean PVR was 205.27±14.76 ml at base line, which became 4.07±8.92 ml at end point and therefore change of mean PVR was -201.21±13.82 ml.

Hence a significant reduction of PVR was found after TURP. The change was test using 'Paired Student 't' test'. The change was found significant (P=<0.001).

Discussion

Recently most of the urologist in our country has been using this surgical method, transurethral resection of prostate of BPH. This present study was done to determine the improvement of symptoms and peak urinary flow rate (Q_{max}) after transurethral resection of prostate. In this study 102 patients of benign prostatic hyperplasia (BPH) from out patient department of urology of NIKDU were selected for transurethral resection of prostate (TURP) and were followed up 2 monthly for 6 months to determine the improvement of IPSS, peak urine flow rate (Q_{max}).

In this study, all cases were purposively selected from out patient department of urology of Dhaka Medical College Hospital age ranging from 60 years to 75 years who has been suffering from lower urinary tract symptoms due to benign prostatic hyperplasia. The age ranges of the separate study done in 1999 and 2000, 60 men with mean age 68 years and had a diagnosis of lower urinary tract symptoms suggestive of BPH (Gacci et. al., 2003).

Another study was done to assess the necessity for routine out patient review following transurethral resection of prostate (TURP) for BPH. 102 patients with histologically proven benign prostatic hyperplasia were prospectively reviewed as out-patients. During a 6 months period from October 1992 to March 1993, 102 consecutive patients (mean age 71 years, range 54-92) attending the out patients department following TURP. 90% of patients expressed satisfied with the results of their operation, 4% were dissatisfied and 6% felt there had been little improvement. Of 8 patient given further out patients department appointment.

After transurethral resection of prostate IPSS scores was showed significant improvements in urinary symptoms.

Effect of TURP was again observed in a separate study by evaluating change of IPSS before TURP irritative mean 6.71; obstructive mean 9.69 and after TURP became irritative 3.06 and obstructive 3.38, showed significant improvement in urinary symptoms with the IPSS for obstructive symptoms than for irritative symptoms or quality of life (QOL) (Gacci et al., 2003). These results are similar with the results of present study.

A significant improvement of Q_{max} was found after transurethral resection of prostate (2 months, 4 months and 6 months follow up) in this study.

Prostatectomy caused a significant change in Q_{max} the mean Q_{max} being 26.1 (14.5-41.2)ml/sec. The mean (SD) improvement in Q_{max} was 17.9 ml/sec at 6 month follow up (Gacci et al., 2003).

Another study included 108 men with symptoms of bladder outlet obstruction using a peak flow rate ≤12ml/sec as an index of obstruction, 65 patients were identified. A flow rate alone was accurate in 95% of cases with 62 patients being obstructed on urodynamic evaluation; 43/108 patients (40%) had flow rate >12 ml/sec. Of 53 patients with outflow obstruction as defined by cystometry who agreed to undergo TURP, 37 (69%) returned 1 year later for a repeat free flow rate and symptomatic assessment. No patient with residual symptoms had a flow rate <12ml/sec at follow up. None of the patients with initially higher flow rates underwent TURP were noted to have residual symptoms at follow up. All patients in this study had improved flow rates compaired with preoperative measurements (Loughlin et. al., 1990).

Hence a significant improvement of voiding time was found after TURP. The change was found significant (P=<0.001). Similar reduction in voiding time also observed in a study on 108 patient with lower urinary tract symptoms due to BPH (Loughlin, Gill KP., et. al., 1990). These results are also consistent with the present study.

A significant reduction of PVR was found after TURP in this study. The change was found significant (P=<0.001).

In a study it was observed 60 men with BPH; prostatectomy caused a significant change in Qmax being 26.1 (14.5-41.2) ml/sec and the mean PVR (0-50) ml. The mean (SD) improvement in Qmax was 17.9 ml/sec and reduction mean PVR 92 ml with 39 patient having no detection PVR at the 6 month follow up (Gacci et. al., 2003). Results of this study are also similar with the present study.

Conclusion:

From the present study it can be concluded that transurethral resection of prostate resolves obstructive symptoms, rapid improvement of urinary flow rate and quality of life that is why it is gold standard treatment for moderate to severe symptomatic BPH patients.

Conflict of Interest : None Declared

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Abbreviations:

BPH: Benign Prostatic Hyperplasia

IPSS: International Prostate Symptoms Score

Q_{max}: Peak Urinary flow rate

PVR: Post voidal residual Urine

TURP: Transurethral Resection of Prostate

REDUCED PAIN, SHORTER HOSPITAL STAY AND EARLY RETURN TO WORK IN PCNL: COMPARATIVE STUDY ON OUTCOME OF PCNL VERSUS OPEN SURGERY IN THE TREATMENT OF LARGE RENAL CALCULI

SYED ALFASANI[1], AKM ZAMANUL ISLAM BHUIYAN[2]

[1]Consultant of Surgery, UHC, Kaliakoir, Gazipur, [2]Head of the Department of Urology, National Institute of Kidney Diseases & Urology.Dhaka-1207

Abstract:

Objective: *To compare the outcome of PCNL & open surgery in the treatment of large renal calculi by assesing the amount of analgesia required to relief pain, mean hospital stay, & convalescence period.*

Materials & Methods: *: This comparative study in during 80 patients diagnosed with kidney stone disease admitted in the NIKDU during the period of Jan' to Dec'2009. They were divided conveniently into two groups. Intervention was done in the formPCNL(40) and open surgery (40). Clinical outcome like, duration of surgery, postoperative hospital stay,doses of narcotic analgesia required to relief pain and convalescence periodwere reviewed. In complete follow up 9 patients were missed in PCNL group resulting in 31 patients. There was no significant difference in preoperative variables such as age,sex, stone size in cm, stone number- single/multiple and stag horn Stone.*

Results *: There were statistically significant difference in the parameters between the groups,(PCNL vs open surgery [mean ± SD]): duration of operation (min), 97.90 ± 24.89 vs 136.62 ± 23.54, postoperative hospital stay (days) ,4.77 ± 3.98 vs 9.55 ± 3.65, mean time return to work (days) , 3.09 ± 1.21vs 6.25 ± 1.53, (p value is <0.001). The amount of analgesia required to relief pain was significantly reduced in PCNL vs open procedure (no patient required > 2 doses vs 27 patient required 3 or >3 doses), p value is <0.001.*

Conclusion: *PCNL is relatively safe & better treatment option than open surgery in the treatment of large renal calculi. It has reduced pain, shorter hospital stay and more rapid return to work.*

Keywords : *PCNL (Percutaneous nephrolithotomy), RCT (Randomised controlled clinical trial), Open surgery, reduced pain, shorter hospital stay.*

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Introduction

Kidney stone disease is existing among mankind since the earliest record of civilization. Hippocrates described the renal stone as first disease of the kidney[1]. High incidence of renal stone disease is found in U.S.A, U.K, Scandinavian countries, Mediterranean countries, portion of the Malayan peninsula and China. Low incidence is found in central and south America, most of Africa and part of Australia[2]. (stoller et al. 2000).

Now four minimally invasive treatment modalities are available for the treatment of kidney stones such as

Correspondence : Syed Alfasani, UHC, Kaliakoir, Gazipur

ESWL (Extra corporeal shock wave lithotripsy). Percutaneous nephrolithotomy (PCNL), retrograde ureteroscopic intra renal surgery and laparoscopic stone surgery[3]. (Lingeman et al. 2002). Now a days all uncomplicated and most of the complicated renal stones are treated by percutaneous method as a routine procedure in the western set up, although the technique is still evolving in the developing country like ours[4].

Open stone surgery is an old and established procedure. In Bangladesh larger kidney stones are mostly treated by open surgery because of poor socioeconomic context[5].

PCNL was not available in Bangladesh till January 2000. In National Institute of Kidney Diseases & Urology, this technique has been regularly undertaken since 2004. The present study is the first prospective randomized work conducted in NIKDU, Dhaka to compare the outcome like efficacy, morbidity and convalescence among PCNL & open surgery. An increasing awareness of this technique by both patients & referring physicians has raised important questions regarding the safety and efficacy of the percutaneous methods Vs standard renal surgery.

If any superiority of treatment by PCNL can be provided or shown that this is relatively safe than the method can further be popularized among the Urologist of our country and this study may be the basis of further research in this field.

Materials & Methods

This Comparative study, initially includes all the patient with kidney stone disease that were admitted In urology department of NIKDU during the period of Jan'2009 to Dec'2009.Total 80 Patients were divided conveniently into two groups PCNL (40) and open surgery (40). Randomization was done by taking consecutive samples. Intervention was done in the form of PCNL and open surgery.

The cases were selected with the Inclusion criteria having stone size more than 2 cm, functioning kidney with sterile urine and the exclusion criteria is renal failure,pregnancy, uncontrolled bleeding disorder, congenital / acquired skeletal abnormalities and infected urine

All patients were evaluated by history, clinical examination and Investigations having similar protocol. Before operation, each patient of two groups were evaluated and compared for age and sex of the patients, size, number, location of the stones and pelvicalyceal dilatation.

Open surgery was performed through standered flank incision with or without rib resection. A standered PCNL was performed with subcostal single puncture in 29 units and double puncture in 2 units. Initially pneumatic, later on ultrasonic lithotripsy was used .18 Fr nephrostomy tube was left in each puncture site and D-J stent (6Fr) was kept in ureter. Radiological evaluation was done postoperatively. Patient who were completely cleared of stones were considered stone free.

Patients were followed monthly for 3 months where 9 patients were missed in PCNL group resulting in 31 patients. Again history, clinical examination and Investigations like urine routine and culture, plain X-ray KUB were done and post PCNL data were recorded . All patients were asked about the time required to return to normal activities.

Statistical analysis was done meticulously by SPSS for windows-14 version program. Data was presented as mean ± SD. probable value of less than 0.05 was considered significant.Test of significance was done by student t-test , z-test and chi-square test.

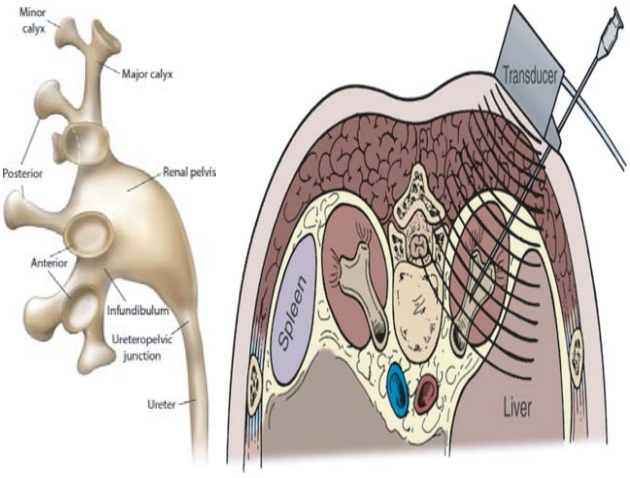

Fig.-1 : *Basic pelvicalyceal anatomy : Wein et al. (2007) p.3230*

Results

Preoperative characteristics (mean ± SD) were as follows: (PCNL vs open surgery): age, 44.48 ± 10.31 vs 45.22 ± 15.53 yrs; sex, (male/female), 20/11vs 24/16; stone size in cm,3.07±0.93 vs 3.44±1.09; stone number- single/multiple, 26(83.9%)/5(16.1%) vs 26(65.0%)/14(35.0%); stag horn Stone,5(16.1%)vs 4(10.0%) . There were no significant difference between the two groups (p>0.05).

Table-I

Reoperative characteristics of the study subjects

Characteristics	Name of Operation	
	PCNL	Open surgery
No of patients	31	40
Age in year (Mean ± SD)	44.48±10.31	45.22±15.53
Sex (male/female)	20/11	24/16
Stone size in cm (Mean ± SD)	3.07±0.93	3.44±1.09
Stone number- Single/Multiple	26(83.9%)/5 (16.1%)	26(65.0%)/14(35) 0%)
Stag horn Stone	5(16.1%)	4(10.0%)

Among the chief complains, pain was present in 27 vs 37 patients, fever in 8 vs 8 patients, haematuriain 5 vs 6 patients and pyuriain 5 vs 6 patients in PCNL and open surgery respectively. Total 3 patient (2 in PCNL, 1 in open surgery) had no complaints of stone disease.

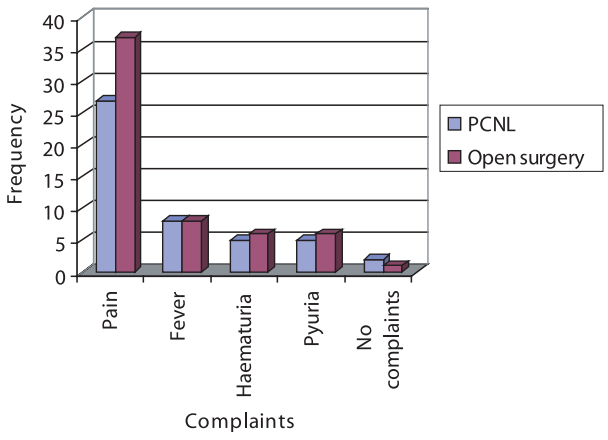

Fig.-3: *Chief complaints of the patients*

Table-II

Total operation time, post operative hospital stay and convalescence period

Parameters	PCNL N= 31	Open surgery N=40	p value
Duration of operation (Min.) (Mean ± SD)	97.90±24.89	136.62±23.54	<0.001
Hospitalstay (days) (Mean ± SD)	4.77±3.98	9.55±3.65	<0.001
Convalescence Period (days) (Mean ± SD)	3.09±1.21	6.25±1.53	<0.001

Table- II shows, time required to complete the operation and the post operative hospital stay in PCNL group and open surgery group. In PCNL group the mean operation time was 97.90 min (SD-24.89) and the post operative hospital stay was 4.77 days (SD- 3.99), whereas in open surgery group the time was 136.62 min (SD-23.55) and hospital stay was 9.55 days (SD- 3.65). The mean operation time (t= -6.704 ;p value is <0.001) and the post operative hospital stay (t= -5.250 ;p value is <0.001) was very significantly lower in PCNL group than in open surgery group. The mean time return to work in PCNL group was 3.09 weeks (SD-1.21) and in open surgery was 6.25 weeks (SD-1.53) . Return to work was significantly faster in PCNL group than open surgery group (p value is <0.001).

Table-III

Narcotic Analgesic Required

Doses of	PCNL	Open surgery
analgesics	N= 31	N=40
Single	25(80.6%)	8(20.0%)
Multiple	6(19.4%)	32(80.0%)

Chi-square = 25.82; p = <0.001

In this study in PCNL group, 25 cases required 1 dose and 6 cases required 2 dose of narcotic analgesics. In open surgery group, 8 cases required 1 dose and 9 cases required 2 dose, 20 cases required 3 dose and 3 cases required >3 dose of narcotic analgesics. So dose

of narcotic analgesia were very significantly reduced in PCNL group than open surgery group (Chi-square=25.82; p value is <0.001).

Post operative pain was compared in both group of patients. In this series dose of narcotics required to relief pain was significantly reduced in PCNL group (no patient required > 2 doses) than open procedure (27 patient required 3 or >3 doses). Chi-square=25.82 ; p value is <0.001.

Discussion:

The present study has been designed to compare the outcome of PCNL and open surgery for the management of renal stone disease more than 2 cm in size. After counseling, taking consent and considering the inclusion and exclusion criteria finally 80 Patients were selected and divided into two groups, PCNL(40) and open surgery (40). In complete follow up 9 patients were missed in PCNL group resulting in 31 patients.

The mean age of the patients was 44.48 years (SD-10.31) in PCNL group and 45.22 years (SD-15.53) in open surgery. The age of the patient was statistically insignificant(>0.05). The age range of the present study is more or less compareable with the study done by Assimos et al[6]. in 1991,(age:23 to 79 years) & by Brannen et al[7]. in 1985,(age:21 to 94 years) . The highest age is higher in those countries is due to long life expectancy of that country and elderly people attending in the clinic .

The mean size of the stone in PCNL group was 3.07 cm (SD-0.94) and in open surgery was 3.44 cm (SD-1.09). The size of the stone in both groups were analysed and found no significant difference (p>.05). In a study by Wong YC,[8]. in 1998,stone size was recorded between 2 to7.5 cm which is almost similar to the size of stone of present study.

In present study, the mean operation time was noted 97.90 min (SD=24.89) in PCNL and 136.62 min (SD=23.55) in open surgery,which was very significantly lower in PCNL (t= -6.704; p value is <0.001). Al-kohlany et al.[9].showed that the mean operation time was 127 vs 204 min in PCNL vs open surgery. Snyder[12]. also showed lower time (155 vs 266 min) required in PCNL than open procedure. The overall time mentioned were longer as because the above studies were conducted on the staghorn calculi absolutely.

Mean hospital stay was 4.77 days for PCNL and 9.55 days for open surgery.In a comparative study between PCNL and open surgery Preminger[9] reported mean hospital stay for PCNL is 4 days and for open surgery is 10 days. Brannen et al.[7] in 1985, reported similar result of 5.5+-0.3 days hospital stay after PCNL and 8.4+-0.5 days after open surgery. The present study is almost similar to the above studies. Time return to work, in PCNL was significantly faster (mean 3.09 weeks) than in open surgery (mean 6.25 weeks) (p value is <0.001). Brannen and associates in 1985[8] (within 2 weeks vs more than 3 weeks) & Al-kohlany et al.[9]. reported the earliar (2.5 weeks vs 4.1 weeks) return to work in PCNL group than open surgery group.

In this study in PCNL group, 25 cases required 1 dose and 6 cases required 2 dose of narcotic analgesics. In open surgery group, 8 cases required 1 dose and 9 cases required 2 dose, 20 cases required 3 dose and 3 cases required >3 dose of narcotic analgesics. So dose of narcotic analgesia were vary significantly reduced in PCNL group. (Chi-square=25.82 ; p value is <0.001).

Likewise, Snyder and Smith in 1986[10] found reduced dose (16 vs 33 doses) of narcotics needed in PCNL group than open operations. The result of the present study was compatible with the above study.

Conclusion:

PCNL is relatively safe & better treatment option than open surgery in the treatment of large renal calculi. It has reduced pain, shorter hospital stay and more rapid return to work, inspite of some limitations like small sample size, purposive samplingtechnique, surgery was not done by single surgeon & stone composition was not considered here. Further research should be conducted on two well matched comparative groups of large sample size to establish the findings of the present study.

Conflict of Interest : None Declared

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Abbreviations

PCNL : Percutaneous nephrolithotomy
ESWL : Extracorporenal Shortwave Lithotripsy

COMPARATIVE STUDY OF OPTICAL INTERNAL URETHROTOMY VERSUS ANASTOMOTIC URETHROPLASTY FOR SHORT SEGMENT BULBAR URETHRAL STRICTURE

ASM SHAFIUL AZAM[1], AKM KAWSAR HABIB[2], SM MAHBUB ALAM[3], MD. HABIBUR RAHMAN[1], MD. ABDUS SALAM[1], HARUN-OR-RASHID[1]

[1]Department of Urology, BSMMU, Dhaka, [2]Department of Urology, Faridpur Medical College, Faridpur, [3]Department of Urology, Dhaka Medical College, Dhaka

Abstract

Objective: *This study was conducted to compare the outcome of anastomotic urethroplasty with that of traditional optical internal urethrotomy in the treatment of short-segment bulbar urethral stricture.*

Methods: *This comparative clinical study was conducted in the Department of Urology, Dhaka Medical College Hospital over a period 1 year from January 2007 to December 2008. A total of 50 patients with short-segment (< 2 cm) bulbar urethral strictures were consecutively included in the study. The test statistics used to analyses the data were Fisher's Exact Probability Test, Student's t-Test. For all analytical tests, the level of significance was set at 0.05 and p < 0.05 was considered significant.*

Results: *About one-quarter (24%) of patients in OI Urethrotomy group experienced bleeding, 4% epididymitis and another 4% incontinence. In contrast, 8% of patients in Anastomotic Urethroplasty group complained of periurethral leakage, 8% fever and another 8% wound infection. Apart from bleeding, all the complications were almost homogeneously distributed between groups.Six (24%) of patients in OI Urethrotomy Group exhibited narrow urinary stream at month 3, as opposed to none in Anastomotic Urethroplasty Group (p = 0.001). Nearly 30% of patients in OI Urethrotomy Group had narrow urinary stream at month 6 compared 4% in Anastomotic Urethroplasty Group (p = 0.024). Of the 25 patients in OI Urethrotomy Group, 1(4%) developed UTI at month 3 and 5(20%) at month 6. None of the patients in Anastomotic Urethropasty Group developed UTI. There was significant difference between groups in terms of UTI at month 6 (p = 0.025).The recurrence rate of stricture in OI Urethrotomy was 24% (6 out of 25 patients) at month 3. However, none in Anastomotic Urethroplasty Group had history of recurrence of stricture (p = 0.011). At baseline the mean uroflowmetry was 5.5 ml/sec in both groups which immediately increased to 25.3 ± 2.6 ml/sec and 23.9 ± 2.2 ml/sec in OI urethrotomy and Anastomotic Urethroplasty groups respectively and then dropped to 18.4 ± 6.3 ml/sec and 20.2 ± 2.6 ml/sec in OI Urethrotomy and Anastomotic Urethroplasty groups respectively at month 3 and to 17.8 ± 6.4 ml/sec and 19.6 ± 2.6 ml/sec respectively at month 6.*

Conclusion: *This study concludes that Anastomotic Urethroplasty is an effective and satisfactory technique for the treatment of short-segment bulbar urethral stricture.*

Key words: *Stricture urethra, Optical Internal Urethrotomy, Anastomotic Urethroplasty*

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Correspondences: ASM Shafiul Azam, E-mail: shafiulazam04 @gmail.com

Introduction :

Urethral stricture disease is a common urological and is one of the most important causes of bladder outflow obstruction which may be resulted from varieties of

pathology e.g. inflammatory disease, injuries of urethra, neoplasm of urethra etc.[1] In the management of urethral strictures the etiology, site, length of stricture are taken into account. Peterson and Webster suggested that no one technique is appropriate for all stricture diseases and the urologist must be familiar with various surgical techniques to deal with any condition of the urethra during surgery. Surgical treatment of urethral strictures includes numerous options such as dilatation, optical internal urethrotomy, stent and reconstructive surgical techniques[2]. Urethroplasty is an open surgical procedure for urethral reconstruction to treat urethral strictures. Urethroplasty can be performed by two methods; primary repair which involves complete excision of the narrowed part of urethra. The proximal and distal patent parts are then rejoined. The second method of urethroplasty utilizes tissue transfer or free graft technique. The gold standard treatment of a short segment bulbar stricture is excision, spatulation of the two ends and an overlapping end to end anastomosis, whether or not the lumen is completely occluded.

Internal urethrotomy refers any procedure that opens the stricture by incising or ablating it transurethrally. The urethrotomy procedure involves incising scar upto healthy tissue to allow the scar to expand (release of scar contracture and the lumen to heal). The goal is for the resultant larger luminal caliber to be maintained after healing. The most common complication of internal urethrotomy is recurrence of stricture. For many, an internal urethrotomy is successful if it offers temporary relief. Therefore, in many cases, internal urethrotomy has been reported as successful despite the fact that it has been associated with eventual stricture recurrence[3]. Optical internal urethrotomy continue to be the most commonly used techniques, but have a high recurrence rate and many patients progress to surgical repair. Moreover optical internal urethrotomy exacerbates scar formation, thus adding to stricture length and predisposing difficult definitive open repair and a lower success rate[4].

Several studies have been conducted in different parts of the world comparing the safety and efficacy between anastomotic urethroplasty and optical internal urethrotomy in short segment bulbar urethral stricture treatment. Urethral mucosa has several unique characteristics that make it superior to any tissues for reconstruction of urethra. Open urethroplasty is regarded as the gold standard treatment for urethral strictures[3]. No such study has yet been carried out in Bangladesh and continuous debate has been going on among urologist about the first & logical treatment option in treating short- segment bulbar urethral stricture.

This study was conducted to compare the outcome of anastomotic urethroplasty with that of traditional optical internal urethrotomy in the treatment of short-segment bulbar urethral stricture.

Patients and methods

The comparatie clinical study was conducted in the Department of Urology, Dhaka Medical College Hospital between January 2007 to December 2008. A total of 50 patients were consecutively included in the study. The required numbers of patients were consecutively included in the study and were randomly assigned either optical internal urethrotomy or anastomotic urethroplasty groups.

The present study has been conducted on the patients with bulbar urethral stricture size < 2 cm admitted in the Department of urology, DMCH for anastomotic urethroplasty or optical internal urethroyomy (OIU).

All patients were evaluated by history, physical examination and some investigations including urine analysis & cultural sensitivity (C/S), serum creatinine, random blood sugar (RBS), ultrasonography, retrograde and micturating cystourethrogram (RGU & MCU) and uroflowmetry. All the cases were further evaluated for fitness of anesthesia. Patients with documented urinary tract infection (UTI) were treated with appropriate antibiotics before the procedure & confirmed by repeat culture sensitivity (C/S). The surgical procedure was performed with the patients under spinal anesthesia. All patients were followed-up by urinary symptoms, uroflowmetry, urine analysis, RGU & MCU at 3 and 6 months.

Data were processed and analyzed using SPSS (Statistical Package for Social Sciences). The test statistics used to analyze the data were descriptive statistics, Fisher Exact Probability Test and Student's t-Test. For all analytical tests, the level of significance was set at 0.05 and $p < 0.05$ was considered significant.

Results :

Twenty four percent of patients in OI Urethrotomy group experienced bleeding, 4% epididymitis and another 4% incontinence. In contrast, 8% of patients in Anastomotic Urethroplasty group complained of periurethral leakage, 8% fever and another 8% wound infection. Apart from bleeding, all the complications were almost homogeneously distributed between groups i.e. not

significant (p > 0.05) (Table I). Fisher Exact Test was done to analyse the data.

Table I
Comparison of complications between groups following intervention

Complications	Group		p-value
	OI Urethrotomy (n = 25)	Anastomotic Urethropasty (n = 25)	
Periurethral leakage	00	2(8.0%)	0.245
Bleeding	6(24.0%)	00	0.011
Fever	00	2(8.0%)	0.245
Epididymitis	1(4.0%)	00	0.500
Incontinence	1(4.0%)	00	0.500
Wound infection	00	2(8.0%)	0.245

Six (24%) of patients in OI Urethrotomy Group exhibited narrow urinary stream at month 3, as opposed to none in Anastomotic Urethroplasty Group (p = 0.001). Nearly 30% of patients in OI Urethrotomy Group had narrow urinary stream at month 6 compared 4% in Anastomotic Urethroplasty Group. The difference was statistically significant in terms of narrow urinary stream (p = 0.024) (Table II). Fisher Exact test was done to analyse the data.

Table II
Comparison of narrow urinary stream between groups

Follow up	Group		p-value
	OI Urethrotomy (n = 25)	Anastomotic Urethroplasty (n = 25)	
Narrow urinary stream at 3 month	6 (24%)	00	0.011
Narrow urinary stream at 6 month	7 (28%)	1(4%)	0.024

Of the 25 patients in OI Urethrotomy Group, 1(4%) developed UTI at 3 month and 5(20%) at 6 month. None of the patients in Anastomotic Urethroplasty Group developed UTI. There was significant difference between groups in terms of UTI at 6 month (p = 0.025) (Table III). Fisher Exact Test was done to analyse the data.

Table III
Comparison of UTI between groups

Follow up	Group		p- value
	OI Urethrotomy (n = 25)	Anastomotic Urethroplasty (n = 25)	
UTI at 3 month	1(4%)	00	0.500
UTI at 6 month	5(20%)	00	0.025

The recurrence rate of stricture in OI Urethrotomy was 24% (6 out of 25 patients) at 3 month. However, none in Anastomotic Urethroplasty Group had history of recurrence of stricture. Seven (28.1%) patients in OI Urethrotomy needed a second urethrotomy, where as only 1(4%) required Anastomotic urethroplasty at 6 month. The differences between the groups in terms of recurrence of stricture at 3 month and at 6 month were statistically significant (p = 0.011 and p = 0.024 respectively) (Table IV). Fisher Exact Test was done to analyse the data.

Table IV
Comparison of recurrence of stricture between groups (n = 50)

Follow up	Group		p- value
	OI Urethrotomy (n = 25)	Anastomotic Urethroplasty (n = 25)	
Recurrence of stricture at month 3	6(24%)	00	0.011
Recurrence of 6 stricture at month	7(28.1%)	1(4%)	0.024

Table V shows the comparison of changes in mean uroflowmetry between groups at different time intervals. At baseline the mean uroflowmetry was 5.5 ml/sec in both groups which immediately increased to 25.3 ± 2.6 ml/sec and 23.9 ± 2.2 ml/sec in OI urethrotomy and Anastomotic Urethroplasty groups respectively and then dropped to 18.4 ± 6.3 ml/sec and 20.2 ± 2.6 ml/sec in OI Urethrotomy and Anastomotic Urethroplasty groups respectively at 3 month and to 17.8 ± 6.4 ml/sec and 19.6 ± 2.6 ml/sec respectively at 6 month. The uroflowmetry improved in both groups compared to their baseline figures, but no significant difference was between the groups with respect to improvement. Data were analysed using Student's t-Test and were presented as mean ± SD.

Table V

Uroflowmetry at different time interval between groups (n = 50)

Uroflowmetry (ml/sec)	Group		p- value
	OI Urethrotomy (n = 25)	Anastomotic Urethropasty (n = 25)	
At baseline	5.5 ± 1.7	5.5 ± 1.8	0.936
Immediate outcome	25.3 ± 2.6	23.9 ±2.2	0.039
Follow up at month 3	18.4 ± 6.3	20.2 ±2.6	0.217
Follow up at month 6	17.8 ± 6.4	19.6 ±2.6	0.218

Discussion :

Andrich et al, 2003 stated that the result of anastomotic urethroplasty is good and sustained in the long term, while the result of optical internal urethrotomy deteriorate steadily with time and there is definite room for development. An anastomotic repair should be performed in preference to an optical internal urethrotomy when possible[5].

Primary end-to-end anastomosis is the gold-standard reconstructivetechnique for short bulbar urethral strictures (< 2 cm). Free grafts and pedicled flaps best reserved for longer strictures. Eltahawy et al. find new onset ED to be negligible following anterior anastomotic urethroplasty 2.3%)[6]. Similarly, Santucci et al. report that new onset of ED occurred in less than 1% of 168 men having bulbar urethroplasty via primary anastomosis[7]. Others have reported a range of 5%-26% of men with anastomotic reconstruction for anterior strictures complaining of ED. These figures, taken together, justify the continued aggressive use of primary anastomosis for short-length urethral strictures[8].

Immediate outcome of intervention shows that 24% of patients in optical internal urethrotomy (OIU) group encountered bleeding, 4% developed epididymitis and another 4% incontinence of urine. In contrast, 8% of patients in anastomotic urethroplasty group had periurethral leakage, 8% fever and another 8% wound infection. All the complications except bleeding were almost identically distributed between groups Stormont et al. (1993) reported that all the complications except bleeding were nearly identical between optical internal urethrotomy (OIU) and anastomotic urethroplasty[9].

Nearly one-quarter (24%) of patients in optical internal urethrotomy (OIU) Group exhibited poor urinary stream at month 3, as opposed to none in anastomotic urethroplasty Group. Narrow urinary stream at month 6 demonstrated its significant presence in Optical internal urethrotomy (OIU) Group (30%) compared to that in anastomotic urethroplasty Group (4%) ($p < 0.05$).

The recurrence of stricture in optical internal urethrotomy OIU at month 3 was 24% as opposed none in anastomotic urethroplasty Group ($p = 0.011$). Seven (28.1%) patients in optical internal urethrotomy (OIU) needed a second urethrotomy, where as only 1(4%) required anastomotic urethroplasty at 6th month ($p = 0.024$) Albers et al. (1996) demonstrated in their study a recurrence rate of 44.8% after primary urethrotomy and 34.6% underwent a second urethrotomy. The recurrence rate of anastomotic urethroplasty was 26.9% and 16.9% needed a second urethroplasty[10].

The mean uroflowmetry at baseline was 5.5 ml/sec in both groups which steeply increased in both optical internal urethrotomy (OIU) and anastomotic urethroplasty groups reaching a mean uroflowmetry of 25.3 ± 2.6 ml/sec and 23.9 ± 2.2 ml/sec respectively and then dropped to 18.4 ± 6.3 ml/sec and 20.2 ± 2.6 ml/sec in optical internal urethrotomy (OIU) and anastomotic urethroplasty groups respectively at month 3 and to 17.8 ± 6.4 ml/sec and 19.6 ± 2.6 ml/sec respectively at month 6. Kane et al. (2002) reported in his study that average peak urinary flow rates increased from 7.9 ml/sec at baseline to 30.1 ml/sec postoperatively in anastomotic group[11].

Conclusion :

From the findings of the study and discussion thereof, it can be concluded that anastomotic urethroplasty is a versatile, effective and a satisfactory technique for the treatment of short segment bulbar urethral strictures. The morbidity and complications are low and outcomes are excellent.

Conflict of Interest : None

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Abbreviations:

UTI: Urinary tract infection

RGU : Retrograde urethrogram

MCU: Micturating urethrogram

OIU: Optical internal urethrotomy

ED: Erectile dysfunction

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REVIEW ARTICLE

OPTIMUM MANAGEMENT OF THE T_1 HIGH GRADE BLADDER CANCER

MD. ABUL HOSSAIN[1], MD. WALIUL ISLAM[2], MD. NURUL HOODA[2], MD. FAZAL NASER[1], MD. SHAFIQUL AZAM[1]

[1]Department of Urology, Shaheed Suhrawardy Medical College, [2]Department of Urology, National Institute of Kidney Diseases & Urology.

Abstract

Objectives: *To determine the optimum treatment option for patients with superficial high grade (T_1Hg) bladder cancer.*

Introduction: *Controversy exists about the most appropriate treatment for superficial high grade (T_1Hg) bladder cancer. Immediate cystectomy offers the best chance for survival but associated with an impaired quality of life compared with conservative therapy. In case of conservative therapy lifelong surveillance is required and there is a high rate of recurrence and risk of disease progression. So optimum treatment option should be determined to treat the disease optimistically.*

Methods: *A comprehensive and systemic search of the pubmed database for English Language articles was performed using the following medical subject Heading (MeSH): Bladder cancer, treatment of superficial high grade (T_1Hg) bladder cancer, treatment options for bladder cancer, natural history of T_1Hg bladder cancer, newer Intravesical agents, cystectomy and in addition reference of relevant articles were searched for additional references.*

Results: *Approximately 70% of all newly diagnosed bladder tumors are non-muscle invasive bladder cancer. The management of these patients entails transurethral resection with or without adjuvant intravesical therapy. After review of obtained articles it is evident that the conservative treatment of T_1Hg bladder cancer should be ended when there is systemic or local toxicity from intravesical therapy or patient is not complaint or persistence of tumor or tumor progression despite therapy.*

Conclusion : *The management of T_1Hg is highly variable due to several factors including divergence in treatment related evidence. The efficacy of treatments must be balanced with their toxicity, so that single treatment option cannot be considered superior across all Non-Muscle Invasive Bladder Cancer (NMIBC). Immediate radical cystectomy may be offered upfront in patients with T_1Hg tumors with concomitant CIS or multiple recurrent high grade tumors.*

Key Words: *Bladder cancer, T_1Highgrade bladder cancer, treatment options for bladder cancer.*

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Introduction:

T_1Hingh Grade transitional cell carcinoma of the urinary bladder represents a highly malignant tumor with a variable and unpredictable biologic potential. Approximately 70% of all newly diagnosed bladder tumors are non-muscle invasive bladder cancers, including stage Ta, stage T_1 and carcinoma in situ (CIS)[1]. The management after these patients entails transurethral resection with or without adjuvant Intravesical therapy. Despite adequate therapy, however, 60-70% of these lesions will recur and 10-20% will progress to muscle – invasive disease, therapy requiring a radical cystectomy[2]. High grade superficial TCC of urinary bladder remains a difficult situation to manage even in premiere centers. Opinion defers as to whether

Correspondences: Md. Abul Hossain, E-mail: drmahossain.qpm@gmail.com

conservative or radical surgery is appropriate when high grade (G_3) tumors are diagnosed. Monaharam et al[3] places the decision making in the management of T_1Hg tumors as the most difficult. In case of conservative therapy like intravesical maintenance BCG instillation, advantage is obvious, since the bladder is spared and therapy does not involve radical surgery with all its morbidity and morbidity. On the other hand, optimal chance of cure is possible in case of cystectomy but chance of overtreatment in a substantial percentage of patients[4]. There are good data supporting bladder conservative therapy with repeat transurethral resection and administration of bacilli Calmette Guerin (BCG) Intravesical therapy[5].

Patients who present with muscle invasive disease and distant metastases are usually managed by radical cystectomy or chemotherapy with or without radical cystectomy. But treatment decision for T_1Hg is not always straightforward. It presents a dilemma to the urologist whether to remove or not to remove the bladder?

Overview of T_1Hg bladder cancer

Bladder cancer is a common malignancy arising from urothelial cells and is responsible for considerable morbidity and mortality[6]. Approximately 70% of nearly diagnosed cases of bladder cancer are non-muscle invasive which is only confined to the urothelial and lamina propria of the bladder[7]. Among non-muscle invasive bladder cancer, around 70% present as Ta lesions (papillary growth invading the lamina propria), and 1% as carcinoma in situ[8]. T_1 tumors which are usually high grade have potential to become more aggressive, with higher rates of progression to muscle invasion and metastasis. Most subsequent studies also suggested that grade is a better prognostic factor to determine mortality than of recurrence [9-10]. Haney and colleagues have shown that the risk of disease progression to muscle invasion is strongly associated with tumor grade[10].

Natural History of T_1Hg Bladder Cancer

Up to one third of patients with NMIBC will progress to muscle invasive disease and have a higher risk of death from bladder cancer than those who do not progress[9]. A population based study of the natural history of the disease in the United States is done by Karim Chamie and colleagues. They analysed 7, 410 individuals with high grade non-muscle invasive disease who were diagnosed between 1992 and 2002. The research suggests that bladder cancer patients are at high risk for recurrence.

According to Christopher Saigal, the risk of recurrence has previously been linked with higher tumor grade and stage at diagnosis, the number of tumors at diagnosis, presence of CIS and continued smoking by the patient. Almost three fourth of the patients with high grade non-muscle invasive bladder cancer had a recurrence, progressed or died within a 10 years period. Approximately 41% of these patients will recur without progression, and an additional 33% will have progressive disease. Among those who progress, the researchers found, 4% will die of their bladder cancer.

The overall recurrence rate of non-muscle invasive bladder cancer is 60% to 70% and overall progression is 2% to 30%.[11-12]. Holmang and colleagues demonstrated that low-grade Ta tumors had a recurrence of 70% with a progression of only 2%. Patients with T_1Hg tumors have ten times the chance of muscle invasion and death than with other Ta – T_1 tumors with a risk of life long progression[13].

T_1Hg tumor progress in more than 50% of cases; deaths from disease occur in 25% of patients in the first 5years and in 10% of patients between 5 to 15 years[14].

Prognostic factors of recurrence and progression

Stage and grade

The two most important prognostic factor in non-muscle invasive bladder cancer are stage and grade. Bladder cancer is the fourth most common male cancer accounting for 7% of all cancers and the eighth highest cancer related mortality rate in American man[15]. Risk factors has been associated with bladder cancer include smoking, chronic inflammatory changes in the bladder (due to persistent bladder stones, recurrent urinary tract infections, indwelling catheters or schistosominsis), and chemotherapeutic exposure, such as cyclo-phosphamide[15-16].

Others factors

Six clinicopathological parameters such as grade, stage, tumor size, prior recurrence rate, presence of concomitant CIS and number of tumors are implicated with recurrence and progression. Tumor multiplicities has been shown to be an important factor in recurrence and progression in case of non-muscle invasive bladder cancer[17-18].

The lack of response to three months of Intravesical therapy has been found to be predictive of progression in T_1Hg disease[19].

Diagnosis:

Correct diagnosis is important for precise decision making. There is 48% of T1 tumors are under staged if muscle was not found in TUR specimen, and 14% of T1 were under staged if muscle was present in the specimen[20].

Biopsy:

To obtain specimen for histological assessment pure cutting current should be used during TURBT. There should always be muscularis propria in contact with the tumor in TURBT specimen. Some advocate cold cup biopsies of the tumor base and many urologists advocate a second TURBT in all patients with pT1 tumor after 10 days[17-20]. Manoharan et al recommend that a second TURBT be considered in patients with a T_1Hg tumor.

Pathology:

World health organization pathology guidelines recommended a conversion from previous classifications of grade G1, G2 or G3 to that of low or high grade papillary urothelial carcinoma[21]. Pathology reports should identify whether muscle tissue is present in the respected specimen or not.

Table-I

2004 WHO/ International society of urologic pathologists: Classification of non-muscle invasive urothelial neoplasia

Hyperplasia (flat and papillary)
Reactive atypia
Atypia of unknown significance
Urothelial dysplasia
Urothelial CIS
Urothelial papilloma
Papillary urothelial neoplasm of low malignant potential
Non muscle invasive low grade papillary urothelial cancer
Urothelial carcinoma

Treatment options

In most cases of non-muscle invasive bladder cancer, tumors are treated initially with TURBT. A careful cystoscopic examination of the entire urethra and bladder surfaces precedes resection[22]. The position of tumors with reference to the bladder neck and ureteral orifices, the tumor configuration, whether tumors are papillary or sessile, and estimates of the number of tumor and their sizes should be noted to assist in future evaluation and follow-up. After resection of all visible tumors, adjuvant Intravesical immunotherapy or chemotherapy can be used.

Table-II

Current treatment options

Treatment	Indications
TURBT	Any suspected urothelial carcinoma; can be the sole treatment
Intravesical chemotherapy and immunotherapy	Non-muscle invasive urothelial carcinoma
Laser ablation therapy	Treatment of select lower and upper-tract cancer treatment of low grade
Conservative management	Papillary tumors
Fulguration or cystoscopic surveillance	Non-muscle invasive papillary bladder tumors Well-documented history of low-grade Ta tumors.

Why Dilemma in Selecting Treatment Option?

Following transurethral resection (TURBT) of the initial T_1Hg tumor without intravesical therapy there is a recurrence rate of 50-70% and progressions rate of 25% to 50%[23-24].

Radical cystectomy in high grade stage T1 transitional cell carcinoma offers excellent results in regard to the prevention of recurrence and progression and survival. The 5 years disease specific mortality after cystectomy for tumor not invading muscularis propria is 20% to 30%, but this mortality rate can be as high as 45% at 5 years and 70% at 10 years in case of conservative therapy[25-26].

So conservative management for those who develop recurrence may be considered as undertreatment. On the other hand radical cystectomy in case of minimal chance of recurrence should be considered as over treatments. Then what should be the optimum treatment option?

TURBT

Transurethral resection of bladder tumor (TURBT) is the first and gold standard treatment option for non-muscle invasive bladder cancer. The quality of the initial TRUBT specimen is of utmost importance. Transurethral resection of bladder tumor should include detrussor muscle in the specimen in an attempt to rule out T2

disease and minimize the risk of understanding. All visible tumors should be resected and resected specimen would provide histological type, grade and depth of invasion. In addition to potentially improving staging accuracy, repeat TURBT may also improve local control of disease[27].

Restaging

One study described that a pathology report of a repeat resection of T1 disease found the incidence of under staging was only 14% and there is also chance of overstaging in 25%-35% cases in the initial specimen. So the standard of care has progressed to mandatory restaging TURBT in case of T1Hg bladder cancer. Repeat resection may also provide prognostic information and improves the efficacy of Intravesical therapy[22].

Even when no residual disease is visible at repeat resection, the prior resection base should be biopsied. Herr has elegantly demonstrated that repeat TUR of non-muscle invasive disease 2 to 6 weeks after initial TUR can up-stage 29% of tumors and change disease management in up to 33%[20]. Therefore, a repeat TUR should be performed to decide the optimum option for management.

Intravesical immunotherapy

Intravesical therapy can be administered is an adjuvant fashion or as part of a maintenance regimen to prevent recurrence[28].

BCG

Bacillus Calmette-Guerin, a live attenuated strain of mycobacterium bovis, first indicated as a tuberculosis vaccine, has had widespread use in Intravesical immunotherapy sice the 1970s[29]. It has be come a first line treatment for carcinoma in situ and has been shown to be effective as prophylaxis to prevent bladder cancer recurrences following TURBT[30].

BCG is the only Intravesical agent that has been shown to affect tumor progression in several randomized trials [30-32]. Herr and colleagues evaluated 86 patients with high-risk superficial cancer and showed that the disease progression and mortality rates in patients treated with BCG decreased from 35% to 28% and 32% to 14% respectively[33]. Pansodoro and colleagues reported on 81 patietns with pT1G3 tumors who received an induction and maintenance regime, with median follow-up of 76 months and recurrence rate was 33%[34].

Table-III

Results of TUR plus BCG for T1G3 tumors.

Series/year	No. of patients	F/U (mo)	Recurrence (%)	Progre-ssion
Perake (2000)	44	43	27	16
Patard (2001)	50	65	52	22
Kulkarni (2002)	69	48	46	12
Bogdanovic	43	53	28	16
Peyromcure	57	53	42	23
Shahin	92	64	70	33

BCG Failure:

Although BCG is an effective adjuvant treatment for T1G3 bladder cancer approximately 50% of patients recur and 15% to 50% of patients within 5 year of BCG therapy[35]. BCG failure is defined as the presence of high-grade NMIBC at 6months from time of TURBT (or at 3 months if the initial tumor is T1G3) or only worsening of the disease (higher grade, stage or number of recurrences, or appearance of CIS) while on BCG therapy despite initial response to BCG [36]. Patients with high risk non-muscle invasive bladder cancer who fail BCG, the option of radical cystectomy should be recommended and discussed with the patient. Herr and colleagues compared the outcome of patients with NMIBC who received a radical cystectomy due to recurrence of disease within 2 years from initial BCG therapy with patients who received radical surgery after 2years; early radical cystectomy was associated with significantly improved survival[37].

Alternative treatments after

BCG failure

Interferon therapy

Patients with a diagnosis of less than stage T1 who do not respond favorably to BCG therapy may be candidates for salvage Intravesical therapy. A multicentre trail of patients with recurrence T1 and lack of response to BCG therapy and treated with reduced dose BCG plus interferon (50 milli units) reported a disease free rate of 42%at 24 months[38]. Intravesical interferon a-2B has been shown to have activity in non-muscle invasive urothelial carcinoma both as monotherapy and most recently in combination with low dose BCG therapy[39-40].

Newer Intravesical Agents

Gemcitabine

Gemcitabine is a newer promising Intravesical agent. In a phase-I study Dalbagni et al[41] reported that Intravesical gemcitabine was well tolerated with minimal bladder

irritation and acceptable myelosuppression. A complete response rate was achieved in 39% cases in a phase II study of patients with BCG refractory transitional cell carcinoma to determine the efficacy of gemcitabine as an Intravesical agent, 28 patients completed the therapy and 16 achieved complete response[42].

Paclitaxel

Paclitaxel is in the early stages of testing.

Cystectomy

Conservative treatment with TUR and Intravesical treatment is associated with continuous decline in survival with life long continuous decline in survival with life long risk of recurrence progression and metastasis[43]. The conservative treatment of T^1Hg bladder cancer should be ended when there is systemic or local toxicity from Intravesical therapy or the patient is not compliant or persistence of tumor or tumor progression despite therapy.

Timing of cystectomy

Early versus deferred: The timing of cystectomy is the most debated issue in the management of T_1Hg tumors. Several groups recommend immediate or early cystectomy without trial of adjuvant Intravesical therapy with or without repeat TUR. Because 5 year survival rate of 90% may decrease to 50% to 60% if radical cystectomy is delayed until progression[44]. In a series of 189 patients who underwent cystectomy within 3 months of diagnosis of muscle invasive disease there was a significantly better 5 year progression free survival than if cystectomy was performed more than 3months following diagnosis (55% and 34% respectively)[45]. Deferring cystectomy until progression to muscle invasive disease may decrease the overall disease specific survival[46]. T1Hg bladder cancer progresses to muscle invasive or metastatic disease at a rate of 30% to 50% after 5 years[47]. As a result some studies advocate initial cystectomy based on the perceived acceptable morbidity and a 5 year disease specific survival rate of 80% to 90%[48-49].

Morbidity and mortality associated with cystectomy

Early complications can occur in upto 28% of patients and most can be managed without additional surgery[50]. Quality of life in bladder cancer patients after radical cystecomy and orthotopic bladder substitution is similar to quality of life of a normal matched population in terms of overall quality of life. Late morbidity is mainly due to the urinary diversion. The risk of impotence is high and age dependent[51]. The per-operative mortality with cystectomy is approximately 3%.

Conclusion

The management of T_1Hg is highly variable due to several factors including divergence in treatment related evidence. The high rates of recurrence and risk of disease progression in bladder cancer often require life long surveillance, making the disease both clinically and economically important. The efficacy of treatments must be balanced with their toxicity, so that single treatment option cannot be considered superior across all NMIBC. Immediate radical cystectomy may be offered upfront in patients with T_1Hg tumors with concomitant CIS or multiple recurrent high grade tumors.

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Abbreviations:

BCG	: Bacillus Calmette Guerin
T1Hg	: T_1Highgrade
TURBT	: Transurethral resection of bladder tumor
CIS	: Carcinoma in Situ
NMIBC	: Non muscle invasive bladder cancer.

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CASE REPORT

RENAL CELL CARCINOMA OF THE KIDNEY PRESENTING AS A RENAL ABSCESS: A RARE CASE REPORT

Nazim Uddin Md. Arif, Ranen Biswas, Waheed Zaman
Department of Urology, Andrology & Renal Transplantation, Apollo Hospitals Dhaka

Abstract:

We report a case of renal tumor presented to us as a case of renal abscess extending to subcutaneous space and finally she was diagnosed as a case of renal cell carcinoma with metastatic para-caval lymphadenopathy. Renal cell carcinoma rarely present with renal and perinephric abscess. The association of renal tumor with renal and subcutaneous abscess can lead to misinterpretation on standard imaging procedures and subsequently mislead to select optimum treatment option. Malignancy may be considered as an underlying cause for the formation of a renal abscess, especially if no other predisposing factors such as diabetes or urinary stones are present.

Key words: *Perinephric abscess, Renal abscess, Renal tumor, Renal cell carcinoma.*

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Introduction:

The association of renal and perinephric abscess with renal cell carcinoma is uncommon. While the diagnosis of pyonephrosis, renal & perinephric abscess is fairly easy, the source of obstruction and infection is an important guide for treatment. Two decades ago *Staphylococcus aureus* antecedent skin lesion may have been the most common cause of renal abscess in children and adults, but now gram-negative organism (*E. coli*) are now the most common cause, and these are more likely associated with retrograde extension of ascending infection and genitourinary abnormalities.[1,2] Anaerobic bacteria may cause perinephric or renal abscesses in patient with history of previous abdominal surgery, renal transplant, malignancy, and oral or dental infection.[3] The association of infective lesion and kidney tumor has not been established adequately in literature. We present a case of renal and perinephric abscess with renal cell carcinoma.

Case Report

A case of 71 years old woman presented to us with fever and swelling in the right loin and lumbar area for 2 weeks. She had been suffering from hypertension for more than 20 years. She has a history of emphysematous pyelonephritis, acute renal failure(sr. creatinine-7.4 mg/dl) 6 years back, which was cured with intravenous antibiotic & double "j" stent placement. She had no haematuria and dysuria, her urinalysis showed numerous pus cell, 2-4 red blood cells per high power field, creatinine was 1.9 mg/dl, urine cultures grew *Escherichia coli* (ELBS). Ultrasonography scan revealed of SOL(space occupying lesion) in right renal region suggestive of abscess with subcutaneous abscess in right loin. Computed tomography revealed hypervascular right renal mass showing large area of necrosis suspicious of renal cell carcinoma, xanthogranulomatous pyelonephritis; with dilated pelvicalyceal system of the right kidney and renal abscess formation extending to perinephric and subcutaneous tissue plane, retroperitoneal lymphadenopathy.

Because of fever and renal abscess extending up to subcutaneous tissue percutaneous drainage was done but patient didn't respond well. Pus culture revealed *Escherichia coli* (ELBS). Nephrectomy was performed. Peroperatively kidney was not very adherent with surrounding structure, tissue plane maintained well, which was against the infectious pathology. Cut surface of the specimen showed a golden yellow tumor with extensive areas of hemorrhage and necrosis. Histologic examination revealed papillary renal cell carcinoma with para-caval lymph node metastasis. At the time of

Correspondences: Nazim Uddin, Department of Urology, Andrology & Renal Transplantation, Apollo Hospitals Dhaka

discharge her sr. creatinine was 1.2 mg/dl. She was advised for radiotherapy to renal bed but refused, however, one year since surgery she is alright now.

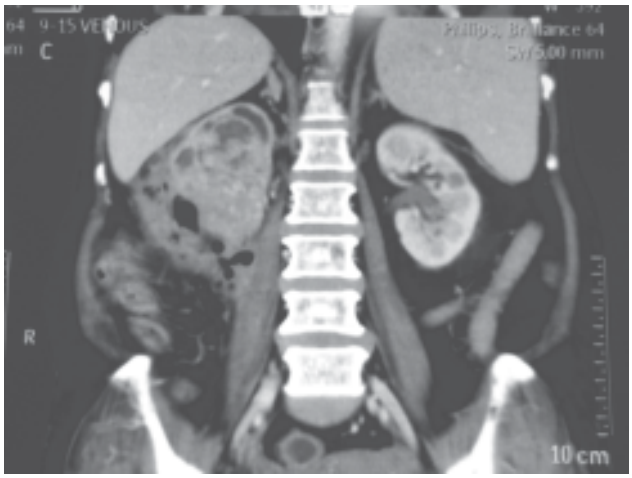

Fig.-1: *Computed tomography revealed hypervascular right renal mass showing large area of necrosis suspicious of renal cell carcinoma, xanthogranulomatous pyelonephritis; with dilated pelvicalyceal system of the right kidney and renal abscess formation extending to perinephric and subcutaneous tissue plane.*

Discussion:

The association of renal cell carcinoma with a renal or perinephric abscess established in published report, its very difficult to diagnose renal tumor when it is present as renal and perinephric abscess.[4] Lo RK et al published a case of perinephric abscess in an adolescent, initially mistaken for tenal tumor, was managed conservatively with antibiotic therapy alone, computed tomography revealed that resolution was complete.[5]

Coexistence of renal tumor and renal abscess is a rare entity, which can lead to misinterpretation on standard diagnostic procedures. It is important to obtain the correct diagnosis, because treatment options for malignant tumor differ from that for abscess.

In our case, absence of gross haematuria and drainage of purulent fluid by puncture misled the differential diagnosis so that cytologic analysis was not obtain, however, retroperitoneal lymphadenopathy was suggestive of some malignant pathology. So, from this case we have learn that, renal abscess treated conservatively with antibiotic & percutaneous drainage need close follow-up after complete remission to exclude any other pathology like malignancy.

Conclusion:

Coexistence of renal tumor and renal abscess is a rare entity, which can lead to misinterpretation on standard diagnostic procedures. It is important to obtain the correct diagnosis, because treatment options for malignant tumor differ from that for abscess. Malignancy may be considered as an underlying cause for the formation of a renal abscess, especially if no other predisposing factors such as diabetes or urinary stones are present.

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