ROLE OF FLEXIBLE CYSTOSCOPY AND ULTRASOUND TOGETHER IN THE DETECTION OF RECURRENT SUPERFICIAL BLADDER TUMORS; A COMPARISON WITH RIGID CYSTOSCOPY

MD. MOYNUL HOQUE CHOWDHURY¹, MD. WALIUL ISLAM², MD. SHAWKAT ALAM³, ANUP ROY CHOWDHURY⁴, MD. LATIFUR RAHMAN MIAH⁵, SHAHARIAR MD. KABIR HASAN⁶, MD. SHARIFUL ISLAM KHAN⁷

Abstract

Objective: To evaluate the role of flexible cystoscopy and ultrasound together in the detection of recurrent superficial bladder tumors

Method: This hospital based prospective comparative study was carried out in the Department of Urology, National Institute of Kidney Diseases and Urology, Sher-E-Bangla nagar, Dhaka from January 2013 to June 2014. A total of 85 patients of post transurethral resection (TUR) and post chemotherapy state for superficial bladder tumors were included in this study. Transabdominal ultrasonography of the bladder was performed for all cases by a consultant radiologist. Flexible cystoscopy was performed by a trained urologist for all. Finally conventional rigid cystoscopy with or without biopsy was performed at the same setting to confirmed the findings.

Result: The mean age was found 62.9±9.7 years with range from 41 to 80 years. Majority (82.4%) patients were male and 15(17.6%) patients were female. Male female ratio was 4.7:1. It was observed that majority (54.1%) patients was found pT1 stage and 39(45.9%) was pTa stage. It was observed that more than two third (67.1%) patients had grade-I and 28(32.9%) had grade-II. Sensitivity, specificity, accuracy, positive and negative predictive values of combine USG and flexible cystoscopy for identification of recurrent tumors were 92.7%, 33.3%, 90.6%, 97.4% and 14.3%.

Conclusion: Ultrasonography and flexible cytoscopy together can detect recurrent superficial bladder tumors as accurate as conventional rigid cytoscopy.

Keywords: USG, flexible cystoscopy, rigid cystoscopy and recurrent superficial bladder.

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Introduction

Worldwide, bladder cancer is the 6th most common cancer in males and the 17th most common cancer in females in 2018. Approximately 75% of patients present with non-muscle invasive disease and have a relatively good prognosis in terms of cancer-specific survival. However, in up to 75% of these patients the cancer will recur despite transurethral resection (TUR) and adjuvant intravesical instillations with either chemotherapy or immunotherapy[1].

Early recurrence rates of superficial bladder cancer after transurethral resection (TUR) remain relatively high at up to 40% at one year. Even patients with papillary neoplasms of low malignant potential have a recurrence rate of 34% at two years increasing to 64% at ten years.
The optimum length of cystoscopic follow-up for patients with superficial bladder cancer is unknown, but patients continue to develop recurrences even after many years of being tumour free[2].

Cystoscopy aided by cytology is the mainstay for the diagnosis of bladder cancer. To date rigid cystoscopy has been the main method of follow-up but flexible cystoscopy is becoming increasingly popular because it can be carried out under local anaesthesia on an out-patient basis[3,4].

Constant improvement in the optics and design of endoscopes have made it possible for the urologist to tackle most urological problems endoscopically, while rigid endoscopes have become extremely popular and are in widespread use all across our country, flexible cystoscopy is still only in its infancy. Flexible cystoscopy allowed much better visualization of the anterior bladder wall and bladder neck than standard rigid cystoscopy.

The flexible cystoscope can provide accurate information about bladder tumors with a specificity of 100 (94-100)% and sensitivity of 96 (80-100)%. Flexible cystoscopy can screen out patients and avoid unnecessary anaesthesia and admission. High cost of the equipment (and its maintenance), however, makes this a somewhat cost-ineffective option. Urologists used to the wide field of vision of a rigid endoscope may also find it difficult to adapt to a flexible one even though the flexiscope can access all areas of the bladder mucosa more easily[5].

Currently, modern sensitive transducers have improved imaging of the urinary tract and therefore transabdominal ultrasound is more effective in visualizing intra-luminal filling defects in the bladder than it was in the past. Moreover, ultrasonography is a non-invasive, well-accepted, and cost-effective diagnostic procedure. Systematic use of ultrasonography has been proposed as the initial test for detection of bladder carcinomas.

Ultrasonography is good but not as good as cystoscopy in the evaluation of the bladder. While the tolerability of cystoscopy is relatively low, it is still superior to ultrasonography in the evaluation of the bladder[6].

The aim of the present study is to evaluate the efficacy of combined flexible cystoscopy and ultrasound in the detection of recurrent superficial bladder tumors and compare with rigid cystoscopy.

Methods:
This hospital based prospective comparative study was carried out in the Department of Urology, National Institute of Kidney Diseases and Urology, Sher-E-Bangla nagar, Dhaka from January 2013 to June 2014 to evaluate the efficacy of combined flexible cystoscopy and ultrasound together in the detection of recurrent superficial bladder tumors. A total of 85 patients of post Transurethral resection (TUR) and post chemotherapy state for superficial bladder tumors of both sex in Urology Department of National Institute of Kidney Diseases and Urology, Sher-E-Bangla Nagar, Dhaka were included in this study. Patient with histologically proved superficial TCCs of urinary bladder (grade-I & II and stage pTa & pT1) were enrolled in this study. Grade-III TCC, muscle invasive TCC at first presentation, associated CIS, associated upper tract TCC and patient refused to give consent were excluded from the study. Transabdominal ultrasonography of the bladder was performed for all cases by a consultant radiologist. Flexible cystoscopy was performed by a trained urologist for all. Finally conventional rigid cystoscopy with or without biopsy was performed at the same settings to confirmed the findings. Statistical analysis was carried out by using the Statistical Package for Social Sciences version 12.0 for Windows (SPSS Inc., Chicago, Illinois, USA). P values <0.05 was considered as statistically significant.

Results

| Variable | Value |
|----------|-------|
| Age in year (mean ±SD) | 62.9±9.7 |
| Sex | |
| Male [n(%)] | 70 (82.4) |
| Female [n(%)] | 15 (17.6) |

The mean age was found 62.9±9.7 years with range from 41 to 80 years. Majority (82.4%) patients were male and 15(17.6%) patients were female. Male female ratio was 4.7:1.
Table II

| Stage  | Number of patients | Percentage |
|--------|--------------------|------------|
| pTa    | 39                 | 45.9       |
| pT1    | 46                 | 54.1       |

Grade

| Grade | Number of patients | Percentage |
|-------|--------------------|------------|
| G-I   | 57                 | 67.1       |
| G-II  | 28                 | 32.9       |

It was observed that majority (54.1%) patients was found pT1 stage and 39(45.9%) was pTa stage. It was observed that more than two third(67.1%) patients had grade-I and 28(32.9%) had grade-II.

Table III

| Type of recurrence | Number of patients | Percentage |
|--------------------|--------------------|------------|
| Rigid cystoscopy   |                    |            |
| Missed lesion      | 3                  | 3.5        |
| Papillary          | 67                 | 78.8       |
| Solid              | 15                 | 17.6       |
| USG                |                    |            |
| Missed lesion      | 8                  | 9.4        |
| Papillary          | 64                 | 75.3       |
| Solid              | 13                 | 15.3       |
| Flexible cystoscopy|                    |            |
| Missed lesion      | 4                  | 9.4        |
| Papillary          | 66                 | 77.6       |
| Solid              | 15                 | 17.6       |

Table III shows recurrence of tumor of the patients, it was observed that majority (78.8%) patients had recurrent papillary tumor in rigid cystoscopy. Sixty four (75.3%) patients had recurrent papillary tumor in USG. Sixty six (77.6%) patients had recurrent papillary tumor in flexible cystoscopy.

Table IV

| Tumor detection | Number of patients | Percentage |
|-----------------|--------------------|------------|
| Rigid cystoscopy|                    |            |
| Positive        | 82                 | 96.5       |
| Negative        | 3                  | 3.5        |
| USG             |                    |            |
| Positive        | 76                 | 89.4       |
| Negative        | 9                  | 10.6       |
| Flexible cystoscopy|                |            |
| Positive        | 81                 | 95.3       |
| Negative        | 4                  | 4.7        |

Table IV shows detection of recurrent tumor in the study patients, it was observed that majority (96.5%) patients had recurrent tumor in rigid cystoscopy. Seventy six (89.4%) patients had recurrent tumor in USG. Eighty one (95.3%) patients had recurrent tumor in flexible cystoscopy.

Table V

Comparison between ultrasonography with rigid cystoscopy in detection of recurrent tumors

| Ultrasonography | Rigid cystoscopy |
|-----------------|------------------|
| Positive (n=82) | Negative (n=3)   |
| Positive (n=76) | 73 (TP)          |
| Negative (n=9)  | 3 (FP)           |

Ultrasonography evaluate true positive 73 cases, false positive 3 cases and false negative 9 cases in comparison with rigid cystoscopy.

Table VI

Comparison between flexible cystoscopy with rigid cystoscopy in detection of recurrent tumors

| Flexible cystoscopy | Rigid cystoscopy |
|---------------------|------------------|
| Positive (n=81)     | Negative (n=4)   |
| Positive (n=81)     | 79 (TP)          |
| Negative (n=4)      | 2 (FP)           |

Flexible cystoscopy evaluate true positive 79 cases, false positive 2 cases and false negative 3 cases and true negative 1 case in comparison with rigid cystoscopy.
**Table VII**

*Sensitivity, specificity, accuracy, positive and negative predictive values of the USG, flexible cystoscopy and combined (USG+flexible cystoscopy) with fixed cystoscopy for identification of recurrent tumors*

| Test of validity          | Ultrasonography | Flexible cystoscopy | Combine  |
|---------------------------|-----------------|---------------------|----------|
| Sensitivity               | 89.0            | 96.3                | 92.7     |
| Specificity               | 0.0             | 33.3                | 33.3     |
| Accuracy                  | 85.9            | 94.1                | 90.6     |
| Positive predictive value | 96.1            | 97.5                | 97.4     |
| Negative predictive value | 0.0             | 25.0                | 14.3     |

Sensitivity, specificity, accuracy, positive and negative predictive values of combine USG and flexible cystoscopy for identification of recurrent tumors were 92.7%, 33.3%, 90.6%, 97.4% and 14.3%.

**Discussion**

This prospective comparative study was carried out with an aim to detect the sensitivity and specificity of flexible cystoscopy and Ultrasound in the detection of recurrent superficial bladder tumors and to compare between them and with conventional rigid cystoscopy and to assess the usefulness of flexible cystoscopy and ultrasound as follow up tools for the detection of recurrent superficial bladder tumors.

In the present study it was observed that recurrent bladder tumors are more common in male subject, where 82.4% and 17.6% patients were male and female respectively. On the other hand male to female ratio was 4.7:1, which is closely resembled with Uddin et al.\[7\]. study, where they found 82.4% male and 17.6% female.

In this current study mean age was found 62.9±9.7 years varied from 41 to 80 years. Similarly, Uddin et al. (2012) showed the mean age of patients with recurrent bladder tumor was 61 years varied from 41-80 years. In another study Stamatiou et al[6]. observed median age was 63.2 years varied from 33 to 85 years in male patients while in female patients median age was 58.6 years varied from 34 to 76 years, which are comparable with the current study.

In this current study it was observed that majority (78.8%) patients had recurrent papillary tumor in rigid cystoscopy. Sixty four (75.3%) patients had recurrent papillary tumor in USG. Sixty six (77.6%) patients had recurrent papillary tumor in flexible cystoscopy. However, lesion that missed are 3.5% in rigid cystoscopy, 9.4% in USG and 4.7% in flexible cystoscopy. Uddin et al.\[7\] evaluated 85 sessions of follow-up investigations-ultrasound and flexible cystoscopy showed 31 recurrences confirmed by rigid cystoscopy and biopsy.

In the present study it was observed that majority (96.5%) patients had recurrent tumor in rigid cystoscopy. Seventy six (89.4%) patients had recurrent tumor in USG and eighty one (95.3%) patients had recurrent tumor in flexible cystoscopy. Uddin et al.\[7\] observed that in rigid cystoscopies, 31 were positive for tumors, ultrasonography was positive in 77.42%, flexible cystoscopy in 90.32% of these positive controls. Rigid cystoscopy was negative for tumor in 54 cases and this was correlated by ultrasounds in 90.74%, flexible cystoscopy in 94.44% of the cases.

Ultrasound evaluation for detection of recurrent tumor, true positive 73 cases, false positive 3 cases and false negative 9 cases in comparison with rigid cystoscopy located in the dome (vault) of the bladder (four), bladder trabeculation (five) or recurrence smaller than 5mm (nine) were the possible causes. False positive rate was 10.0% in the study by Malone[8]; severe trabeculation and diverticula of the bladder (one), prominent median lobe (one), blood clot and debris (one) were the possible causes. There was a close correlation between the results of rigid cystoscopy and those of flexible cystoscopy in 92.94%. Correlation between the results of rigid cystoscopy and ultrasonography was in 85.88%[7]. There was discordance between the results of two modalities of cystoscopy in 6 cases (3 false positive and 3 false negative).Discordance between the results of rigid cystoscopy and ultrasonography was 12 (5 false positive and 7 false negative) observed by Uddin et al [7].
Flexible cystoscopy evaluation for detection of recurrent tumor, true positive 79 cases, false positive 2 cases and false negative 3 cases and true negative 1 case in comparison with rigid cystoscopy. Uddin et al.7 mentioned in their study that there was a close correlation between the results of rigid cystoscopy and those of flexible cystoscopy in 79 of the 85 cases (92.94%). Correlation between the results of rigid cystoscopy and ultrasonography was in 73 of the 85 cases (85.88%), which is comparable with the current study.

So, it was observed that for detection of recurrent tumor, ultrasonography sensitivity 89.0%, flexible cystoscopy 96.3% and combine 92.7%. ultrasonography specificity 0%, flexible cystoscopy 33.3% and combine 33.3%. Ultrasonography accuracy 85.9%, flexible cystoscopy 94.1% and combine 90.6% for detection of recurrent tumor. Ultrasonography positive predictive values 96.1%, flexible cystoscopy 97.5% and combine 97.4% for detection of recurrent tumor. Ultrasonography negative predictive values 0%, flexible cystoscopy 25.0% and combine 14.3% for detection of recurrent tumor. Uddin et al[7] mentioned in their study that sensitivity, the most important parameter, was 97% for the two examinations together. Each method separately had the following sensitivity: ultrasound 77%; flexible cystoscopy 90%. Sensitivity and specificity of USG in detecting recurrent bladder tumors were 77.42% and 90.74% respectively; and for flexible cystoscopy were 90.32% and 94.44%. In Uddin et al[7] study, accuracy rate of ultrasound was 86.0% and that of flexible cystoscopy was 93.0% (6.0% of 31 tumor diagnoses missed, 95% confidence interval), which was comparable well with combination of ultrasound and flexible cystoscopy (accuracy rate 99.0%; 95% confidence interval) and conventional rigid cystoscopy. So, their study showed that, when comparing rigid cystoscopy and combination of ultrasound and flexible cystoscopy, good correlation between detection rates are encouraging. The flexible cystoscope can provide accurate information about bladder tumor with a specificity of 100 (94-100)% and sensitivity of 96 (80-100)% [5]. Rod-lens cystoscopy has been a yardstick of the accuracy of alternative tests such as ultrasound and cystology[8,9,10]. Positive findings on ultrasonography that are not confirmed at conventional cystoscopy have been interpreted as false-positive ultrasound scans, not false-negative cystoscopies[11]. In this study, 4 of the 85 tumor episodes were missed by the flexible cystoscopy, which was similar to the study of Walker et al[11]. and three tumors were on the right lateral wall and it could be due to the fact that cystoscopist always stood on the patient’s right, the right wall was more difficulty to examine thoroughly. The missed fourth tumor was on the left lateral wall in a bladder filled with turbid urine. For ultrasonography, the sensitivity 87.1%, specificity (98.1%), positive predictive value 94.4% and negative predictive value 95.4% were good but not as good as cystoscopy obtained by Stamatiou et al[6].

Conclusion

It can be concluded that ultrasonography and flexible cystoscopy together can detect recurrent superficial bladder tumors as accurate as conventional rigid cystoscopy and patients can be followed-up as out-patient basis.

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