

## RESEARCH ARTICLE

# Hematuria Screening Test for Urinary Bladder Mucosal Infiltration in Cervical Cancer

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### Abstract

**Objective:** To determine the diagnostic performance of hematuria as a screening test for urinary bladder infiltration in cervical cancer patients with a prospective study design. **Materials and Methods:** Newly diagnosed cervical cancer patients at Srinagarind hospital from 14 June 2011 to 30 April 2012 were enrolled in this study. We collected midstream urine samples for urinalysis from every patient before routine cystoscopic exam for clinical staging. The presence of 3 or more red blood cells (RBCs) per high power field was defined as positive for hematuria. A two-by-two table was used to determine the diagnostic performance of hematuria to detect urinary bladder mucosal infiltration using cystoscopy and biopsy as the gold standard. **Result:** A total of 130 were patients included, 54 of which (41.5%) had hematuria. Of these, four patients (3.08%) had pathological report from cystoscopic biopsy confirmed metastatic squamous cell carcinoma. The sensitivity, specificity, PPV, NPV, and accuracy of hematuria as a screening test to detect urinary bladder mucosal infiltration of cervical cancer were 100%, 60.3%, 7.4%, 100%, and 61.5%, respectively. There was no single case of urinary bladder mucosal infiltration in patients initially staged less than stage III. **Conclusions:** Hematuria can be used as a screening test to detect urinary bladder mucosal infiltration of cervical cancer. This can reduce the number of cervical cancer patients who really need to undergo cystoscopy as a staging procedure to less than half and to less than 20% if stage III or more were included without missing a single case of urinary bladder mucosal infiltration.

**Keywords:** Hematuria - screening test - urinary bladder mucosal infiltration - cervical cancer

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### Introduction

Cervical cancer is a common cancer in Thai women. The incidence rate is 25 in 100,000 women per year (Wilailak, 2009) with the death rate of 10.79 in 100,000 people (Ferlay et al., 2000). There are 6000-7000 new cases of cervical cancer per year (Wilailak, 2009).

Cervical cancer is clinically staged. The International Federation of Gynecology and Obstetrics (FIGO) staging system 2009 (Pecorelli, 2009) defined stage IVA as having tumor involved the mucosa of the urinary bladder and/or rectum.

Cystoscopy is the investigation of choice accepted by the FIGO for the diagnosis of bladder mucosa infiltration (Pecorelli et al., 1997). At Srinagarind Hospital, we perform cystoscopy as a routine procedure for clinical staging. The prevalence of invasive urinary bladder mucosal infiltration in cervical cancer ranged from 1.76-7.72% (Shingleton et al., 1971; Van Nagell et al., 1975; Griffin et al., 1976; Udomthavornsuk et al., 1987). Cystoscopy requires specific equipment, skill, cost, and time. According to the very low prevalence of urinary bladder mucosal involvement, a large proportion of patients unnecessarily underwent this procedure without any benefit.

Eighty percent of patients with bladder cancer have painless, intermittent hematuria as the primary symptom (Cummings et al., 1992). Messing et al. (2006). in a study of healthy 1576 men, revealed 258 cases of hematuria. Of these 258 cases, there were 21 cases of urothelial cancer of urinary bladder. Udomthavornsuk et al. (1987) retrospectively studied the cervical cancer patients with urinary bladder mucosal involvement. All the patients with urinary bladder mucosal involvement proved by cystoscopy had abnormal amount of red blood cells in their urine. Data from these studies give us the idea that hematuria may be a screening test for urinary bladder mucosal infiltration in cervical cancer to select patients who really need to undergo cystoscopy in clinical staging.

### Materials and Methods

This prospective study was undertaken between 14 June 2011 and 30 April 2012 at Srinagarind Hospital, Faculty of Medicine, Khon Kaen University, Thailand. All newly diagnosed cervical cancer patients were included in this study. The study was approved by the ethics committee on 14 June 2011. Written informed consents were obtained from all the participants entered into the study.

Midstream urine sample was collected for urinalysis just before every cystoscopic procedure. Hematuria was defined as the presence of 3 or more RBCs per high-power field (Mariani et al., 1989). Cystoscopy was done as part of the routine staging work-up in all patients. Bladder biopsy was done when there was any suspicious lesion of mucosal invasion. Two-by-two table was used to determine the diagnostic performance of hematuria to detect urinary bladder mucosal infiltration using cystoscopy and biopsy as gold standard.

## Results

There were 130 newly diagnosed cervical cancer patients between 14 June 2011 and 30 April 2012. The average age of the patients was 52.28 years-old (range 33-81). Underlying diseases of the patients were shown in Table 1. Table 2 shows the distribution of the initial stages of the patients. The majority of patients (38.46%) were in stage IIIB.

The urinalysis results were shown in Table 3. Fifty four patients (41.54%) had hematuria, with 31 patients (23.85%) initially staged (before bladder biopsy) less than

**Table 1. Underlying Diseases of 130 Patients**

Underlying disease	No. of patients
None	107
Hyperthyroid	3
Heart disease	2
HIV serology positive	4
Diabetic mellitus or Hypertension or Dyslipidemia	14

**Table 2. Distribution of Initial Stages of 130 Patients (Before Bladder Biopsy)**

FIGO stage	No. of patients	%
IA1	4	3.08
IA2	1	0.76
IB1	22	16.92
IB2	2	1.54
IIA1	2	1.54
IIA2	2	1.54
IIB	38	29.23
IIIA	1	0.77
IIIB	50	38.46
IVA	0	0
IVB	3	2.31
Unstaged	5	3.85

**Table 3. Classification of Staging and Hematuria in 130 Patients**

Staging	No. of patients (%)	Hematuria (%)
Less than stage III and unstaged	76 (52.46%)	31 (23.85%)
Stage III or more	54 (47.54%)	23 (17.69%)
Total	130 (100%)	54 (41.54%)

**Table 4. Results of the 16 Urinary Bladder Biopsies**

Pathological report	No. of patients
Metastatic squamous cell carcinoma	4
Cystitis	6
Inflammation	3
Fibrosis	1
Squamous metaplasia	2

**Table 5. Hematuria and Cystoscopy and Biopsy of Urinary Bladder Mucosal Infiltration**

	Cystoscopy and biopsy		Total
	Positive	Negative	
Hematuria: Positive	4	50	54
Negative	0	76	76
Total	4	126	130

**Table 6. Distribution of the Final Stages in 130 Patients (After Bladder Biopsy)**

FIGO stage	No. of patients	%
IA1	4	3.08
IA2	1	0.76
IB1	22	16.92
IB2	2	1.54
IIA1	2	1.54
IIA2	2	1.54
IIB	38	29.23
IIIA	1	0.77
IIIB	47	36.15
IVA	3	2.31
IVB	3	2.31
Unstaged	5	3.85

III and 23 patients (17.69%) initially staged III or more. At cystoscopy, 16 patients were reported having bladder mucosal lesions suspicious of malignant infiltration. Table 4 shows the result of the urinary bladder mucosal biopsies. Four patients were pathologically confirmed to have metastatic squamous cell carcinoma to bladder mucosa. Of these 4 patients, 3 were initially had stage IIIB and 1 was initially had stage IVB (lung metastasis).

Table 5 shows the results of urinalysis and cystoscopic findings. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of hematuria as a screening test using cystoscopy and biopsy as gold standard were 100%, 60.32%, 7.41%, 100%, and 61.54% respectively.

Distribution of the final stages (after bladder biopsy) is shown in Table 6.

## Discussion

Cystoscopy is a routine clinical staging work-up of all cervical cancer patients at Srinagarind Hospital. The prevalence of urinary bladder mucosal infiltration in our study is only 3.08% and all of these patients are in stage III or more advanced stage. Many studies had demonstrated in the same way. The data from Shingleton et al. (1971); Van Nagell et al. (1975); Griffin et al. (1976); Udomthavornsuk et al. (1987) showed the prevalence of urinary bladder mucosal infiltration in cervical cancer of 5.7%, 7.72%, 1.76%, and 3.25%, respectively. All of these patients had stage III or more advanced diseases. If we use the criterion of stage III or more to do cystoscopy for staging, we can reduce the number of patients who really need to do cystoscopy from 130 to 54 (47.54%) (Table 3).

From Table 5, all patients with urinary bladder mucosal involvement confirmed by cystoscopic and pathologic findings had hematuria. Both the sensitivity and NPV of hematuria to detect urinary bladder mucosal involvement

were 100%. Therefore, hematuria is a very good screening test to rule out urinary bladder mucosal involvement in cervical cancer. There was no single case of negative hematuria having urinary bladder mucosal involvement from cystoscopy and biopsy. However, the specificity and PPV were low (60.32% and 7.41%, respectively). Therefore, if we use hematuria as the only criterion for cystoscopy in the clinical staging for cervical cancer, there still are many patients who will undergo cystoscopy unnecessarily.

If we combine stage III or more advanced stage with hematuria as the criteria for cystoscopy in clinical staging, the number of patients who really need cystoscopy will be only 23 from 130 or 17.69% (Table 3). We can omit more than 80% of the patients from cystoscopy and save quite a lot of cost and time consumed by the procedure.

In conclusion, hematuria can be used as a screening test to detect urinary bladder mucosal infiltration of cervical cancer. This can reduce the number of cervical cancer patients who really need to undergo cystoscopy as a staging procedure to less than half and to less than 20% if stage III or more was included without missing a single case of urinary bladder mucosal infiltration.

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