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The usefulness of urinary cytology testing in the evaluation of irritative voiding symptoms

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KEY WORDS
Urinary cytology
Urothelial cancer
Irritative voiding symptoms

Objective: The purpose of this study was to assess the clinical usefulness of urinary cytology testing for the evaluation of urothelial cancer in women with irritative voiding symptoms who were examined at a urogynecology service.

Study design: Urinary cytology studies results that were obtained from January 1, 2000, to December 31, 2002, were cross-matched with the Rhode Island Department of Health Cancer Registry to identify those women who were diagnosed with urinary tract malignancies. The prevalence of urothelial cancer was determined, and the sensitivity, specificity, and positive and negative predictive values of urinary cytologic testing were calculated for 2 common classification strategies: (1) consideration of atypical cytologic test results to be normal and (2) consideration of atypical cytologic test results to be abnormal.

Results: Among 1516 cross-matched cytologic test results from 1324 patients, 5 urothelial cancers were identified. Two of the 5 malignancies were associated with positive cytology results. The prevalence of urothelial cancer was 0.38% (95% CI, 0.1%, 0.9%). When atypical cytology studies were classified as normal, the sensitivity of urinary cytology was 40% (95% CI, 7.2%, 83.0%); the specificity was 99.9% (95% CI, 99.5%, 100%); the positive predictive value was 66.7% (95% CI, 12.5%, 98.2%), and negative predictive value was 99.8% (95% CI, 99.2%, 100%). In contrast, when atypical cytology results were classified as abnormal, the sensitivity and negative predictive value remained the same, but the specificity declined to 93.6% (95% CI, 92.1%, 94.8%), and the positive predictive value decreased to 2.3% (95% CI, 0.4%, 8.8%).

Conclusion: The low prevalence of urothelial cancers and low sensitivity of urinary cytology studies severely limit the usefulness of this test in the evaluation of women with irritative voiding symptoms.

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Irritative urinary voiding symptoms that include urinary urgency, frequency, nocturia, and dysuria are the second most common presentation of bladder cancer, with hematuria being the most common complaint.[1-3] However, only one third of patients who are diagnosed with bladder cancer have irritative voiding symptoms, which makes treatment decisions that are based on symptoms alone difficult.[2] Urinary cytology is often used in the evaluation of patients with irritative voiding symptoms to aid in the detection of urothelial tract malignancies, but its role remains controversial, with some authors arguing for cytology only in high-risk patients.[4]

The presence of neoplastic urothelial cells in the urine was first reported by Sanders[5] in 1864, but the use of urinary cytology for the diagnosis of urothelial malignancy was not described until 1945 by Papanicolaou and Marshall.[6] Since then, the subject of urinary cytology as a test for urothelial cancer has been discussed in numerous reports.[7,8] Although the sensitivity and specificity of urinary cytology is thought to be higher in women with a history of urinary tract malignancy or hematuria, the clinical usefulness of this test in the evaluation of women with irritative voiding symptoms is uncertain.

The objective of this study was to assess the clinical usefulness of urinary cytology for the detection of urothelial cancer in women with irritative voiding symptoms at an academic urogynecology service. Specifically, we sought to determine the prevalence of urothelial cancer in our study population and to determine the sensitivity, specificity, and positive and negative predictive values of urinary cytology for the diagnosis of urinary tract malignancy in these women using the 2 most common classification strategies. Our hypothesis was that urinary cytology has limited usefulness for the evaluation of urinary tract malignancy in women with complaints of irritative voiding symptoms.

Material and methods

This study was approved by the Institutional Review Boards at Women and Infants' Hospital of Rhode Island and by the Rhode Island Department of Health. All urinary cytology studies that were sent from the Division of Urogynecology at Women and Infants' Hospital of Rhode Island from January 1, 2000, to December 31, 2002, in the course of the evaluation of women with irritative voiding symptoms were included in this study. We defined irritative voiding symptoms as urinary urgency, pain or burning with urination, urinary frequency, and/or nocturia. Definitions conform to the standards recommended by the International Continence Society.[9] In accordance with accepted nomenclature, final urinary cytologic testing results were classified by 1 of 2 board-certified attending cytopathologists into 1 of 4 categories: normal, atypical/indeterminate, suspicious, or malignant.[10] Fresh urine specimens that were analyzed in the cytopathology laboratory were centrifuged, and the precipitate was put into "thin preparation" vials. After being processed, the specimens were read in a standardized fashion in a manner that was similar to the reading of "thin preparation" Papanicolaou smears. It has been our standard practice to obtain urinary cytology studies for women with irritative voiding symptoms and to send repeat cytologic tests for women with atypical or suspicious results. Treatment decisions are then based on the most abnormal cytologic test reading.

Table I Common classification strategies for grouping atypical urinary cytology studies

Strategy 1		Strategy 2	
Low risk	High risk	Normal	Abnormal
Normal Atypical	Suspicious Malignant	Normal	Atypical Suspicious Malignant

Urinary cytology studies that were sent from our division during the study period were identified through the Women and Infants' Hospital cytology laboratory and compiled into a master list. Social security numbers and cytologic testing dates were then extracted from this list and electronically cross-matched with the Cancer Registry database at the Rhode Island Department of Health to identify those women who were diagnosed subsequently with urinary tract malignancies during the study period. We set search parameters for the cross-match using International Classification of Diseases Oncology incidence codes for *bladder* (C67.0-C67.9), *ureter* (C66.9), *urothelial* (C67), *urethra* (C68.0, C67.5), and *kidney* (C64.9, C65.9). Results from the database cross-match were then confirmed with the master cytologic test list and individual medical records to ensure accuracy.

Through the database cross-match, types of urothelial cancer and tumor behavior (malignant or in situ) were noted, and the prevalence of urothelial cancer in our study population was determined. We then calculated the sensitivity, specificity, and positive and negative predictive values of urinary cytology (with 95% CIs) using 2 different common classification strategies: (1) grouping atypical/indeterminate urinary cytologic results into a low-risk category with "normal" cytologic testing readings and (2) grouping atypical/indeterminate cytology studies into a high-risk category with all "abnormal" cytology test readings (including atypical/indeterminate, suspicious, and malignant cytologic results; Table I). To evaluate the impact of varying