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# COMMITTEE OPINION

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## Committee on Gynecologic Practice American Urogynecologic Society

*This Committee Opinion was developed by the American College of Obstetricians and Gynecologists' Committee on Gynecologic Practice and the American Urogynecologic Society in collaboration with committee members Charles W. Nager, MD, Vivian W. Sung, MD, and James L. Whiteside, MD.*

*This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.*

## Asymptomatic Microscopic Hematuria in Women

**ABSTRACT:** Asymptomatic microscopic hematuria is an important clinical sign of urinary tract malignancy. Asymptomatic microscopic hematuria has been variably defined over the years. In addition, the evidence primarily is based on data from male patients. However, whether the patient is a man or a woman influences the differential diagnosis of asymptomatic microscopic hematuria, and the risk of urinary tract malignancy (bladder, ureter, and kidney) is significantly less in women than in men. Among women, being older than 60 years, having a history of smoking, and having gross hematuria are the strongest predictors of urologic cancer. In low-risk, never-smoking women younger than 50 years without gross hematuria and with fewer than 25 red blood cells per high-power field, the risk of urinary tract malignancy is less than or equal to 0.5%. Furthermore, the evaluation may result in more harm than benefit and is unlikely to be cost effective. Thus, data support changing current hematuria recommendations in this low-risk group. The American College of Obstetricians and Gynecologists and the American Urogynecologic Society encourage organizations producing future guidelines on the evaluation of microscopic hematuria to perform sex-specific analysis of the data and produce practical sex-specific recommendations. In the meantime, the American College of Obstetricians and Gynecologists and the American Urogynecologic Society recommend that asymptomatic, low-risk, never-smoking women aged 35–50 years undergo evaluation only if they have more than 25 red blood cells per high-power field.

### Recommendations and Conclusions

The American College of Obstetricians and Gynecologists (the College) and the American Urogynecologic Society (AUGS) make the following recommendations and conclusions:

- Urinalysis is a commonly performed test and microscopic hematuria is a common finding.
- Renal cancer and bladder cancer are more common in men than women.
- In low-risk, never-smoking women younger than 50 years without gross hematuria and with fewer than 25 red blood cells per high-power field, the risk of urinary tract malignancy is less than or equal to 0.5%.
- The College and AUGS encourage organizations producing future guidelines on the evaluation of microscopic hematuria to perform sex-specific anal-

ysis of the data and produce practical sex-specific recommendations.

- The College and AUGS recommend that asymptomatic, low-risk, never-smoking women aged 35–50 years undergo evaluation only if they have more than 25 red blood cells per high-power field.

### Background

Over the years, asymptomatic microscopic hematuria has been variably defined. Past guidelines required two microscopic urinalyses to establish a diagnosis of asymptomatic microscopic hematuria (1, 2). The 2012 American Urological Association guidelines on the evaluation and diagnosis of asymptomatic microscopic hematuria require only a single positive properly collected specimen with three or more red blood cells per high-power field with no obvious benign cause (3). Additionally, those



guidelines have lowered the age threshold for evaluation from older than 40 years to 35 years. The recommended evaluation for all patients meeting the criteria for asymptomatic microscopic hematuria (after other causes have been ruled out) includes cystoscopy and upper tract imaging with multiphasic computed tomography (CT) urography, with and without intravenous contrast. It should be emphasized that “blood” on a dipstick urinalysis is not hematuria, and this finding indicates the need for a microscopic urinalysis to evaluate for red blood cells. In contrast to the American Urological Association recommendations, the U.S. Preventive Services Task Force in 2011 concluded the current evidence is insufficient to assess the balance of benefits and harms of screening for bladder cancer in asymptomatic adults (4).

The strength of the evidence behind the American Urological Association recommendations is Grade C (observational studies that are inconsistent, have small sample sizes, or have other problems that potentially confound interpretation of data) (3). In addition, the evidence primarily is based on data from male patients. However, whether the patient is a man or a woman influences the differential diagnosis of asymptomatic microscopic hematuria, and the risk of urinary tract malignancy (bladder, ureter, and kidney) is significantly less in women than in men. Therefore, female-specific data should be evaluated and female-specific recommendations should be made for the diagnostic evaluation of asymptomatic microscopic hematuria.

### **Urinalysis and the Prevalence of Microscopic Hematuria**

Urinalysis is a commonly performed test and microscopic hematuria is a common finding. For example, in a large Kaiser Permanente database that spanned 6 years, 3,742,348 urinalyses were performed on 2,705,696 women, and 552,119 (20%) of them had microscopic hematuria; however, this number includes some women with an identified cause of microscopic hematuria, such as urinary tract infection (5). In the American Urological Association systematic review of 80,000 women and men, the prevalence of asymptomatic microscopic hematuria ranged from 2.4% to 31.1% (3).

### **Specimen Collection**

A voided midstream sample is the recommended method to collect a urine specimen from women. Based on the anatomic differences between men and women, this collection approach will result in more genital flora contamination in samples from women. Menstruation, urogenital tract atrophy, and pelvic organ prolapse are exclusively female conditions that can lead to urine contamination. Obesity also increases the risk of contamination. Although the hematuria guidelines panel noted nonlife-threatening diagnoses (eg, benign prostatic hypertrophy [12.9%] and urethral stricture [1.4%]) can be discovered during a microscopic hematuria evalua-

tion (3), such conditions are not common to or relevant for women.

### **Prevalence of Urinary Tract Malignancies**

Asymptomatic microscopic hematuria is an important clinical sign for urinary tract malignancy. Risk factors for urinary tract malignancy include being male, being older, being a past or current smoker, having gross hematuria, and having a history of pelvic irradiation. In 2017, there are estimated to be 3.3 times more new cases of bladder cancer in men than in women (60,490 versus 18,540) (6). Bladder cancer accounts for approximately 6% of cases of cancer in males and is the fourth most common cancer among men. In contrast, bladder cancer accounts for only 2% of cases of cancer in females and is not in the top 10 most common types of cancer among women. Similarly, there are estimated to be 1.7 times more new cases of renal cancer in men compared with women (40,610 versus 23,380). In terms of lethality, bladder cancer is the eighth most common cause of death in men, but is not in the top 10 for women. Men are 2.2 times more likely to die of urinary tract cancer than women (22,260 versus 9,930 estimated deaths) (6).

### **The Evaluation of Microscopic Hematuria and the Detection of Urinary Tract Malignancy**

Among the 10 studies that assessed bladder cancer rates by sex and were included in the 2012 microscopic hematuria guidelines, six studies found no cases of bladder cancer among female patients. The rate of female bladder cancer across these studies was 0–0.3% (7–16). In addition, a 2011 study of 100,000 women with hematuria that was not included in the 2012 American Urological Association guidelines (because it was published after the literature search) found that the rate of any urologic malignancy among women younger than 40 years with any degree of microscopic hematuria was 0.02%, and the rate among women older than 40 years was 0.4% (17). The identified risk factors for malignancy were having a history of gross hematuria, being male, being older than 50 years, and having a history of smoking. Table 1 lists the prevalence of urinary tract cancer by the degree of hematuria in women older than 40 years. The authors proposed using a cutoff of greater than 25 red blood cells per high-power field among women older than 40 years, noting this approach had a better sensitivity, specificity, and positive predictive value than the 2012 recommendations (17). In addition, a follow-up study of 3,573 women referred for urologic evaluation for asymptomatic hematuria, performed by Kaiser Permanente Southern California, found that being older than 60 years and having a history of smoking, gross hematuria, or both, were the strongest predictors of urologic cancer (5). Absent these risk factors, the rate of urologic cancer did



**Table 1.** The Prevalence of Urinary Tract Cancer by Degree of Hematuria in Women Older Than 40 Years ⇐

Red Blood Cells Per High-Power Field	Urinary Tract Cancer (%)
3–10	0.22
11–25	0.40
26–99	0.87
More than 100	1.77

Data from Jung H, Gleason JM, Loo RK, Patel HS, Slezak JM, Jacobsen SJ. Association of hematuria on microscopic urinalysis and risk of urinary tract cancer. *J Urol* 2011;185:1698–703. [PubMed]

not exceed 0.6% (Table 2). The risk scoring system suggests that women younger than 50 years have a very low rate of urinary tract cancer. Of note, in women without gross hematuria in the previous 6 months, microscopic hematuria was not significantly associated with the risk of urologic cancer (5). Of concern, several studies have failed to confirm the utility of asymptomatic microscopic hematuria as a screening tool for renal cancer. In one series that evaluated microscopic hematuria as a screening tool for renal cancer, the rate of renal cancer was only 0.33% (8, 18). Up to 60% of cases of renal cancer are diagnosed incidentally with imaging for unrelated symptoms (19).

### Risk of Diagnostic Testing

Routine evaluation of all men and women older than 35 years with cystoscopy and CT urography has substantial cost and adverse event implications. In patients undergoing outpatient cystoscopy, 50% reported dysuria and 3% had a documented urinary tract infection (20). In addition, nephropathy from intravenous contrast has been calculated to be greater than 2% in the general population and greater than 20–30% in high-risk patients (21). Diagnostic CT scans involve much higher doses of

radiation compared with plain-film radiography. It has been estimated that up to 2% of future malignancies may be iatrogenic secondary to CT radiation exposure, and the risk is greater when CT radiation exposure is administered to individuals younger than 40 years (22). The expected detection rate of cancer from a given test should exceed the potential risk of cancer that the test precipitates. Computed tomography scans for women younger than 40 years have the greatest risk and lowest yield in the evaluation of microscopic hematuria.

### Implementation of the Evaluation of Microscopic Hematuria Recommendations

Because of the high prevalence of microscopic hematuria and the very low risk of urinary tract cancer, compliance with the recommendations among health care providers has been limited. For example, a survey of primary care physicians from two U.S. metropolitan areas reported that 64% of microscopic hematuria findings were not routinely referred for urologic evaluation (23). Another large primary care cohort study showed similar results and revealed that only 13.9% of patients with microscopic hematuria underwent imaging, 13.7% had cystoscopy, and only 5.7% received complete evaluation (24). Women had significantly lower evaluation rates (complete evaluation in only 3.8% of female patients), and this implies that health care providers already are using sex-specific risk factors to make clinical decisions about whom should be evaluated (24). At a large academic center, 35.6% of patients with microscopic hematuria underwent any imaging, 9% had cystoscopy, and 8.2% underwent both, further supporting these results (25). “Alarm fatigue” generated by the aggressive hematuria evaluation combined with the low rate of urologic cancer in this large segment of patients presenting with microscopic hematuria, as well as the potential for iatrogenic harm, warrant reconsideration of the guidelines.

**Table 2.** Hematuria Risk Score in Female Patients\* ⇐

	No Cancer	Urologic Cancer	P	95% Confidence Interval	Bladder Cancer	Renal Cancer	Ureteral Cancer
Low (score 0–4)	1938 (99.5%)	9 (0.5%)	<.01	0.2–0.9%	3 (0.2%)	6 (0.3%)	0
Moderate (score 5–8)	1431 (98.7%)	19 (1.3%)		0.8–2.0%	18 (1.2%)	1 (0.1%)	0
High (score 9–10)	157 (89.2%)	19 (10.8%)		6.6–16.3%	13 (7.4%)	3 (1.7%)	3 (1.7%)*

\*To calculate the hematuria risk score, attribute four points for age greater than 50 years or history of gross hematuria; attribute one point for smoking or more than 25 blood cells per high-powered field.

Reprinted from Lippmann QK, Slezak JM, Meneffee SA, Ng CK, Whitcomb EL, Loo RK. Evaluation of microscopic hematuria and risk of urologic cancer in female patients. *Am J Obstet Gynecol* 2017;216:146.e1–7. [PubMed]



## Conclusions

Asymptomatic microscopic hematuria in women is common; however, it is less likely to be associated with urinary tract malignancy among women than men. For women, being older than 60 years, having a history of smoking, and having gross hematuria are the strongest predictors of urologic cancer. In low-risk, never-smoking women younger than 50 years without gross hematuria and with fewer than 25 red blood cells per high-power field, the risk of urinary tract malignancy is less than or equal to 0.5%. Furthermore, the evaluation may result in more harm than benefit and is unlikely to be cost effective. Thus, data support changing current hematuria recommendations in this low-risk group. The College and AUGS encourage organizations producing future guidelines on the evaluation of microscopic hematuria to perform sex-specific analysis of the data and produce practical sex-specific recommendations. In the meantime, the College and AUGS recommend that asymptomatic, low-risk, never-smoking women aged 35–50 years undergo evaluation only if they have more than 25 red blood cells per high-power field.

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