

Practice Guidelines

Microscopic Hematuria in Adults: Updated Recommendations from the American Urological Association

Key Points for Practice

- Consider repeating urinalysis in women found to have microscopic hematuria associated with UTI following successful treatment.
- With microscopic hematuria in patients at low risk of cancer, performing repeat urinalysis at six months is a reasonable alternative to imaging and cystoscopy.
- Although gross hematuria is strongly associated with malignancy, microscopic hematuria is more common and has a lower malignancy risk.

From the *AFP* Editors

Previous guidelines from the American Urological Association (AUA) recommended that all patients with microscopic hematuria be fully evaluated for urinary tract cancer without regard to the patient's risk of malignancy. Although this strategy results in the fewest missed cancers in modeling studies, it is costly, increases patient risk, and can result in overdiagnosis. The AUA released an updated guideline for risk-based evaluation of microscopic hematuria.

Defining Microscopic Hematuria

The AUA defines microscopic hematuria as three or more red blood cells per high-power field (RBC/HPF) on urine microscopy. A threshold between three and 10 RBC/HPF has the highest sensitivity for detecting bladder cancer and the lowest negative likelihood ratio. A single urinalysis is

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This series is coordinated by Michael J. Arnold, MD, contributing editor.

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Author disclosure: No relevant financial affiliations.

sufficient because 95% of microscopic hematuria is detected in one sample. Because at least 20% of positive dipstick tests for blood have no red blood cells on subsequent urine microscopy, any positive dipstick should be confirmed.

Initial Evaluation

Initial evaluation for patients with microscopic hematuria involves searching for a likely cause to be addressed. Common causes include urinary tract infections (UTIs), menstruation, external genital lesions, vaginal atrophy, pelvic organ prolapse, urolithiasis, benign prostatic enlargement, and urethral stricture. After addressing any of these issues, a repeat urinalysis should be performed. With conditions such as prostatic hypertrophy, vaginal atrophy, and pelvic organ prolapse, microscopic hematuria may not completely resolve. In these cases, full evaluation may be warranted. Obtaining a catheter urine sample also may be helpful.

Women with urologic malignancies are often treated repeatedly for UTI before cancer is diagnosed. Repeating urinalysis with microscopy after identifying hematuria associated with UTI should be considered, although this strategy has not been prospectively validated.

Anticoagulation does not appear to explain microscopic hematuria, and the appropriate workup should be performed in these patients. Patients taking antithrombotic medications are more likely to be diagnosed with bladder cancer, suggesting these medications may increase bleeding from underlying malignancies.

Risk Stratification

If the initial evaluation suggests no obvious source of microscopic hematuria, possible risk factors should be assessed. Smoking, higher numbers of RBC/HPF, persistent hematuria, and history of gross hematuria increase the risk of malignancy (*Table 1*).

The AUA risk categories combine factors from two validated risk scores. These risk categories

TABLE 1

American Urological Association Microhematuria Risk Stratification System

Low (patient meets all criteria)

Men age < 40 years; women age < 50 years
3 to 10 RBC/HPF on a single urinalysis
Never smoker or < 10 pack-years
No risk factors for urothelial cancer

Intermediate (patient meets any one of these criteria)

Men age 40 to 59 years; women age 50 to 59 years
11 to 25 RBC/HPF on a single urinalysis
10 to 30 pack-years
Low-risk patient with no prior evaluation and 3 to 10 RBC/HPF on repeat urinalysis
Additional risk factors for urothelial cancer

High (patient meets any one of these criteria)

Women or men age \geq 60 years
> 25 RBC/HPF on a single urinalysis
> 30 pack-years
History of gross hematuria

RBC/HPF = red blood cells per high-power field.

Reprinted with permission from Barocas DA, Boorjian SA, Alvarez RD, et al. Microhematuria: AUA/SUFU guideline. *J Urol.* 2020;204(4):783.

have not been prospectively validated, and no prospective evidence demonstrates the clinical outcomes of using them for risk scoring.

Less common risk factors for urinary tract cancer include a family history of cancer or cancer-related syndromes, occupational exposure to benzene or aromatic amines, previous pelvic radiation therapy, previous cyclophosphamide chemotherapy, or chronic indwelling catheter or foreign body. Irritative urinary symptoms without UTI suggest increased cancer risk. With no evidence to guide evaluation, the AUA recommends considering a full evaluation in these cases.

LOW RISK

Patients at low risk include men younger than 40 years and women younger than 50 years with microscopic hematuria between three and 10 RBC/HPF. Low-risk patients have less than a

10 pack-year smoking history and no other risk factors. The AUA recommends repeating urinalysis in six months, although an evaluation with cystoscopy and renal ultrasonography is also reasonable.

INTERMEDIATE RISK

Patients at intermediate risk have at least one risk factor that takes them out of the low-risk category, such as ages 40 to 59 years in men and 50 to 59 years in women, a 10 to 30 pack-year smoking history, 11 to 25 RBC/HPF on microscopic urinalysis, and persistent microscopic hematuria after an initial low-risk determination.

For these patients, the guideline recommends cystoscopy and renal ultrasonography. Renal ultrasonography is recommended over computed tomography urography because of reasonable discrimination of cortical lesions, decreased expense, and lack of ionizing radiation. The drawback of renal ultrasonography is poor sensitivity for upper urinary tract cancers.

HIGH RISK

Patients at high risk have at least one high-risk factor, including age 60 years or older, more than a 30 pack-year smoking history, more than 25 RBC/HPF on microscopic urinalysis, and a history of gross hematuria. For these patients, the guideline recommends cystoscopy and computed tomography urography. Magnetic resonance urography and retrograde pyelography with renal imaging are reasonable if contrast media is contraindicated because of kidney disease or allergy.

After a Negative Evaluation

Based on limited study, malignancy risk is low in patients with a negative microscopic hematuria evaluation. Over 14 years of follow-up of 258 patients, only two bladder cancers were diagnosed. Repeat urinalysis within 12 months of the negative workup should be considered, and evaluation may be discontinued if no microscopic hematuria is found. The benefits of additional evaluation for recurrent microscopic hematuria are unclear.

Urine cytology and urine-based tumor marker testing should be avoided in the initial evaluation of microscopic hematuria. Positive cytology has a 10% false-positive rate and rarely leads to a bladder cancer diagnosis after negative cystoscopy. The role of cytology in the evaluation of persistent microscopic hematuria is unknown.

PRACTICE GUIDELINES

The views expressed are those of the author and do not necessarily reflect the official policy or position of the Department of the Navy, Uniformed Services University of the Health Sciences, Department of Defense, or the U.S. government.

Editor's Note: The updated guideline is important because it provides a framework for risk stratification and targeted evaluation. If this framework had been prospectively validated, it would be more useful. The AUA combined risk factors from two validated risk scores to propose three risk levels and evaluation paradigms. The AUA acknowledges the need for validation of the guideline.

The guideline does contain an important warning: the need to consider a microscopic hematuria evaluation in patients with recurrent UTI, especially with negative culture results. About one in 10 women and one in 20 men with bladder cancer receive more than three antibiotic courses for UTI before cancer is diagnosed.

The recommendation to repeat urinalysis after six months in patients at low risk and within a year after a negative workup might be controversial in primary care. Because the future laboratory evaluations are often missed by patients, the shaky evidence behind this recommendation is concerning. The AUA cites a single study showing a slightly higher malignancy rate in patients with persistent microscopic hematuria, yet most of these patients were diagnosed with malignancy following a UTI.¹ Without more evidence, it may be more important to perform a repeat urinalysis after resolution of UTI symptoms rather than a six-month repeat in all patients.—Michael J. Arnold, MD, Contributing Editor

Reference

1. Ghandour R, Freifeld Y, Singla N, et al. Evaluation of hematuria in a large public health care system. *Bladder Cancer*. 2019;5(2):119-129.

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Q1. B	Q7. C	Q13. A	Q19. D
Q2. C	Q8. B	Q14. D	Q20. C
Q3. B	Q9. D	Q15. C	Q21. A
Q4. D	Q10. B	Q16. B	Q22. C
Q5. A	Q11. A	Q17. B	Q23. C
Q6. C	Q12. B	Q18. D	Q24. D