# Microhematuria: AUA/SUFU Guideline

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**Abbreviations and Acronyms**

CIS = carcinoma in situ

GRADE = Grading of Recommendations, Assessment, Development, and Evaluation

MH = microhematuria

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

RCC = renal cell carcinoma

UA = urinalysis

UTUC = upper tract urothelial carcinoma

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**Purpose:** Patients presenting with microhematuria represent a heterogeneous population with a broad spectrum of risk for genitourinary malignancy. Recognizing that patient-specific characteristics modify the risk of underlying malignant etiologies, this guideline sought to provide a personalized diagnostic testing strategy.

**Materials and Methods:** The systematic review incorporated evidence published from January 2010 through February 2019, with an updated literature search to include studies published up to December 2019. Evidence-based statements were developed by the expert Panel, with statement type linked to evidence strength, level of certainty, and the Panel's judgment regarding the balance between benefits and risks/burdens.

**Results:** Microhematuria should be defined as $\geq$ 3 red blood cells per high power field on microscopic evaluation of a single specimen. In patients diagnosed with gynecologic or non-malignant genitourinary sources of microhematuria, clinicians should repeat urinalysis following resolution of the gynecologic or non-malignant genitourinary cause. The Panel created a risk classification system for patients with microhematuria, stratified as low-, intermediate-, or high-risk for genitourinary malignancy. Risk groups were based on factors including age, sex, smoking and other urothelial cancer risk factors, degree and persistence of microhematuria, as well as prior gross hematuria. Diagnostic evaluation with cystoscopy and upper tract imaging was recommended according to patient risk and involving shared decision-making. Statements also inform follow-up after a negative microhematuria evaluation.

**Conclusions:** Patients with microhematuria should be classified based on their risk of genitourinary malignancy and evaluated with a risk-based strategy. Future high-quality studies are required to improve the care of these patients.

**Key Words:** hematuria, cystoscopy, CT Urogram, bladder cancer, urothelial carcinoma, urine markers

Hematuria is one of the most common urologic diagnoses, estimated to account for over 20% of urology evaluations.[1] Indeed, screening studies have noted a prevalence range of microhematuria (MH) among healthy volunteers of 2.4%-31.1% depending on the specific population evaluated.[2]

The differential diagnosis of MH encompasses a wide range of urologic, nephrologic, as well as gynecologic conditions. Importantly, while genitourinary malignancy has been diagnosed in approximately 3% of patients evaluated for MH,[2,3] the risk of detecting an underlying cancer has

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been found to be highly dependent on factors such as sex, age, smoking history, and degree of hematuria.[4]

As the aggregate likelihood of identifying a malignancy among patients with MH is relatively low, the benefits and potential harms of diagnostic evaluation must be considered both at the patient and health system level.

At the same time, practice-pattern assessments have demonstrated significant deficiencies in the evaluation of patients presenting with hematuria. For example, one study found that less than 50% of patients with hematuria diagnosed in a primary care setting were subsequently referred for urologic evaluation.[5] Furthermore, performance of both cystoscopy and imaging occurs in less than 20% of patients in most series, and varies to some degree by sex and race.[6–8] The underuse of cystoscopy, and the tendency to rely solely on imaging for evaluation, is particularly concerning since the vast majority of cancers diagnosed among persons with hematuria are bladder cancers, optimally detected with cystoscopy.[4,6–14]

As such, there is a need for updated, evidence-based guideline recommendations for evaluation of hematuria that limit the unnecessary risks and costs associated with the over-evaluation of patients who are at low risk for malignancy, while at the same time clearly identifying clinical scenarios in which work-up is warranted in order to address the delays in diagnosis of important urologic conditions. In addition, since deciding how aggressively to pursue an etiology for MH involves tradeoffs at the individual level (risk of malignancy versus harms of evaluation), it is necessary for the clinician and patient to engage in shared decision-making, particularly in situations where the ratio of benefits to harms is uncertain, equivalent, or "preference sensitive."[15] The purpose of this guideline and the associated algorithm (figure 1) is, therefore, to provide a clinical framework for the diagnosis, evaluation, and follow-up of MH.

## METHODOLOGY

### Searches and Article Selection

A systematic review was conducted to inform on appropriate diagnosis, evaluation, and follow-up in patients with suspected and confirmed MH. The methodologist, in consultation with the expert panel, developed criteria for inclusion and exclusion of studies based on the Key Questions and the populations, interventions, comparators, and outcomes of interest. OVID was used to systematically search MEDLINE and EMBASE databases for articles evaluating hematuria using the criteria determined by the expert panel. Five systematic reviews and 91 primary literature studies met the study selection criteria and were chosen to form the evidence base. The initial draft evidence report included evidence published from January 2010 through February 2019. A second search was conducted to update the report to include studies published up to December 2019.

### Determination of Evidence Strength

Certainty of evidence underpinning the recommendation statements were defined using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system. The AUA employs a three-tiered strength of evidence system to inform evidence-based guideline statements.[16] In short, high certainty by GRADE translates to AUA A-category strength of evidence, moderate to B, and both low and very low to C (table 1).

### AUA Nomenclature: Linking Statement Type to Evidence Strength

The AUA nomenclature system explicitly links statement type to the body of evidence strength, level of certainty, magnitude of benefit or risk/burdens, and the Panel's judgment regarding the balance between benefits and risks/burdens (table 2).

A full description of the AUA methodology system can be found in the unabridged version of this guideline available at www.auanet.org/guidelines.

### Guideline Statements

#### *Diagnosis and Definition of Microhematuria (MH)*

1. Clinicians should define MH as >3 red blood cells per high-power field (RBC/HPF) on microscopic evaluation of a single, properly collected urine specimen. (Strong Recommendation; Evidence Level: Grade C)
2. Clinicians should not define MH by positive dipstick testing alone. A positive urine dipstick test (trace blood or greater) should prompt formal microscopic evaluation of the urine. (Strong Recommendation; Evidence Level: Grade C)

The literature review from the 2012 guideline and more recent data support the definition of MH as > 3 RBC/HPF on microscopic evaluation of a single urine specimen.[2,17] Dipstick testing remains insufficient as it measures peroxidase activity, which can be confounded by factors including (but not limited to) the use of povidone iodine, myoglobinuria, and dehydration. In order to inform clinicians of the degree of hematuria a patient has with sufficient detail to determine whether further evaluation is warranted, the Panel emphasizes the importance of utilizing laboratories reporting RBC/HPF quantitatively.

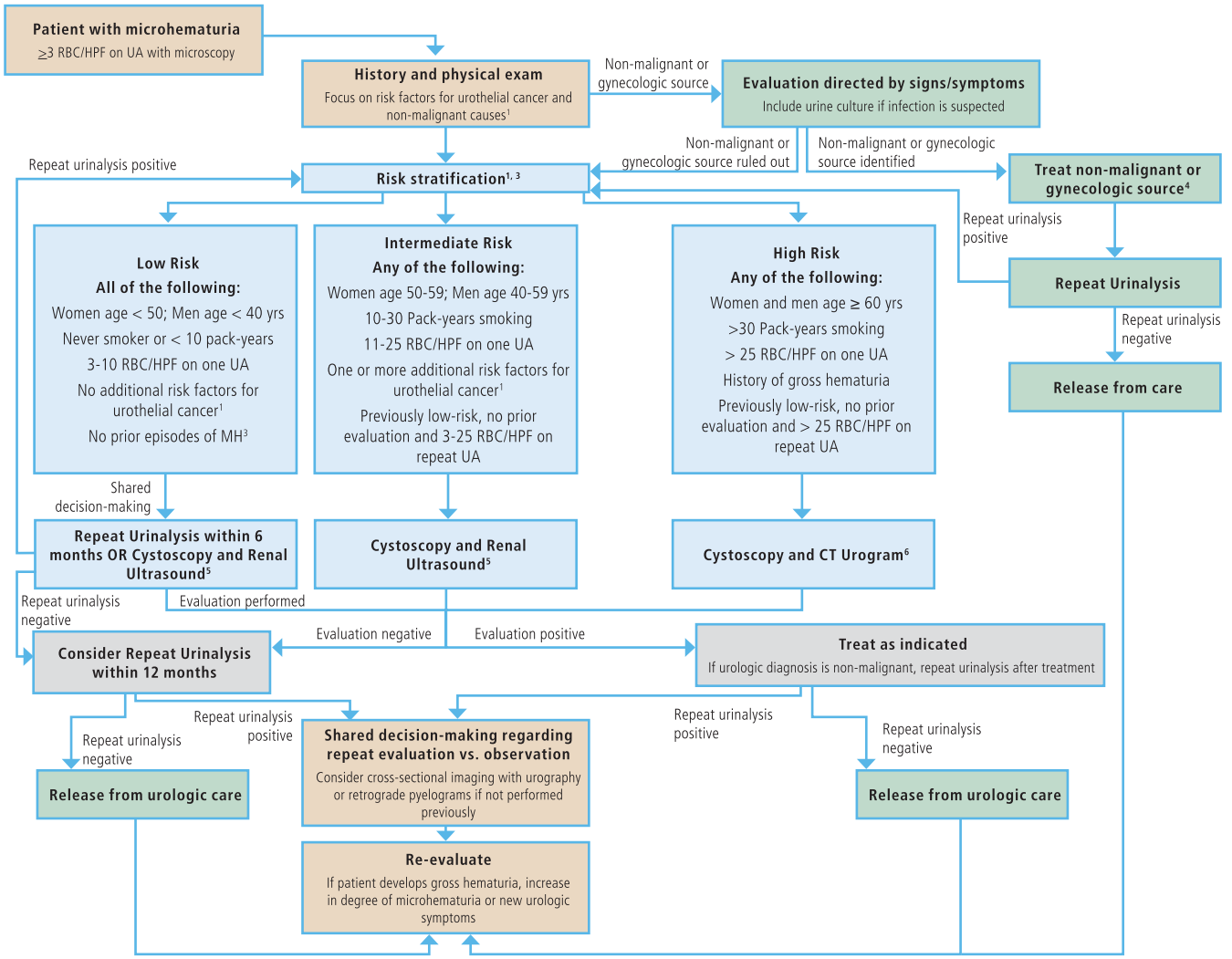
#### *Initial Evaluation.*

3. In patients with MH, clinicians should perform a history and physical examination to assess risk factors for genitourinary malignancy, medical renal disease, gynecologic and non-malignant genitourinary causes of MH. (Clinical Principle)

Careful consideration should be given to risk factors for malignancy (tables 3 and 4). Physical examination should include measurement of blood pressure and a genitourinary examination as dictated by the clinical history. For example, in women, examination of the external genitalia, introitus, and periurethral tissue may identify urethral pathology or other gynecologic pathology to explain the MH.

4. Clinicians should perform the same evaluation of patients with MH who are taking antiplatelet agents or anticoagulants (regardless of the type or level of therapy) as patients not on these agents. (Strong Recommendation; Evidence Level: Grade C)

## Microhematuria Evaluation Algorithm




1. Main risk factors for urothelial cancer are those in the AUA risk stratification system (age, male sex, smoking, degree of microhematuria and history of gross hematuria). Additional risk factors for urothelial carcinoma include but are not limited to irritative lower urinary tract voiding symptoms, history of cyclophosphamide or ifosfamide chemotherapy, family history of urothelial carcinoma or Lynch Syndrome, occupational exposures to benzene chemicals or aromatic amines, history of chronic indwelling foreign body in the urinary tract
2. If medical renal disease is suspected, consider nephrologic evaluation, but pursue concurrent risk-based urological evaluation
3. Patients may be low-risk at first presentation with microhematuria, but may only be considered intermediate- or high-risk if found to have persistent microhematuria
4. There are non-malignant and gynecologic sources of hematuria that do not require treatment and/or may confound the diagnosis of MH. Clinicians can consider catheterized urine specimen in women with vaginal atrophy or pelvic organ prolapse. Clinicians must use careful judgment and patient engagement to decide whether to pursue MH evaluation in the setting of chronic conditions that do not require treatment, such as the aforementioned gynecologic conditions, non-obstructing stones or BPH.
5. Clinician may perform cross-sectional imaging with urography or retrograde pyelograms if hematuria persists after negative renal ultrasound
6. MR Urogram or Non-contrast imaging plus retrograde pyelograms if contraindications to CT Urogram



**Figure 1.**

Patients on anticoagulants should be assessed in the same fashion as patients who are not anticoagulated because these patients have a malignancy risk similar to other populations.[18–20]

5. In patients with findings suggestive of a gynecologic or non-malignant urologic etiology, clinicians should evaluate the patients with appropriate physical examination techniques and tests to identify such an etiology. (Clinical Principle)
6. In patients diagnosed with gynecologic or non-malignant genitourinary sources of MH, clinicians should repeat urinalysis (UA) following resolution of the gynecologic or non-malignant genitourinary cause. If MH persists or the etiology cannot be identified, clinicians should perform risk-based urologic evaluation. (Clinical Principle)
7. In patients with hematuria attributed to a urinary tract infection, clinicians should obtain a UA with microscopic evaluation following treatment to ensure resolution of the hematuria. (Strong Recommendation; Evidence Level: Grade C)

If the history and physical examination suggest the presence of a gynecologic or non-malignant source of MH, the clinician should perform a directed evaluation to rule in or rule out such an etiology.

**Table 1:** *Strength of Evidence Definitions*

| AUA Strength of Evidence Category | GRADE Certainty Rating | Definition |
|---|---|---|
| A | High | • We are very confident that the true effect lies close to that of the estimate of the effect |
| B | Moderate | • We are moderately confident in the effect estimate<br>• The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different |
| C | Low | • Our confidence in the effect estimate is limited |
| | Very Low | • The true effect may be substantially different from the estimate of the effect<br>• We have very little confidence in the effect estimate<br>• The true effect is likely to be substantially different from the estimate of effect |

In light of noted practice patterns, the Panel believes it is important to emphasize the need for a follow-up UA following resolution of a presumed gynecologic or non-malignant urologic cause of MH, particularly urinary tract infection, to confirm resolution of the MH. If the MH persists, a risk-based urologic evaluation should be performed.

The Panel acknowledges that there are some non-malignant urologic and gynecologic conditions, such as non-obstructing nephrolithiasis or pelvic organ prolapse, which will not merit treatment or in which the MH may not resolve completely even with appropriate management. In these cases, clinicians must use careful judgment and shared decision-making to decide whether to pursue MH evaluation. Attention to the patient's risk factors for urologic malignancy should guide these decisions.

8. Clinicians should refer patients with MH for nephrologic evaluation if medical renal disease is suspected. However, risk-based urologic evaluation should still be performed. (Clinical Principle)

Patients with proteinuria, dysmorphic RBCs, cellular casts, or renal insufficiency may have medical renal disease, which can cause hematuria. Therefore, patients with these features should be referred to a nephrologist. While evaluation for medical renal disease should be performed, this does not preclude the need for risk-based urologic evaluation to identify coexistent urologic pathology.

### *Risk Stratification.*

9. Following initial evaluation, clinicians should categorize patients presenting with MH as low-, intermediate-, or high-risk for genitourinary malignancy based on the accompanying tables (tables 3 and 4). (Strong Recommendation; Evidence Level: Grade C)

Patients presenting with hematuria represent a heterogeneous population with a broad spectrum of risk for underlying malignancy based on clinical and demographic features. The Panel, therefore, created categories, summarized as 'low-,' 'intermediate-,' and 'high-' risk for a diagnosis of genitourinary malignancy (table 4), in order to facilitate patient-centered testing strategies.

Several available risk stratification systems were considered, which, broadly stated, estimate risk of urothelial carcinoma as <1% for those deemed low-risk, 1-2% for intermediate-risk, and 10% or greater for high-risk.[4,21] The Panel also considered the contribution to patient risk of each individual risk factor for urothelial carcinoma based on an extensive literature review. The risk stratification system designed for this guideline was based on this systematic review and received unanimous approval from members of the Panel.

Recognizing that there remains variability in risk *within* each risk group and that this classification system will require validation, several strengths merit highlighting. First, the stratification incorporates age-specific thresholds for men and women, drawing on observations of greater risk for malignancy for male patients at younger ages than their female counterparts.[4,9,22–27] Additionally, this system incorporates stratification based on degree of MH, as large series have found increased risks associated with higher numbers of RBC/HPF on microscopic UA.[23,26] With respect to tobacco exposure, this system incorporates considerations of duration and intensity of tobacco exposure, in accord with standards from the cancer screening literature.[28,29] Further, the framework provides guidance to recategorize initially low-risk patients with persistent hematuria on follow-up evaluations. Finally, the AUA Guideline Risk Stratification System explicitly incorporates recognized risk factors for urothelial cancer (table 3) into the considerations for recommending diagnostic evaluation.

## Urinary Tract Evaluation

### *Low-Risk.*

10. In low-risk patients with MH, clinicians should engage patients in shared decision-making to decide between repeating UA within six months or proceeding with cystoscopy and renal ultrasound. (Moderate Recommendation; Evidence Level: Grade C)

The Panel acknowledges that the likelihood of diagnosing malignancy in a low-risk MH patient is very low; therefore, the diagnostic yield in such patients must be balanced against the potential harms of obtaining imaging, including the implications of false positive detection.[30]

Further, while cystoscopy represents the current standard for diagnosing bladder tumors[31–34] it does involve a relatively invasive procedure, with potential patient discomfort and anxiety, as well as a low risk of UTI, and, from a healthcare system vantage point, cost.[35,36]

Understanding then that some low-risk patients may choose to repeat a UA rather than undergo evaluation at the time of initial MH diagnosis, the Panel advises a repeat UA within six months to limit the likelihood of delayed diagnosis of a treatable urologic condition.

### *Initially Low-Risk With Hematuria on Repeat Urinalysis (UA).*

11. Low-risk patients who initially elected not to undergo cystoscopy or upper tract imaging and who are found to have MH on repeat urine testing should be reclassified as intermediate- or high-risk. In such patients, clinicians should perform cystoscopy and

**Table 2:** *AUA Nomenclature Linking Statement Type to Level of Certainty, Magnitude of Benefit or Risk/Burden, and Body of Evidence Strength*

| Evidence Grade | Evidence Strength A (High Certainty) | Evidence Strength B (Moderate Certainty) | Evidence Strength C (Low Certainty) |
|---|---|---|---|
| Strong Recommendation (Net benefit or harm substantial) | -Benefits > Risks/Burdens (or vice versa)<br>-Net benefit (or net harm) is substantial<br>-Applies to most patients in most circumstances and future research is unlikely to change confidence | -Benefits > Risks/Burdens (or vice versa)<br>-Net benefit (or net harm) is substantial<br>-Applies to most patients in most circumstances but better evidence could change confidence | -Benefits > Risks/Burdens (or vice versa)<br>-Net benefit (or net harm) appears substantial<br>-Applies to most patients in most circumstances but better evidence is likely to change confidence |
| Moderate Recommendation (Net benefit or harm moderate) | -Benefits > Risks/Burdens (or vice versa)<br>-Net benefit (or net harm) is moderate<br>-Applies to most patients in most circumstances and future research is unlikely to change confidence | -Benefits > Risks/Burdens (or vice versa)<br>-Net benefit (or net harm) is moderate<br>-Applies to most patients in most circumstances but better evidence could change confidence | -Benefits > Risks/Burdens (or vice versa)<br>-Net benefit (or net harm) appears moderate<br>-Applies to most patients in most circumstances but better evidence is likely to change confidence |
| Conditional Recommendation (Net benefit or harm comparable to other options) | -Benefits = Risks/Burdens<br>-Best action depends on individual patient circumstances<br>-Future Research is unlikely to change confidence | -Benefits = Risks/Burdens<br>-Best action appears to depend on individual patient circumstances<br>-Better evidence could change confidence | -Balance between Benefits & Risks/Burdens unclear<br>-Net benefit (or net harm) comparable to other options<br>-Alternative strategies may be equally reasonable<br>-Better evidence likely to change confidence |
| Clinical Principle | A Clinical Principle is a statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature. | | |
| Expert Opinion | Expert Opinion refers to a statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment. | | |

upper tract imaging in accordance with recommendations for these risk strata. (Strong Recommendation; Evidence Level: Grade C)

In one large study, patients who had persistent MH on repeat urine testing had a higher rate of malignancy on subsequent evaluation as compared with those who had negative repeat urine testing.[37] According to the risk stratification schema above, patients with *persistent* MH are, therefore, re-classified as either intermediate- or high-risk for malignancy, in part dependent upon the degree of MH present at the repeat UA (table 4). Such re-classification ensures that patients with recurrent or persistent hematuria undergo a risk-stratified evaluation.

***Intermediate-Risk.***

12. Clinicians should perform cystoscopy and renal ultrasound in patients with MH categorized as intermediate-risk for malignancy. (Strong Recommendation; Evidence Level: Grade C)

Studies of MH patients have consistently demonstrated that when a urologic malignancy is detected during evaluation, the most frequent cancer found is bladder cancer.[4,6–14], Whereas imaging has poor sensitivity for identifying bladder cancer,[4] cystoscopy is 98% sensitive.[38] As such, cystoscopy should be performed in intermediate-risk MH patients. Regarding the choice of upper tract imaging, renal ultrasound has adequate sensitivity and specificity for renal cortical tumors compared to axial imaging, at lower cost and with less risk (e.g., ionizing radiation, intravenous contrast reactions, and false-positive results).[30,39–41] While the reported sensitivity of renal ultrasound for upper tract urothelial carcinoma (UTUC) is poor (14%), the Panel's recommendation here is based on the low incidence of this diagnosis,[24] and, therefore, limited benefit of axial imaging over ultrasound.

***High-Risk.***

13. Clinicians should perform cystoscopy and axial upper tract imaging in patients with MH categorized as high-risk for malignancy. (Strong Recommendation; Evidence Level: Grade C)

    Options for Upper Tract Imaging in High-Risk Patients:

a. If there are no contraindications to its use, clinicians should perform multiphasic CT urography (including imaging of the urothelium). (Moderate Recommendation; Evidence Level: Grade C)
b. If there are contraindications to multiphasic CT urography, clinicians may utilize MR urography. (Moderate Recommendation; Evidence Level: Grade C)
c. If there are contraindications to multiphasic CT urography and MR urography, clinicians may utilize retrograde pyelography in conjunction with non-contrast axial imaging or renal ultrasound. (Expert Opinion)

Cystoscopy is a critical component of the work-up of patients with MH identified as high-risk for malignancy because of the risk of bladder cancer in this population.

The Panel concluded that patients who meet the high-risk criteria are at a sufficient risk for harboring an upper tract malignancy to also warrant multiphasic cross-sectional imaging to evaluate both the renal parenchyma

**Table 3:** *Urothelial Cancer Risk Factors*

| Risk Factors Included in AUA Microhematuria Risk Stratification System | Additional Urothelial Cancer Risk Factors* |
|---|---|
| Age | Irritative lower urinary tract symptoms |
| Male sex | Prior pelvic radiation therapy |
| Smoking history | Prior cyclophosphamide/ifosfamide chemotherapy |
| Degree of microhematuria | Family history of urothelial cancer or Lynch Syndrome |
| Persistence of microhematuria | Occupational exposures to benzene chemicals or aromatic amines (e.g., rubber, petrochemicals, dyes) |
| History of gross hematuria | Chronic indwelling foreign body in the urinary tract |

* The Panel recognizes that this list is not exhaustive.

and the urothelium, using CT urography if there are no contraindications to its use.

In patients with contraindications to contrast-enhanced CT, such as chronic kidney disease or allergy to iodine-based contrast, the Panel recommends MR urography.

For patients with contraindications to both CT and MR urography, either non-contrast CT or renal ultrasound may be used to assess the renal cortex with the addition of retrograde pyelography to assess the upper urinary tracts.

14. Clinicians should perform white light cystoscopy in patients undergoing evaluation of the bladder for MH. (Moderate Recommendation; Evidence Level: Grade C)

White light cystoscopy remains the standard for evaluation of MH.[42] The Panel acknowledges the development of enhanced cystoscopic techniques such as blue light cystoscopy to improve bladder cancer detection and resection among patients previously diagnosed with bladder cancer.[43,44] Nevertheless, blue light cystoscopy studies to date have been reported among patients with an established diagnosis of bladder cancer rather than MH cohorts being screened for bladder cancer. As such, the generalizability of this approach to MH patients remains uncertain.

15. In patients with persistent or recurrent MH previously evaluated with renal ultrasound, clinicians may perform additional imaging of the urinary tract. (Conditional Recommendation; Evidence Level: Grade C)

The patient with persistent or recurrent MH who has undergone prior renal ultrasound represents a clinical scenario in which the diagnosis of UTUC is possible, although admittedly still uncommon. In these cases, clinicians may choose to obtain further imaging to include delineation of the urothelium such as CT urography, MR urography, or retrograde pyelography.

16. In patients with MH who have a family history of renal cell carcinoma (RCC) or a known genetic renal tumor syndrome, clinicians should perform upper tract imaging regardless of risk category. (Expert Opinion)

RCC is associated with several genetic syndromes (table 5)[45–48] and with a family history of RCC;[49] therefore, such patients who have MH should undergo upper tract imaging. Insufficient evidence exists regarding the preferred modality in this scenario.

### *Urinary Markers.*

17. Clinicians should not use urine cytology or urine-based tumor markers in the initial evaluation of patients with MH. (Strong Recommendation; Evidence Level: Grade C)
18. Clinicians may obtain urine cytology for patients with persistent MH after a negative workup who have irritative voiding symptoms or risk factors for carcinoma in situ. (Expert Opinion)

The Panel does not recommend using urine cytology or urine-based tumor markers in the initial evaluation of MH because, to date, markers have not demonstrated incrementally additive information to cystoscopy in the MH population, nor have they been found to be of sufficient predictive value to obviate cystoscopy.

One area for which cytology may have a role is in improving detection of carcinoma in situ (CIS), which occasionally may evade detection by white light cystoscopy.[50] As such, there may be a role for cytology in patients with persistent MH in patients who have irritative voiding symptoms or other risk factors for CIS.

### *Follow-Up.*

19. In patients with a negative hematuria evaluation, clinicians may obtain a repeat UA within 12 months. (Conditional Recommendation; Evidence Level: Grade C)
20. For patients with a prior negative hematuria evaluation and subsequent negative UA, clinicians may discontinue further evaluation for MH. (Conditional Recommendation; Evidence Level: Grade C)
21. For patients with a prior negative hematuria evaluation who have persistent or recurrent MH at the time of repeat UA, clinicians should engage in shared decision-making regarding need for additional evaluation. (Expert Opinion)

**Table 4:** *AUA Microhematuria Risk Stratification System*

| Low (patient meets all criteria) | Intermediate (patient meets any one of these criteria) | High (patient meets any one of these criteria) |
|---|---|---|
| • Women age <50 years; Men age <40 years<br>• Never smoker or <10 pack years<br>• 3-10 RBC/HPF on a single urinalysis<br>• No risk factors for urothelial cancer (see Table 3) | • Women age 50-59 years; Men age 40-59 years<br>• 10-30 pack years<br>• 11-25 RBC/HPF on a single urinalysis<br>• Low-risk patient with no prior evaluation and 3-10 RBC/HPF on repeat urinalysis<br>• Additional risk factors for urothelial cancer (see Table 3) | • Women or Men age ≥60 years<br>• >30 pack years<br>• >25 RBC/HPF on a single urinalysis<br>• History of gross hematuria |

**Table 5:** *Known Genetic Renal Tumor Syndromes**

| Known genetic renal tumor syndrome |
|---|
| 1. von Hippel-Lindau |
| 2. Birt-Hogg-Dube |
| 3. Hereditary Papillary Renal Cell Cancer |
| 4. Hereditary Leiomyomatosis Renal Cell Cancer |
| 5. Tuberous sclerosis |

* The Panel recognizes that this list is not exhaustive.

22. For patients with a prior negative hematuria evaluation who develop gross hematuria, significant increase in degree of MH, or new urologic symptoms, clinicians should initiate further evaluation. (Moderate Recommendation; Evidence Level: Grade C)

The intensity of follow-up after completion of a negative hematuria evaluation must balance the small risk of a false-negative initial evaluation with the anxiety, cost, inconvenience, and risks of ongoing monitoring and repeat investigation.

The very limited diagnostic yield of repeated evaluations noted to date from studies of patients followed after a negative hematuria evaluation must be recognized. However, the Panel recognizes that select patients may benefit from and/or request follow-up after a negative hematuria evaluation, or after a negative follow-up UA in a low-risk patient who has not been evaluated. A repeat UA represents an initial, non-invasive modality for continued monitoring. Patients with a negative follow-up UA may be discharged from further hematuria evaluation given the very low risk of malignancy, while patients with persistent MH merit shared decision-making regarding next steps in care. Importantly, changes in a patient's clinical status, particularly the development of gross hematuria, should prompt clinical review.

## FUTURE DIRECTIONS

The goal of this guideline is to improve the evaluation and management of patients with hematuria. Due to the combination of a relatively high prevalence of MH in the adult population with a low prevalence of clinically-significant disease, this guideline aims to provide a risk-based framework for testing. Moreover, it is recognized that, in the current state, many patients with hematuria do not undergo evaluation. Accordingly, an important goal of risk-based recommendations is to provide guidance for patients and clinicians regarding appropriate evaluation. Nevertheless, the Panel recognizes the paucity of high-level supporting evidence for the guideline statements and acknowledges several notable areas where gaps in knowledge exist. These represent opportunities for future investigation to meaningfully enhance care. Such areas include the use of new automated instruments for UA, validation of risk groups, utility of urinary biomarkers and enhanced cystoscopy for MH, refinement of imaging techniques to reduce radiation exposure, and further investigation of the natural history of patients with MH following negative evaluation.

**Disclaimer:** This document was written by the Microhematuria Guideline Panel of the American Urological Association Education and Research, Inc., which was created in 2018. The Practice Guidelines Committee (PGC) of the AUA selected the committee chair. Panel members were selected by the chair. Membership of the Panel included specialists in urology, gynecology, and primary care with specific expertise on this disorder. The mission of the panel was to develop recommendations that are analysis based or consensus-based, depending on panel processes and available data, for optimal clinical practices in the evaluation of microhematuria. Funding of the panel was provided by the AUA. Panel members received no remuneration for their work. Each member of the panel provides an ongoing conflict of interest disclosure to the AUA, and the Panel Chair, with the support of AUA Guidelines staff and the PGC, reviews all disclosures and addresses any potential conflicts per AUA's Principles, Policies and Procedures for Managing Conflicts of Interest. While these guidelines do not necessarily establish the standard of care, AUA seeks to recommend and to encourage compliance by practitioners with current best practices related to the condition being treated. As medical knowledge expands and technology advances, the guidelines will change. Today these evidence-based guidelines statements represent not absolute mandates but provisional proposals for treatment under the specific conditions described in each document. For all these reasons, the guidelines do not pre-empt physician judgment in individual cases. Treating physicians must take into account variations in resources, and patient tolerances, needs, and preferences. Conformance with any clinical guideline does not guarantee a successful outcome. The guideline text may include information or recommendations about certain drug uses ('off label') that are not approved by the Food and Drug Administration (FDA), or about medications or substances not subject to the FDA approval process. AUA urges strict compliance with all government regulations and protocols for prescription and use of these substances. The physician is encouraged to carefully follow all available prescribing information about indications, contraindications, precautions and warnings. These guidelines and best practice statements are not intended to provide legal advice about use and misuse of these substances. Although guidelines are intended to encourage best practices and potentially encompass available technologies with sufficient data as of close of the literature review, they are necessarily time-limited. Guidelines cannot include evaluation of all data on emerging technologies or management, including those that are FDA-approved, which may immediately come to represent accepted clinical practices. For this reason,

the AUA does not regard technologies or management which are too new to be addressed by this guideline as necessarily experimental or investigational.

## CONFLICT OF INTEREST DISCLOSURES

All panel members completed COI disclosures. Disclosures listed include both topic- and non-topic-related relationships. Panel members not listed below have nothing to disclose. Consultant/Advisor: Ronald Alvarez, Abbvie, Esai, Genentech, Unleash, Vaccitech; Stephen Boorjian, ArTara, Ferring, Sanofi; Blake Hamilton, NextMed, Inc., Dornier MedTech, Ambu; Kathleen Kobashi, Allergan, Medtronic, Contura; Yair Lotan, Photocure, Astra Zeneca, Nucleix, Merck, Engene, Zymo Research, CAPs Medical; Matthew Nielsen, Grand Rounds, Inc., American College of Physicians, American Urological Association; Andrew Peterson, BSCI: American Medical Systems, Inc.; Jay Raman, Urogen Pharma. Meeting Participant or Lecturer: Tracy Downs, Photocure; Cary Gross, Flatiron, Inc. Scientific Study or Trial: Stephen Boorjian, SUO-CTC Organized Trial; Cary Gross, NCCN/Pfizer, NCCN/Astra Zeneca; Yair Lotan, Cepheid, Pacific Edge, FKD, MDxHealth, Anchiano, GenomeDx Biosciences, Inc.; Andrew Peterson, Movember Foundation; Jay Raman, MDx Health, Pacific Edge Biotechnologies. Investment Interest: Blake Hamilton, StreamDx; Jay Raman, American Kidney Stone Management, United Medical Systems, Inc. Leadership Position: Yair Lotan, Vessi Medical. Other: Cary Gross, Johnson & Johnson; Yair Lotan, Urogen, Synergo.

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