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Asymptomatic Microhematuria in Adults: Risk-Stratified Evaluation, Diagnostic Yield and Strategies to Avoid Unnecessary Testing

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Abstract

Introduction and Purpose. Asymptomatic microhematuria is a common finding in adults, but the probability of clinically significant genitourinary malignancy varies considerably between patients. This review evaluates current approaches to microhematuria, focusing on risk stratification, diagnostic yield, and strategies that may reduce unnecessary invasive or imaging-based investigations.

Materials and Methods. A structured narrative review of PubMed/MEDLINE was performed and supplemented by current clinical practice guidelines and relevant systematic reviews, meta-analyses, and original studies. Publications from January 2015 to August 2026 were primarily considered, with earlier landmark studies included when relevant.

Results. Current evidence supports risk-based rather than uniform evaluation. Patients at very low risk can often be managed initially with repeat urinalysis, whereas cystoscopy and upper urinary tract imaging are increasingly justified as malignancy risk rises. Ultrasonography provides an appropriate first-line imaging option in many intermediate-risk patients, while CT urography remains important in higher-risk settings. Urine cytology and molecular urine-based markers may help refine decisions in selected intermediate-risk patients but cannot broadly replace cystoscopy. After a complete negative evaluation, subsequent malignancy detection is uncommon, and routine repeated invasive investigation has a low diagnostic yield.

Conclusions. Risk-stratified evaluation can reduce unnecessary testing while maintaining more intensive assessment for patients with a meaningful probability of malignancy. Further refinement of risk models and prospective validation of biomarker-guided pathways may allow more individualized diagnostic strategies.

Keywords: microhematuria, microscopic hematuria, risk stratification, cystoscopy, CT urography, urinary biomarkers, genitourinary malignancy

1. Introduction

Microhematuria is commonly detected during routine urinalysis in adults without urinary symptoms. In many patients it is transient or associated with a benign condition, but it may also be the first sign of renal or urological disease, including malignancy. Its clinical relevance therefore depends strongly on the context in which it occurs. A positive urine dipstick alone is insufficient to establish the diagnosis and should be followed by microscopic confirmation in a properly collected specimen [1].

The difficulty lies in deciding how extensively a patient with confirmed microhematuria should be investigated. Historically, unexplained cases were often evaluated with cystoscopy and upper urinary tract imaging irrespective of individual cancer risk. While this approach reduces the chance of missing significant pathology, its diagnostic yield is low in unselected populations and many patients are exposed to invasive procedures, radiation, contrast media, incidental findings and additional costs despite a low probability of malignancy [2–5].

This has led to increasing use of risk-based diagnostic pathways. Current strategies take into account factors such as age, sex, smoking exposure, the degree and persistence of microhematuria, and previous gross hematuria. The 2025 amendment to the AUA/SUFU guideline further refined this approach, reducing the intensity of initial evaluation in patients at very low risk while maintaining more extensive assessment for those with a higher estimated probability of urothelial malignancy [1,6].

Several areas remain uncertain despite this shift. The optimal choice of upper urinary tract imaging is not identical across risk groups, and the clinical role of urine cytology and molecular urine-based markers continues to evolve. Management after a negative initial evaluation is also debated, particularly when microhematuria persists or recurs. In these situations, repeating invasive investigations may offer little additional diagnostic benefit, but the threshold for stopping surveillance is not always clear [7–11].

The aim of this review is to critically evaluate current evidence on the assessment of asymptomatic microhematuria in adults. The review focuses on malignancy risk stratification, the appropriate use and diagnostic yield of cystoscopy and upper urinary tract imaging, the emerging role of urine-based biomarkers, and follow-up after a negative evaluation. Particular consideration is given to whether contemporary risk-based strategies can reduce unnecessary

diagnostic procedures without compromising the detection of clinically significant genitourinary disease.

2. Research Materials and Methods

A structured narrative review was conducted to examine current evidence on the assessment of asymptomatic microhematuria in adults. PubMed/MEDLINE was used as the primary database. The search was supplemented by current clinical practice guidelines and by screening the reference lists of relevant systematic reviews, meta-analyses, and key original studies. The final search was completed on 16 August 2026.

The review focused mainly on publications from January 2015 to August 2026, with earlier landmark studies included when relevant to current definitions or diagnostic practice. Search terms combined concepts related to microhematuria, malignancy risk stratification, cystoscopy, upper urinary tract imaging, urine-based biomarkers, diagnostic yield, and follow-up.

Clinical practice guidelines, systematic reviews, meta-analyses, cohort studies, diagnostic accuracy studies, and relevant original investigations involving adults were considered. Studies limited to pediatric populations and those focused exclusively on gross hematuria were excluded. The review included evidence addressing malignancy risk, contemporary risk-stratification systems, cystoscopy and upper urinary tract imaging, urine-based diagnostic tests, and follow-up after a negative initial evaluation.

The findings were synthesized narratively, with attention to clinically relevant differences between diagnostic strategies, consistency between available studies and current recommendations, and areas in which evidence remains uncertain.

3. Definition and Confirmation of Microhematuria

Microhematuria is defined as ≥3 red blood cells per high-power field (RBC/HPF) on microscopic examination of a single, properly collected urine specimen. Under current AUA/SUFU recommendations, multiple positive samples are not required to confirm the finding when an adequate specimen has been examined microscopically [1].

A positive urine dipstick alone is insufficient for diagnosis. Dipstick testing detects heme activity and may be positive in the presence of hemoglobin or myoglobin even when intact

erythrocytes are absent from the urinary sediment. Trace blood or greater on dipstick testing should therefore be followed by microscopic examination [1].

Specimen quality and the clinical setting should also be considered when interpreting the result. Contamination and temporary causes of urinary bleeding may produce an abnormal finding that does not persist. When microhematuria is associated with an identifiable gynecological or non-malignant genitourinary condition, urinalysis should be repeated after the condition has resolved. The same applies when hematuria is attributed to urinary tract infection. Persistence after treatment or resolution of an apparent temporary cause warrants further assessment based on the patient's clinical profile and malignancy risk [1].

Microscopic confirmation establishes the presence of microhematuria but does not determine its source or clinical significance. These depend on the underlying cause and the patient's individual risk factors.

4. Etiology and Initial Clinical Assessment

After microhematuria has been confirmed, evaluation should focus on whether an identifiable cause is present and whether the findings suggest a renal parenchymal or urological source of bleeding. Potential causes range from transient or benign conditions to glomerular disease, structural urinary tract abnormalities, and malignancy. Establishing this clinical context is necessary before malignancy risk can be assessed reliably [1].

The medical history should include previous urinary tract infections, nephrolithiasis, urological procedures or trauma, known renal disease, and episodes of visible hematuria. Benign prostatic enlargement and other lower urinary tract disorders may contribute to microscopic bleeding in men, while gynecological bleeding or specimen contamination should be considered in women when clinically plausible. An apparently benign explanation should not be accepted as definitive if microhematuria persists after the suspected cause has resolved [1].

Blood pressure and serum creatinine are important components of the initial assessment. Urinalysis may also help distinguish a possible renal source of bleeding. Proteinuria, dysmorphic erythrocytes, red blood cell or other cellular casts, impaired renal function, and hypertension increase suspicion of medical renal disease and may warrant nephrological evaluation. Glomerular disorders, including IgA nephropathy and hereditary basement

membrane disease, may present with microscopic hematuria before a substantial decline in kidney function becomes evident [1,12].

Findings suggestive of renal disease do not exclude concurrent urological pathology. Patients with proteinuria, abnormal urinary sediment, or reduced kidney function may require nephrological assessment while still undergoing urological evaluation when their clinical profile indicates a relevant risk of genitourinary malignancy [1,12].

Common non-malignant urological causes include urinary tract infection, urinary calculi, benign prostatic disease, urethral pathology, structural abnormalities, and recent instrumentation. When microhematuria is attributed to a treatable condition, its resolution should be confirmed after treatment. Persistent or recurrent hematuria should prompt reassessment rather than continued attribution to the original benign diagnosis [1].

The initial evaluation should therefore identify patients who require a nephrological pathway, those in whom repeat urinalysis after treatment is appropriate, and those with persistent or unexplained microhematuria who need further risk-based urological assessment.

5. Microhematuria and Risk of Genitourinary Malignancy

Genitourinary malignancy is an important consideration in patients with otherwise unexplained microhematuria, although cancer is identified in only a small proportion of those investigated. Bladder cancer accounts for most detected malignancies, while upper tract urothelial carcinoma (UTUC) and renal cell carcinoma are substantially less common. The challenge is therefore to identify patients in whom microhematuria reflects a clinically relevant cancer risk without subjecting large numbers of low-risk individuals to unnecessary invasive or imaging-based evaluation [1,2].

A systematic review and meta-analysis of 30 studies including 24,366 patients illustrates the relatively low overall diagnostic yield. Bladder cancer was detected in 2.00% of patients, UTUC in 0.02%, and renal cell carcinoma in 0.18%. Even in studies in which cystoscopy or computed tomography urography was performed in at least 95% of participants, upper urinary tract malignancy remained uncommon. Detection rates increased in cohorts with a higher baseline risk, supporting a more selective approach to diagnostic testing. However, substantial heterogeneity between the included studies limits the direct application of a single pooled estimate to every patient with microhematuria [2].

The probability of malignancy varies considerably according to clinical characteristics. Increasing age, male sex, smoking exposure, a greater degree or persistence of microhematuria, and a history of gross hematuria are associated with higher urothelial cancer risk. Younger patients without smoking exposure or other established risk factors have a much lower probability of malignancy. The same microscopic finding may therefore carry very different implications depending on the patient in whom it occurs [1,2].

A history of gross hematuria deserves separate consideration because visible bleeding is associated with a higher probability of urinary tract malignancy than incidentally detected microhematuria. Studies that combine visible and non-visible hematuria should therefore be interpreted cautiously when their results are applied specifically to asymptomatic patients with microscopic findings [1,2].

The low overall prevalence of cancer does not justify dismissing unexplained microhematuria, but neither does the possibility of malignancy justify identical evaluation in every patient. Extensive investigation in those with very low baseline risk may lead to unnecessary cystoscopy, radiation exposure, contrast administration, incidental findings, additional procedures, and cost, while providing little additional diagnostic benefit. Conversely, insufficient evaluation in a higher-risk patient may delay recognition of clinically significant disease [2–5].

6. Risk Stratification: From Uniform Evaluation to an Individualized Approach

The probability of malignancy differs considerably among patients with microhematuria, making uniform diagnostic evaluation difficult to justify. Current strategies therefore use clinical characteristics to estimate cancer risk before deciding how extensively the urinary tract should be investigated. The AUA/SUFU guideline introduced a formal low-, intermediate-, and high-risk classification in 2020, with further revisions incorporated into the 2025 amendment [1,6].

Risk assessment combines several variables, including age, sex, smoking history, the degree and persistence of microhematuria, previous gross hematuria, and other recognized risk factors for urothelial malignancy. None of these variables should be interpreted in isolation. A similar degree of microhematuria, for example, may have very different clinical implications in a young non-smoker and in an older patient with substantial tobacco exposure [1,6,13].

The 2025 amendment introduced relevant changes in the assessment of women. Data published after the 2020 guideline showed a very low malignancy rate among younger women without additional risk factors. The age threshold used to define lower-risk women was therefore increased, and age alone no longer places a woman in the highest-risk category. This reduces unnecessary intensive evaluation in a group in which the probability of urothelial cancer is generally low [1,14].

Risk classification may also change during follow-up. Persistence of microhematuria or the appearance of additional risk factors can move a patient from an initially low-risk group into a category in which further investigation is justified. The classification is therefore better viewed as a practical estimate based on the information available at a given time rather than as a permanent diagnosis [1].

Recent validation data support the ability of the updated model to separate patients with different probabilities of urothelial malignancy. In a 2026 retrospective cohort of 4,550 adults with asymptomatic microhematuria who underwent cystoscopy and upper urinary tract imaging, urothelial neoplasms were detected in 0.2% of low-risk, 0.8% of intermediate-risk, and 3.8% of high-risk patients according to the 2025 AUA criteria. Age, male sex, smoking exposure, and urinary red blood cell count were independently associated with urothelial malignancy [15].

The same study also identified limitations of the current classification. Renal cortical neoplasms did not show a comparable increase across the three risk groups, suggesting that a model centered on urothelial cancer predictors may be less useful for estimating the risk of some renal malignancies. Bladder cancer was also identified in 2.2% of women aged 70 years or older, raising the possibility that risk in older women may not be fully captured by the revised age criteria [15].

Any categorical system also simplifies a continuous spectrum of risk. Patients immediately above and below a threshold for age, smoking exposure, or urinary red blood cell count are unlikely to differ biologically to the same extent suggested by their placement in separate categories. Less common exposures, family history, previous pelvic radiation, and hereditary predisposition may further influence risk without being fully reflected in the core model [1,6].

Risk stratification is therefore useful primarily because it identifies groups with substantially different probabilities of urothelial malignancy and allows the intensity of investigation to be

adjusted accordingly. It should not be interpreted as an exact prediction of cancer risk. Current models appear less informative for some non-urothelial malignancies and still require clinical judgment, particularly in patients near category boundaries or with risk factors not adequately represented in the classification [15].

Table 1. Risk stratification and recommended evaluation of asymptomatic microhematuria in adults

Risk category	Main clinical criteria	Cystoscopy	Upper urinary tract evaluation	Initial approach
Low/negligible risk	Women <60 years; men <40 years; 3–10 RBC/HPF; never smoker or <10 pack-years; no additional urothelial cancer risk factors	Not routinely indicated initially	No immediate imaging	Repeat urinalysis within 6 months
Intermediate risk	Women ≥60 years; men 40–59 years; 11–25 RBC/HPF; 10–30 pack-years; persistent microhematuria after an initially low-risk assessment; or additional urothelial	Recommended	Renal ultrasonography	Cystoscopy and renal ultrasonography; in appropriately counseled patients wishing to avoid immediate cystoscopy, urine cytology or a validated urine-based tumor marker may

	cancer risk factor(s)			assist decision-making
High risk	High-risk features include men ≥60 years, >30 pack-years, >25 RBC/HPF, previous gross hematuria, or other features resulting in a high-risk profile; women should not be classified as high risk on the basis of age alone	Recommended	Axial upper tract imaging; multiphasic CT urography preferred when possible	Cystoscopy and upper tract imaging; MR urography or alternative imaging may be used when CT urography is contraindicated

Abbreviations: RBC/HPF, red blood cells per high-power field; CT, computed tomography; MR, magnetic resonance.

Source: authors' own elaboration based on AUA/SUFU Guideline 2025 [1].

7. Diagnostic Evaluation According to Risk

Risk stratification determines how extensively patients with microhematuria should be investigated. The aim is not to minimize testing, but to reserve invasive procedures and more intensive imaging for patients in whom the probability of clinically significant disease is sufficient to justify them [1].

Patients classified as low or negligible risk do not require immediate cystoscopy or upper urinary tract imaging. Current AUA/SUFU recommendations favor repeat urinalysis within six months. Persistent microhematuria should lead to reassessment of risk rather than prolonged observation under the original low-risk classification [1].

Intermediate-risk patients generally undergo cystoscopy and renal ultrasonography. Cystoscopy allows direct assessment of the bladder mucosa, while ultrasonography provides non-invasive evaluation of the kidneys without radiation or intravenous contrast. Selected patients who wish to avoid immediate cystoscopy may also consider urine cytology or a validated urine-based tumor marker after appropriate counseling, although the role of these tests is discussed separately [1,16].

High-risk patients require more extensive evaluation. Cystoscopy is combined with axial imaging of the upper urinary tract, with multiphasic CT urography preferred when no contraindication is present. Magnetic resonance urography can be used when CT urography is unsuitable, while alternative combinations of retrograde pyelography and non-contrast imaging may be required when neither modality can be performed [1].

The choice between ultrasonography and CT urography is particularly relevant because the two methods differ in both diagnostic performance and burden. CT urography is more sensitive for upper tract urothelial lesions and provides detailed assessment of the renal parenchyma and ureters. Its greater sensitivity comes at the cost of radiation exposure, intravenous contrast, incidental findings, and additional investigations prompted by abnormalities unrelated to the original indication. These disadvantages become more important when the baseline probability of upper tract malignancy is very low [3,5,7,17].

The prospective DETECT I study illustrates this problem. Among patients presenting with microscopic hematuria, bladder cancer was detected more often than renal malignancy, while upper tract urothelial carcinoma was exceptionally uncommon. Renal and bladder

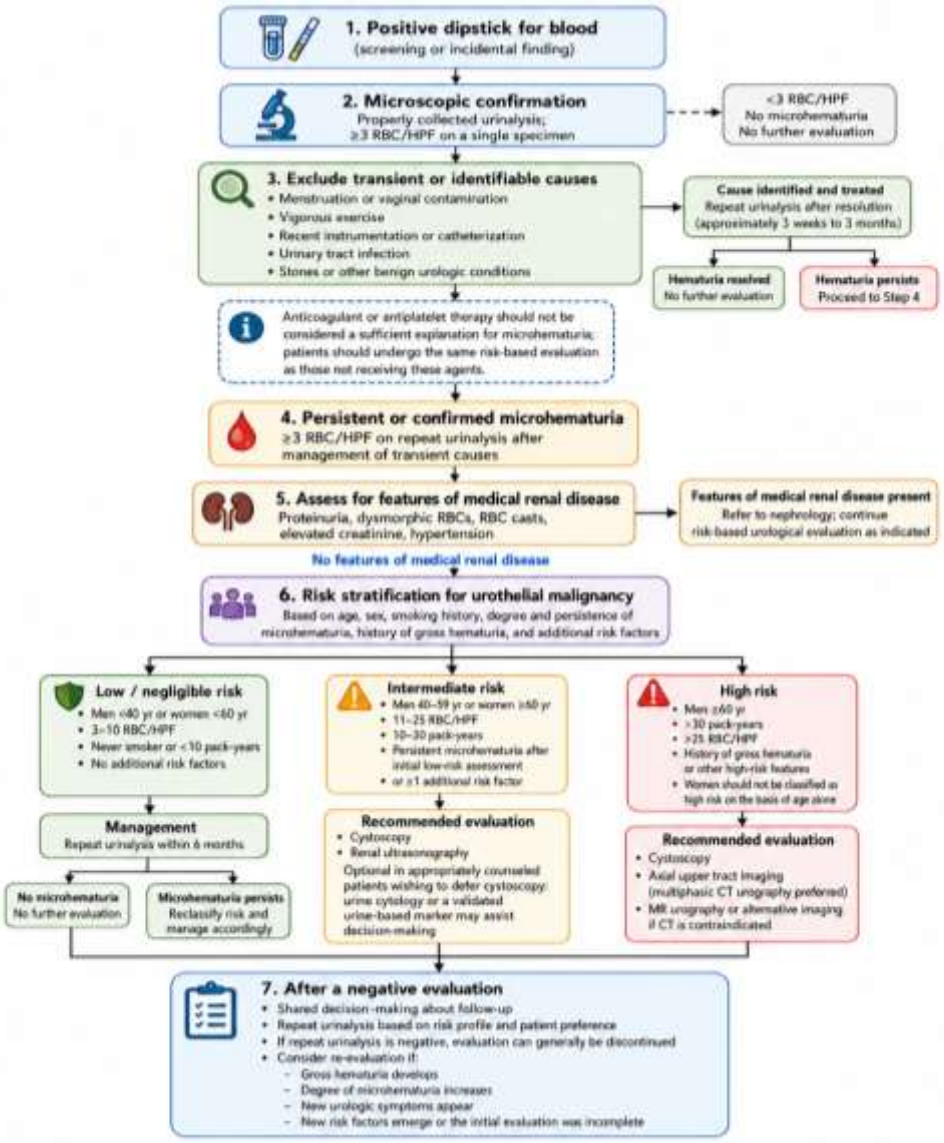
ultrasonography performed reasonably well for renal cancer but had low sensitivity for upper tract urothelial lesions. These results support ultrasonography as an appropriate first-line imaging method in selected patients with microscopic hematuria, but they also show why it cannot be considered equivalent to CT urography when suspicion of upper tract malignancy is higher [7,17,18].

Imaging does not replace evaluation of the bladder. Bladder cancer accounts for most malignancies detected during microhematuria assessment, and cross-sectional imaging cannot provide the same direct assessment of the bladder mucosa as cystoscopy. Cystoscopy therefore remains the reference method when a patient's estimated risk justifies lower urinary tract evaluation [1,2,7,16].

The intensity of investigation should ultimately reflect both the probability and the type of pathology being sought. Repeat urinalysis is sufficient initially for many patients at negligible risk, ultrasonography offers an appropriate balance of diagnostic yield and burden in the intermediate-risk setting, and CT urography becomes more appropriate as the likelihood of significant upper urinary tract disease increases. No single diagnostic test provides equivalent information about the bladder, renal parenchyma, and upper urinary tract, which is why appropriate risk classification remains central to selecting the diagnostic pathway [1,7].

Figure 1. Risk-adapted diagnostic pathway for the evaluation of asymptomatic microhematuria in adults.

The pathway integrates microscopic confirmation of hematuria, assessment of potentially reversible causes and features of medical renal disease, malignancy risk stratification, and subsequent risk-based urological evaluation.



Abbreviations: RBC/HPF, red blood cells per high-power field; CT, computed tomography; MR, magnetic resonance; AUA/SUFU, American Urological Association/Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction.

Source: authors' own elaboration based on AUA/SUFU Guideline 2025 [1].

8. Urine Cytology and Urine-Based Biomarkers

The invasive nature of cystoscopy has increased interest in non-invasive urine-based tests for urothelial malignancy. Their potential value is greatest when they can identify patients with a sufficiently low probability of bladder cancer to avoid or defer cystoscopy. At present, however, neither urine cytology nor molecular urine-based markers can replace cystoscopy across the full spectrum of patients with microhematuria [1,9].

Urine cytology is characterized by high specificity, particularly for high-grade urothelial carcinoma, but considerably lower sensitivity for low-grade disease. Its interpretation may also be affected by inflammation, recent instrumentation, inadequate specimens, and atypical findings of uncertain significance. These limitations make cytology unsuitable as a routine screening test for all patients with microhematuria, although it remains useful when high-grade disease or carcinoma in situ is specifically suspected [1,9].

The 2025 AUA/SUFU amendment gives urine-based testing a selective rather than universal role. Cytology and validated urine-based tumor markers are not routinely recommended to determine the need for cystoscopy in low/negligible-risk or high-risk patients. In the former group, the baseline probability of malignancy is already very low, whereas in high-risk patients a negative urinary test does not provide sufficient reassurance to omit direct bladder evaluation. Their most relevant application is therefore in selected intermediate-risk patients who wish to avoid immediate cystoscopy after appropriate counseling [1].

Prospective data suggest that such an approach can reduce the use of invasive procedures. In the randomized STRATA trial, incorporation of a molecular urine test into the evaluation of lower-risk patients with microhematuria substantially reduced cystoscopy use compared with standard care. This finding is clinically relevant, but fewer cystoscopies should not automatically be interpreted as equivalent long-term outcomes. A strategy that safely reduces invasive testing must also demonstrate that clinically important cancers are not missed or diagnosed at a later stage [8].

Interpretation of biomarker performance also depends strongly on the population being tested. High negative predictive values are easier to achieve when the prevalence of bladder cancer is low, and the same assay may provide less reassurance in patients with a higher pre-test probability of malignancy. Available tests also differ considerably in methodology, study

populations, thresholds, and validation. Reported performance of one assay should therefore not be generalized to urine-based tumor markers as a single diagnostic category [9].

Some newer molecular tests have shown high sensitivity and negative predictive values in patients evaluated for hematuria, suggesting potential utility as rule-out tools in selected populations. Their positive predictive values are generally more modest, and favorable diagnostic accuracy in a validation cohort does not establish that cystoscopy can be safely omitted over long-term follow-up. Independent validation and direct comparisons between assays remain limited [9].

Urine cytology retains a separate role in selected high-risk patients, particularly when cystoscopy is equivocal or when persistent microhematuria and other clinical features raise concern for carcinoma in situ despite an otherwise negative evaluation. Its usefulness in this setting reflects its better performance for high-grade than low-grade urothelial disease [1].

Urine-based tests should therefore be regarded as tools for refining risk-based decisions rather than as general substitutes for cystoscopy. Their current role is most convincing in selected intermediate-risk patients, where avoiding an invasive procedure may provide meaningful benefit. Whether biomarker-guided pathways can achieve this without delaying clinically significant cancer diagnoses remains the more important unresolved question [1,8,9].

Table 2. Diagnostic methods used in the evaluation of microhematuria: clinical role, advantages, and limitations

Diagnostic method	Main clinical role	Main advantages	Limitations and most appropriate use
Cystoscopy	Direct evaluation of the bladder mucosa	Direct visualization; remains the reference method for bladder assessment	Invasive, may cause discomfort and has a low expected yield in very-low-risk patients. Recommended when malignancy risk justifies lower urinary tract evaluation

Renal and bladder ultrasonography	Initial upper urinary tract imaging, particularly in intermediate-risk patients	No ionizing radiation or intravenous contrast; widely available; useful for renal masses and structural abnormalities	Lower sensitivity for UTUC and some ureteral lesions than CT urography. Appropriate when upper tract cancer probability is relatively low
CT urography	Comprehensive evaluation of the renal parenchyma and upper urinary tract	High diagnostic performance for upper tract urothelial and structural lesions; detailed anatomical assessment	Radiation exposure, intravenous contrast, incidental findings, and greater diagnostic burden. Most appropriate in high-risk patients
MR urography	Alternative upper urinary tract imaging when CT urography is contraindicated	No ionizing radiation; allows cross-sectional assessment of the kidneys and urinary tract	Less widely available, more costly, and not routinely required when CT urography can be performed. Mainly an alternative in selected high-risk patients
Urine cytology	Adjunctive assessment for high-grade urothelial carcinoma or carcinoma in situ	High specificity, particularly for high-grade disease	Limited sensitivity for low-grade tumors; atypical results may be difficult to interpret. Most useful in selected high-risk or diagnostically uncertain cases

Urine-based molecular markers	Refinement of the decision to perform cystoscopy in selected patients	Non-invasive; some assays provide high sensitivity and negative predictive value and may reduce cystoscopy use	Performance varies between assays and depends on baseline cancer prevalence; long-term evidence remains limited. Most relevant in appropriately counseled intermediate-risk patients rather than as a universal substitute for cystoscopy

Abbreviations: CT, computed tomography; MR, magnetic resonance; UTUC, upper tract urothelial carcinoma.

Source: authors' own elaboration based on current evidence and AUA/SUFU Guideline 2025 [1].

9. Clinical Situations Associated with Diagnostic Misattribution

Microhematuria may be prematurely attributed to a plausible benign cause, delaying further evaluation when the abnormality persists. Antithrombotic therapy and urinary tract infection are common examples because both can readily be accepted as sufficient explanations for urinary bleeding [1,19,20].

Patients receiving anticoagulant or antiplatelet therapy should be evaluated according to the same risk-based principles as those not taking these medications. Antithrombotic therapy may increase the tendency to bleed, but it does not establish the source of hematuria. In some cases, it may simply make bleeding from an underlying urinary tract lesion more apparent. Anticoagulation or antiplatelet use should therefore not be used to exclude malignancy risk assessment or otherwise indicated urological evaluation [1].

Urinary tract infection is another frequent source of diagnostic misattribution. Hematuria occurring during a documented infection may reasonably be related to inflammation, but resolution should be confirmed after treatment. Persistent or recurrent microhematuria requires reassessment rather than continued attribution to infection. Repeated empirical treatment without confirming disappearance of the urinary abnormality may delay recognition of other urinary tract pathology [1,19].

This concern is especially relevant in women. Although their overall risk of urothelial malignancy is lower than that of men, observational studies have shown longer diagnostic intervals before bladder cancer diagnosis and more frequent intervening diagnoses of urinary tract infection. These findings do not justify invasive investigation after every episode of infection-associated hematuria, but they support repeat assessment when bleeding persists or recurs after treatment [19,20].

A presumed reversible cause should therefore be considered resolved only when the hematuria itself also resolves. If it does not, further evaluation should proceed according to the patient's malignancy risk rather than the original benign explanation [1].

10. Follow-Up After a Negative Evaluation

A complete negative risk-based evaluation is associated with a low subsequent probability of detecting genitourinary malignancy. Follow-up should therefore distinguish persistent microscopic findings from a genuine change in the clinical presentation rather than rely on routine repetition of invasive investigations [1,10,11].

Current AUA/SUFU recommendations do not require mandatory long-term surveillance after a negative evaluation. Instead, the decision to repeat urinalysis should be individualized through shared decision-making. When repeat urinalysis is negative, further follow-up for the previous episode of microhematuria can generally be discontinued [1].

Long-term observational data provide some reassurance. In a retrospective study of 8,465 patients who had undergone negative cystoscopy and CT urography, subsequent urinary tract malignancy was diagnosed in 0.74%, compared with 0.83% among matched controls without microhematuria. No significant difference in cancer incidence was observed between the groups [10].

Persistent or recurrent microhematuria after a negative evaluation is more difficult to interpret, but its diagnostic yield on repeated investigation appears low. In a cohort of 637 patients with persistent or recurrent microhematuria after an initially negative work-up, repeat cystoscopy detected bladder cancer in 2 of 161 patients, while repeat upper tract imaging identified a new suspicious renal mass in 4 of 317. Repeat investigations were performed at a median of 39 months after the initial assessment. These findings argue against automatic repetition of the complete diagnostic pathway solely because microscopic hematuria persists [11].

A change in clinical presentation carries greater importance. Gross hematuria, a substantial increase in the degree of microhematuria, or new urological symptoms should prompt renewed

evaluation after a previous negative work-up. Reassessment may also be appropriate when the original investigation was incomplete or when the patient's risk profile has changed [1].

Stable persistent microhematuria after an adequate negative evaluation should therefore be managed differently from newly developed warning signs. For many patients, a negative repeat urinalysis provides a reasonable endpoint to follow-up. When microhematuria persists, the decision to repeat cystoscopy or imaging should reflect the previous evaluation, current risk factors, and any change in symptoms rather than a fixed surveillance schedule [1,10,11].

11. Current Controversies and Limitations of Risk-Based Strategies

Risk-stratified evaluation is preferable to uniform investigation of all patients with microhematuria, but current models remain imperfect. They divide a continuous spectrum of malignancy risk into discrete categories based on a limited number of clinical variables. Patients close to thresholds for age, smoking exposure, or degree of hematuria may have similar underlying risk despite being assigned to different diagnostic pathways. Risk categories are therefore practical tools rather than precise estimates for individual patients [1,6,13,15].

A further limitation is that existing systems are primarily designed to predict urothelial malignancy. Validation of the 2025 AUA framework showed increasing rates of urothelial neoplasia across successive risk groups, whereas renal cortical tumors did not follow the same pattern. A model that performs well for bladder and upper tract urothelial cancer may therefore be less informative for other renal malignancies [15].

The revised approach to women illustrates another area requiring refinement. The 2025 amendment reduces unnecessary evaluation in younger women with a very low baseline risk, but available data suggest that bladder cancer risk becomes more relevant at advanced age. Older women with additional risk factors may therefore not fit neatly into simplified age-based assumptions [1,14,15].

Uncertainty also remains over the optimal use of upper urinary tract imaging. Ultrasonography avoids radiation and intravenous contrast but is less sensitive for upper tract urothelial carcinoma. CT urography provides more complete assessment, although the additional diagnostic yield must be weighed against radiation exposure, contrast administration, incidental findings, and cost. Because upper tract malignancy is rare in asymptomatic microhematuria, greater test sensitivity does not automatically justify CT urography in every patient [2–5,7,17,18].

Urine-based biomarkers may reduce cystoscopy in selected intermediate-risk patients, but evidence that such strategies provide equivalent long-term oncological outcomes is still limited. Their performance depends on pre-test cancer probability, and substantial differences between available assays make broad generalization difficult. For now, they are better suited to refining selected decisions than replacing cystoscopy routinely [1,8,9].

Similar uncertainty applies to follow-up after a negative evaluation. Subsequent malignancy detection is uncommon and repeated cystoscopy or imaging generally has a low yield, yet the optimal duration of surveillance is not well defined for patients with persistent microhematuria and substantial ongoing risk factors [1,10,11].

The remaining challenge is to identify the relatively small group of patients who benefit from intensive investigation without exposing much larger low-risk populations to unnecessary procedures. More precise risk prediction, external validation in relevant subgroups, and prospective assessment of biomarker-guided pathways will be needed to move beyond the limitations of current categorical models [8,9,13,15].

12. Future Perspectives

More precise evaluation of microhematuria will probably require a shift from broad risk categories toward individualized estimates of malignancy probability. The current AUA/SUFU framework separates patients with substantially different risks of urothelial neoplasia, but considerable variation remains within each category. Continuous models incorporating age, sex, smoking exposure, degree of microhematuria, and additional clinical factors may eventually provide more useful estimates than fixed low-, intermediate-, and high-risk thresholds [1,13,15].

Urine-based molecular tests may become part of such models. Their most plausible role is not as an independent alternative to cystoscopy, but as an additional source of information in patients whose clinical risk does not clearly justify or exclude invasive evaluation. Comparative studies should assess competing assays in well-defined microhematuria populations and determine whether they add predictive value beyond established clinical variables. High sensitivity or negative predictive value alone is not sufficient; biomarker-guided pathways must also show that fewer cystoscopies do not result in delayed diagnosis of clinically significant bladder cancer [8,9].

The approach to upper urinary tract imaging also requires refinement. Current risk models appear more informative for urothelial malignancy than for renal cortical tumors, while

ultrasonography and CT urography offer different balances between sensitivity and diagnostic burden. Future comparisons should therefore examine not only additional lesions detected by more intensive imaging, but whether their detection changes cancer stage, treatment, or long-term outcome [3,5,7,15,17,18].

Several patient groups remain difficult to classify, including older women, patients with persistent microhematuria after a negative evaluation, and those with less common but clinically relevant cancer risk factors. Validation in diverse populations and healthcare settings will be important if diagnostic pathways become increasingly selective [1,10,11,14,15,20].

Diagnostic yield should also not be the only measure of success. Reducing cystoscopy or CT urography is valuable only when clinically important disease is not missed or diagnosed later. Cancer stage, treatment consequences, procedure-related harm, incidental findings, costs, and patient preferences should therefore be incorporated into future evaluations of risk-based strategies [3–5,8,10,11].

The next step in microhematuria assessment is likely to involve combining clinical risk estimation with selected non-invasive biomarkers and appropriately targeted imaging rather than relying on a single new diagnostic test. Whether this approach can safely improve on current categorical pathways will require prospective validation and long-term outcome data [8,9,13,15].

13. Conclusions

Asymptomatic microhematuria is a common finding, but the probability of clinically significant genitourinary malignancy varies markedly between patients. This variability favors a risk-stratified rather than uniform diagnostic approach.

Cystoscopy and upper urinary tract imaging should be concentrated in patients with a meaningful probability of malignancy, while unnecessary procedures can be avoided in those at very low risk. The choice of diagnostic method should reflect not only test sensitivity but also the absolute likelihood of disease, potential harms, and the likelihood that the result will influence clinical management.

Urine cytology and molecular urine-based markers may refine evaluation in selected patients, particularly those at intermediate risk, but they cannot currently replace cystoscopy across the broader microhematuria population. Persistent microhematuria after a complete negative evaluation likewise does not automatically justify repeated invasive investigation.

Risk-based models remain imperfect and should complement rather than replace clinical judgment. More precise risk prediction, better integration of validated non-invasive biomarkers, and prospective evidence on less intensive diagnostic pathways will be needed to reduce unnecessary testing without compromising detection of clinically significant disease.

Author's contribution

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References

1. Barocas DA, Lotan Y, Matulewicz RS, Raman JD, Westerman ME, Kirkby E, Pak LJ, Souter L. Updates to Microhematuria: AUA/SUFU Guideline (2025). J Urol. 2025;213(5):547-557. doi:10.1097/JU.0000000000004490.
2. Waisbrod S, Natsos A, Wettstein MS, Saba K, Hermanns T, Fankhauser CD, Müller A. Assessment of Diagnostic Yield of Cystoscopy and Computed Tomographic Urography for Urinary Tract Cancers in Patients Evaluated for Microhematuria: A Systematic Review and Meta-analysis. JAMA Netw Open. 2021;4(5):e218409. doi:10.1001/jamanetworkopen.2021.8409.
3. Yecies T, Bandari J, Fam M, Macleod L, Jacobs B, Davies B. Risk of Radiation from Computerized Tomography Urography in the Evaluation of Asymptomatic Microscopic Hematuria. J Urol. 2018;200(5):967-972. doi:10.1016/j.juro.2018.05.118.
4. Halpern JA, Chughtai B, Ghomrawi H. Cost-effectiveness of Common Diagnostic Approaches for Evaluation of Asymptomatic Microscopic Hematuria. JAMA Intern Med. 2017;177(6):800-807. doi:10.1001/jamainternmed.2017.0739.
5. Georgieva MV, Wheeler SB, Erim D, Smith-Bindman R, Loo R, Ng C, Garg T, Raynor M, Nielsen ME. Comparison of the Harms, Advantages, and Costs Associated With Alternative Guidelines for the Evaluation of Hematuria. JAMA Intern Med. 2019;179(10):1352-1362. doi:10.1001/jamainternmed.2019.2280.
6. Barocas DA, Boorjian SA, Alvarez RD, Downs TM, Gross CP, Hamilton BD, Kobashi KC, Lipman RR, Lotan Y, Ng CK, Nielsen ME, Peterson AC, Raman JD, Smith-Bindman R, Souter LH. Microhematuria: AUA/SUFU Guideline. J Urol. 2020;204(4):778-786. doi:10.1097/JU.0000000000001297.
7. Tan WS, Sarpong R, Khetrapal P, Rodney S, Mostafid H, Cresswell J, Hicks J, Rane A, Henderson A, Watson D, Cherian J, Williams N, Brew-Graves C, Feber A, Kelly JD, DETECT I trial collaborators. Can Renal and Bladder Ultrasound Replace Computerized Tomography Urogram in Patients Investigated for Microscopic Hematuria? J Urol. 2018;200(5):973-980. doi:10.1016/j.juro.2018.04.065.
8. Lotan Y, Daneshmand S, Shore N, Black P, Scarpato KR, Patel A, Lough T, Shoskes DA, Raman JD. A Multicenter Prospective Randomized Controlled Trial Comparing Cxbladder Triage to Cystoscopy in Patients With Microhematuria: The Safe Testing of Risk for Asymptomatic Microhematuria Trial. J Urol. 2024;212(1):41-51. doi:10.1097/JU.0000000000003991.

9. Siguencia F, Heard J, Smith SM, Pagano I, Furuya H, Wu X, Ahdoot M, Rosser CJ. Diagnostic Performance of Urinary Biomarker Tests in Detecting Bladder Cancer: A Systematic Review, Meta-analysis, and Network Meta-analysis. Urology. 2026;210:145-152. doi:10.1016/j.urology.2026.01.035.
10. Lisanti CJ, Graeber A, Syed H, Moeck A, Rittel AG, Aden JK, Schwope R, Jellison F. What Is the Relative Risk of Urologic Malignancy in Microscopic Hematuria Patients After Negative Evaluation? A Long-term Population-based Retrospective Analysis of 8465 Patients. Abdom Radiol (NY). 2023;48(3):1011-1019. doi:10.1007/s00261-022-03793-x.
11. Pak JS, Wang EY, Lee K, Pina LA, McKiernan JM, Anderson CB. Diagnostic Yield of Repeat Evaluation for Asymptomatic Microscopic Hematuria After Negative Initial Workup. Urol Oncol. 2021;39(5):300.e1-300.e6. doi:10.1016/j.urolonc.2020.11.032.
12. Saha MK, Massicotte-Azarniouch D, Reynolds ML, Mottl AK, Falk RJ, Jennette JC, Derebail VK. Glomerular Hematuria and the Utility of Urine Microscopy: A Review. Am J Kidney Dis. 2022;80(3):383-392. doi:10.1053/j.ajkd.2022.02.022.
13. Woldu SL, Ng CK, Loo RK, Slezak JM, Jacobsen SJ, Tan WS, Kelly JD, Lough T, Darling D, van Kessel KEM, de Jong JJ, van Criekinge W, Shariat SF, Hiar A, Brown S, Boorjian SA, Barocas DA, Svatek RS, Lotan Y. Evaluation of the New American Urological Association Guidelines Risk Classification for Hematuria. J Urol. 2021;205(5):1387-1393. doi:10.1097/JU.0000000000001550.
14. Saxon GM, Patil D, Hammett J. Microhematuria in Women: Prevalence of Malignancy and Risk Score Evaluation. Urology. 2022;160:34-39. doi:10.1016/j.urology.2021.11.003.
15. Udedibia E, Solosky K, Macdonald EJ, Gaines J, Huang K, Diefenbach M, Vira M, Hall SJ. Critical Analysis of the AUA 2020/2025 Microscopic Hematuria Guidelines to Predict Urothelial but Not Renal Cortical Neoplasms and Validation of the Individual Clinical Components in Risk Stratification for Urothelial Neoplasms but Not Renal Cortical Neoplasms. J Urol. 2026;215(4):441-449. doi:10.1097/JU.0000000000004854.
16. Devlies W, de Jong JJ, Hofmann F, Bruins HM, Zuiverloon TCM, Smith EJ, Yuan Y, van Rhijn BWG, Mostafid H, Santesso N, Violette P, Omar MI. The Diagnostic Accuracy of Cystoscopy for Detecting Bladder Cancer in Adults Presenting with Haematuria: A Systematic Review from the European Association of Urology Guidelines Office. Eur Urol Focus. 2024;10(1):115-122. doi:10.1016/j.euf.2023.08.002.

17. Taylor JI, Souter LH, Barocas DA, Boorjian SA, Raman JD, Lotan Y. Diagnostic Imaging in the Evaluation of Asymptomatic Microhematuria: Systematic Review and Meta-analysis. J Urol. 2023;209(6):1099-1106. doi:10.1097/JU.0000000000003395.
18. Bochner E, Ibezue C, Banerji D, Attia S, Taylor J, Lotan Y. Assessing the Diagnostic Performance of Renal Ultrasound in Microhematuria Evaluation: Validation of the AUA Microhematuria 2020 Guidelines. Urology. 2026;207:196-200. doi:10.1016/j.urology.2025.09.012.
19. Liedberg F, Gårdmark T, Hagberg O, Aljabery F, Ströck V, Hosseini A, Malmström PU, Söderkvist K, Ullén A, Jerlström T, Jahnson S, Holmberg L, Häggström C. Treatment Related to Urinary Tract Infections Is Associated with Delayed Diagnosis of Urinary Bladder Cancer: A Nationwide Population-based Study. Eur Urol Oncol. 2025;8(1):119-125. doi:10.1016/j.euo.2024.07.008.
20. Zhang EZ, Millot JC, Balasubramanian A, Davis L, Wald G, Arenas-Gallo C, McCann J, Ponsky LE, Calaway AC, Barata PC, Scherr DS, Basourakos SP, Dreyfuss LD, Bohorquez Caballero AD, Rhodes S, Shoag JE. Persistent Sex Disparities in Bladder Cancer Diagnosis: An Analysis of National Trends From 2012 to 2021. Urol Pract. 2026;13(1):42-50. doi:10.1097/UPJ.0000000000000904.