

I'm not robot!

TABLE 2. Type of bleeding and type of treatment of the 52 bleeding sites treated with TC-325/Hemospray

Type of treatment	Spurting bleeding, n (%)	Oozing bleeding, n (%)	Other bleeding, (%)*
Monotherapy	0 (0)	13 (25.0)	0 (0)
Combination therapy	3 (5.8)	18 (34.6)	1 (1.9)
Rescue therapy	2 (3.8)	14 (26.9)	1 (1.9)
Total no. of bleeding sites	5 (9.6)	45 (86.5)	2 (3.8)

*Other bleeding qualities included 1 patient with a spurting bleed that was banded ligated but continued to ooze and one patient who had multiple areas of angiodysplasia.

	LRP	RaLRP	P
No patients	80	49	
Median age (SD)	65 (5.49)	63 (4.87)	0.125
Median follow-up, month	78	14	0.010
PSA level, ng/mL (%)			
<10	13 (16)	14 (29)	0.146
10-20	42 (53)	19 (38)	
>20	25 (31)	16 (33)	
Clinical T stage (%)			
cT1	31 (39)	6 (12)	0.001
cT2	39 (49)	27 (55)	
cT3	10 (12)	16 (33)	
Biopsy GS (%)			
<7	13 (16)	14 (29)	0.146
7	42 (53)	18 (37)	
>7	25 (31)	16 (33)	

LRP: Laparoscopic radical prostatectomy, RaLRP: Robotic-assisted laparoscopic radical prostatectomy, SD: Standard deviation, PSA: Prostate-specific antigen, GS: Gleason score

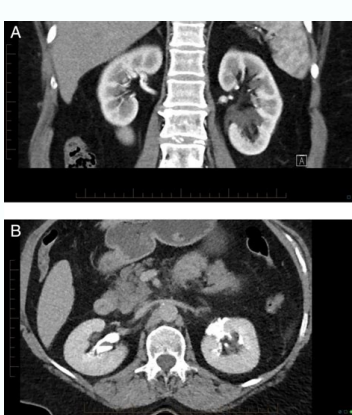
FEATURES OF DHF



Physical examination



- Measurement of the blood pressure and volume status is especially important when glomerulonephritis is a consideration.
- Evaluation for the presence of periorbital puffiness or peripheral edema
- Detailed skin examination to look for purpura.
- Abdominal examination to look for palpable mass reveals a renal tumor or hydronephrosis may exist.
- A palpable bladder after voiding indicates obstruction or retention



Eau guidelines microscopic hematuria. Eau guidelines haematuria. Eau bladder cancer guidelines. Eau nmibc guidelines. Eau utuc guidelines.

Dr. Matthew Nielsen, Professor and Interim Chair of the Department, was a panelist and contributing author to the American Urological Association's new 2020 Guideline for the evaluation of hematuria, released this week. The guideline will be presented by panel co-Chairs at the AUA Live Virtual Experience at 3:45pm on Saturday, June 27. Hematuria is a common finding in clinical practice, with over 2 million American patients referred each year for evaluation, representing one of the most common diagnoses seen by urologists. The AUA panel aimed to develop and disseminate clear guideline recommendations for the evaluation of hematuria. This work sought to mitigate potentially avoidable risks and costs associated with the over-evaluation of patients at low risk for malignancy, while at the same time addressing the delays in diagnosis of important urologic conditions caused by widespread under-evaluation and variations in care. The new 2020 AUA Guideline provides an individualized, risk-stratified approach to hematuria evaluation based on the patient's risk of harboring a urinary tract cancer. Nielsen's work in this area started with a collaboration with the American College of Physicians' High Value Care Task Force, published in 2016. This effort highlighted unexplained variation in care and raised questions related to potentially avoidable costs and harms from existing recommendations at that time, which recommended uniform evaluation with CT for all adults with hematuria. Last summer, a team of investigators from UNC published a simulation modeling study in JAMA Internal Medicine examining tradeoffs of harm, benefit and cost associated with various strategies for hematuria evaluation, finding substantial potentially avoidable costs and harms from radiation exposure with a uniformly intensive approach. "It was a privilege to be a part of this important effort from the AUA, and I'm very grateful for the leadership of the co-Chairs, other panelists, and AUA staff. We are hopeful that these new guidelines will provide clearer guidance and a patient-centered approach, reducing avoidable harms and costs for low-risk patients while enhancing early detection of disease for patients at greater risk." Matthew Nielsen, MD, MS, FACS Interim Chair, Department of Urology Filed Under: Categories: News Tags: Nielsen Our aim is to develop best practice clinical guidelines primarily for frontline urologists, but also for patients to support shared decision making and, increasingly, the shift to more individualized patient-centered care. Read more about our methodology or the guidelines office. (UroToday.com) The guidelines for microhematuria were formulated by a multidisciplinary panel with representations from the American Urological Association (AUA), Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU), and American College of Obstetricians and Gynecologists (ACOG), as well as Bladder Cancer Advocacy Network (BCAN) patient advocate. The guidelines were based on systematic review search dates between January 2010 until December 2019. The evidence base includes five systematic reviews and 91 primary literature studies. Hematuria is one of the most common urological diagnoses, with over 25% of urological evaluations. The prevalence of microscopic hematuria from screening healthy volunteers is approximately 6.5%, with ranges between 2.4 and 31.1%, depending on the specific population evaluated. The possible urological etiologies for haematuria include: malignancy in approximately 3% of cases infection Inflammation Stone disease benign prostatic hyperplasia congenital or acquired anatomic abnormalities There is significant variability across the current guidelines and consensus statements regarding the evaluation of microscopic haematuria, whether it should entail cystoscopy and upper tract imaging. It is known that aside from the conflicting guidelines regarding the evaluation of microscopic hematuria, there is an overall low yield of the evaluation with malignancy diagnosed in only 3% of the cases, with less than 1% diagnosed in patients without any kind of risk factors, and more than 10% diagnosis in patients with multiple risk factors. Additionally, the evaluation also has potential harms, which include risks to the patient and cost to the health system. Moreover, currently, there is poor adherence to the existing guidelines. The aim of the 2020 AUA guidelines regarding microscopic haematuria is to provide a risk-stratified approach to hematuria evaluation based on the patient's risk of harboring a urinary tract cancer and concordant with the patients' values. Microhematuria is defined as three or above red blood cells per high power field on microscopic evaluation of a single, properly collected urine specimen (Evidence level grade C). Clinicians should not define microhematuria by a positive dipstick testing alone. Positive dipstick test trace blood should prompt formal microscopic evaluation of the urine. In patients diagnosed with gynecological or non-malignant genitourinary sources of microhematuria, clinicians should repeat urinalysis following the resolution of the gynecological or non-malignant genitourinary cause. If microhematuria persists or the etiology cannot be identified, clinicians should perform a risk-based urologic evaluation. If the hematuria is attributed to a urinary tract infection, clinicians should obtain a urinalysis with microscopic evaluation following treatment of the infection to ensure that hematuria has been resolved (Evidence level grade C). Following the initial evaluation, clinicians should categorize patients presenting with microhematuria either as low, intermediate, or high risk for genitourinary malignancy based on the following tables (Table 1). Table 1- Specifically, in patients with low risk of malignancy, the clinician should engage in a shared decision-making process with the patient in an attempt to decide between repeating the urinalysis within six months or proceeding with cystoscopy and renal ultrasound. If these low-risk patients initially elect not to undergo cystoscopy or upper tract imaging and are found to have microhematuria on repeat urine testing, they should be reclassified as intermediate or high-risk. In these patients, upper tract imaging and cystoscopy should be done in accordance with recommendations for these extra risk strata. In intermediate-risk patients, clinicians should perform cystoscopy and renal ultrasound. Lastly, in high-risk patients, cystoscopy and upper tract imaging should be performed as well. Specifically, in high-risk patients, if there is no contraindication to its use, clinicians should perform multiphasic CT urography. If there is a contraindication to CT urography, clinicians may utilize MRU. If there are contraindications to both CTU and MRU, retrograde pyelography in conjunction with non-contrast axial imaging or renal ultrasound should be done. No urinary markers, including urine cytology, should be used in the initial evaluation of patients with microhematuria. Urine cytology may be obtained for patients with persistent microhematuria after negative workup, who also have irritative voiding symptoms or risk factors for carcinoma-in-situ. In patients with a negative workup, clinicians may obtain repeat urinalysis within 12 months. The patient with a prior negative workup and subsequent negative urinalysis clinicians may discontinue further evaluation for microhematuria. If patients with a prior negative hematuria evaluation have persistent or recurrent microhematuria at the time of repeat urinalysis, clinicians should engage in shared decision making regarding the need for additional evaluation. Patients with prior negative hematuria evaluation, who developed gross hematuria, a significant increase in the degree of their microhematuria, or new urologic symptoms, the clinician should initiate further evaluation. The panel does acknowledge several notable areas where there are considerable gaps in knowledge. These present opportunities for further investigation to enhance care. These include: automated instrumentation Validation of risk groups lower radiation imaging enhanced cystoscopy urinary biomarkers follow up procedures The algorithm for the AUA microhematuria guidelines is depicted in Figure 1. Figure 1- Microscopic hematuria AUA algorithm guidelines: Home Guidelines Guidelines Clinical Guidelines Microhematuria Daniel Barocas, MD, MPH* Stephen Boorjian, MD* Ronald Alvarez, MD, MBA; Tracy M. Downs, MD; Cary Gross, MD; Blake Hamilton, MD; Kathleen Kobashi, MD; Robert Lipman; Yair Lotan, MD; Casey Ng, MD; Matthew Nielsen, MD, MS; Andrew Peterson, MD; Jay Raman, MD; Rebecca Smith-Bindman, MD; Lesley Souter, PhD * Equal author contribution The purpose of this guideline is to provide a clinical framework for the diagnosis, evaluation, and follow-up of microhematuria (MH). MethodologyOVID was used to systematically search MEDLINE and EMBASE databases for articles evaluating hematuria using criteria determined by the expert panel. The initial draft evidence report included evidence published from January 2010 through February 2019. A second search conducted to update the report included studies published up to December 2019. Five systematic reviews and 91 primary literature studies met the study selection criteria and were chosen to form the evidence base. When sufficient evidence existed, the body of evidence for a particular modality was assigned a strength rating of A (high), B (moderate), or C (low); and evidence-based statements of Strong, Moderate, or Conditional Recommendation were developed. Additional information is provided as Clinical Principles and Expert Opinions when insufficient evidence existed. See text and algorithm for definitions and detailed diagnostic, evaluation, and follow-up information.Guideline StatementsDiagnosis and Definition of Microhematuria1. Clinicians should define microhematuria as ≥ 3 red blood cells per high-power field on microscopic evaluation of a single, properly collected urine specimen. (Strong Recommendation; Evidence Level: Grade C)2. Clinicians should not define microhematuria 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)Initial Evaluation3. In patients with microhematuria, 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 microhematuria. (Clinical Principle)4. Clinicians should perform the same evaluation of patients with microhematuria 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)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 microhematuria, clinicians should repeat urinalysis following resolution of the gynecologic or non-malignant genitourinary cause. If microhematuria 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 urinalysis with microscopic evaluation following treatment to ensure resolution of the hematuria. (Strong Recommendation; Evidence Level: Grade C)8. Clinicians should refer patients with microhematuria for nephrologic evaluation if medical renal disease is suspected. However, risk-based urologic evaluation should still be performed. (Clinical Principle)Risk Stratification9. Following initial evaluation, clinicians should categorize patients presenting with microhematuria as low-, intermediate-, or high-risk for genitourinary malignancy based on the accompanying tables (Tables 3 and 4). (Strong Recommendation; Evidence Level: Grade C)Urinary Tract EvaluationLow-Risk10. In low-risk patients with microhematuria, clinicians should engage patients in shared decision-making to decide between repeating urinalysis within six months or proceeding with cystoscopy and renal ultrasound. (Moderate Recommendation; Evidence Level: Grade C)Initially Low-Risk with Hematuria on Repeat Urinalysis11. Low-risk patients who initially elected not to undergo cystoscopy or upper tract imaging and who are found to have microhematuria on repeat urine testing should be reclassified as intermediate- or high-risk. In such patients, clinicians should perform cystoscopy and upper tract imaging in accordance with recommendations for these risk strata (Strong Recommendation; Evidence Level: Grade

Risk-12. Clinicians should perform cystoscopy and renal ultrasound in patients with microhematuria categorized as intermediate-risk for malignancy. (Strong Recommendation; Evidence Level: Grade C)High-Risk13. Clinicians should perform cystoscopy and axial upper tract imaging in patients with microhematuria categorized as high-risk for malignancy. (Strong Recommendation; Evidence Level: Grade C)Options for Upper Tract Imaging in High-Risk Patient.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)If there are contraindications to multiphasic CT urography, clinicians may utilize MR urography. (Moderate Recommendation; Evidence Level: Grade 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)14. Clinicians should perform white light cystoscopy in patients undergoing evaluation of the bladder for microhematuria. (Moderate Recommendation; Evidence Level: Grade C)15. In patients with persistent or recurrent microhematuria previously evaluated with renal ultrasound, clinicians may perform additional imaging of the urinary tract. (Conditional Recommendation; Evidence Level: Grade C)16. In patients with microhematuria who have a family history of renal cell carcinoma or a known genetic renal tumor syndrome, clinicians should perform upper tract imaging regardless of risk category. (Expert Opinion)Urinary Markers17. Clinicians should not use urine cytology or urine-based tumor markers in the initial evaluation of patients with microhematuria. (Strong Recommendation; Evidence Level: Grade C)18. Clinicians may obtain urine cytology for patients with persistent microhematuria after a negative workup who have irritative voiding symptoms or risk factors for carcinoma in situ. (Expert Opinion)Follow-Up19. In patients with a negative hematuria evaluation, clinicians may obtain a repeat urinalysis within 12 months. (Conditional Recommendation; Evidence Level: Grade C)20. For patients with a prior negative hematuria evaluation and subsequent negative urinalysis, clinicians may discontinue further evaluation for microhematuria. (Conditional Recommendation; Evidence Level: Grade C)21. For patients with a prior negative hematuria evaluation who have persistent or recurrent microhematuria at the time of repeat urinalysis, clinicians should engage in shared decision-making regarding need for additional evaluation. (Expert Opinion)22. For patients with a prior negative hematuria evaluation who develop gross hematuria, significant increase in degree of microhematuria, or new urologic symptoms, clinicians should initiate further evaluation. (Moderate Recommendation; Evidence Level: Grade C) Hematuria remains 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 EtiologiesUrologic etiologies for hematuria include malignancy, infection, inflammation, calculus disease, benign prostatic hyperplasia (BPH), and congenital or acquired anatomic abnormalities.3 Hematuria may also be confused with gynecological sources of bleeding, myoglobinuria, or pigmentation of the urine from the ingestion of certain foods and drugs. When considering the risk of malignancy in patients with hematuria, a recent prospective observational study over 3,500 patients referred for evaluation of hematuria noted a 10.0% rate of urinary tract cancer: 13.2% for patients with gross hematuria (GH) and 3.1% among patients with MH.4 Similarly, aggregate data from 17 prior MH screening studies published between 1980 to 2011 identified in the 2012 AUA Guideline reported a urinary tract malignancy rate of 2.6% (range 0% to 25.8%), the vast majority of which were bladder cancers.2 Eleven more contemporary studies enrolling MH patients in the current evidence base dating from 2010 to 2019 reported an aggregate urinary tract malignancy rate of 1% (range 0.3% to 6.25%), which varied according to the presence or absence of risk factors for malignancy.5-15Diagnostic Evaluation of MicrohematuriaWhile most experts agree that patients with GH should be evaluated with cystoscopy, upper tract imaging and urinary cytology, significant variability exists across current guidelines and consensus statements regarding MH, particularly the definition of MH, criteria for evaluation, as well as the appropriate components of the evaluation, including the optimal imaging modality.16,17 The 2012 AUA Guideline recommended computed tomography (CT) urography and cystoscopy in all patients over 35 years of age with MH, and were largely crafted without regard to patients' risk of malignancy. Indeed, the principal goal of the 2012 Guideline was to minimize the likelihood of missing a malignancy diagnosis.2 Consistent with this intention, a theoretical simulation model determined that this evaluation would miss detection of the fewest number of cancers relative to other existing guidelines.17 Nevertheless, this approach has attendant patient risk (e.g., discomfort and risk of infection with cystoscopy, risk of contrast reactions, potential for radiation-induced cancers attributed to CT, detection of false-positive findings leading to further investigation),17 and an incremental healthcare cost approximately twice that of guidelines from other organizations.17,18 In light of the overall low rate of cancers detected among patients with MH, the implications of diagnostic studies must be considered both at the patient and health system level.At the same time, practice-pattern assessments have demonstrated significant inconsistencies 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.19 Moreover, in a series of patients presenting with hematuria who had known risk factors for bladder cancer, only 23% received any type of imaging, and only 13% underwent cystoscopy.10 The underuse of cystoscopy, and the tendency to use only imaging for evaluation, is particularly concerning when one considers that the vast majority of cancers diagnosed among persons with hematuria are bladder cancers, optimally detected with cystoscopy.7,8,10,13-15,20-23Women with hematuria have been especially prone to delays in evaluation, often due to practitioners ascribing hematuria to a urinary tract infection (UTI) or gynecologic source, resulting in inadequate evaluation and delay in cancer diagnosis.19,24 Similarly, studies have found that African American patients are less likely than Caucasian counterparts to undergo any aspect of hematuria evaluation, including urology referral, cystoscopy, and imaging.25 In turn, despite having a lower incidence of bladder cancer than men, women diagnosed with bladder cancer have a lower 5-year survival than men (73.3% versus 78.2%), which may be in part attributable to delay in diagnosis leading to higher stage disease at diagnosis.26 Likewise, racial differences in five-year survival and stage at diagnosis for urothelial cancer have also been noted, with evidence demonstrating lower rates of referral to urology and lower use of imaging in women and African Americans with hematuria compared to men and whites, which may explain some of this variation in disease burden at diagnosis and in survival.25,27,28 Delays in diagnosis of bladder cancer have been suggested to contribute to a 34% increased risk of cancer-specific mortality and a 15% increased risk of all-cause mortality.29As such, the need exists to develop and disseminate clear 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 addressing the delays in diagnosis of important urologic conditions caused by widespread under-evaluation and variations in care. Furthermore, 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" (e.g., dependent on the value that an individual patient may place on them).30This 2020 AUA Guideline for MH was developed with these goals in mind. The aim is to provide an individualized approach to hematuria evaluation based on the patient's risk of harboring a urinary tract cancer and concordant with the patient's values. In the process, it is recognized that tailoring the intensity of evaluation to patient risk, as opposed to recommending intensive evaluation for every patient irrespective of harms and costs, will inevitably introduce the potential for some missed cancers. Nonetheless, the proposed approach seeks to optimize the balance of detection and risk at both the patient and health system level. In addition, the Panel aims to put forth an actionable set of recommendations that will facilitate standardization in order to minimize unnecessary variations and the risk of under-evaluation and delayed diagnosis of important urologic conditions. The recommendations herein, based on analysis of the best available evidence, represent a patient-centered approach by maximizing the opportunities to diagnose important urologic conditions in a timely fashion, while avoiding unnecessary evaluations in low-risk patients.MethodologyThe systematic review utilized to inform this guideline was conducted by an independent methodological consultant. Determination of the guideline scope and review of the final systematic review to inform guideline statements was conducted in conjunction with the MH Panel.Panel FormationThe Panel was created in 2018 by the American Urological Association Education and Research, Inc. (AUAEER). This guideline was developed in collaboration with the Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU). The Practice Guidelines Committee (PGC) of the AUA selected the Panel Chairs who in turn appointed the additional panel members with specific expertise in this area in conjunction with SUFU. Additionally, the Panel included representation from the American College of Obstetricians and Gynecologists (ACOG) as well as a patient advocate. Funding of the Panel was provided by the AUA; panel members received no remuneration for their work.Searches and Article SelectionA 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 (PICO) 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. Based on a low volume of studies identified enrolling solely MH patients, studies that enrolled a combination MH and GH population were included in the evidence base. Studies enrolling the two populations were described separately in text and tables.Control articles, which were deemed important and relevant by the Panel, were compared with the draft literature search strategy output, and the final strategy was updated as necessary to capture all control articles. In addition to the MEDLINE and EMBASE databases searches, reference lists of included systematic reviews and primary literature were scanned for potentially useful studies.All hits from the OVID literature search were input into reference management software (EndNote X7), where duplicate citations were removed. Abstracts were reviewed by the methodologist to determine if the study addressed the Key Questions and if the study met study design inclusion criteria. For all research questions, randomized controlled trials (RCTs), observational studies, and case-control studies were considered for inclusion in the evidence base. Studies had to enroll at least 30 patients per study arm. Case series, letters, editorials, in vitro studies, studies conducted in animal models, and studies not published in English were excluded from the evidence base.Full-text review was conducted on studies that passed the abstract screening phase. Studies were compared to the predetermined PICO as outlined below. Nine panel members were paired with the methodologist and completed duplicate full-text study selection of 10% of studies undergoing full-text review. The dual-review trained the methodologist, who then completed full-time review of the remaining studies.PopulationAll adult (≥18 years) patients with suspected or confirmed MHStudies enrolling mixed population MH and GH patients were considered for inclusionStudies enrolling solely GH populations were excludedInterventionsHematuria detection by urinalysis (UA) or dipstickComplete hematuria work-up componentsRisk factors for malignancy and/or mortalityImaging modalitiesCystoscopyUrinary marker assaysPatient engagement tools and decision aidsFollow-up schedules in patients with initial negative hematuria evaluationComparatorsAny of the included interventions of interest when defined as the control group and compared to another interventionIt was anticipated that a majority of the identified studies would be single armOutcomesCritical outcomesHematuria detection concordance (UA versus dipstick)Diagnostic yield, incorporating prevalence of malignant and/or benign diagnosesDiagnostic test characteristics, including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and false positive rateRisk stratification for urologic malignancyRisk stratification system performance characteristics, including predictive ability, prognostic number needed to screenRate of adverse events and number needed to harmImpact on outcomesDisease specific survival ratesDiagnostic grade/stage of malignancyPrevalence of risk factors in the study patientsPatient satisfactionQuality of lifeThe 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.Data AbstractionData were extracted from all studies that passed full-text review by the methodologist. All extracted data were audited by an independent auditor.Risk of Bias AssessmentQuality assessment for all retained studies was conducted. Using this method, studies deemed to be of low quality would not be excluded from the systematic review, but would be retained, and their methodological strengths and weaknesses discussed where relevant. To define an overall study quality rating for each included study, risk of bias as determined by validated study-type specific tools, was paired with additional important quality features. To evaluate the risk of bias within the identified studies, the Assessment of Multiple Systematic Reviews (AMSTAR)31 tool was used for systematic reviews, the Cochrane Risk of Bias Tool32 was used for randomized studies, and a Risk of Bias in Non-Randomized Studies - of Intervention (ROBINS-1)33 was used for observational studies. Additional important quality features, such as study design, comparison type, power of statistical analysis, and sources of funding were extracted for each study.The Grading of Recommendations Assessment, Development, and Evaluation (GRADE)34 system was used to determine the aggregate evidence quality for each guideline statement. GRADE defines a body of evidence in relation to how confident guideline developers can be that the estimate of effects as reported by that body of evidence is correct. Evidence is categorized as high, moderate, low, and very low; and assessment is based on the aggregate risk of bias for the evidence base plus limitations introduced as a consequence of inconsistency, indirectness, imprecision, and publication bias across the studies.35 Additionally, certainty of evidence can be downgraded if confounding across the studies has resulted in the potential for the evidence base to overestimate the effect. Upgrading of evidence is possible if the body of evidence indicates a large effect or if confounding would suggest either spurious effects or would reduce the demonstrated effect.Data SynthesisOne of the main objectives for the guideline is to establish a risk model to stratify patients based on their risk for underlying urologic malignancy. To this end, pooling of data was conducted in three areas using RevMan.36 For studies that reported adjusted odds ratios (without raw data) for risk factors associated with malignancy, the odds ratios were pooled using a random-effects inverse-variance method. For studies that reported raw data on patient factors and their association with malignant diagnosis, unadjusted odds ratios were calculated and pooled using a random-effects Mantel-Haenszel method. Finally, prevalence of both malignant and benign diagnoses in relation to the type of hematuria work-up received by patients were calculated and pooled using a random-effects inverse-variance method. For all other areas, pooling was determined to be inappropriate based on heterogeneity of population, reference standard, or reported outcomes.Determination of Evidence StrengthThe AUA employs a three-tiered strength of evidence system to underpin evidence-based guideline statements. 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)The AUA categorizes body of evidence strength as Grade A (well-conducted and highly-generalizable RCTs or exceptionally strong observational studies with consistent findings), Grade B (RCTs with some weaknesses of procedure or generalizability or moderately strong observational studies with consistent findings), or Grade C (RCTs with serious deficiencies of procedure or generalizability or extremely small sample sizes or observational studies that are inconsistent, have small sample sizes, or have other problems that potentially confound interpretation of data). By definition, Grade A evidence is evidence about which the Panel has a high level of certainty, Grade B evidence is evidence about which the Panel has a moderate level of certainty, and Grade C evidence is evidence about which the Panel has a low level of certainty.37Table 1: Strength of Evidence DefinitionsAUA Strength of Evidence CategoryGRADE Certainty RatingDefinitionAHigh Very confident that the true effect lies close to that of the estimate of the effectBModerate Moderately confident in the effect estimate* The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially differentCLow Very Low* Confidence in the effect estimate is limited* The true effect may be substantially different from the estimate of the effect * Very little confidence in the effect estimate* The true effect is likely to be substantially different from the estimate of effectAUA Nomenclature. Linking Statement Type to Evidence StrengthThe AUA nomenclature system explicitly links statement type to body of evidence certainty, level of certainty, magnitude of benefit or risk/burdens, and the Panel's judgment regarding the balance between benefits and risks/burdens (Table 2). Strong Recommendations are directive statements that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be undertaken because net benefit or net harm is substantial. Moderate Recommendations are directive statements that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be undertaken because net benefit or net harm is moderate. Conditional Recommendations are non-directive statements used when the evidence indicates that there is no apparent net benefit or harm, when benefits and harms are finely balanced, or when the balance between benefits and risks/burden is unclear. All three statement types may be supported by any body of evidence strength grade. Body of evidence strength Grade A in support of a Strong or Moderate Recommendation indicates that the statement can be applied to most patients in most circumstances but that better evidence could change confidence. Body of evidence strength Grade C in support of a Strong or Moderate Recommendation indicates that the statement can be applied to most patients in most circumstances but that better evidence is likely to change confidence. Conditional Recommendations also can be supported by any evidence strength. When body of evidence strength is Grade A, the statement indicates that benefits and risks/burdens appear balanced, the best action depends on patient circumstances, and future research is unlikely to change confidence. When body of evidence strength Grade B is used, benefits and risks/burdens appear balanced, the best action also depends on individual patient circumstances and better evidence could change confidence. When body of evidence strength Grade C is used, there is uncertainty regarding the balance between benefits and risks/burdens; therefore, alternative strategies may be equally reasonable, and better evidence is likely to change confidence. Where gaps in the evidence existed, the Panel provides guidance in the form of Clinical Principles or Expert Opinions with consensus achieved using a modified Delphi technique if differences of opinion emerged.38 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 refers to a statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment for which there may or may not be evidence.TABLE 2: AUA Nomenclature Linking Statement Type to Level of Certainty, Magnitude of Benefit or Risk/Burden, and Body of Evidence StrengthEvidence Strength (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)Net benefit (or net harm) is substantialApplies to most patients in most circumstances and future research unlikely to change confidenceBenefits > Risks/Burdens (or vice versa)Net benefit (or net harm) is substantialApplies to most patients in most circumstances but better evidence could change confidenceBenefits > Risks/Burdens (or vice versa)Net benefit (or net harm) appears substantialApplies to most patients in most circumstances but better evidence is likely to change confidenceConditional Recommendation (No apparent net benefit or harm)Benefits = Risks/BurdensBest action depends on individual patient circumstancesFuture research unlikely to change confidenceBenefits = Risks/BurdensBest action depends on individual patient circumstancesBetter evidence is likely to change confidenceBalance between Benefits & Risks/Burdens unclearAlternative strategies may be equally reasonableBetter evidence likely to change confidenceClinical PrincipleA 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 literatureExpert OpinionA statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment for which there is no evidencePeer Review and Document ApprovalAn integral part of the guideline development process at the AUA is external peer review. The AUA conducted a thorough peer review process to ensure that the document was reviewed by experts in the diagnosis, evaluation, and follow-up of MH. In addition to reviewers from the AUA PGC, Science and Quality Council (SQC), and Board of Directors (BOD), the document was reviewed by representatives from SUFU and ACOG as well as external content experts. Additionally, a call for reviewers was placed on the AUA website from December 2-16, 2019 to allow any additional interested parties to request a copy of the document for review. The guideline was also sent to the Urology Care Foundation and representatives of the Bladder Cancer Advocacy Network (BCAN) to open the document further to the patient perspective. The draft guideline document was distributed to 115 peer reviewers. All peer review comments were blinded and sent to the Panel for review. In total, 66 reviewers provided comments, including 51 external reviewers. At the end of the peer review process, a total of 443 comments were received. Following comment discussion, the Panel revised the draft as needed. Once finalized, the guideline was submitted for approval to the AUA PGC, SQC, and BOD as well as the governing body of SUFU for final approval. 1. Clinicians should define microhematuria as ≥3 red blood cells per high-power field on microscopic evaluation of a single, properly collected urine specimen. (Strong Recommendation; Evidence Level: Grade C) Discussion 2. Clinicians should not define microhematuria 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) Discussion 3. In patients with microhematuria, clinicians should engage patients in shared decision-making to decide between repeating urinalysis within six months or proceeding with cystoscopy and renal ultrasound. (Moderate Recommendation; Evidence Level: Grade C) Discussion Initially Low-Risk with Hematuria on Repeat Urinalysis 11. Low-risk patients who initially elected not to undergo cystoscopy or upper tract imaging and who are found to have microhematuria on repeat urine testing should be reclassified as intermediate- or high-risk. In such patients, clinicians should perform cystoscopy and upper tract imaging in accordance with recommendations for these risk strata. (Strong Recommendation; Evidence Level: Grade C) Discussion Intermediate-Risk 12. Clinicians should perform cystoscopy and renal ultrasound in patients with microhematuria categorized as intermediate-risk for malignancy. (Strong Recommendation; Evidence Level: Grade C) Discussion High-Risk 13. Clinicians should perform cystoscopy and axial upper tract imaging in patients with microhematuria categorized as high-risk for malignancy. (Strong Recommendation; Evidence Level: Grade C)Options for Upper Tract Imaging in High-Risk Patients.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)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) Discussion Guideline Statement 14 14. Clinicians should perform white light cystoscopy in patients undergoing evaluation of the bladder for microhematuria. (Moderate Recommendation; Evidence Level: Grade C) Discussion Guideline Statement 15 15. In patients with persistent or recurrent microhematuria previously evaluated with renal ultrasound, clinicians may perform additional imaging of the urinary tract. (Conditional Recommendation; Evidence Level: Grade C) Discussion Guideline Statement 16 16. In patients with microhematuria who have a family history of renal cell carcinoma or a known genetic renal tumor syndrome, clinicians should perform upper tract imaging regardless of risk category. (Expert Opinion) Discussion Urinary Markers 17. Clinicians should not use urine cytology or urine-based tumor markers in the initial evaluation of patients with microhematuria. (Strong Recommendation; Evidence Level: Grade C) 18. Clinicians may obtain urine cytology for patients with persistent microhematuria after a negative workup who have irritative voiding symptoms or risk factors for carcinoma in situ. (Expert Opinion) Discussion 19. In patients with a negative hematuria evaluation, clinicians may obtain a repeat urinalysis within 12 months. (Conditional Recommendation; Evidence Level: Grade C) 20. For patients with a prior negative hematuria evaluation and subsequent negative urinalysis, clinicians may discontinue further evaluation for microhematuria. (Conditional Recommendation; Evidence Level: Grade C) 21. For patients with a prior negative hematuria evaluation who have persistent or recurrent microhematuria at the time of repeat urinalysis, clinicians should engage in shared decision-making regarding need for additional evaluation. (Expert Opinion) 22. For patients with a prior negative hematuria evaluation who develop gross hematuria, significant increase in degree of microhematuria, or new urologic symptoms, clinicians should initiate further evaluation. (Moderate Recommendation; Evidence Level: Grade C) Discussion 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 likelihood of identifying clinically-significant disease, this guideline aims to provide a risk-based framework for testing. Moreover, it is recognized that many patients with hematuria are not currently undergoing evaluation, and thus another goal of risk-based recommendations is to improve utilization of the guideline by patients and clinicians. 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, which represent opportunities for future investigation to meaningfully enhance care. For example, new automated instruments, based either on flow cytometry or digitized microscopy, are increasingly utilized to perform UA. These machines may not correlate directly with traditional urine microscopy, and thus it will be important to determine if the threshold of ≥3RBC/HPF used in the guideline will be an equivalent predictor of risk when these new technologies are used in evaluation. 124One area of particular importance for additional study will be to validate the risk groups that have been outlined herein. Specifically, it remains to be determined whether these current divisions between risk groups accurately reflect differences in cancer risk. Ideally, large prospective cohort studies will form the basis for such validation. Moreover, the current risk stratification focuses primarily on risk factors for urothelial cancer. That is, smoking, obesity, hypertension, and chronic kidney disease represent established risk factors for RCC, of which only smoking is represented in current risk stratification. 25 Whether a different risk stratification is necessary to improve recommendations regarding imaging will also require further study. The potential benefits of reducing exposure to radiation and contrast agents (with attendant risk of renal issues and allergies) and decreasing healthcare cost are substantial; 17,18,94 however, there exists the risk with this approach of missing small renal masses, upper tract urothelial cancers, and small stones. 4,17,52,109,126 The balance of these pros and cons will need to be determined. At the same time, the potential health system benefits of a risk-based approach, as well as implementation/adherence to the guideline recommendations, will need to be documented.Another topic that merits continued investigation is the potential role of urinary biomarkers in the evaluation of patients with MH. Urothelial cancers are in contact with the urine, and this fact has been utilized to evaluate the differential expression of proteins, RNA, DNA, and changes in methylation and cells among patients with malignant and benign conditions. There are multiple markers currently available and in development to help with detection of bladder cancer in hematuria patients. While there is insufficient evidence to recommend use of these markers routinely in the evaluation of patients with MH, the potential exists for these markers to improve risk stratification over the clinical variables put forth herein, and thereby improve an individualized approach to MH evaluation. For example, biomarkers may in the future be used to calculate a pre-test probability of finding urothelial carcinoma, which may in turn guide the intensity of subsequent evaluation. If, for example, a negative test result yields a pre-test probability of

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