National Practice Recommendations for Hematuria: How to Evaluate in the Absence of Strong Evidence?

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Abstract

Hematuria is one of the most common conditions confronting clinical urologists and is present in many genitourinary pathology conditions. Although researchers have studied hematuria symptoms in an effort to determine the best diagnostic pathway, the existing lack of scientific evidence has created variations in clinical practice. The literature does not provide enough evidence to significantly alter the need to assess these patients. Consequently, many patients with microscopic or gross hematuria undergo low-yield workups that include invasive testing and imaging with radiation. In 2007, a national group of Kaiser Permanente (KP) urology chiefs agreed that national practice recommendations were needed to address existing variations in the management and workup of hematuria. Using a KP guideline methodology, the group reached a consensus agreement on the following recommendations: 1) referral to urology is recommended for all people with gross hematuria or high-grade hematuria (>50 red blood cells per high-power field [RBCs/HPF]) on a single urinalysis (UA); 2) referral to urology and urologic evaluation is recommended for men or women with asymptomatic microscopic hematuria or symptomatic hematuria that produces >3 RBCs/HPF on two of three properly performed and collected urinalyses; and 3) voided urinary cytology should be eliminated from asymptomatic hematuria screening protocol. The test is not sensitive enough to obviate further workup if findings are negative, and elimination of this screening test is estimated to save millions of dollars across the US. Hematuria on a UA should be reported as 0 to 3 RBC/HPF, 4 to 10 RBC/HPF, 11 to 25 RBC/HPF, 26 to 50 RBC/HPF, >50 RBC/HPF, or gross hematuria. This approach will also reduce radiation exposure.

Introduction

Background

Quality improvement requires physicians to systematically explore new scientific evidence, integrate this information into practice, and evaluate their performance. In addition, Kaiser Permanente (KP) clinicians need to effectively leverage our integrated delivery system in providing preventive care, improving early detection, and managing complex clinical conditions. Daily, clinicians face situations that require a comprehensive understanding of the complex variables involved in patient care, aggressive decision making, and prioritization of work and of resources.

The Interregional Chiefs of Urology Service (IRCUS) is one of many KP groups that embrace quality-improvement methods and activities. With support from the regional Clinical Practice Guidelines team, the national KP HealthConnect team, and The Permanente Federation, these clinicians have elected to work on several areas of focus as a national quality-improvement agenda. On the basis of an identified need and many years of clinical practice, the group decided to focus on a standardized hematuria evaluation.

Lack of Scientific Evidence

Adult microhematuria is an example of a clinical symptom for which the lack of scientific evidence has created variations in clinical practice. Hematuria is one of the most common conditions confronting clinical urologists and is present in a number of genitourinary pathology conditions. According to KP experts, it is estimated to account for 20% of all urologic visits and up to 13.9% of urologic hospitalizations.

Similar efforts to address hematuria symptoms have been initiated by professional associations and individual clinicians. In 2001, the American Urological Association (AUA) convened the Best Practice Policy

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Table 1. The Kaiser Permanente Interregional Chiefs of Urology Service
Colorado Edward Swartz, MD
Georgia David Starr, MD
Group Health Permanente; Seattle, WA Marc A Lowe, MD
Hawaii Howard Landa, MD Albert Mariani, MD Michelle Aspera, MD
Ohio Nabil Chehade, MD
Northern California Gary Nicolaisen, MD
Northwest Stephen Lieberman, MD
Southern California Ron Loo, MD James Murphy, MD Marguerite Koster Thomas Vandergast, MD Joel Whittaker, MPH
The Permanente Federation Jed Weissberg, MD Violeta Rabrenovich, MHA, CHIE

Panel on Asymptomatic Microscopic Hematuria to formulate policy statements and recommendations for the evaluation of asymptomatic microhematuria in adults.[1] As a result of these efforts, the AUA recommended that an appropriate renal or urologic evaluation be performed for all patients with asymptomatic microscopic hematuria who are at risk for urologic disease or primary renal disease; however, there was no consensus on when to test for microscopic hematuria in the primary care setting, and screening was not addressed in this report.

In addition, the current literature does not provide enough evidence to significantly alter the need to assess these patients. Consequently, many patients undergo low-yield workups that include invasive testing and imaging with radiation.

Methodology

IRCUS is a multidisciplinary group (Table 1) that works to ensure that KP provides safe, effective, and high-quality care; to reduce practice variation; and to create organizational improvement in urologic care. In 2007, they sponsored a review of the literature to address core clinical questions relating to hematuria management and workup (Table 2). Evaluation of recommendations issued by the AUA and input were obtained both from national and regional KP Guideline Development Units.

Although the AUA recommendations represented a consensus statement of urologists from across the US, our clinicians believed the KP guideline methodology (*Common Methodology*),[2] developed by interregional guideline experts, to be more rigorous. (In accordance with KP's *Common Guideline Methodology,* consensus-based recommendations are developed when an important clinical question needs to be answered and the evidence is insufficient to support evidence-based recommendations.) The group believed that the existing situation warranted development of national practice recommendations. In addition, they believed that KP,

Table 2. Core clinical questions and evidence search strategy
Core clinical questions
1. For patients with microhematuria, what threshold of red blood cells per high power field (RBC/HPF) is associated with a sufficient probability of urologic pathology to warrant a referral to urology?
2. How should hematuria be reported on the urinalysis?
3. What is the role of urine cytology and/or bladder tumor markers in the detection of urologic pathology among patients with hematuria?
4. For patients with hematuria, what imaging tests (ie, CT urogram, modified CT urogram, intravenous pyelogram, helical CT, and/or renal ultrasonography) should be employed for the detection of urologic cancers?
5. Is routine urinalysis screening effective for reducing urologic pathology in the asymptomatic population?
To answer the group's clinical questions, a literature search included the following databases and specialty sites:
• Kaiser Permanente Clinical Library
• Clinical Evidence via OVID
• PUBMED
• Hayes
• Blue Cross
• Blue Shield TEC, Health Tech Assessment database
• Southern California Permanente Medical Group Medical Tech Assessment Database
• Turning Research Into Practice database (Bandolier, Agency for Healthcare Research and Quality, New Zealand Guideline Group, Monash, National Institute for Clinical Excellence, Scottish Intercollegiate Guideline Network)
• American Urological Association
• American College of Radiology

CT = computed tomography

as an integrated delivery system, offers a unique opportunity to manage patient care across care settings in a more effective way. Finally, as with many other specialties, KP Urology Departments have a long and outstanding history of research and quality-improvement efforts that can be leveraged.

This initiative was sponsored by the Associate Executive Medical Directors—Quality, Southern California Permanente Medical Group Technology Assessment and Guideline Unit, and The Permanente Federation.

Results

Kaiser Permanente National Practice Resource

After reviewing the literature, the group concluded that evidence relating to the diagnostic follow-up care of hematuria was insufficient for developing "evidence-based" practice recommendations. Despite insufficient evidence, the clinicians agreed that consensus-based national practice recommendations were nonetheless warranted to reduce the variation in hematuria management.

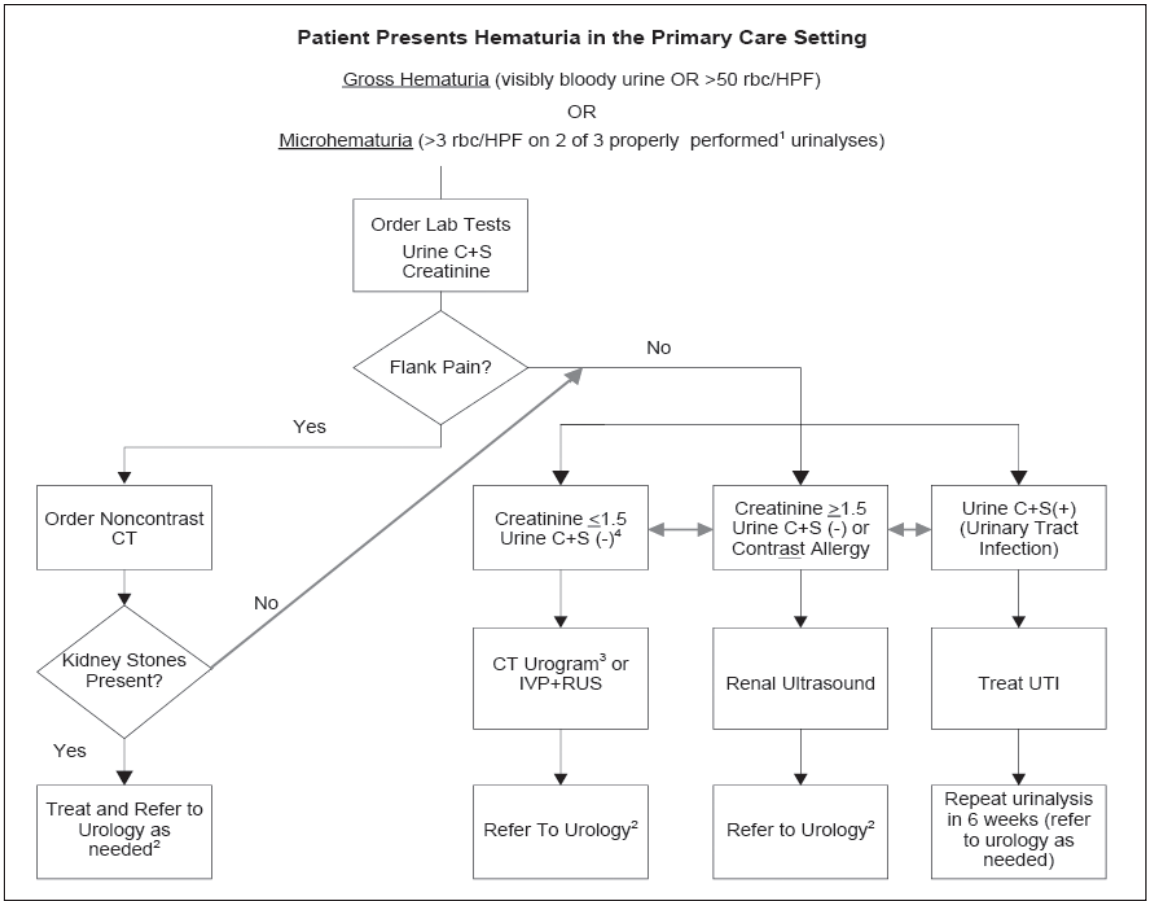

Figure 1. Adult hematuria workup algorithm.

C + S = culture and sensitivity; e-gfr = estimated glomerular filtration rate; HPF = high-power field; rbc = red blood cells; IVP = intravenous pyelogram; KUB = kidneys, ureter, bladder; NSAIDs = nonsteroidal anti-inflammatory drugs; RUS = renal ultrasound; U/A = urinalysis.

[1] Urine specimens should be collected >48 hours after exercise. The U/A should be analyzed fresh if possible, by a standardized methodology to avoid the lysus of formed elements from heat for chemical breakdown.

[2] After urologic evaluation is completed, re-referral for persistent microhematuria is not needed unless there is a change in clinical situation, such as the occurrence of gross hematuria or another sign or symptom suggestive of possible urologic pathology.

[3] CT Urogram is defined as a two-phase study (noncontrast followed by postcontrast delay) and KUB reconstruction. When IVP is ordered, clinicians should take into consideration patient history of chronic illness (diabetes, heart failure, and other comorbidities), as well as a patient being on certain medications (metformin, NSAIDS, and others).

[4] Patients receiving contrast should have a serum e-gfr testing performed prior to the procedure.

The Standardized Hematuria Evaluation Practice Resource[3] describes the evidence and steps for screening adult patients, the making of risk assessments, and summarizes suggested diagnostic follow-up treatment. The goals of this work—in the face of insufficient evidence—are to standardize and optimize a proper workup for patients with hematuria and to minimize radiation exposure from unnecessary testing among those patients unlikely to have serious disease (Figure 1).

An additional goal is to provide clinicians with adequate background and resources to increase their comfort in evaluating patients with asymptomatic microscopic hematuria. This practice resource is not intended to replace a clinician's judgment or to establish a protocol for all patients with this clinical issue.

The clinicians agreed on and supported the following consensus-based recommendations.

Recommendation 1

Referral to urology is recommended for all patients with gross hematuria or high-grade hematuria (>50 RBC/HPF) on a single urinalysis (UA).

Referral to urology and urologic evaluation is recommended for men or women with asymptomatic microscopic hematuria or symptomatic hematuria (unilateral flank pain, lower irritative voiding symptoms, recurrent urinary tract infections despite appropriate use of antibiotics, etc) that produces >3 RBC/HPF on two of three properly performed and collected UAs. (Note: Urine specimens should be collected >48 hours after exercise. The UA should also done when the urine is fresh if possible, by a standardized methodology, to avoid the lysis of formed elements from heat or chemical breakdown.)

Evidence review and rationale: A review of the evidence identified one evidence review by Southern California Permanente Medical Group (SCPMG),[4] which identified 18 studies evaluating hematuria and the risk of urologic disease. Eleven of the 18 studies did not provide the data needed to evaluate urologic cancer rates at specific cutoff points below 8 RBC/HPF. Among the seven remaining studies where cutoff points of >2 to 5 RBC/HPF were used to define microhematuria, urologic or renal cancers were detected 1.3% to 8.3% of the time among patients who were older than 33 years.[5–7] The review also examined laboratory case series studies to determine the upper limit of normal (95th percentile) among "healthy" patients receiving microscopic UA. These studies show a strong trend toward "normal" limits, ranging from 0 to 2 RBC/HPF in men and from 0 to 5 RBC/HPF in women. It is important to note that although the normal limits varied between men and women, the studies did not provide information regarding the actual presence or absence of urologic disease in the populations studied. Ultimately, the SCPMG review concluded that there is insufficient evidence to determine the "optimal" RBC/HPF cutoff point for detecting clinically significant asymptomatic microhematuria. A subsequent literature search was conducted in 2007 to update the 2003 SCPMG review. No additional systematic reviews, meta-analyses, or randomized, controlled trials (RCTs) were identified.

In the absence of high-quality RCTs or systematic reviews, the Interregional Urology Chiefs Group agreed, on a consensus basis, that referral to urology for further diagnostic workup is recommended for asymptomatic patients whose microscopic UA yields >3 RBC/HPF on two of three properly urinalyses, regardless of patient sex. The chiefs also agreed that urine samples should be collected after avoiding strenuous physical exercise for >48 hours to avoid glomerular or urothelial exercise hematuria; urine should also be analyzed fresh if possible, by a standardized methodology, to avoid the lysis of formed elements from heat or chemical breakdown. The chiefs recommend evaluating three urine specimens because of evidence from one study showing that 18% of patients with a life-threatening lesion had negative findings on at least one UA within six months of the diagnosis.[8]

Hematuria evaluation: This evaluation should *not* be performed if the risk of the testing exceeds the risk of the medical condition that is diagnosed. Thus, if the life-threatening risk of a hematuria evaluation (instrumentation urosepsis, contrast anaphylaxis, radiation risk, contrast nephropathy) is greater than the yield of the evaluation for a defined population, then the evaluation should not be performed.

National recommendations
1. Referral to urology is recommended for all patients with gross hematuria or high-grade hematuria (>50 RBC/HPF) on a single urinalysis (UA).
2. Hematuria on a UA should be reported out as 0 to 3 RBC/HPF, 4 to 10 RBC/HPF, 11 to 25 RBC/HPF, 26 to 50 RBC/HPF, >50 RBC/HPF, or gross hematuria.
3. There was no consensus on the role of urine cytology and/or bladder tumor markers in the evaluation of patients with hematuria.
4. A modified computed tomography (CT) urogram or IVP with concurrent renal ultrasound is recommended for patients with significant hematuria.
5. There is insufficient evidence to recommend routine UA to screen for asymptomatic hematuria in the absence of clinical indicators.

Follow-up care: Hematuria is likely to persist in the majority of patients who are monitored. The evidence for the risk of cancer developing within two to five years in patients with hematuria who have been evaluated is scanty, but it is in the range of 0% to 3%.

A retrospective study (which did not distinguish between gross hematuria and microhematuria) of 823 patients who did not have a malignancy and whose medical charts were available found that the average follow-up monitoring was 14.7 years. Using intravenous pyelogram (IVP) as the lone imaging modality, transitional cell carcinoma (TCC) was found in 7 of 740 (0.95%) patients at an average of 14.3 years after diagnosis (range, 5.3–23.9 years). Renal cell carcinoma (RCC) developed in 5 of 740 (0.68%) of patients at an average of 15.7 years after diagnosis (range, 2.5–23.2 years). Overall, 1.5% of the evaluated patients developed TCC or RCC. Gross hematuria or a smoking history was present in 77%. Although the data on which to base recommendations for hematuria follow-up care is limited, consideration may be given to reevaluating any patient with gross hematuria or persistent microhematuria and a smoking history at two to five years.[9]

Recommendation 2

Hematuria on a UA should be reported out as 0 to 3 RBC/HPF, 4 to 10 RBC/HPF, 11 to 25 RBC/HPF, 26 to 50 RBC/HPF, >50 RBC/HPF, or gross hematuria.

Evidence review and rationale: Literature sources that specifically compared the effect of reporting UA results according to varied cutoff points were not identified. One large prospective study[10] of 1000 consecutive patients with asymptomatic hematuria found that the incidence of urologic pathology was greater for people with high-grade hematuria vs low-grade microhematuria; no difference between low (4–10 RBC/HPF) and intermediate grades of hematuria was found.

To gain a better understanding of how hematuria correlates with the presence or absence of urologic disease, IRCUS agreed to standardize the reporting of UA results according to the following cutoffs: 0 to 3 RBC/HPF, 4 to 10 RBC/HPF, 11 to 25 RBC/HPF, 26 to 50 RBC/HPF, >50 RBC/HPF, or gross hematuria. Examination of UA data that are reported in a standard fashion may provide insight to clinicians on how to best to stratify hematuria workups on the basis of the yield of urologic disease in each category.

Recommendation 3

There was no consensus on the role of urine cytology and/or bladder tumor markers in the evaluation of patients with hematuria.

Evidence review and rationale: A literature search was conducted to identify studies evaluating the effectiveness of urine cytology and bladder tumor markers for the detection of urologic cancer among patients with hematuria. Several systematic reviews were identified.

One systematic review[11–13] identified 15 studies evaluating urine cytology and NMP22 BladderChek Test (Matritech, Inc, Newton, MA, USA) as tests for detecting urinary tract malignancy. Pooled data from these studies showed that sensitivity for the urine cytology test ranged from 3% to 100%, whereas specificity ranged from 62% to 100%. The review also found inconsistent data from five heterogeneous studies regarding the sensitivity (58%–91%) and specificity (60%–84%) of the NMP22 BladderChek Test for the detection of urologic disease. The authors caution against drawing definitive conclusions, given that the studies included were heterogeneous, methodologically flawed, and subject to potential bias. Ultimately, the study authors agreed with the AUA statement that the available data are insufficient to recommend routine use of voided urinary markers in patients with microscopic hematuria.

These studies show a strong trend toward "normal" limits ranging from 0 to 2 RBC/HPF in males and from 0 to 5 RBC/HPF in females.

In 2005, the KP Southern California Technology Assessment and Guidelines Team reviewed the literature for the use of the NMP22 BladderChek Test to detect primary or recurrent TCC of the urinary tract.[4] No RCTs were identified. They did, however, find 22 uncontrolled studies evaluating the accuracy of the test. The NMP22 BladderChek Test had a sensitivity ranging from 30% to 100%, specificity of 60% to 90%, and positive predictive value (PPV) of 34% to 76%. The team concluded that the sensitivity of the NMP22 BladderChek Test suggests that it may help to detect low-grade primary carcinomas, but the specificity and PPV of the NMP22 BladderChek Test also suggest that the test would result in an increased number of unnecessary cystoscopic procedures. However, most results highlight increased specificity and sensitivity.[14]

Another systematic review[15] pooled data from 42 studies (n = 5706) and compared the diagnostic accuracy of urine cytology vs other tests (BTA [Polymedco, Inc, Cortlandt Manor, NY, USA], BTA stat [Polymedco, Inc], BTA TRAK [Polymedco, Inc], telomerase, or NMP22 BladderChek Test) against the reference standard of cystoscopy and/or histopathology. They found that cytology had a pooled specificity of 94%, which was

significantly higher than for the other tests evaluated in the study. The authors also stated that none of the tests evaluated in the studies reached levels of sensitivity that are acceptable in lieu of cystoscopy for clinical practice. In addition, 22 of 42 studies used a case-control design, which provides greater potential for bias.

A cross-sectional study[14] (n = 668) compared the NMP22 BladderChek Test with urine cytology and with reference standard (cystoscopy and pathology findings) for detection of recurrent bladder cancer. They found that the NMP22 BladderChek Test had a sensitivity of approximately 49% and specificity ranging from 83% to 91%. The degree to which these findings can be applied to primary prevention in populations with bladder cancer is unclear.

The purpose of a bladder tumor marker is to increase the clinician's index of suspicion for TCC of the urinary tract. Questions have been raised about the appropriateness of urine cytology as part of a hematuria study. This was studied from the KP Hawaii Hematuria 1000-patient hematuria database. We found a sensitivity of 55% and a specificity of 99.3%. Unique information that led to a diagnosis of urinary tract TCC was found in four patients. The cost to diagnose a cancer by this test and no other (unique information) in the hematuria evaluation was $8367 vs $5616 for IVP, $3235 for cystoscopy, and $3291 for creatinine. The cost of the test to diagnose a life-threatening lesion (in support of other tests whose findings might also have made the diagnosis) was $1521 for cytology, $1695 for IVP, $3044 for cystoscopy, and $3291 for creatinine. This study supported the use of urine cytology in that it diagnosed TCC not diagnosed by other tests, and the cost of the test was comparable to other well-established costs.[15,16]

Table 3. Summary of radiation exposure by imaging test

Imaging (CPT code)	Millisieverts (mSv)
Intravenous urogram or intravenous pyelogram (76497)	1.6
Renal and bladder ultrasound (76775)	0
KUB (radiograph plain film) (74000)	0.07
CT without contrast, abdomen and pelvis (74150, 72192)	10
CT with contrast, abdomen and pelvis (74160, 72193)	14
CT with and without contrast, abdomen and pelvis (74170, 72194)	24

CT = computed tomography; CPT = current procedural terminology; KUB = kidneys, ureter, bladder

The KP Hawaii Region did an analysis of the current well-established bladder tumor markers. A frank malignancy reading for urine cytology (cost, $60.25) had a 41% sensitivity but a 97.2% specificity in 17 studies encompassing 4,685 patients. In four BTA (cost, $98.00) studies encompassing 455 patients, there was a 78% sensitivity and a 80% specificity. In five NMP22 BladderChek Test (cost, $15.50) studies encompassing 846 patients, there was a 80% sensitivity and a 77% specificity. In a study of the FISH test encompassing 456 patients, Sarosdy et al[17] found a sensitivity of 68% and a specificity of 80%.

For a clinical test to be useful, it must change what the clinician does. A specificity of 97.2% (2.8% false positive rate) for cytology would likely cause a urologist to have a lower threshold for ordering a biopsy of indeterminate bladder or prostatic urethral lesions and might prompt ureteroscopy.

Recommendation 4

A modified computed tomography (CT) urogram or IVP with concurrent renal ultrasound is recommended for patients with significant hematuria (as already defined).

As long as the renal ultrasound is done concurrently with IVP, there is no need for renal tomography. This approach will reduce radiation exposure (Table 3). One caveat: the radiation exposure associated with the modified CT urogram has been reported to be 12 to 24 times higher than with IVP. The modified CT urogram should be conducted with a protocol capable of visualizing any collecting-system lesions using the lowest radiation dose possible. Patients receiving contrast should have a serum estimated glomerular filtration rate (eGFR) test performed before the procedure. When IVP is ordered, clinicians should take into consideration the patient's history of chronic illness (diabetes, heart failure, and other comorbidities), as well as whether the patient takes certain medications (metformin, nonsteroidal anti-inflammatory drugs, and others).

Evidence review and rationale: A review of the literature was conducted to identify studies that evaluate the effectiveness of CT urogram and/or IVP for detecting urologic disease. A complementary search of the literature was also conducted to identify studies that compare the relative differences in radiation exposure that may exist between the two imaging modalities. One systematic review and two cohort studies (reports about which were published subsequently to the systematic review) were identified. A brief summary of this evidence is provided below.

One systematic review by Rogers et al[11] identified three studies evaluating the use of the CT urogram to

identify any abnormality that may cause hematuria. According to that review:

One study combined CT with IVP as the reference standard and reported a sensitivity of 100% and a specificity of 97%.

A second study used histopathology as the reference standard and reported a sensitivity of 92% and a specificity of 94%.

A third study evaluated the CT as a method to detect filling defects or strictures in the urinary tract and reported a sensitivity of 82% and a specificity of 97%.

The authors concluded that there is some evidence to support the use of CT to determine the cause of hematuria. However, they also reported that the evidence base is limited evidence to three diagnostic accuracy studies, one of which was poorly reported and not designed for the purpose of detecting significant urologic pathology.

Turney et al[18] conducted a cohort study (n = 200) comparing CT urogram findings with those for cystoscopy and pathology to determine the diagnostic accuracy of CT urography (CTU) for detection of bladder cancer. They reported a sensitivity of 93%, a specificity of 98%, a PPV of 98%, and a negative predictive value of 97%. In this publication's introduction, the study authors claimed that CTU is becoming recognized as the diagnostic tool of choice for many urologic conditions and represents the "gold standard" for examining upper urinary tracts. This explicit bias suggests caution when interpreting the study results.

Another nonrandomized cohort study (n = 512), conducted by Albani et al,[19] examined the diagnostic accuracy of CTU vs IVP in adults with hematuria.

For the identification of upper tract lesions, CTU had a sensitivity of 94% and a PPV of 89%, whereas IVP had a sensitivity of 50% and a PPV of 40%. Owing to the lack of a gold-standard examination for upper tract evaluation, specificity could not be calculated.

For the identification of lower urinary tract lesions, CTU had a sensitivity of 40% and specificity of 93%, whereas IVP had a sensitivity of 37% and a specificity of 97%. Both imaging modalities failed to detect more than 60% of bladder lesions smaller than 2 cm.

The overall detection rates were 25.5% for CTU and 19.4% for IVP.

Methodologic issues: The authors identified two cohorts and included in the analysis only those study subjects who could make the required follow-up visits. The effect of this design in reaching definitive conclusions is uncertain.

The authors acknowledged that CTU and IVP were not performed in the same patients and that the increased radiation exposure provided by two tests could not be justified.

The two cohorts were unmatched, but analysis indicated that there were no statistically significant differences in patient characteristics.

Patients were not stratified by risk of disease, and the authors believe that this contributed to the relatively low overall detection rate.

… the radiation exposure associated with the modified CT urogram has been reported to be 12 to 24 times higher than with IVP.

Rogers et al[11] also identified seven nonrandomized studies evaluating IVP (also known as intravenous urography, or IVU) as an index test for the detection of urologic cancer among people with hematuria. They reported the following results:

"Seven studies evaluated IVU as an index test … . [Four] studies evaluated IVU against final diagnosis, but for different target conditions: upper urinary tract tumors (sensitivity 89%, specificity 95%), lower tract tumors (sensitivity 56%, specificity 98%), any upper tract pathology (sensitivity 67%, specificity 91%), any renal abnormality (sensitivity 90%, specificity 98%) or any filling defect or structure in the urinary tract (sensitivity 68%, specificity 98%). Across the IVU studies, specificity values (range 91%-100%) appeared to be more consistent than sensitivity values (range 55%-90%), although it is difficult to estimate the overall value of IVU as a test owing to the clinical and statistical heterogeneity between studies."[11]

Radiation exposure: Several studies evaluating the radiation exposure levels from CT urography and IVP among adults with hematuria and flank pain (suspected renal colic) were identified (Kim et al,[20] Homer et al,[21] Thomson et al,[22] and others[23–30]). The data suggest that radiation may be higher for noncontrast CT (range, 1.4–10.0 millisieverts [mSv]) and noncontrast helical CT (range, 2.806–5.004 mSv) than for IVP (range, 1.48–4.46 mSv). With CT, exposures were consistently higher for women than for men. (Table 3 provides a summary of radiation exposures by imaging test.)

Studies that explicitly evaluated the health impact of different levels of radiation exposure from the CT urogram versus IVP among patients with hematuria were not identified (summary of average doses from American College of Radiology and Radiological Society of North America).[31]

There is no clear consensus that CTU is superior to IVP for a hematuria evaluation; however, there is emerging evidence that this may be the case. Although radiation exposures are higher for CTU than for IVP, newer

CT protocols and technologic advances are reducing radiation dose while increasing the anatomic detail of images in addition to identifying pathology in other organ systems that would not be noted on IVP. The interregional urology chiefs agreed, on a consensus basis, that CTU can be used to evaluate patients with significant hematuria according to a protocol capable of visualizing collecting-system lesions using the lowest radiation dose possible. Patients receiving contrast CT should have a serum creatinine test performed before the procedure. Alternatively, a concurrent IVP and renal ultrasound would also provide acceptable imaging of significant renal masses and collecting-system lesions with less radiation but less standardization (more operator-dependent) (Mariani AJ, personal communication, 2007 May 19).[a,32]

The interregional urology chiefs also took the following into consideration:

A CT of the abdomen and pelvis with and without contrast exposes the patient to about 20 times the radiation dose of an IVP. (Note: renal ultrasound has no associated radiation exposure.)

It has been estimated that … a significant number of future cancers will be caused by iatrogenic unnecessary imaging.[39]

An IVP will detect only 10% of 1-cm lesions and 52% of 2- to 3-cm lesions. Fortunately <4% of renal masses that are <3 cm in size will behave malignantly, even though ≤90% are RCCs. This may be the reason why IVP served urology as well as it did for so long as the standard imaging for a hematuria evaluation.

CT is superior to renal ultrasound for the detection of small renal masses, but renal ultrasound detected 100% of lesions >2.5 cm and the majority of lesions >1.5 cm in one well-designed study.[33] Again, most small lesions do not behave malignantly.

Fine-cut CT images can approach the collecting-system detail of an IVP and provide additional functional information. On IVP, tumors present as negative filling defects (as do clots and radiolucent stones). On CT, a tumor will usually opacify after contrast, and a radiolucent stone is easily distinguished from a blood clot. Renal ultrasound can also easily distinguish a clot from a radiolucent stone.

The cost of a CT urogram (~$282) would be approximately the same as the cost of an IVP plus a renal ultrasound (~$228 + ~$87 = ~$315), according to data from KP Hawaii Region 2007 (Mariani AJ, personal communication, 2007 May 19).[a]

CT scans account for 70% of all medical x-ray exposure even though they represent 20% of diagnostic imaging studies. It is estimated that a single dose of 10 mSv (<1 CT scan) has a lifetime cancer risk of 1/1000 and a death rate of 1/2000.

Recommendation 5

There is insufficient evidence to recommend routine UA to screen for asymptomatic hematuria in the absence of clinical indicators.

Evidence review and rationale: Hematuria screening for cancer in the asymptomatic population has not been clinically established. RCTs and high-quality epidemiologic studies supporting the use of routine UA screening among asymptomatic adults are lacking. Furthermore, in a 2006 report, the US Preventive Services Task Force recommended against routine bladder screening among asymptomatic persons.[34,35]

Routine screening for bladder cancer with urine dipstick, microscopic UA, or urine cytology is not recommended in asymptomatic persons. All patients who smoke tobacco should be routinely counseled to quit smoking.

In patients without significant urologic symptoms, microscopic hematuria is occasionally detected on routine UA. At present, routine screening of adults for microscopic hematuria with UA is not recommended because of the intermittent occurrence of this finding and the low incidence of significant associated urologic disease.

Discussion

Implementation: Collaboration and Tools

Implementation of a nationwide adult asymptomatic microhematuria screening and management program is a result of the collaborative efforts of clinicians representing multiple areas of medical care: urology, primary care, radiology, and laboratory. Many other departments—including guideline development, regional continuing medical education, regional laboratory, and national and regional KP HealthConnect implementation teams—were consulted in both the planning and implementation.

Standardized implementation tools were developed:

- A hematuria-management standardized presentation that is used during chiefs' Departments of Urology, Primary Care, Radiology, and other meetings to provide an overview of the recommendations and to educate clinicians and staff
- Hematuria practice resource pocket cards to assist clinicians during patient care
- Continuing medical education materials
- KP HealthConnect hematuria diagnosis SmartSet list
- Standardization of reporting of hematuria by laboratory departments
- Implementation and adherence to national practice

recommendations will be evaluated in the future, and the lessons that this provides will be used to modify practice recommendations, provide feedback to clinicians, and support ongoing performance improvement efforts.

Eliminate One-Quarter of Future Workups

In an effort to minimize variations in reporting and to collect definitive evidence to completely eliminate the need to assess the lowest-risk patients with hematuria in the near future, a KP HealthConnect SmartSet list data collection tool has been developed to allow concurrent electronic data analysis of hematuria workup outcomes. It will be used nationwide by KP urologists to document their workup findings; we estimate that within one year, enough data will be captured to eliminate the need to assess 25% or more of the patients currently being evaluated. A valuable outcome goal is to demonstrate the power and capability of KP HealthConnect in population-based clinical research. To reinforce continuity of care, the KP HealthConnect tool will generate patient-care instructions for further follow-up treatment.

High Radiation Risk

It has been estimated that acute radiation exposures as low as 10 mSv pose significant cancer risk, so much so that a significant number of future cancers will be caused by iatrogenic unnecessary imaging.[36]

Conclusions

More than 62 million CT scans are performed annually in the US, a large number of which are due to screening and assessment of asymptomatic patients with microhematuria. Clearly, major efforts to curtail unnecessary radiation exposure are sorely needed. As advocated by the KP IRCUS, an immediate reduction in radiation exposure by collectively switching to a modified CT urogram and a commitment to support the collection of evidence through KP HealthConnect to completely eliminate unnecessary workup underscore our dedication to the KP promise.[37]

The KP National Hematuria Guideline has been a tremendous inspiration to all participants. The work illustrates the potential that KP possesses in effecting safer and more reliable evidence-based care as well as its obligation as a health care leader in striving to answer previously unanswerable questions and to change the way that medicine is practiced for our patients and worldwide. ❖

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