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Use of Automated Urine Microscopy Analysis in Clinical Diagnosis of Urinary Tract Infection: Defining an Optimal Diagnostic Score in an Academic Medical Center Population

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ABSTRACT A retrospective case record study was conducted that established a scoring tool based on clinical and iQ200 parameters, able to predict or rule out the clinical diagnosis of UTI in the majority of adult patients in an academic hospital. Automated standardized quantitative urine analysis, such as iQ200 analysis, is on the rise because of its high accuracy and efficiency compared to those of traditional urine analysis. Previous research on automated urinalysis focused mainly on predicting culture results but not on the clinical diagnosis of urinary tract infection (UTI). A retrospective analysis was conducted of consecutive urine samples sent in for culture because of suspected UTI. UTI was defined by expert opinion, based on reported symptoms, conventional urine sediment analysis, and urine cultures. Parameters of iQ200 analysis and clinical symptoms and signs were compared between cases and controls. Optimal cutoff values were determined for iQ200 parameters, and multivariate logistic regression analysis was used to identify the set of variables that best predicts the clinical diagnosis of UTI for development of a scoring tool. A total of 382 patients were included. Optimal cutoff values of iQ200 analysis were 74 white blood cells (WBC)/μl, 6,250 "all small particles" (ASP)/μl, and a bacterial score of 2 on an ordinal scale of 0 to 5. The scoring tool attributed 1 point for frequent micturition or increased urge, 2 points for dysuria, 1 point for a bacterial score of $\geq$2, 2 points for WBC/μl of $\geq$50, and an additional point for WBC/μl of $\geq$150. This score had a sensitivity of 86% and a specificity of 92% when using a threshold of $<$4 points. The combination of iQ200 analysis and a simple survey could predict or rule out UTIs in a majority of patients in an academic medical center.

KEYWORDS automated urine analysis, expert opinion, multivariate logistic regression, retrospective case record study, urinary tract infection

Urinary tract infection (UTI) is among the most frequently occurring infections and is the second most frequent clinical indication for empirical antibiotic treatment in primary and secondary care (1, 2). The gold standard for diagnosis is detection of a pathogen in the urine in the presence of clinical symptoms. Because the result of a traditional urine culture is not readily available, presumptive diagnosis of UTI is based on diagnostic tests such as dipstick or urinary sediment analysis (3).

In some populations, the diagnosis of UTI is not as straightforward and should be distinguished from asymptomatic bacteriuria or inflammatory conditions, such as interstitial cystitis (2). This is especially the case in a tertiary hospital, where relatively many patients have complex urinary tract problems or kidney transplants or are treated with immunosuppressive medication.

In the past few years, automated, standardized, quantitative urine analysis has been

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introduced in clinical practice and has shown high efficiency and accuracy compared to traditional sediment analysis (4). One of these systems is the IRIS Diagnostics iQ200 Elite (iQ200), currently marketed by Beckman Coulter Inc., which analyzes urinary samples using flow imaging technology and auto particle recognition. The iQ200 classifies and quantifies particles, including bacteria, yeasts, white blood cells (WBC), and squamous epithelial cells, and correlates well with traditional urinary sediment examination with manual cell counts (5). Our group and other research groups have so far focused mainly on the use of automated urinalysis as a screening tool to predict negative urine cultures and thus to reduce the culture workload in the laboratory (6–9).

For this purpose, a positive culture was used as the "laboratory" gold standard of UTI without taking clinical symptoms into account, therefore predicting the presence of bacteriuria, but not of symptomatic UTI (10, 11). This distinction is important because it is currently thought that there is no role for treatment of patients with asymptomatic bacteriuria other than for pregnant women and patients undergoing urologic procedures (12).

The test results of automated urine analysis are, however, subject to different clinical interpretations. This is partly because of unfamiliarity with quantitative results, instead of the semiquantitative test results that clinicians used before, and the lack of optimal cutoff values for the clinical diagnosis of UTI.

The goal of the current study was to establish cutoff values for parameters of iQ200 analysis, to be used in diagnosing symptomatic UTI in a tertiary hospital population. Subsequently, we aimed to develop a scoring model to predict the clinical diagnosis of urinary tract infection, based on both symptoms and these cutoff values.

MATERIALS AND METHODS

Setting and patient population. A retrospective study was performed at Leiden University Medical Center, which is an academic tertiary hospital in Leiden, the Netherlands. It has approximately 400 hospital beds and focuses on transplant medicine (solid organ transplants and stem cell transplants), resulting in a large proportion of immunocompromised patients. Samples from inpatients and outpatients of the hospital constitute the majority of samples sent to the clinical chemistry and microbiological laboratories (6). The study was approved by the Ethics Committee.

Urine samples. Upon receipt at the Department of Medical Microbiology, all urine samples submitted for bacterial culture during a 12-week period from 25 February to 17 May 2013 were divided into two portions under sterile conditions if they had sufficient volume (at least 2 ml for culture and Gram stain and 3 ml for the iQ200 screening). One portion was analyzed by the iQ200 system in the clinical chemistry laboratory within 2 h after receipt from the microbiological laboratory. Results were not reported to the clinician because the iQ200 was still under validation. The other portion was analyzed by the microbiological laboratory. For more detailed information regarding procedures we refer to Russcher et al. (6).

For the purpose of this study, urine samples from children, pregnant women, and patients with an indwelling urinary catheter for more than 24 h, a nephrostomy, or a urostomy were excluded because the diagnosis of UTI is defined differently within these groups. Urine samples from patients without clinical data or clinical suspicion for UTI (e.g., preoperative routine urine controls) were excluded as well. Only the first sample of each patient was included.

Microbiological analysis. Urine samples were analyzed using local standard microbiological methods for Gram stain and culture (6). The bacterial load was assessed and scored from $<$100 CFU/ml (no growth) to $\geq 10^5$ CFU/ml. The relevance of the urine sample was assessed according to our standard protocol for urine cultures, taking a quality score (the Q score) based on white blood cell (WBC) and squamous epithelial cell (SEC) counts in the Gram stain into account, as previously described (6). In urine samples with a high Q score ($\geq$1, corresponding with a high WBC and low SEC count), all growth was identified to the species level. Colonies in samples with a Q score of zero were only identified to the species level if a monoculture with a bacterial load of $\geq 10^5$ CFU/ml was present. Samples with Q scores of $\leq$0 were generally classified as mixed flora.

A positive culture was defined as having $\geq 10^3$ CFU/ml of not more than two different usual uropathogens or as having $\geq 10^5$ CFU/ml of a single unusual urinary pathogen. Common and uncommon pathogens and nonpathogens that were cultured are listed in Table 1.

Automated urine microscopic analysis. All samples derived from the Department of Medical Microbiology were tested by the iQ200 Elite analyzer (Iris Diagnostics, Chatsworth, CA), which is an automated urine microscopy analyzer that uses flow cytometry and digital photography. Automatic particle recognition software categorizes urine particles into 12 groups, including leukocytes, erythrocytes, bacteria, and "all small particles" (ASP). The ASP group consists of unclassified particles of <3 μm, such as cocci, which are not recognized well by the iQ200, some other bacteria, crystals, and other formed elements (4, 6, 10). All elements other than bacteria were quantitatively reported (per microliter), and bacteria were reported semiquantitatively (on a scale from 0 to 5). After automatic classification, a

TABLE 1 Pathogens isolated from urine cultures of 381 patients with and without UTIs

Pathogen group or pathogen	No. with UTI (n = 59)	No. without UTI (n = 322)
Usual urinary pathogens		
Escherichia coli	31	26
Klebsiella spp.	4	6
Enterococcus spp.	2	5
Pseudomonas aeruginosa	2	4
Aerococcus urinae	2	2
Proteus mirabilis	0	3
Unusual urinary pathogens		
Other *Enterobacteriaceae*	2	4
Beta-hemolytic streptococci	2	3
Staphylococcus aureus	2	0
Haemophilus parainfluenzae	1	0
Candida spp.	0	2
Nonurinary pathogens		
Staphylococcus haemolyticus	2	0
Other staphylococci	0	3
Gardnerella vaginalis	0	1
Remaining groups		
Mixed flora	6	186
No growth	3	77

trained technician reviewed all images. Misplaced or unclassified images were placed in the correct categories, and bacterial counts were adjusted in cases when cocci were present.

Conventional urine analysis. In a vast majority of patients from whom a urine sample was sent in for culture, a different sample was sent to the clinical chemistry for dipstick analysis. If the dipstick tested positive for leukocytes or erythrocytes, sediment analysis was performed using local standard protocol. The positively tested urine was centrifuged for 5 min at 2,000 rpm. Subsequently, urine was poured off until 0.5 ml supernatant remained. This was shaken, and one drop was analyzed on a slide under a microscope. Observed elements were quantified as the number per high power field and reported qualitatively in the medical record.

Clinical assessment. Clinical data and characteristics of included patients were obtained from the electronic medical records. Patients were retrospectively classified as either cases having a UTI or controls who did not have a UTI by two infectious diseases specialists using medical chart review. The expert reviewers used data on symptoms, signs, antibiotic (pre)treatment, and outcome, as documented in the electronic patient files. They used data on culture results and conventional urine analysis, which consisted of dipstick and sediment analysis. They also considered whether another diagnosis was more likely or could be the cause of complaints and/or fever. They were blinded to the iQ200 results, which were not reported in the medical records. If they differed in opinion, they reached consensus by means of discussion.

Statistical analysis. Baseline characteristics were compared with χ^2 tests for dichotomous variables and an unpaired t test for age. Symptoms and signs were compared with χ^2 tests. Parameters from the iQ200 analysis were compared using unpaired t tests, and receiver operating characteristic (ROC) curves were plotted. Cutoff values were determined based on the optimal tradeoff between sensitivity and specificity. These cutoffs correspond with coordinates on the ROC curves that are closest to 0.1 (the upper left corner) (13). Distances for all coordinates on the ROC curves to 0.1 were calculated by the formula $d = (1 - \text{sensitivity})^2 + (1 - \text{specificity})^2$.

A logistic regression model was established, using symptoms and parameters from the iQ200. In the case of information on a specific sign or symptom not being documented in the electronic patient file, that patient was excluded for this specific analysis. Backward selection excluded parameters based on likelihood ratios without significantly changing the fit of the model. The final model retained all variables significantly associated with the presence of UTI at a $P < 0.05$ level. A numerical scoring tool was developed using the model by simplifying β-coefficients of all independent predictor variables. We calculated the area under the receiver operating characteristic curve (AUC) with 95% confidence interval (CI) to assess the scoring tool's discriminatory power to predict or rule out UTI. ROC curves were also plotted for the separate iQ200 and clinical variables derived from the model.

Cutoff values were considered based on sensitivity, specificity, and positive and negative predictive values (PPV and NPV, respectively). All analyses were performed using SPSS 21.0 (SPSS Inc., Chicago, IL).

RESULTS

Population characteristics. During the study period, 1,442 urine samples from 1,084 unique patients were submitted. The following samples were excluded: 641

TABLE 2 Baseline characteristics of 381 patients with and without UTIs

Characteristic	With UTI ($n = 59$)	Without UTI ($n = 322$)	*P* value
Age in yrs (mean [SD])[a]	61.1 (17.7)	55.8 (18.2)	0.04
Male (no. [%])	33 (56)	152 (47)	0.22
Hospitalized (no. [%])	23 (39)	151 (47)	0.26
Indwelling catheter removed <7 days prior to culture (no. [%])	4 (7)	27 (8)	0.70
Immunosuppressive medication <3 mo prior to culture (no. [%])	16 (28)	113 (35)	0.26
Neutropenia (no. [%])	0 (0)	15 (5)	0.09
Antibiotics <48 h prior to culture (no. [%])	16 (29)	98 (31)	0.74
Renal transplant (no. [%])	6 (10)	39 (12)	0.70
Pancreatic transplant (no. [%])	0 (0)	8 (3)	0.23
Hematopoietic stem cell transplant (no. [%])	2 (3)	14 (4)	0.75
Fever (no. [%])[b]	14 (25)	100 (31)	0.31

[a]$P < 0.05$.
[b]Fever was defined as a temperature higher than 38.1 °C.

samples from patients not suspected of having a UTI, 152 samples from patients with an indwelling urinary catheter for >24 h, 76 samples from pregnant patients, 62 samples of children below the age of 18, 33 samples from a nephrostomy or urostomy drain, 91 subsequent samples of patients already included, and 13 samples lacking data in the corresponding electronic patient files. After exclusion, 381 unique patients and urine samples remained. A total of 29 of 381 urine samples submitted were obtained by one-time catheterization and the rest by midstream clean catch. The prevalence of UTI among the 381 patients according to the expert review was 59. The expert reviewers initially differed in opinion in 30 of 381 patients (7.8%), but reached consensus for all patients by means of discussion. Table 2 shows demographic and clinical characteristics of the two patient groups (with and without urinary tract infections). Patients who had a UTI were significantly older ($P = 0.041$) than those who did not. None of the other characteristics differed significantly between both groups.

Culture results. Table 1 shows culture results of cases and controls. *Escherichia coli* was the most prevalent pathogen ($n = 57$). A total of 192 cultures displayed mixed flora, and 80 cultures showed no growth. Patients who were assessed as cases with a UTI while their culture showed no growth were all treated with antibiotics in the 48 h prior to culture ($n = 3$).

Signs and symptoms. The prevalences of signs and symptoms among both patient groups are listed in Table 3. Dysuria, recognition of symptoms from a previous UTI, frequent micturition, and cloudy urine were most strongly associated with UTI. Subgroup analysis was conducted for aggravated lower urinary tract symptoms (LUTS) in

TABLE 3 Signs and symptoms of 381 patients with and without UTIs

Sign/symptom[a]	With UTI (no. [%])	Without UTI (no. [%])	Odds ratio (CI)	*P* value[c]
Frequent micturition/increased urgency[b]	27 (54)	56 (19)	5.0 (2.7–9.3)	0.00
Dysuria	36 (69)	55 (18)	10.1 (5.2–19.5)	0.00
Aggravated LUTS	5 (10)	23 (8)	1.3 (0.5–3.6)	0.59
Suprapubic pain[b]	7 (13)	15 (5)	2.9 (1.1–7.4)	0.02
Recognition of symptoms from a previous UTI[b]	14 (27)	15 (5)	7.0 (3.1–15.6)	0.00
Increased incontinence	7 (13)	21 (7)	2.1 (0.8–5.3)	0.10
Macroscopic hematuria	3 (6)	16 (5)	1.1 (0.3–4.0)	0.87
Cloudy urine[b]	12 (24)	18 (6)	4.9 (2.2–11.0)	0.00
Foul smelling urine[b]	10 (20)	21 (7)	3.3 (1.4–7.5)	0.00
Increased cognitive impairment	6 (10)	30 (9)	1.1 (0.4–2.8)	0.82
Suprapubic tenderness	5 (18)	16 (9)	2.2 (0.7–6.5)	0.16
Costovertebral angle tenderness	3 (19)	9 (16)	1.3 (0.3–5.3)	0.76
All signs/symptoms	59 (15)	322 (85)		

[a]All symptoms and signs as reported in the patient file. LUTS, lower urinary tract symptoms.
[b]$P < 0.05$.
[c]CI, confidence interval.

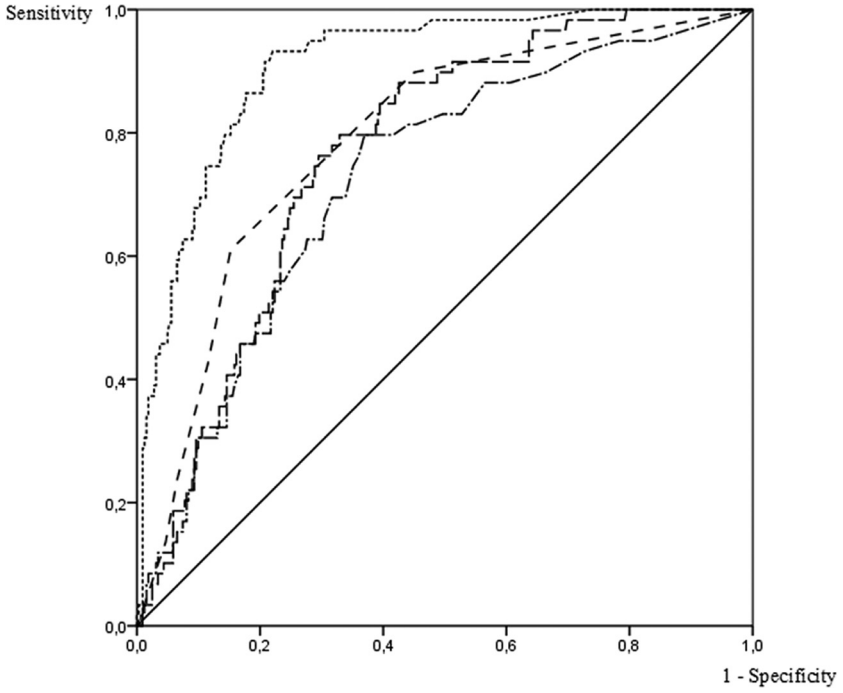

FIG 1 Receiver operating characteristic curves of different iQ200 parameters predicting UTI. On the *y* axis, sensitivity; on the *x* axis, 1 − specificity. AUC, area under the receiver operating characteristic curve; CI, 95% confidence interval. ···, WBC/μl (AUC, 0.91; CI, 0.87 to 0.94); – –, bacteria (AUC, 0.79; CI, 0.73 to 0.85); - - -, ASP/μl (AUC, 0.77; CI, 0.71 to 0.82); - - - · - - -, red blood cells (RBC)/μl (AUC, 0.72; CI, 0.66 to 0.79); —, reference line.

male patients, increased cognitive impairment in patients older than 59 years of age, and vaginal irritation or changed discharge in women. None of these three symptoms was significantly associated with UTI in their respective subgroups (data not shown). The concentration of C-reactive protein in serum and leukocyte count in blood did not differ significantly between patients with and without UTIs (*P* values were 0.95 and 0.69, respectively). The same applied to the proportion of patients with positive blood cultures when comparing both groups ($P = 0.31$).

iQ200 parameters. The difference in distribution of white blood cells in urine between cases and controls was obvious. Most cases had a count of >20 leukocytes/μl (97%), while most controls had a count of ≤20 leukocytes/μl (69%) ($P < 0.01$). A somewhat similar result was found for the concentration of bacteria. The iQ200 analysis reported a bacterial score of 2 or more for 61% of the cases and <2 for 85% of the controls ($P < 0.01$). ROC curves were plotted for iQ200 parameters and are shown in Fig. 1. The count of white blood cells per microliter (WBC/μl) had the largest area under curve (AUC, 0.91; CI, 0.87–0.94) and the highest discriminative value compared to those of the other parameters. Optimal cutoff values were calculated for WBC/μl, bacterial score, and ASP/μl and are shown in Table 4.

Because of the high discriminative value of WBC/μl, this parameter was subsequently divided into 3 categories, using the cutoffs of 50 and 150. The first cutoff, 50,

TABLE 4 Cutoff values of iQ200 parameters and corresponding sensitivity and specificity

Parameter	Cutoff value	Sensitivity (%)	Specificity (%)
WBC/μl (optimal calculated)	<74	86	82
WBC/μl (selected for categorization)	<50	91	79
	<150	69	89
Bacteria	<2	61	84
ASP/μl[a]	<6,250	76	70

[a]ASP, all small particles.

TABLE 5 Variables retained after logistic regression analysis of factors independently associated with UTI and attribution of points based on β coefficients

Variable	AOR (CI)[a]	β Coefficient	Points attributed
Frequent micturition/increased urge	2.8 (1.1–7.3)	1.0	1
Bacterial score, ≥2	3.7 (1.3–10.2)	1.3	1
Dysuria	12.1 (4.5–32.5)	2.5	2
WBC/μl, 50–149	15.6 (4.1–59.8)	2.8	2
WBC/μl, ≥150	44.5 (12.1–164.1)	3.8	3

[a]AOR, adjusted odds ratio; CI, confidence interval.

was selected by prioritizing sensitivity over specificity while maintaining a good tradeoff between both of them (sensitivity, 91%; specificity, 79%). The second cutoff, 74, was the optimal calculated cutoff (sensitivity, 86%; specificity, 82%), and the third cutoff, 150, was selected by approximately reducing the number of false negatives by half (sensitivity, 69%; specificity, 89%). Cutoffs were rounded to increase clinical applicability.

Establishment of a scoring tool. Logistic regression analysis was performed. Symptoms significantly associated with UTI were entered into the model, together with the categorized concentration of WBC/μl (using the two selected cutoff values from Table 4) and the iQ200 parameter "bacteria." We did not use ASP/μl in our model because we aimed to establish a clinically applicable model, and this parameter is nonspecific for measurement of bacteria. A scoring tool was developed to confirm or rule out the diagnosis of UTI (Table 5). Points were attributed based on β coefficients, with 1 point being given to the parameter with the smallest coefficient (14, 15). The maximum possible score was 7.

ROC curves of the scoring tool (AUC, 0.95; CI, 0.93 to 0.98) and of its separate components, iQ200 analysis (AUC, 0.90; CI, 0.86 to 0.93) and clinical (AUC, 0.80; CI, 0.73 to 0.88) variables, are shown in Fig. 2. As expected, the scoring tool had a higher

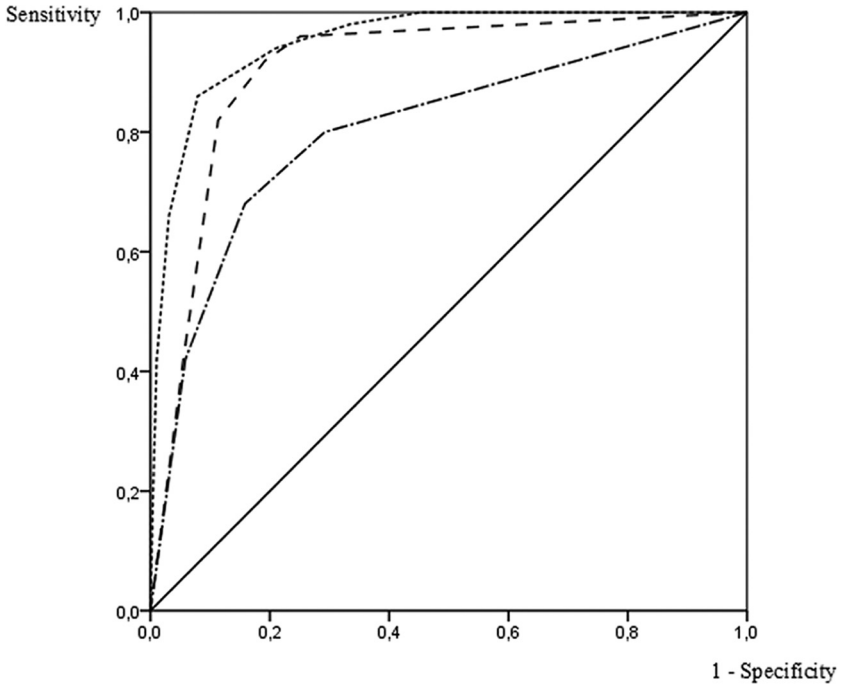

FIG 2 Receiver operating characteristic curves of the scoring tool and its separate components (iQ200 and clinical variables) predicting UTI. On the *y* axis, sensitivity; on the *x* axis, 1 −specificity. AUC area under the receiver operating characteristic curve; CI, 95% confidence interval. ···, combined score (AUC, 0.95; CI, 0.93 to 0.98); – –, WBC/μl and bacteria (AUC, 0.90; CI, 0.86 to 0.93); - - - -·- - - -, dysuria and frequent micturion/increased urge (AUC, 0.80; CI, 0.73 to 0.88); —, reference line.

TABLE 6 Possible thresholds for the scoring tool and corresponding characteristics

Score threshold	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
<2	98	67	34	100
<3[a]	94	79	44	99
<4	86	92	65	98
<5[b]	66	97	79	94
<6	42	99	88	91

[a]Threshold selected to rule out UTI.
[b]Threshold selected to confirm UTI.

sensitivity and specificity in predicting UTI compared to the separate iQ200 and clinical parameters as derived from the model, as well as the single iQ200 parameters (Fig. 1). Different cutoff scores and corresponding characteristics of the scoring tool are displayed in Table 6. When using a single threshold, a score of <4 has the optimal tradeoff between sensitivity (86%) and specificity (92%), which are both remarkably high, given the complexity of the study population. Using this cutoff, 7 patients would incorrectly be scored as negative (14% of cases), while 23 patients would incorrectly be scored as positive (8% of controls). If two cutoffs were to be used, three categories are formed, as follows: UTI likely, UTI possible, or UTI unlikely (Table 7). By using one threshold of below 3 and one of 5 or more, both false negatives and false positives are reduced by more than half compared to those when using a single threshold of 4. However, 19% of all patients would be classified as possibly having a UTI.

DISCUSSION

Our study defined cutoff values for parameters measured by an automated urine analysis system, the IRIS iQ200, for prediction of the clinical diagnosis of urinary tract infection in a heterogeneous, academic population of adult patients. In contrast to previous research on automated urine analysis by the iQ200 (6, 7, 10), we did not solely use a positive urine culture as the "gold" standard, but focused on clinical symptoms and course of disease in combination with culture results. This clinical assessment allowed exclusion of false-positive urine cultures of patients without urinary symptoms and with a diagnosis other than UTI, limiting unnecessary treatment of UTI. Prudent use of antibiotics has become increasingly relevant because of the problem of antibiotic resistance, which currently has become one of the most serious and growing threats to public health (16).

We found that urinary white blood cell count had the highest discriminative value for UTI (AUC, 0.91) compared to the other individual parameters, bacterial score and ASP/μl. The calculated optimal cutoff for WBC/μl was 74, with a sensitivity of 86% and specificity of 82%. For development of the scoring tool, we choose to use a lower cutoff of 50 WBC/μl, with a higher sensitivity of 91% and acceptable specificity of 79% (AUC, 0.85), to reduce the amount of false-negative results.

The finding that only 3% of the cases had a concentration of $\leq$20 WBC/μl in urine corresponds with findings of previous research using conventional urine analysis (17, 18). The role of the count of ASP/μl in UTI diagnosis by iQ200 remains to be determined. One study reported that ASP/μl has a better test performance than bacterial score at certain cutoffs (8), but our findings confirm the observation of Parta et al., who did not find ASP count to contribute in ruling out UTIs (8, 10).

The optimal scoring tool for diagnosis of UTI obtained by multivariable analysis included the iQ200 parameters "WBC/μl" and "bacteria" and the clinical symptoms "dysuria" and "frequent micturition/increased urge." The test characteristics of the scoring tool depend on the chosen threshold(s). Through the selection of different cutoff criteria, the score can be adapted to different clinical situations, depending on the relative benefits of maximizing sensitivity or specificity.

While a high sensitivity is important to minimize the number of false negatives, specificity might be of equal importance to minimize the number of false positives and limit inappropriate antibiotic use.

TABLE 7 Number of patients with and without UTI in each score group and predictive values using two cutoffs

Score	With UTI (n = 50)	Without UTI (n = 291)	Positive predictive value (%)	Negative predictive value (%)
<3	3	230	1	99
3–4	14	52	21	79
>4	33	9	79	21

Obviously, the selection of the best cutoff depends on the setting, the clinical condition and individual characteristics of the patient, and the risk of delaying antibiotic treatment. In the case of a febrile patient with suspected invasive UTI, a threshold of <2 seems appropriate to rule out UTI and search for an alternative diagnosis, whereas in the case of suspected cystitis, the threshold of 4 could be used to withhold antibiotics. Therefore, the use of three categories (UTI likely [≥5], UTI possible [3 to 4] or UTI unlikely [Is<3]) is probably most useful for application in patient care, leaving room for interpretation and risk analysis by the clinician.

Previous research on automated urine analysis showed that its findings correspond well with those of conventional urine sedimentation (5). Most research on analysis by the IRIS iQ200 aimed to predict a positive urine culture in order to reduce laboratory workload and associated costs (6, 8, 10). One of these articles also took clinical data into account, which led to a reduction of cases considered to be false positive using only urine culture as the gold standard (10). Since the purpose of this study by Parta was to evaluate the iQ200 as a screening tool to decrease unnecessary urine culture, a low cutoff for WBC (≥6/μl) was chosen to achieve high sensitivity, resulting in a poor specificity of 67 to 70%.

Luciano developed a risk score, combining both dipstick and iQ200 sediment reading results with age, which improved UTI diagnosis in a pediatric population (19).

Similar studies were performed on different commercial systems using flow cytometry, e.g., the Sysmex UF-1000i (Sysmex, Japan) to define optimal cutoff points for WBC/μl or bacterial score for ruling out bacterial UTI, but these data cannot be extrapolated directly to the iQ200 because both systems work differently. The UF-1000i is laser based and uses fluorescent dye, which the iQ200 does not (7, 9, 20, 21).

The strengths of our study are the particular academic population and its reflection of a real-world situation, which includes a very heterogeneous group of both inpatients and outpatients, of whom some had renal transplants, had a fever, were already treated with antibiotics, had contaminated urine samples, or were difficult to classify as either having a UTI or not.

The present study has its limitations. First, data from electronic patient files was obtained retrospectively and might not always have been complete. Second, the entire available data set was used for the prediction score, which as a result could not be validated in a different patient set. Validation is therefore required before the score can be implemented in clinical use. Third, the diagnosis of UTI lacks a gold standard. However, we feel that assessment by two independent blinded experts who take clinical data and conventional sediment analysis, as well as culture results, into account is the best reference test currently available. Finally, the study population was too small to distinguish between uncomplicated cystitis and invasive UTIs and to determine if cutoff values of iQ200 parameters would be different for certain subgroups, such as patients with neutropenia or renal transplants (2, 22).

Further research should prospectively validate the scoring tool for diagnosis of UTI on a new set of data and in different subgroups of patients and demonstrate potential benefits, such as reduction in the unnecessary use of antibiotics.

In conclusion, although the diagnosis of UTI can be challenging in an adult academic patient population, the combination of a simple survey and the results of the iQ200 could rule out infection in the majority of patients and therefore improve antibiotic stewardship in suspected UTI cases.

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