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The ability of Dipsticks to identify bacteria in urine in patients with hip fractures

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Abstract
Purpose: Urine dipstick is a commonly used test for detecting urinary tract infections because of its rapidity and low cost. Urine culture is the traditional golden standard for detecting urinary tract infection diagnosis.
In comparison to the golden standard, urine culture, this paper investigates whether the use of a urine dipstick is a valid method to identify the presence of bacteria in urine and thereby diagnose it as a urinary tract infection, in a Danish context, where the definition of a positive urine culture is 104 CFU/ml (10,000) bacteria in the urine.
This study is performed by testing sensitivity and specificity in dipsticks and by sending urine for culture.
Results: The study included 65 patients with hip fractures. ROC curves gave an AUC value of 0.72 (95% confidence interval [CI], 0.630–0.825). ROC was used to measure positive urine sticks.
There were 26 true positive and 22 false positive dipsticks in total. The sensitivity of the urine cultures was a total of 66.6. There is significant uncertainty about whether dipsticks can identify urinary tract infections, as the results were between 0.49 and 0.80. The specificity in our study was 78.8 in total. The accuracy was 75.5.
The confidence interval at 95% for the true positive dipstick was between 0.39 and 0.68. The false positive was between 0.31 and 0.60. The true negative tests showed results between 0.77 and 0.92. The false negative result was between 0.07 and 0.22.
Conclusion: The sensitivity and specificity of the urine dipstick to identify bacteriuria were 0.66 and 0.78, respectively, meaning that bacteriuria was overlooked in one-third of the tested urine. However, the combination of nitrite and leucocyte esterase in testing correctly excluded bacteriuria in 86% of the tests.

Keywords: Urinary tract infection, UTI, urine dipstick, hip fracture

Introduction

Urinary tract infection (UTI) is a common bacterial infection, estimated at 150 million episodes annually worldwide [1]. The frequency of UTI has been reported to be between 2 and 52% [2], and in patients with hip fracture UTI is associated with a 2.4-fold increase in surgical site infections [3]. Even with timely surgery and aggressive management through rehabilitation, hip fracture is associated with a high mortality rate. This mortality rate can mostly be attributed to the high prevalence of pre-fracture comorbidities and the high rate of postoperative complications, such as surgical wound infection, pneumonia, bleeding, ileus, delirium, and UTI [4]. Thus, it is paramount to have a strategy to identify and treat UTIs to improve the quality of care and reduce the risk of complications for frail patients, and the burden for strained healthcare organizations.

Background

The number of older people is increasing throughout the world, and the number of patients presenting with a fractured hip is rising because of that [5]. Hip fractures are a very serious event for an elderly person. Most women sustain hip fractures. Hip fractures nearly always require hospitalization and are fatal in almost a quarter of all cases (2). In Denmark, 6000–7000 patients incur hip fractures every year, and the number has been increasing over the last decade. If patients have UTI at the time of surgery, length of stay > 5 days, infectious complications (OR 1.71), non-infectious complications (OR 1.28), 30-day unplanned re-operations (OR 1.96), and 30-day readmissions (OR 2.04) are all increased. Regarding infectious complications, the presence of a UTI at the time of surgery is an independent predictor of sepsis (OR 2.44) and septic shock (OR 4.05) [6]. Furthermore, UTI is a predictor for the development of delirium (OR 2.67) and prolonged hospitalization and rehabilitation [7, 8].
The gold standard for the diagnosis of a urinary tract infection is the detection of the pathogen in the presence of clinical symptoms. The pathogen is detected and identified by urine culture. This also allows an estimate of the level of the bacteriuria. However, the minimum level of bacteriuria demonstrating an infection of the urinary tract has not been defined in scientific literature or standardized by microbiological laboratories. Many laboratories define 105 colony-forming units of CFU/ m urine as the threshold [9, 10]. Making a urine culture is costly and takes at least 24 hours. Urine culture yields either positive results (growth of more than 105 CFU/mL) or negative results [10]. However, in Denmark, the definition of a positive urine culture is 103 - 104 CFU/ml (1,000-10,000) bacteria in the urine [11].
A urine dipstick is a useful and commonly used test for detecting the presence of bacteria in urine. The dipstick test can detect urinary parameters such as glucose, protein, nitrite, and leukocyte esterase. The presence of nitrite and leukocyte esterase in urine may indicate the presence of bacteria [10]. The dipstick test requires only limited technical expertise, is cheap, and enables a quick diagnosis in high-

risk patients [12]. However, the value of dipsticks has been questioned [10]. However, the studies included in the meta-analysis are difficult to compare, as there are differences in the definition of UTI and different urine tests [13]. Furthermore, nitrite tests only identify the metabolites of nitrite reductase, an enzyme generated by a variety of microorganisms. Unless there is a bacteriuria, these compounds are not generally present in urine. This test has a sensitivity and specificity of 25% and 94%-100%, respectively. The limited sensitivity has been linked to bacteriuria caused by enzyme-deficient bacteria or low-grade bacteriuria. A positive nitrite test result is specific for UTI, mainly due to urease-positive organisms such as *Proteus* species and, on rare occasions, *E. coli*; nevertheless, it is very insensitive as a screening tool, with only 25% of UTI patients having a positive nitrite test result [12]. A negative test for nitrite does not imply the absence of bacteriuria, but only the absence of some types of bacteria.

Only a few studies reporting the accuracy of diagnosis based on the precision of dipsticks have been carried out on samples of patients including elderly surgical patients [14]. The presence of bacteriuria might have an important impact on the outcome of patients' surgery and rehabilitation and results from international studies cannot directly be translated to a Danish context. Thus, clinicians in orthopedics are faced with the dilemma that it is recommended to carry out surgery within 24 hours to optimize the best outcome for the patients [15], but identifying bacteriuria might take 24-48 hours. Therefore, it is relevant to test the accuracy and precision of dipsticks to identify bacteriuria in a population of Danish orthopedic patients with hip fractures.

AIM

The purpose of this study was to test the precision of urine dipsticks in identifying bacteriuria. The objectives were to measure the sensitivity and specificity of urine dipsticks in identifying bacteriuria compared to the reference test, urine culture.

Methods

The study was conducted with patients admitted within a year to two departments of orthopedic surgery in Farsoe and Hjoerring, Denmark. During the recruitment period, the two departments received 447 patients with hip fractures, including 307 female patients and 140 male patients.

Design

A descriptive prospective design was used. Urine samples were collected and tested at three points: on admission, by signs of UTI during hospitalization, and at discharge.

Participants

The inclusion criteria were patients over the age of 18 years who were admitted for surgery for intracapsular or extracapsular hip fracture. The exclusion criteria were as follows: patients with an indwelling urinary catheter; patients who were already receiving antibiotic treatment on admission; patients who had been transferred to other departments; and patients who had been diagnosed with dementia or were unable to talk or understand Danish.

Data Collection

Demographic data, including age, gender, and fracture type, were collected from medical records. To diagnose bacteriuria, all urine samples were tested with dipstick screening and sent for microbiological analysis.

All patients had urine samples collected on admission and at discharge with sterile intermittent catheterization according to an aseptic technique by the hospital policy [16, 17].

The dipstick screening test was performed within eight hours after patient admission. The dipstick screening test was performed on CLINITEK Status+ Analyzer (Siemens) using Siemens Multistix 7 for urinalysis [18]. The Siemens Multistix 7 is a diagnostic test strip that needs to be dipped in the urine until all pads are wet. The dipstick is placed on a paper towel and analyzed in the CLINITEK Status+ Analyzer. The results are visible after two minutes, and the results are automatically printed. Multistix 7 shows leucocyte, nitrate, protein, pH, blood, ketones, and glucose. In this study, positive results of urine measurements could be seen at 1+ or more in the dipstick response. CLINITEK Status+ Analyzer was used to read the dipstick. A positive dipstick for bacteriuria was present when urine was tested positive for both leucocyte esterase and nitrite.

Statistical analysis

Data were processed using the statistical program SPSS, version 27. Mean and SD were used to summarize normally distributed continuous data. Prevalence, sensitivity, specificity. The area under the curve (AUC) was summarized. The confidence interval (CI) at the 95% level was calculated.

Results

The study included 65 patients with hip fractures. Altogether, 57 (87.7%) females and 8 (12.3) males, with a mean age of 80.82 years (55–96) participated. A total of 382 patients were excluded due the following reasons: a diagnosis of dementia (n=40), receiving of antibiotic treatment at admission (n=19), being hospitalized more than eight hours in the emergency room (n=29), being transferred to other departments (n=4), not understanding or speaking Danish (n=3), having permanent catheterization (n=9), using pure intermittent catheterization (n=1), cognitive disease (n=2), cancer (n=2), multiple trauma (n=1), problems with urination (n= 2), alcohol intoxicated (n= 1), not wanting to participate (n=33) and, finally, with no reason given (n=236).

During the study period, 143 urine tests were sent for culture, and 143 dipstick tests were performed in the departments. Table 1 presents the results of the urine culture and dipsticks at admission, the results of dipsticks and urine culture for patients who were suspected to have developed bacteriuria during admission, and the dipsticks and result of urine culture at discharge. In total, there were 39 positive urine cultures and 48 positive dipsticks.

Table 1: Number of positive and negative cultures and dipsticks.

	Admission N =65 (%), [CI 95%]	**During hospital stay n=13 N =65 (%), [CI 95%]**	**At discharge N= 65 N =65 (%), [CI9 5%]**	**Total n=143 N =65 (%), [CI 95%]**
Positive urine culture (Reference test)	15 (23) [0.13-0.35]	10(77) [0.46-0.94]	14(22) [0.12-0.33]	39(29) [0.20-0.35]
Negative urine culture	50 (76) [0.64-0.86]	3(23) (0.05-0.53]	51(78) [0.66-0.8]	104 (73) [0.64-0.79]

(Reference test)				
Positive dipstick	19(29) [0.18-0.41}	12(92) [0.63-0.99]	17[26] [0.16-0.38]	48(34) [0.26-0.42]
Negative dipstick	46(70) [0.58-0.81]	1(8) [0.01-0.36]	48(74) [0.61-0.83]	95(66) [0.58-0.74]

Of the 143 dipstick tests, 35 (25%) were either false positive or negative about the result of false positive and negative urine cultures (Table 2).

Table 2: True and false positive or negative results of dipstick test of urine for bacteriuria.

	Admission N=65 (%), [CI 95%]	**During hospital stay N=13(%), [CI 95%]**	**At discharge N=65 (%), [CI 95%]**	**Total N=143 (%), [CI 95%]**
True positive	10	9	7	26(18) [0.12-0.25]
False positive	9	3	10	22(15) [0.09-0.22]
True negative	41	0	41	82(57) [0.48-0.65]
False negative	5	1	7	13(0.09) [0.04-0.15]

The specificity to correctly identify bacteriuria was between 50-0.66 (Table 3), the accuracy was 0.73-0.78 and the specificity was between 0.80-0.82 at admission or discharge.

Table 3: Sensitivity, specificity and accuracy of the dipstick versus urine cultures on admission and at discharge.

	Admission N=65	**At discharge N=65**
Sensitivity	0.667	0.50
Specificity	0.82	0.804
Accuracy	0.785	0.738

*Results in “During hospital stay” are not calculated, as this was not possible due to a "0” true negative test.

The confidence interval at 95% for the true positive dipstick was between [CI95: 0.39- 0.68]. The false positives were between [CI95:0.31- 0.60] (Table 4). The true negative tests showed results between [CI95: 0.77- 0.92] (Table 4). The false negative result was between [CI95:0.07- 0.22] (Table 4).

Table 4: Total sensitivity, specificity, prevalence of bacteriuria and true and false test of the dipstick

	Estimated value N=143	**95% Confidence Interval**	
		Lower limit	**Upper limit**
Prevalence	0.27	0.20	0.35
Sensitivity	0.66	0.49	0.80
Specificity	0.78	0.69	0.85
True positive	0.54	0.39	0.68
False positive	0.45	0.31	0.60
True negative	0.86	0.77	0.92
False negative	0.13	0.07	0.22

versus urine cultures.
versus urine cultures.

With a comparison of the sensitivity and specificity of the urine dipsticks as shown in a ROC curve, the ability of the dipsticks to positively identify bacteriuria (AUC 0.72 (95% [CI95; 0.630- 0.825] is summarized in Figure 1.

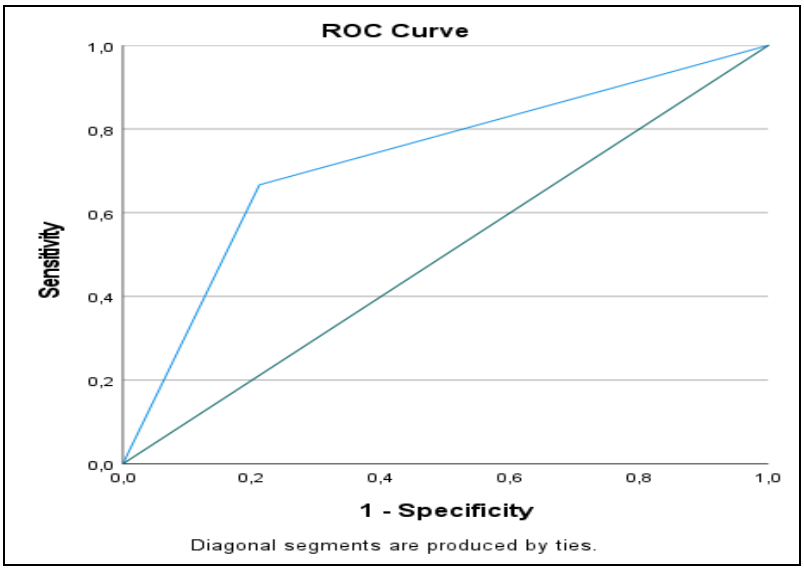

Fig 1: ROC curve for dipsticks positive for leucocyte esterase and nitrite. During admission, 10 (15.3%) [CI95: 0.07-0.26] patients developed bacteriuria.

Discussion

This is the first study including a Danish orthopedic population to test the sensitivity and specificity of dipsticks for identifying bacteriuria using a CLINITEK Status+ Analyzer compared to urine culture. The study included elderly patients admitted for fractured hips. Patients undergoing hip-fracture surgery with concurrent bacteriuria at the time of surgery have more adverse 30-day outcomes compared with patients who have not been diagnosed with bacteriuria. This highlights the need for quick and precise methods to identify bacteriuria at the time of geriatric hip fracture surgery to reduce complications and improve 30-day outcomes [6].

Diagnosis of UTI

The diagnosis of UTI is based on a combination of clinical symptoms and the presence of bacteriuria. Dysuria is the most common symptom of UTI, but dysuria is a complaint in vaginitis, chlamydial urethritis, and pyelonephritis [19]. Furthermore, UTI can be categorized as asymptomatic or have atypical symptoms and signs. Hence, laboratory tests are required to support the diagnosis of UTI. Several tests are available for the identification of bacteriuria. An ideal test is cheap and needs less time and expertise, with high accuracy enabling a reliable and rapid diagnosis in high-risk patients. Though urine culture is the gold standard for the diagnosis of bacteriuria, it is expensive and time-consuming, requiring at least 48 hours to produce results [19]. Treatment of urine culture without regard to the symptomatology of the patient (pain and burning when urinating, frequent urination, suprapubic pain, temperature above 37.9 centigrade) all too often results in useless antibiotic treatment due to random bacterial findings [20-22]. The literature shows overtreatment of bacteriuria to be a known problem [23]. A study showed that when doctors used only the dipstick test to diagnose classical lower urinary tract symptoms, 47% of the patients received unnecessary antibiotics, while 11% did not receive proper treatment [24]. Therefore, it is important to ensure treatment with antibiotics for those patients who have bacteriuria with symptoms and not for those with asymptomatic bacteriuria. The incidence of asymptomatic bacteriuria increases from 3.5% in the general population to 16–18% in women older than 70 years. One longitudinal study report that it affects 50% of older women [25]. Asymptomatic bacteriuria is defined as uropathogenic bacteria in amounts of at least 105 CFU/ ml without any associated symptoms.

Comparing results

In our study, we used the Danish recommendation for bacteriuria of 104 CFU/ml whereas the international studies used a definition of bacteriuria of 105 CFU/ml, which makes a direct comparison difficult. In a study of a urine dipstick analysis of 635 urine culture-positive patients, the sensitivity of nitrite alone and leukocyte esterase alone was 23.31% and 48.5%, respectively. The sensitivity of blood alone in a positive urine culture was 63.94%. The sensitivity was 72.28% if leukocyte esterase and/or blood were present [19]. The sensitivity was found to be the highest when nitrite, leukocyte, and blood were considered together. Out of 136 positive culture results, 103 were dipstick positive and 33 were negative. Sensitivity, specificity, positive predictive value, and negative predictive value of both nitrite and leukocyte esterase were 75.74%, 68.90%, 66.66%, and 77.40%, respectively, with culture being considered the gold standard [26]. The highest specificity value, positive predictive value, positive likelihood ratio, and negative likelihood ratio were recorded for the "nitrite-positive and leucocyte esterase-positive" results. The combined "nitrite-positive or leucocyte-positive" result was relatively the best indicator for accurate dipstick diagnosis, with AUC=0.7242 [27].

In this study, the sensitivity and specificity were 0.66 and 0.78, respectively. This is in line with the findings from previous studies [6].

Sensitivity and specificity are summarized in a ROC curve. The ROC curve can be considered as the average value of sensitivity for a test over all possible values of specificity [28]. The area under the curve (AUC) summarizes the diagnostic accuracy of the test. It takes values from 0 to 1. The value of 0 shows a perfectly inaccurate test, and the value of 1 shows a perfectly accurate test. An AUC of 0.5 suggests no discrimination, 0.7- 0.8 is acceptable, 0.8- 0.9 is excellent and over 0.9 is outstanding [29].

In this study, the AUC curve was 0.72. These results are in line with a previous study (27) and reflect how nearly 30% of patients with UTI would not be diagnosed and receive relevant treatment. This is not appropriate for patients receiving osteosynthesis material for hip fractures.

The study shows a high probability of a true negative dipstick (0.86%). Data from this study support the significance of dipstick test results that are negative and might be a predictor for ruling out positive urine cultures. This is also seen in other studies and the meta-analysis of Devillé *et al*. [10, 30]. A dipstick can be used to screen for UTI. Positive dipsticks should be sent for culture to verify the results. Use of the CLINITEK Status+ Analyzer machine is practical in busy everyday life on hospital wards, as care staff, can easily get on with other tasks before the dipstick needs to be read. With the manual use of a dipstick, an overly long interval between obtaining the stick of urine and making the reading can have a negative impact on the result because the time can change the actual result.

Implication for clinical practice

Previously treatment was initiated based on dipsticks and symptoms presented by the patients. The false positive dipsticks could have led to overtreatment of antibiotics, which would have been the routine in the ward before the study was completed. Healthcare organizations are faced with the challenges of reducing the use of antibiotics to reduce the risk of developing multiple-resistant bacteria. Accuracy and precision in diagnosing bacteriuria is an important tool to achieve this goal [1].

Strengths and limitations

In this study, the dipstick was measured against the urine culture as the reference test using the Danish recommendation for bacteriuria which is more relevant for a Danish clinical context. The dipstick was, in practice, considered positive if it tested positive for both leucocyte esterase and nitrite. A strength of the study is that mechanical extraction of urine was used and that the urine for the urine cultures was obtained in sterile conditions, as recommended. Mid-stream urine has often been used in studies that increase the risk of contamination [16]. The procedure of automatic reading of dipsticks is less susceptible to erroneous labeling and registration of test results compared with manual handling and therefore has the potential to enhance patient safety and increase precision

in diagnosing bacteriuria (31). The CLINITEK Status+ Analyzer machine was new to the staff as it had not previously been used in their departments. Nevertheless, the staff did not experience much difficulty in using it.

A weakness was that a total of 236 patients were not included for unknown reasons. One reason (which was expressed by staff) could be that it was time-consuming for the staff to ensure that the urine for the reference test was obtained within eight hours of admission.

Conclusion

The sensitivity and specificity of urine dipstick to identify bacteriuria were 0.66 and 0.78, respectively, with bacteriuria being overlooked in one-third of the tested urine in patients with a fractured hip.

Ethical approval

The Danish Ethics Committee in the region of North Jutland (notification number 48712) approved the study. Information about the study was given to the patients both in writing and orally. Patients provided written informed consent.

Conflict of interest statement

There are no conflicts of interest for the authors of this manuscript.

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