

Diagnosing Catheter-associated Urinary Tract Infection in Critically Ill Patients: Do the Guidelines Help?

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Abstract

Catheter-associated urinary tract infection (CAUTI) is the leading cause of hospital-acquired infections in hospitalized patients in medical and surgical wards, but it is still commonly underdiagnosed in critically ill patients despite a higher device usage rate. The most commonly employed diagnostic criteria for such diagnosis come from the Infectious Disease Society of America and Centers for Disease Control and Prevention National Health Safety Network surveillance definition. It is surprising that no separate diagnostic criteria of CAUTI exist, for the critically ill patients – though these patients are of a different class of patients' altogether, due to decreased immunity, existence on multiple organ supports, and invasive lines, and an inability to communicate with a clinician. In this review, we highlight the difficulties in applying the available guidelines to diagnose CAUTI in critically ill patients. We also suggest an algorithm for the diagnosis of CAUTI in these patients.

Keywords: Catheter-associated urinary tract infection, critically ill, guidelines

INTRODUCTION

Catheter-associated urinary tract infection (CAUTI) is the leading cause of hospital-acquired infections, with an incidence around 1.4–1.7/1000 catheter days in hospitalized patients in medical and surgical wards, but it is still commonly underdiagnosed in critically ill patients. This is despite a device usage around 45%–79% in the Intensive Care Unit (ICU) versus 17%–23% in the wards.^[1] Approximately 66% of patients have the device in place throughout the ICU stay for a prolonged period.^[1] Infection hierarchy in the ICUs from developing countries is topped by ventilator-associated pneumonia (VAP) in 24.1 cases per 1000 ventilator days, catheter-related bloodstream infections (CRBSIs) in 12.5/1000 catheter days, and CAUTI in 8.9/1000 catheter days.^[2] CAUTI is the second most common cause of nosocomial bloodstream infection, with around 15%–25% mortality.^[3] CAUTI also leads to excessive use of health-care resources.^[4] The most commonly employed diagnostic criteria for such diagnosis come from the Infectious Disease Society of America (IDSA)^[5] and Centers for Disease Control and Prevention (CDC) National Health Safety Network (NHSN) surveillance definition.^[6] The latest from IDSA for the

diagnosis of CAUTI came in 2010^[5] and CDC NHSN surveillance definition was updated in 2017, as represented in Figure 1.^[6] It is surprising that no separate diagnostic criteria of CAUTI exist, for the critically ill patients – though these patients are of a different class of patients' altogether, due to decreased immunity, existence on multiple organ supports, and invasive lines, and an inability to communicate with a clinician. Differentiating asymptomatic bacteriuria (ASB) from CAUTI poses a tough challenge in this environment. A previous review cautioned against an increased temptation to initiate antimicrobial therapy on the basis of positive urine culture.^[7] In this review, we highlight the difficulties in applying the available guidelines to diagnose CAUTI in critically ill patients. We also suggest an algorithm for the diagnosis of CAUTI in these patients.

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Diagnosis of CAUTI by the existing guidelines	
<p>IDSA 2010 Guideline for diagnosis of CAUTI: [5]</p> <ul style="list-style-type: none"> CA-UTI in patients with indwelling urethral, indwelling suprapubic, or intermittent catheterization is defined by the presence of symptoms or signs compatible with UTI with no other identified source of infection along with $\geq 10^3$ colony forming units (CFU/mL) of ≥ 1 bacterial species in a single catheter urine specimen or in a midstream voided urine specimen from a patient whose urethral, suprapubic, or condom catheter has been removed within the previous 48 h In the catheterized patient, pyuria is not diagnostic of CA-bacteriuria or CA-UTI. 	<p>CDC NHSN surveillance definition for diagnosis of CAUTI 2017: [6]</p> <p>Patient must meet A, B, and C below:</p> <ul style="list-style-type: none"> A. Patient had an indwelling urinary catheter that had been in place for > 2 days on the date of event (day of device placement = Day 1) AND was either present for any portion of the calendar day on the date of event or removed the day before the date of event. B. Patient has at least one of the following signs or symptoms: fever ($> 38.0^\circ\text{C}$), suprapubic tenderness, costovertebral angle pain or tenderness, urinary urgency, urinary frequency or dysuria. C. Patient has a urine culture with no more than two species of organisms identified, at least one of which is a bacterium of $\geq 10^3$ CFU/ml. The following excluded organisms cannot be used to meet the UTI definition: <i>Candida</i> species or yeast not otherwise specified mold, dimorphic fungi or parasites. An acceptable urine specimen may include these organisms as long as one bacterium of $\geq 10^3$ CFU/ml is also present. Additionally, these non-bacterial organisms identified from blood cannot be deemed secondary to a UTI since they are excluded as organisms in the UTI definition.

Figure 1: Current Infectious Disease Society of America and Centers for Disease Control and Prevention guidelines for the diagnosis of catheter-associated urinary tract infection

LIMITATION 1: RELIANCE ON CLINICAL SIGNS AND SYMPTOMS FOR THE DIAGNOSIS OF CATHETER-ASSOCIATED URINARY TRACT INFECTION

Bacteriuria in short-term catheterized patients (2–10 days) occurs in around 25%, among which only 25% develop symptoms of UTI and around 3%–4% of these develop bacteremia.[4] The risk of bacteriuria and candiduria which increases by 3%–7%/day can go up to 100% by day 30.[4,7]

It is well known that ASB and UTI need to be differentiated as the former is common and rarely leads to bacteremia and clinical adverse outcomes, while the latter is an important cause for in-hospital morbidity and mortality. However, the distinction is less clear in the ICU setting.

First, clinical signs and symptoms (apart from fever), such as suprapubic tenderness, costovertebral angle tenderness, urinary urgency, frequency, and dysuria can be elicited very rarely in intubated critically ill patients; hence, meeting all three requirements for the diagnosis of CAUTI is difficult.[7,8]

A retrospective study done at a US tertiary care academic center by Tedja *et al.* in 2015 showed that for a total of 105 CAUTIs (by the CDC definition) identified over 2 years, 51% had alternative explanation for fever (primarily pneumonia, bloodstream infections) and only 6% of patients of CAUTI became bacteremic.[8] Yeast was isolated in 50% of cases, which made the diagnosis of CAUTI redundant (CDC removed candiduria from the CAUTI definition in 2015, by which time the study was completed). It is pertinent to note that CAUTI rates by CDC definition are used to judge the quality of hospital care in the US and also determine penalties imposed by Medicare. Therefore, the authors pointed out that excessive reliance on a combination of fever and positive urine cultures to diagnose CAUTI may

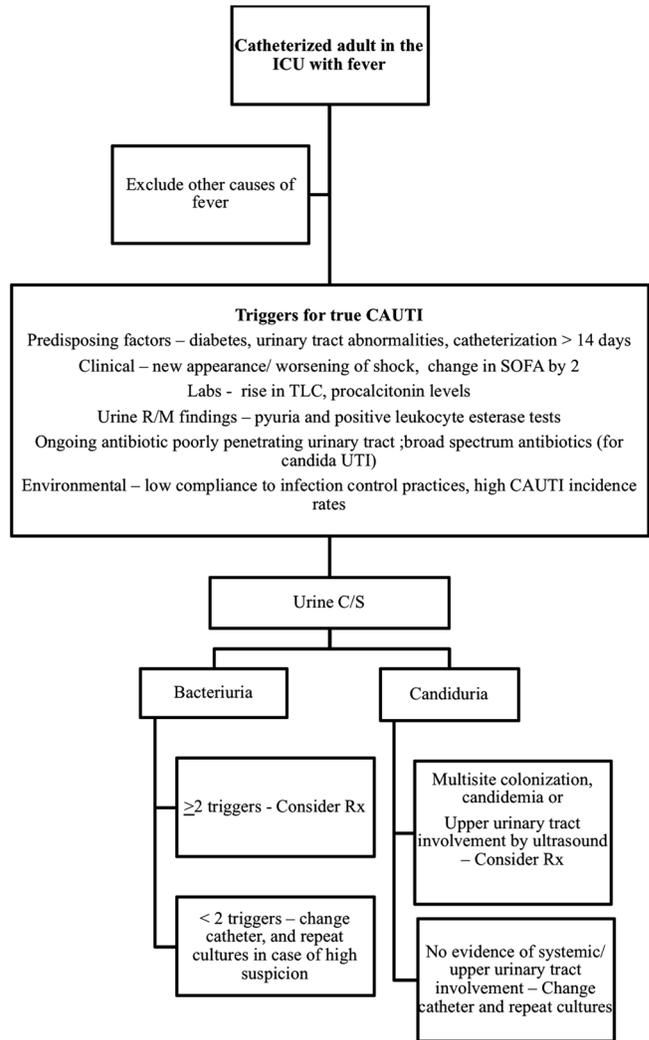


Figure 2: Suggested approach to catheter-associated urinary tract infection in catheterized patient with fever in Intensive Care Unit

unnecessarily worsen hospital burden in managing clinically “irrelevant” infections. Secondary bacteremia (especially with uropathogenic bacteria) is highly suggestive of a “true” CAUTI, but it is not justifiable to label a CAUTI episode as irrelevant if bacteremia does not occur and/or the clinician is not compelled to change the antibiotic. Furthermore, one must take into account that in the study by Tedja *et al.*, most patients with CAUTI were already on antibiotics; therefore, true rates of secondary bacteremia could not have been ascertained.

A sizeable portion of ICU patients are immunocompromised and do not present with fever, and worsening of clinical parameters may be the only sign of a new infection. In this backdrop, is bacteriuria truly asymptomatic? Complicated UTIs have been known to develop in patients with “asymptomatic” bacteriuria and varying anatomic and functional defects.[6] Until a well-designed prospective trial determines the outcomes in immunocompromised bacteriuric patients, we may not know the answer.

LIMITATION 2: CENTERS FOR DISEASE CONTROL AND PREVENTION DOES NOT RECOGNIZE POLYMICROBIAL URINARY TRACT INFECTION – A REALITY IN CRITICALLY ILL PATIENTS

Kline and Lewis, in their 2016 review, discussed the conundrum of urine contamination by mixed flora versus true polymicrobial UTI. They point out that the microorganisms if present in levels sufficient for UTI diagnosis ($>10^5$ cfu/ml) could represent a true polymicrobial infection and simultaneous detection of two or more of the same pathogens from blood cultures may help in making the diagnosis.^[9] It is thought that that synergy between different species of microbes may be seen in the urinary tract, promoting polymicrobial infections. Recently, microorganisms previously considered as contaminants, such as *Staphylococcus saprophyticus*, *Enterococcus*, and Group B *Streptococcus*, have been recognized as uropathogens.^[10] Exclusion of mixed flora from CAUTI is simple when it appears to patients in the wards or outpatients, but in critically ill patients with multiorgan failure, such exclusion (as suggested by CDC) can be counterproductive.^[9,10] Availability of advanced automated systems such as Vitek and MALDI-TOF has led to a surge in the detection of fastidious microorganisms. Till their uropathogenicity is disproven, it is not safe to ignore growth of more than two microorganisms as mixed flora.

LIMITATION 3: DIFFERENT CUTOFFS FOR BACTERIAL COUNTS IN CENTERS FOR DISEASE CONTROL AND PREVENTION AND INFECTIOUS DISEASE SOCIETY OF AMERICA – DO THEY NOT CONFUSE A CRITICAL CARE PHYSICIAN?

While the IDSA guidelines have been designed keeping clinical decision-making in mind, CDC guidelines are primarily for surveillance purpose. In fact, no standard definition of significant bacteriuria exists. The National Institute on Disability and Rehabilitation Research consensus statement defined significant bacteriuria in patients on in-dwelling catheters as $>10^2$ cfu/ml.^[11] With standard methods, the minimum level of detection is 10^3 cfu/ml. The IDSA guidelines point out that in situations where the detection of significant bacteriuria would result in treatment (as in pregnancy), where even asymptomatic bacteriuria requires treatment, the higher threshold of 10^5 should be considered to increase the diagnostic accuracy. Nevertheless, varied cutoffs for bacterial counts (10^3 in IDSA versus 10^5 in CDC) in the two definitions create ambiguity for the treating physician, especially in patients who are not improving despite ongoing antimicrobial therapy. Existence of different cutoffs for surveillance and diagnosis is not a feature of the algorithms for VAP and CRBSI.^[12]

LIMITATION 4: DISREGARDING PYURIA IN CRITICALLY ILL PATIENTS

Pyuria has a positive predictive value exceeding 95% in the identification of UTIs in noncatheterized patients, so much so that, in the absence of pyuria, urine cultures need not be obtained. On the contrary, pyuria should not be a sole criterion for obtaining urine cultures in catheterized patients. This was the primary conclusion of a landmark study by Tambyah and Maki in 2000, where 761 newly catheterized-hospitalized patients were cultured daily and had their urine white blood cell (WBC) concentration monitored daily.^[13] Mean urine WBC count was significantly higher in patients with CAUTI, especially those caused by Gram-negative bacilli, than by coagulase-negative staphylococci and yeasts. In fact, pyuria with >5 WBCs/high power field had a specificity of 90% in diagnosing CAUTI with $>10^5$ cfu/ml.^[13] However, this study did neither distinguish between asymptomatic bacteriuria and UTI nor was it limited to ICU patients. In a 2017 study by Lee *et al.*, involving 169 catheterized ICU patients, pyuria and leukocyte esterase had high sensitivity (73% and 87.5%, respectively) and nitrite test had a high specificity (100%).^[14] Ignoring pyuria in a critically ill febrile-catheterized patient needs to be elucidated, where other signs and symptoms cannot be elicited. We suggest that it needs to be incorporated in the diagnostic algorithm for critically ill.

LIMITATION 5: CANDIDURIA IN CRITICALLY ILL PATIENTS – IS IT TRULY BENIGN?

Fungal UTIs are typically asymptomatic. Even pyuria is uncommon in candiduric patients. Candiduria occurs late in the hospital stay. In a French ICU study, the mean onset of candiduria after ICU admission was at 17 days.^[15] Furthermore, it is often difficult to differentiate upper and lower tract infection in candiduric patients. In one study that used ¹¹¹In-labeled leukocyte scintigraphy (the study excluded critically ill patients), 50% of candiduric patients had renal uptake, raising a concern that subclinical pyelonephritis may be a common phenomenon in candiduric patients.^[16] As critically ill patients are most susceptible to candidemia after candiduria, it is well possible that *Candida* pyelonephritis may be coexisting in many such patients. The CDC guidelines however exclude candiduria from the definition of CAUTI. Before the exclusion in 2015, *Candida* was the most common organism causing CAUTI. An epidemiologic study was conducted involving 137 adult ICUs in the US, after the definition change excluding candiduria. This study by Fakih *et al.* threw up some interesting results.^[17] The standardized incidence rate (SIR) of CAUTI reduced by 44%, after the definition change, while SIR of central line-associated bloodstream infection (CLABSI) increased by 30%. CDC guidelines attribute infection to CLABSI after exclusion of other sources. Therefore, these simultaneous changes, also coupled with rise in specifically *Candida*- and *Enterococcus*-related CLABSI, indicate that disregarding

candiduria may have led to increased rates of candidemia, which were then attributed to CLABSI.^[17]

Excluding candiduria from the definition of CAUTI is questionable, when kidneys are the most common site of disseminated candidiasis.^[18,19] Concomitant candidemia can occur in up to 8% in such patients.^[20] Fever with candiduria may be the only initial manifestation of systemic candidiasis in some patients. We question its ignorance even if the counts are $\geq 10^5$ in critically ill, with ICU patients being at highest risk for candidemia.^[21] Recent reviews suggest that multisite colonization by *Candida* in an ICU patient deserves to be treated.^[21,22]

We suggest an algorithm [Figure 2] to approach CAUTI in a critically ill febrile adult with a urinary catheter. We propose that the decision to treat a positive urine culture (bacterial/candida) in the ICU should be based on the presence of two/more of several factors, which we have compiled together as “triggers to treat.” However, guidelines can only steer clinicians in decision-making; finally, it is the treating clinician who judges whether a positive test result needs to be acted on, or not – that art also continues to evolve with time.

CONCLUSION

We propose that there is a need for diagnostic criteria for CAUTI for ICU patients as the current guidelines might not help critical care physicians dealing with patients on multiple organs supports with majority of the patients unable to communicate.

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Conflicts of interest

There are no conflicts of interest.

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