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Original Contribution

Diagnostic performance of initial serum lactate for predicting bacteremia in female patients with acute pyelonephritis

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ABSTRACT

Objectives: The purpose of the present study was to investigate the diagnostic value of lactate for predicting bacteremia in female patients with acute pyelonephritis (APN).
Methods: We conducted a retrospective study of female patients with APN who visited the study hospital emergency department. The demographics, comorbidities, physiologies, and laboratory variables including white blood cell count and segmented neutrophil count, C-reactive protein, and initial serum lactate levels were collected and analyzed to identify associations with the presence of bacteremia.
Results: During the study period, a total of 314 patients were enrolled. One hundred twenty-three patients (39.2%) had bacteremia. *Escherichia coli* was the most frequent pathogen. Logistic regression analysis demonstrated that the lactate level was independently associated with the presence of bacteremia (odds ratio, 1.39 [95% confidence interval, 1.08-1.78]). The C-statistic of the lactate level was 0.67 (95% CI, 0.60-0.73). At a cutoff value of 1.4 mmol/L, the lactate level predicted bacteremia with a sensitivity (53.7%), specificity (72.3%), positive predictive value (55.5%), negative predictive value (70.8%), positive likelihood ratio (1.93), and negative likelihood ratio (0.64).
Conclusion: The initial serum lactate level showed poor discriminative performance for predicting bacteremia in female patients with APN.

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1. Introduction

1.1. Background

Acute pyelonephritis (APN) is frequent and requires hospitalization in most females [1–3]. The decision to admit female patients with APN is a clinical one based on consideration of comorbidities and structural and functional abnormalities. Bacteremia is a potentially critical condition, which may result in severe sepsis, septic shock, and death. Therefore, identification of bacteremia should be an important factor for deciding whether to admit patient [4–6].

Unfortunately, it takes a few days for blood culture result to reveal the presence of bacteremia; as a result, blood cultures barely contribute to the admission decision. Researchers have tried to identify easy, rapid laboratory tests for predicting bacteremia in APN, and procalcitonin (PCT) is considered a possible surrogate for bacteremia in APN [7]. Midregional proatrial natriuretic peptide (MRproANP) and C-reactive protein (CRP) were less accurate than PCT [8].

Lactate is one of the important sepsis markers in addition to CRP, proatrial natriuretic peptide, and PCT. However, previous studies targeting female patients with APN did not analyze the diagnostic value of lactate. With growing interest in the prognostic usefulness of lactate in sepsis, we evaluated the role of lactate in female patients with APN. The purpose of the present study was to investigate the diagnostic value of lactate for predicting bacteremia in female patients with APN and compare its performance with that of other laboratory markers.

2. Methods

2.1. Study design and subjects

We performed a retrospective chart review study. The present study was approved by the institutional review board of the study hospital, and the institutional review board waived the requirement for informed

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consent for all subjects in the present study. The study hospital is a 1200-bed urban academic, tertiary care, university hospital.

Adult patients who were diagnosed with APN in the study hospital emergency department (ED) between January 2013 and December 2014 were eligible for inclusion in the present study. In the study hospital, the diagnostic criteria for APN included the following: (1) a body temperature (BT) higher than 38°C, (2) lumbar tenderness, and (3) pyuria on urinalysis (≥5 to 9 leukocytes/high-power field) and bacteriuria with a colony count of greater than or equal to 100 000 colony-forming units per milliliter for clean voided urine [9,10]. If the patient had taken any antipyretic agent before visiting the ED, a BT higher than 38°C was not required for diagnosis. Patients were excluded from the study based on following criteria: (1) male sex, (2) no blood culture test, or (3) no evaluation of lactate and CRP levels within 2 hours after ED arrival.

Blood cultures were obtained before starting antibiotics. At least 2 sets of 10-mL blood samples were collected in 2 sets of bottles—BacT/ALERT FA Plus (for detection of aerobic and facultative microorganisms) and BacT/ALERT FN Plus (for detection of anaerobic microorganisms)—and were incubated under aerobic and anaerobic conditions in an automatic machine (BacT/ALERT 3D; bioMérieux, Durham, NC). The bacterial growth was automatically monitored. A single isolation of coagulase-negative staphylococci, *Corynebacterium* species, *Bacillus* species other than *Bacillus anthracis*, or *Micrococcus* species in the blood was considered contamination.

The serum lactate level was primarily measured using arterial blood, but the venous blood lactate level was also permitted. The lactate level was measured using a Stat Profile Critical Care Xpress Analyzer (Nova Biomedical, Waltham, MA). The measurement capacity for lactate in this instrument ranges from 0.3 to 20 mmol/L. This machine was periodically inspected by the manufacturer staff.

2.2. Outcome measures

The primary outcome measure was bacteremia. *Bacteremia* was defined as growth of any pathogen in the blood culture. The cases that were considered contaminated as above were excluded.

2.3. Data collection and processing

Demographics, clinical data, physical findings at ED presentation, and initial laboratory results (within 2 hours of ED arrival) were collected by a trained abstractor according to the guidelines recommended by Gilbert et al [11]. These included the age; sex; comorbidities, such as hypertension (HTN), diabetes mellitus (DM), cerebrovascular disease, chronic renal disease, malignancy, and indwelling Foley catheter; initial vital signs; white blood cell (WBC) count; hemoglobin level; platelet (PLT) count; blood urea nitrogen (BUN) level; creatinine (Cr) level; WBC count in urine analysis; nitrite level in urine analysis; initial lactate level; initial CRP level; whether to admit; ED length of stay; and hospital length of stay (if admitted).

2.4. Statistical analysis

All continuous data are presented as the mean and SD, and discrete data are presented as both the count and percentage. Results of logistic regression analyses are presented as the odds ratio (OR) with a 95% confidence interval (CI). Statistical significance was defined as a 2-sided $P < .05$.

Comparison of normally distributed data was performed using an independent-sample *t* test. For nonnormally distributed data, comparisons were performed using the Mann-Whitney *U* test or Kruskal-Wallis test. For categorical data, the χ^2 test with a Fisher exact test for 2×2 tables was used. Results were considered significant at a threshold of $P < .05$ (2 tailed).

We referred to the Standards for the Reporting of Diagnostic Accuracy recommendations when analyzing of the results [12,13].

Associations between the presence of bacteremia and each potential variable were first quantified using univariate logistic regression analyses. Then, multivariable logistic regression analysis was performed for trend factors ($P < .10$) in the univariate analysis. Model 1 adjusted for lactate and CRP. Model 2 adjusted for lactate, CRP, and other laboratory findings, and model 3 adjusted for model 2 variables and basic characteristics, clinical symptoms, and physiologic variables. Regression results are expressed as ORs with 95% CI.

The predictive values of the lactate and CRP were tested using area under the receiver operating characteristic (AUROC) analysis. The SEM and *P* values for the AUROC and comparisons between laboratory variables were calculated according to the methods of Hanley and McNeil [14,15]. The cutoff value that maximized the sum of the sensitivity and specificity (Youden index) was calculated for lactate [16]. A diagnostic test was performed at various cut points of the lactate and CRP level, including evaluation of the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio, and negative likelihood ratio.

All analyses were performed using STATA 11.1 (StataCorp LP, College Station, TX) and SAS 9.1 (SAS Institute, Inc, Cary, NC).

3. Results

3.1. Study subject characteristics

During the study period, 540 patients met the initial eligibility criteria. Among these patients, we excluded the following: (1) 184 male patients, (2) 11 patients who did not undergo a blood culture

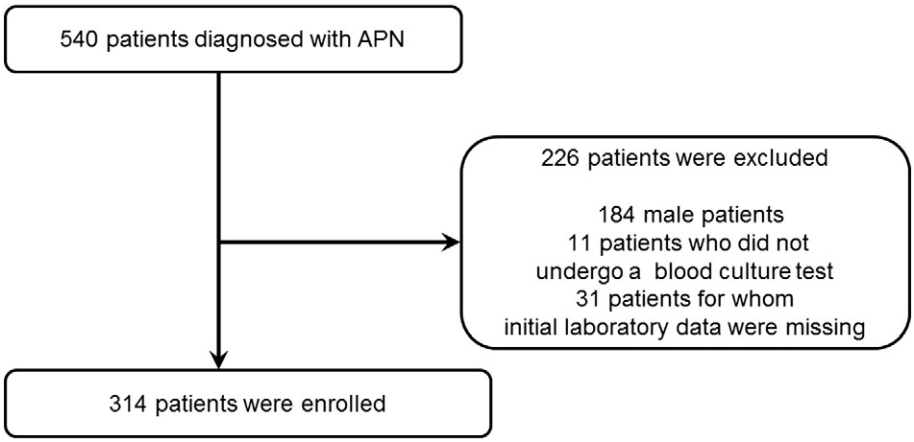

Fig. 1. Flow of the study.

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