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Original article

Comparison of diagnostic and prognostic utility of lactate and procalcitonin for sepsis in adult cancer patients presenting to emergency department with systemic inflammatory response syndrome

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ABSTRACT

Objectives: Differentiating sepsis from other noninfectious causes of systemic inflammatory response syndrome (SIRS) in cancer patients is often challenging. Although lactate and procalcitonin have been studied extensively regarding sepsis management, little is known about their utility in cancer patients. This study aimed to compare the diagnostic and prognostic utility of lactate and procalcitonin for sepsis in cancer patients.

Material and methods: This prospective case-control study was conducted with adult cancer patients presenting to emergency department (ED) with at least two SIRS criteria. The infection status of each patient was determined retrospectively.

Main diagnostic variables were calculated for diagnostic and prognostic utilities of lactate and procalcitonin.

Results: Among 86 patients, mean age was 61. Twenty-two (25.6%) were determined in the sepsis group. In the ROC analysis, a lactate value of 1 mmol/L predicted sepsis with 86.36% (95%CI: 65.1%–97.1%) sensitivity and 28.12% (95%CI: 17.6%–40.76%) specificity. A procalcitonin value of 0.8 ng/mL yielded a sensitivity of 63.64% (95%CI: 40.7%–82.8%) and 76.56% (95%CI: 63.4%–86.2%) specificity for differential diagnosis of sepsis in cancer patients.

Lactate and procalcitonin showed similar abilities in differentiating sepsis from non-infective SIRS in cancer patients [AUROCs of 0.638 (95%CI:0.527–0.739) vs 0.637 (95%CI:0.527–0.738), respectively. $p = 0.994$].

They were also similar in predicting poor clinical outcome with AUROCs of 0.629 (95%CI:0.518–0.731) and 0.584 (95%CI: 0.473–0.69), respectively ($p = 0.577$).

Conclusions: The results of this study indicated that, none of the lactate and procalcitonin can be recommended alone to differentiate sepsis from non-infectious SIRS and to predict the poor clinical outcomes in adult cancer patients with SIRS in the ED.

1. Introduction

Sepsis is defined as the presence of probable or documented infection together with systemic inflammatory response syndrome (SIRS).[1] Early diagnosis of sepsis and timely initiation of evidence-based treatment strategies are known to improve the clinical outcomes and to reduce sepsis-related mortality.[1,2]

The emergency department (ED) is a frequent first point of contact for cancer patients. Cancer patients are ten times more likely to develop sepsis since they are immunocompromised. In addition to be the most common comorbidity in septic patients, cancer is the highest risk factor for mortality in sepsis.[3] Early diagnosis of sepsis and distinguishing it from noninfectious processes are of paramount importance to initiate an appropriate treatment on time in these patients.[4] Besides its low specificity, the

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variable presentation of SIRS in cancer patients makes this distinction challenging for emergency physicians.[5,6] A biomarker can be very helpful in the appropriate management of these patients in the ED and may help to avoid unnecessary diagnostic tests, hospitalization, and unwarranted antimicrobial therapy.

There have been sufficient studies on diagnosis and prediction of severity for procalcitonin and lactate sepsis.[7,8] However, little is known about their utility in cancer patients.[9]

The aim of this study was to compare diagnostic and prognostic values of lactate and procalcitonin levels for sepsis in cancer patients presenting to ED with SIRS.

2. Materials and methods

2.1. Design and setting

This prospective case-control study was conducted in the ED of a teaching hospital in XXXX, Turkey between February 2014 and August 2014. Institutional ethics committee approval (Project Number: XXXX 2014/45) and written informed consent of patients were obtained.

The study site is a tertiary hospital in which about 2000 cancer patients receive care per year. The ED provides care for about 40,000 patients annually. An average of 10% of the ED patients is cancer patients.

2.2. Participants

The study group was composed of adult cancer patients who met at least two of the SIRS criteria presented to ED at times in which the principal investigator (EK) was accessible. Exclusion criteria were hematologic and thyroid malignancies, liver dysfunction, trauma patients, patients who presented to the ED because of seizure or missing data for follow-up. In addition, patients who were treated with intravenous fluid therapy of more than 500cc when they were determined as candidates for study, patients whose blood was obtained for lactate and procalcitonin levels, patients using antibiotics at presentation, or those receiving parenteral fluid therapy at home were also excluded.

2.3. Protocol

All cancer patients who met the inclusion criteria were recorded regardless of the complaint. Blood samples were taken for lactate and procalcitonin levels immediately, at the time that patients were identified to be eligible for the study. The procalcitonin levels were studied bedside using an immunoassay method and detected by an i-CHROMA Reader (Boditech Med. Inc., KOREA, 2013) device.

For procalcitonin levels, 2 cc blood taken into a mere vacuum tube was centrifuged for 10 min at 4000 rpm, then serum of 150 μL was taken and aliquoted into 1.5 mL tubes. An aliquot of 75 μL was used for the procalcitonin kit. After waiting 12 min, it was processed in the device and results were obtained in 5 s. The limits of detection were indicated as 0.25–100 ng/mL. The procalcitonin level of greater than 0.5 ng/ml was accepted as probable infection, and the level of greater than 10.0 ng/mL was accepted as severe sepsis or septic shock according to the manufacture protocol.

Lactate levels from radial artery blood administered to a heparin syringe of 2.5 cc was sent to the emergency laboratory pneumatically, followed by analysis with an electrode method by blind technicians using Radiometer ABL 700 Copenhagen (Denmark, 2012) device. The results of lactate levels were obtained as mg/dl, and were converted into mmol/L by multiplying by the constant '0.111' in order to compare with literature.

The presentation characteristics of patients, radiology and laboratory results data with emergency management, lactate levels, and ED outcomes were recorded by the caregiver emergency physician. These doctors were unaware of the procalcitonin levels. However, lactate levels were used in patient care without any changes specific to this study. Hospital database and phone contacts by the principal investigator with patients or their relatives were used for a 28-day follow-up. In addition, radiographic and laboratory data in the form of data were checked from the medical records and ED charts.

Patients whose probable cause of SIRS were assumed to be infection and had been verified clinically infected were accepted as sepsis. In this study, the presence of infection was decided by the lead investigator retrospectively with clinical evidence, laboratory findings, and imaging results based on the criteria of "International Sepsis Forum Consensus Conference on Definitions of Infection".[10] All inpatient and outpatient follow-up data were reviewed for evidence or probability of infection as defined by the consensus. Those for whom infection had not been considered or shown were determined as the 'sepsis negative group'. Intensive care unit (ICU) requirements or mortality were considered as "poor clinical outcome".

2.4. Outcome measures

The primary outcome was the detection of sepsis with lactate and procalcitonin levels. The secondary outcome was the comparison of utility of the biomarkers for predicting poor clinical outcomes.

2.5. Statistical analysis

Statistical analyses were performed using MedCalc for Windows, version 13.1.0.0 (MedCalc Software, Ostend, Belgium). All continuous variables were presented with 95% confidence intervals (CI). Categorical variables were expressed as percentages or ratios.

Independent samples t-test or Mann Whitney U test were used in the comparison of continuous variables between groups. Chi-square or Fisher's exact test were used in the comparison of categorical variables between groups where appropriate.

Sensitivity, specificity, positive and negative likelihood ratios (LRs) of markers at potential and determined thresholds were calculated with 95% CI. Diagnostic and prognostic performances of markers were assessed with Receiver operating characteristic (ROC) curve analysis. The area-under-the-curve (AUC) comparisons were conducted with nonparametric DeLong method which is used in the comparison of ROC curves of tests performed on the same individual. A p-value of 0.05 was considered statistically significant.

3. Results

Among 94 eligible patients, 86 were included in the study (Fig. 1). The median age of was 61 (95% CI: 58–64). The most common malignancy in this study was lung cancer. However, cancer stage data of half of the patients could not be achieved. A total of 39 patients (45.3%) had no comorbid diseases in the study group. The demographic and clinical characteristics are presented in Table 1.

Infection foci considered by the caregiver physician of patients were as follows: lung (n = 16), bladder (n = 6), gallbladder (n = 2), bowel (n = 2), tonsils (n = 1), and ear (n = 1). A total of 6 out of those (lung-4, bladder-1, bowel-1) were assessed as sepsis negative since it was not supported by clinical, laboratory, and radiological evidences in the retrospective evaluation. As a result, sepsis was observed in 22 (25.6%) of patients in the study group. There was a