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ORIGINAL ARTICLE

Urinary albumin/creatinine ratio as an early predictor of outcome in critically-ill septic patients

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Abstract Several cumbersome scoring systems were developed for prognosis and outcome prediction in sepsis. We intended in this study to evaluate the urinary albumin/creatinine ratio (ACR) as a prognostic predictor in sepsis.

We included 40 adult septic patients in a prospective observational study. We excluded patients with preexisting chronic kidney disease or diabetes mellitus.

After clinical evaluation, urine spot samples were collected on admission and 24 h later for ACR1 and ACR2. Admission APACHE IV score and the highest recorded SOFA score of their daily estimation were considered. We also evaluated the need for mechanical ventilation, inotropic and/or vasoactive support, renal replacement therapy (RRT), and in-hospital mortality.

In a population with 63 (55–71) year old with 29 (72.5%) males, we found that the ACR2 is correlated with the SOFA score ($r = 0.4$, $P = 0.03$). SOFA was higher in patients with increasing ACR [14(4.8–16.8) vs 5(3–8), $P = 0.01$]. None of the ACR measures was correlated with APACHE IV score. ACR2 was higher in patients who needed mechanical ventilation and inotropic and/or vasoactive support [140(125–207) and 151(127–218) mg/g respectively] compared to [65(47–174) and 74(54–162) mg/g], $P = 0.01$ and 0.009. None of the measured parameters was related to the need of RRT. ACR1, ACR2, APACHE IV and increasing ACR were predictors of mortality. The AUC for mortality prediction was largest for APACHE IV (0.90) then ACR2 (0.88). ACR2 of 110.5 mg/g was 100% sensitive and 86% specific to predict mortality.

We concluded that the urinary ACR may be used as a simple test for prognosis and mortality prediction in sepsis.

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1. Introduction

Sepsis occurs in 1–2% of all hospitalized patients and accounts for as much as 25% of ICU cases. In the United States, sepsis causes more than 200,000 deaths each year [1]. Sepsis is marked by a severe host defense response that involves

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triggering of potent inflammatory cascades which release a plethora of pro-inflammatory and anti-inflammatory molecules into the circulation [2]. The endothelial dysfunction is a milestone in sepsis pathogenesis. An early feature of sepsis is the loss of endothelial barrier integrity leading to systemic capillary leak [3]. This enhanced capillary permeability causes increased glomerular excretion of albumin in the urine [4]. Microalbuminuria has been accordingly seen by several studies to occur early after severe inflammatory process and to persist in more severe cases [5–8].

Early prediction of mortality among critically ill sepsis patients and early institution of intensive therapy are of paramount importance. Various intensive care units scoring systems like the Acute Physiology and Chronic Health Evaluation (APACHE) II, APACHE IV, and Simplified Acute Physiology (SAPS II) scores to predict mortality are in current use. These scoring systems require a large number of variables derived from the patient's history, examination, and initial laboratory data.

Microalbuminuria was shown to be promising as a predictor of organ failure, vasopressor requirement and mortality prediction. It was shown to be even better than APACHE II and SOFA scores in some studies [9–14].

We intended in our study to evaluate the prognostic value of urinary albumin/creatinine ratio (ACR) in patients with sepsis and to compare this prognostic value with the APACHE IV and Sepsis-related Organ Failure Assessment Score (SOFA) scoring systems.

2. Patients and methods

This is a prospective observational study that recruited all adult critically ill patients admitted to the surgical/medical ICU department, Electricity Hospital, Cairo, Egypt from May 2013 to May 2014. We included in the study patients with diagnosis of sepsis syndrome with the presence of SIRS based on the diagnostic criteria of 1992 ACCP/SCCM [15] and its update in 2001 International Sepsis Definition Conference [16], exhibiting two or more of the following signs: (1) temperature of >38 °C or <36 °C, (2) pulse rate of >90 beats/min, (3) respiratory rate of >20 breaths/min or hyperventilation with a $PaCO_2$ of <32 mmHg, or (4) white blood cell (WBC) count of $>12{,}000\ \mu L^{-1}$ or $<4000\ \mu L^{-1}$, or $>10\%$ immature cells. The presence of infection was defined according to the clinical and microbiological criteria of the Centers for Disease Control and Prevention (CDC) definitions [17] and was held as a gold standard. It was determined by two independent experts who examined the patients daily for the first 48 h of admission.

We excluded from the study patients less than 18 year old, patients with anuria or hematuria, patients with preexisting chronic kidney disease, patients with diabetes mellitus, patients with proteinuria due to renal or post renal causes, patients with urinary tract infection, and patients with ICU length of stay less than 24 h.

The study protocol was approved by the institutional review board at Cairo University together with representatives of study conduction site.

All included patients were subjected for clinical evaluation including history, physical examination, routine laboratory investigations (capillary blood glucose, coagulation profile, arterial blood gases, liver function tests, kidney function tests, random blood sugar, and serum electrolytes), and cultures from suspected sources of infection including sputum, urine, ... etc. together with at least two blood cultures obtained from different venipuncture were obtained prior to antibiotic administration.

APACHE IV score was calculated in an integer score form that is web based computed by applying worst values of the measurements observed during 24 h following ICU admission, with a maximum score of 286 [18]. The score was previously validated in sepsis patients [19].

The SOFA score is a scoring system to determine the extent of organ dysfunction [20]. SOFA score was evaluated daily until ICU discharge or demise or up to a total of 28 days. The highest recorded SOFA score was considered for statistical analysis.

Other parameters of disease severity that were studied included need for mechanical ventilation, need for inotropic and/or vasoactive support and need for renal replacement therapy (RRT). Outcome was evaluated by ICU length of stay (ICU-LOS) and the in-hospital mortality.

2.1. Urinary albumin creatinine ratio

Urine spot samples were collected at the time of ICU admission for Albumin Creatinine Ratio 1 (ACR1) and 24 h following ICU admission for Albumin Creatinine Ratio 2 (ACR2).

Urinary microalbumin was measured by the immunoturbidimetric method and urinary creatinine by modified kinetic Jaffe reaction (Dimension RxL Max, Dade Behring Inc., U.S.A.).

Trends of microalbuminuria was assessed as the change from ACR1 to ACR2. The difference between those values represents the delta albumin/creatinine ratio (Δ ACR) and is calculated as $\Delta\ ACR = ACR2 - ACR1$. When Δ ACR is negative, it is defined as decreasing ACR and when it is positive, it is defined as increasing ACR.

2.2. Statistical method

Data were prospectively collected and coded prior to analysis using the statistical package of social science (SPSS version 16). Normal distribution of different dependent variables in relation to their independent variables was studied. A variable was considered normally distributed if the Shapiro–Wilk's test had a $P > 0.05$ [21,22] and with z-value of skewness and kurtosis between -1.96 and $+1.96$ [23].

Our variables were found to be non-normally distributed. Continuous variables were accordingly expressed as median (Q1–Q3). Categorical variables were expressed as frequency and proportion. Nonparametric test (Mann–Whitney U test) was used for comparison between two groups as regards quantitative variable. Chi-Square Test (x^2) was used for comparison between two groups as regards qualitative data. Exact test was used instead when the expected frequency is less than 5. Spearman correlation coefficient test (r) was used to test a positive or negative relationship between two variables. Receiver operator characteristic (ROC) analysis was performed to define a cutoff value of a variable. Sensitivity was estimated as $\frac{\text{True positive}}{(\text{True positive}+\text{False negative})}$ and specificity was estimated as $\frac{\text{True negative}}{(\text{True negative}+\text{False positive})}$. Results were considered statistically significant if $P \leqslant 0.05$.