Research Journal of Clinical Pediatrics

Commentary A SCITECHNOL JOURNAL

A Prospective Cohort Study of Individuals with Albuminuria in Critical Illness

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Received date: 03 January, 2022; Manuscript No. RJCP-22-56271;

Editor assigned date: 05 January, 2022; PreQC No. RJCP-22-56271(PQ);

Reviewed date: 15 January, 2022; QC No RJCP-22-56271;

Revised date: 26 January, 2022; Manuscript No. RJCP-22-56271(R);

Published date: 02 February, 2022; DOI: 10.4172/rjcp.1000117.

Abstract

Purpose: To determine the course of albuminuria in critically sick patients and its relationship to the APACHE II score, SOFA score, infection markers, and outcome.

Methods: We Measured Albumin Creatinine Ratio (MACR) for all sequentially hospitalized ICU patients in a prospective cohort study. Gender, age, admission diagnosis, type of admission (medical, surgical), length of stay, and days of follow up were all recorded as baseline data. Medical and surgical subgroups, as well as diabetes and non-diabetes, were created from the cohort. When possible, patients were followed for ten days.

Results: A total of 150 individuals were included in the study, with a median age of 68.6 years. The patients' APACHE II scores were 20.5 and their SOFA scores averaged 5.0. In the first five days, the ACR rises in all patients. On day 1, the median ACR was 29.2 mg/mmol, and on day 5, the median ACR was 45.5 mg/mmol. The ACR reduced after day five for all subgroups except diabetes individuals. A significant association was found between mean ACR per patient and age (r=0.19), APACHE II (r=0.48), mean SOFA score (r=0.41), and serum creatinine (r=0.25) using Spearman rho correlation. A correlation between ACR and CRP was discovered only in surgical patients.

Serum creatinine is linked to ACR and acts as a confounder in the relationship between ACR and the SOFA score. There was no significant difference in mean micro albuminuria between survivors and non-survivors on the first day.

Conclusion: All critically ill patients ACR rises in the first five days. Except for diabetic and medical patients, there was a link between ACR and physiologic severity scores of disease.

Keywords: Albuminuria; Albumin creatinine ratio; Critically ill; Intensive care; Severity of disease

Introduction

When patients are brought to the Intensive Care Unit (ICU), clinicians face a difficult task: Predicting patient outcome. Several tools have been created for this goal over time. The Acute Physiology and Chronic Health Evaluation (APACHE) and Sepsis-related Organ Failure Assessment (SOFA) score systems are two examples of scoring systems.

These tools are complicated, despite their use. The APACHE score, for example, takes 24 hours to acquire the data needed to calculate prediction mortality. It might be possible to target our treatment interventions more precisely if we could identify individuals who are most at risk of major complications and bad outcomes sooner [1-3]. In addition to the existing scoring systems, there is a need for a non-invasive and direct way for quantifying the severity of sickness.

Micro albuminuria has been proposed as a prognostic marker in the ICU, for acute kidney injury in septic patients and in pediatric intensive care [4-9]. Critical illness is associated with endothelial dysfunction that results from a cytokine cascade following injury and infection. Increased capillary permeability to plasma proteins is a consequence [10]. The glomerulus will leak albumin as a reaction to increased endothelial permeability, which will cause (micro) albuminuria. Frequently, patients admitted to an ICU are coping with multiple organ failure including kidney failure. Because of this, there is a rationale for using kidney functions to score the severity of illness [11].

Few preliminary studies examined the use of albuminuria in the intensive care as a prognostic marker. In 2006, a study by Gosling concluded that urine albumin predicts ICU mortality and inotrope requirement as well as or better than APACHE II and SOFA scores [12]. A systematic review by Gopal 2006 describes that albuminuria may hold promise as a predictor of illness severity, and mortality on the intensive care. However, it was concluded that future studies need to be conducted to determine the optimal timing as well as the threshold reference value for the urine albumin creatinine ratio in the adult intensive care population [13].

In this prospective study we record the presence of albuminuria over time and study the association between albuminuria and the conventional severity of illness scoring systems (APACHE and SOFA), infection parameters (C-Reactive Protein (CRP) and White Blood Cell count (WBC)) and outcome.

Patients and Methods

In a teaching hospital with a 26-bed mixed medical-surgical tertiary ICU, a prospective cohort study was conducted. Patients over the age of 18 who had been in intensive care for a period of time were included. Patients with chronic kidney disease (creatinine levels greater than 177 mol/l) and those on chronic dialyses were excluded from the study. For practical reasons, the follow-up period was ten days or until the patient was discharged from the ICU.

Gender, age, admission diagnosis, type of admission (medical, surgical), length of stay, days of follow up, and outcome were all recorded as baseline data. The ICU and hospital databases were used to derive the results. The cohort was separated into two subgroups based on the kind of admission: Medical and surgical patients and diabetes and non-diabetic patients based on a documented diagnosis of

diabetes prior to ICU admission. Diabetes mellitus, hypertension, and renal function were all pre-defined potential confounders. After 24 hours in the ICU, the APACHE II score was calculated using the original definitions and the NICE data dictionary. The Albumin Creatinine Ratio (ACR), the Sepsis-related Organ Failure Assessment (SOFA), and plasma WBC count were all recorded daily from the enrolled patients using the XE-2100 automated blood cell counter.

Informed consent was waived by the ethical review board because of the observational design of the study in accordance with Dutch and European legislation.

Urine Analyses

Urine samples were collected daily at 9 am. Approximately 15 ml was extracted from the urinary catheter, and urine analysis was performed on the same day. Albumin and creatinine levels were analyzed on the modular analytics paralyzer (Roche Diagnostics), and the ACR was calculated. The ACR is the preferred test for diagnosis of albuminuria because it corrects for the confounding effect of variations in urine volume on the urine albumin concentration [14].

The normal rate of albumin excretion is less than 20 mg/mmol, persistent albumin excretion between 30 mg/mmol and 300 mg/mmol is in the literature defined as micro albuminuria. However, we defined albuminuria as any amount of albumin excretion in the urine.

Treatment: All patients were treated according to standard intensive care treatment according to national and international guidelines.

Statistical Analyses

Statistical analyses were performed with SPSS version 17.0 (SPSS Inc., Chicago, Illinois, USA). Data are expressed as mean and Standard Deviation (SD) for normally distributed data and as median and Inter Quartile Range (IQR) for skewed data. However, when the data from one patient is used as a variable, the arithmetic mean for that patient is used. A p-value less than 0.05 were considered statistically significant for all analyses.

Evaluation of an association between ACR and physiologic scores, markers of inflammation, plasma creatinine and outcome were made using the two-tailed Spearman rank correlation procedure [15]. Spearman rank correlation was used instead of Pearson correlation because of the non-normal distribution of the ACR values. Because ACR showed a skewed distribution, medians were compared between patient groups using the mann-whitney nonparametric test and between time points using the Wilcoxon signed rank test.

Univariate regression analyses were performed for categorical ACR in relation to SOFA score, WBC, CRP, diabetes mellitus, hypertension and plasma creatinine. The ACR categories were chosen based on the normal value of 3.4 mg/mmol. The presence of confounding for these relations was tested through logistic regression analyses. The same was done for the relation between ACR day one (ACR1) and APACHE II score.

Characteristics

During a two-month period 150 patients were included. One patient was excluded because of chronic kidney failure for which he received chronic dialyses. The remaining 149 patients had a mean age 68.6 range 31 years-88 years [16]. The patient group included 106 (71.2%) men and 43 (28.8%) women. All patients were treated with vasoactive medication (noradrenalin, dopamine or enoximone) and nearly all patients were mechanically ventilated. There were no differences in ACR between men and women. Spearman rho correlation showed a significant correlation between mean ACR per patient and age (r=0.19), APACHE II (r=0.48), mean SOFA score (r=0.41) and serum creatinine (r=0.25). APACHE II score, ICU stay, ACR, SOFA and predictive mortality for the categories surgical and medical, diabetes and non-diabetes [17]. The surgical patient group included mainly patients after heart valve replacement (76 patients). In addition, 9 patients after gastrointestinal surgery, 8 patients after major vascular surgery, and 4 miscellaneous. The medical patient group consisted of patients with respiratory failure (11 patients), cardiogenic shock (11 patients), sepsis (9 patients), and pulmonary infection (7 patients), after cardiac arrest (6 patients), intoxication (2 patients) and miscellaneous (8 patients). Approximately 27% of the patients had diabetes and 32% had preexisting hypertension. The median admission creatinine was 83 (IQR 36 μmol/L. 19% had a pre-admission creatinine of >120 μmol/L).

Discussion

This study showed that the ACR of the cohort decreases between the first and the second day but increases until day 5 of ICU treatment in all patient groups. This is followed by a decrease in all patients except for the patients suffering from diabetes mellitus. ACR may be a marker of endothelial dysfunction caused by the primary insult and the subsequent inflammation. This inflammation wanes in several days resulting in a decreased ACR. The observation of an increasing ACR until day 5 is in conflict with a conclusion drawn by Gosling et al. [18]. This author concluded that the ACR decreases significantly after four to six hours. This contradiction may in part be explained by the differences in baseline characteristics between these study populations. Our study was different in two respects. First, the mean age in the Gosling study is 55.5 years versus 68.6 years in our study. We did confirm the finding in the Gosling study that showed that urine albumin on ICU admission increased significantly with patient age. Second, patients in the Gosling study had lower median APACHE scores then in our study, 18.0 versus 20.5. The current study established a significant relation between ACR and APACHE II score. This could be an explanation for the higher ACR values in the current study.

Conclusion

The goal of this observational study was to describe the progression of microalbuminuria across time. In contrast to earlier research, it was discovered that the mean ACR increased in all patients until day 5. Except for diabetic and medical patients, the ACR is substantially associated with the APACHE II score. A substantial relationship between ACR and CRP was discovered in surgical patients. Plasma creatinine has been found to be a confounder in the ACR-SOFA relationship. There was no significant difference in mean albuminuria between survivors and non-survivors on the first day. Although the ACR in the urine is linked to disease severity, it cannot be utilized as a routine prognostic measure.

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