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Original article

Low caloric and protein intake is associated with mortality in patients with acute kidney injury

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SUMMARY

Background: Acute renal injury (AKI) interferes greatly with nutritional status, affecting the metabolism of all macronutrients and increased mortality rates in hospitalized patients. Our objective was to evaluate the association of nutritional parameters (albumin, cholesterol, caloric and protein intake and nitrogen balance (NB)) with mortality in patients with AKI.

Methods: This is a prospective observational study that evaluated 595 consecutive patients over the age of 18 years with AKI, requiring enteral or parenteral feeding. At the time of the patient's enrollment, demographic and laboratorial data, caloric and protein supply and NB were recorded on the first day of referral to the nephrologist. All patients were followed throughout the hospital stay and mortality rate was also recorded.

Results: The medium age of patients with AKI was 64 (54–75) years, 64.5% male, 62% admitted to intensive care unit (ICU), 52% on dialysis and the majority (48%) were at stage 3 by AKIN. Length of stay and hospital mortality were 18 (10–31) days and 46%, respectively. Superior age, AKI severity, lower body weight and body mass index (BMI), higher need for dialysis, ICU admission and shorter hospital stay were associated with higher mortality. At logistic regression, caloric (OR: 0.946; CI:95%: 0.901–0.994; *p*:0.029) and protein intake (OR: 0.947; CI:95%: 0.988–0.992; $p = 0.028$) and serum albumin (OR: 0.545; CI:95%: 0.401–0741; $p < 0.001$) were associated with hospital mortality. Cholesterol (OR: 0.995; CI:95%: 0.991–1.000; $p = 0.052$) was not associated with increased mortality in the adjusted analysis. Analysis of the receiver operating characteristic (ROC) curve showed that calorie intake < 12 kcal/kg (AUC: 0.745; CI:95%: 0.684–0.765; $p < 0.001$) and protein intake < 0.5 g/kg (AUC: 0.726; CI:95%: 0.686–0.767; $p < 0.001$) were predictors of hospital mortality, as well as a negative NB < −6.47 g N/day (AUC: 0.745; CI:95%: 0.704–0.786; $p < 0.001$).

Conclusions: In conclusion, low caloric and protein intake, negative NB and low albumin value are conditions associated with higher hospital mortality in patients with AKI.

1. Introduction

Acute renal injury (AKI) is a clinical condition associated with increased mortality rates in hospitalized patients [1]. Its diagnosis is usually based on elevated serum creatinine and/or detection of oliguria [2]. In addition to contributing to increased morbidity and mortality, AKI interferes greatly with nutritional status by providing a pro-inflammatory and pro-antioxidant state, affecting the metabolism of all macronutrients, culminating in body mass depletion [3].

In a classic study by Fiaccadori et al. in 1999 [4], the complete nutritional status of more than 300 patients with AKI was evaluated. In the results, the authors identified the influence of severe malnutrition diagnosed by subjective global assessment with a higher incidence of acute complications, days of hospitalization and mortality. Since then, other studies with smaller numbers of patients have been developed in order to find associations of nutritional parameters with adverse outcomes.

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Some nutritional conditions are associated with higher mortality in this population, such as severe malnutrition, low caloric supply, negative nitrogen balance (NB), hypoalbuminaemia, hypocholesterolaemia and less resistance measured by electrical bioimpedance [4–8]. Although some studies demonstrate the association of these nutritional parameters with survival, regardless of interference such as the presence of edema or inflammation, in practice, the use of these parameters as nutritional markers is still questionable.

Considering the limitations of the majority of conventional methods of nutritional assessment caused by the alteration in volume and/or inflammatory status, identification of the degree of catabolism through the calculation of NB has been pointed out as a more reliable and consolidated measure to monitor nutritional adequacy in this population [9,10].

Thus, the objective of our study was to evaluate the association of nutritional parameters as albumin, cholesterol, caloric and protein intake and nitrogen balance with mortality in patients with AKI.

2. Materials and methods

This prospective observational study was conducted from March 2011 to December 2014 with patients admitted to the Clinical Hospital of Botucatu Medical School of the State University of São Paulo, accompanied by the AKI Group of the Nephrology discipline of the Department of Clinical Medicine. The protocol was approved by the Ethics Committee of our institution (protocol number 3938-2011). Written informed consent was obtained from all patients or relatives prior to their inclusion in the study.

Patients were eligible for enrollment if they were 18 years or older, diagnosed with AKI according to the acute kidney injury network (AKIN) criteria [2], with clinical characteristics suggestive of acute tubular necrosis (ATN), requiring renal support therapy (hemodialysis (HD) or high volume peritoneal dialysis (HVPD)), enteral or parenteral feeding and a minimum follow-up of 24 h after referral to the nephrologist. Patients with AKI of other etiologies, advanced chronic renal failure (baseline serum creatinine > 4 mg/dL) or a need for chronic renal replacement therapy (dialysis or renal transplantation) were excluded.

2.1. Study protocol

Patients included were submitted to a study protocol consisting of clinical and laboratory data, caloric and protein supply data, urea nitrogen appearance (UNA) and NB. Data were recorded on the first day of referral to the nephrologist. All patients were followed during their hospital stay and mortality rate and the length of the hospital stay were also recorded.

For analysis of nutritional intake, the amount of protein (g) and total calories (kcal) offered by industrialized formulas according to enteral and parenteral feeding patterns were considered. Total serum levels of C-reactive protein (CRP), cholesterol, albumin, creatinine and urea were measured using the dry chemistry method (Ortho-Clinical Diagnostics VITROS 950®, Johnson & Johnson).

UNA and NB: calculated daily using the following formulas [3]:

$$\begin{aligned}\text{NB} &= \text{dietetic nitrogen} - (\text{UNA} + \text{sensible losses}) \\ &\quad + \text{faecal losses (2 g) UNA (g/day)} \\ &= \text{urinary ureic nitrogen losses} \\ &\quad + \text{variation of serum urea nitrogen} \\ &\quad + \text{dialysate nitrogen (g/day)}\end{aligned}$$

$$\begin{aligned}\text{UNA} &= (\text{UUN} \times \text{V}) + (\text{SUN2} - \text{SUN1}) \times 0.006 \times \text{BW} \\ &\quad + (\text{BW2} - \text{BW1}) \times \text{SUN2}/100 + (\text{DN} \times \text{VD})\end{aligned}$$

Insensible losses [11]: $0.031 \times \text{BW}$

$$\text{RPCn} = (\text{UNA} \times 6.25)/\text{BW}$$

NB: nitrogen balance; UNA: urea nitrogen appearance; UUN: urinary urea nitrogen (g/day); V: volume of urine (L); SUN1 and SUN2: serum urea nitrogen (mg/dL) on days 1 and 2; BW: body weight (kg); DN: dialysate nitrogen (g/L); VD: volume of dialysate (L); RPCn: normalized rate of protein catabolism.

2.2. Statistical analysis

Data are expressed as the mean ± standard deviation (SD), median (including the lower and upper quartiles) or percentage. Comparisons between two groups for continuous variables were performed using the Mann–Whitney test. Comparisons between two groups for categorical variables were performed using the χ^2 test or Fisher's exact test. A logistic regression model was used to predict mortality. NB, protein and caloric supply, albumin and cholesterol were tested as continuous independent variables. These variables were adjusted with parameters that exhibited significant differences in the univariate analysis and did not exhibit high collinearity among them.

A receiver operating characteristic (ROC) curve was constructed to identify the cut-off of the nutritional parameters mentioned above associated with mortality. The parameters were tested as continuous variables. Data analysis was performed using Sigma Plot software for Windows v12.0 (Systat Software Inc., San Jose, CA, USA). p Values lower than 0.05 were considered statistically significant.

3. Results

A total of 595 patients with an average age of 64 (54–75) years, 64.5% male, 62% admitted to ICU and 52% on dialysis were included in the study. Regarding classification by AKIN stage, 77 (13%) were at stage 1, 232 (39%) at stage 2 and the majority, 286 (48%) patients, were at stage 3. Length of stay and hospital mortality were 18 (10–31) days and 46%, respectively. The hospitalization period prior to referral to the nephrologist was 6 (3–13) days.

Table 1 describes the clinical data of the patients divided according to evolution to death. Superior age, AKI severity, lower body weight and body mass index (BMI), higher need for dialysis, intensive care unit (ICU) admission and shorter hospital stay were associated with higher mortality.

Comparing the laboratory data, dietary intake and catabolism of patients through univariate analysis, as shown in Table 2, it is observed that lower concentrations of albumin an cholesterol and higher concentrations of CRP and urea were associated with increased mortality. Lower caloric and protein intake as well as a more negative NB were also associated with mortality.

In the logistic regression model (Table 3), three of the five nutritional parameters evaluated were associated with hospital mortality, even when adjusted for sex, age, and CRP, caloric (OR: 0.946; CI:95%: 0.901–0.994; p: 0.029) and protein intake (OR: 0.947; CI:95%: 0.988–0.992; $p = 0.028$) and serum albumin (OR: 0.545; CI:95%: 0.401–0.741; $p < 0.001$). Although the serum concentrations of cholesterol were also associated with mortality, this relationship was not maintained after correction for the confounding variables.

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