Pre-albumin is a strong prognostic marker in elderly intensive care unit patients

Abstract

Objectives: Pre-albumin (PAB) can be used to evaluate the association between nutrition status and in-hospital mortality. However, there is no literature to compare if PAB is the best indicator to predict in-hospital mortality among the nutrition indexes in a study.

Methods: We operated a retrospective study including 145 patients admitted to our institution’s elderly intensive care unit (ICU) from January, 2017 to December, 2019. Admission laboratory results were collected. Regression analysis and receiver operating curve (ROC) were analyzed to explore the performance of different nutrition indexes.

Results: The levels of PAB were significantly different between the survivor and non-survivor group (p=0.001). Univariate analysis showed nutrition indexes (lymphocytes, albumin, body mass index [BMI], geriatric nutritional risk index (GNRI), prognostic nutritional index [PNI] and PAB) were associated with in-hospital mortality (all p<0.1). Following adjustment for age, platelets and creatinine (CREA), only BMI and PAB remained statistically significant (BMI: HR 2.799, 95% CI 1.167–6.715, p=0.021; PAB: HR 6.329, 95% CI 2.660–15.151, p<0.001). In addition, PAB had the highest area under the curve (AUC) for predicting in-hospital mortality (AUC = 0.696) followed by BMI (AUC = 0.561) and other factors.

Conclusions: PAB is a better predictor of in-hospital mortality than other nutrition indexes in elderly ICU patients.

Keywords: elderly; in-hospital mortality; intensive care unit; pre-albumin.

Introduction

Intensive care unit (ICU) patients are often coupled with one or more system dysfunctions, acute illness, immobility and impaired diet, causing poor nutrition status. Thus, malnutrition is common in ICU patients [1]. Advanced age, persistent eating disorders and accompanied by comorbidities, leading to aggravation of malnutrition [2]. It is pointed out that malnutrition is a risk factor to predict ICU patients with poor outcomes [3]. During hospital, active and effective nutrition supplement can ameliorate the treatment effect and reduce the occurrence of complications. So it is necessary to assess the nutritional status of ICU patients when admission; however, the levels of nutritional indices are affected by diet, inflammation or/and insufficient organ function, monitoring the nutritional status is challenging.

Serum albumin, lymphocytes and body mass index (BMI) are indicators of nutritional status [4, 5]. Nutritional indices (geriatric nutritional risk index [GNRI], prognostic nutritional index (PNI)) are also useful prognostic markers for diseases [4]. Serum pre-albumin (PAB) level is closely linked to metabolism in the body [5]. However, there are few studies to clarify which of these nutritional indices is the best prognostic marker for patients, especially in elderly ICU. Thus, in the study, we seek to discuss and compare those factors in elderly ICU patients.

Materials and methods

Patients

We operated a retrospective observational study including 145 patients admitted to our institution’s elderly ICU from January 2017 to December 2019. Patients with admission laboratory results were included. Patients with age <18 years old or incomplete data were excluded. For patients admitted multiple times within 30 days, only the first admission data were extracted and analyzed. Follow-up results were checked from medical records or telephone contacts. The outcome evaluated was in-hospital mortality. The investigation was in line with the Declaration of Helsinki and authorized by the local Institutional Review Board (Nanjing, China).

Data collection

The following factors were collected: gender, age, body weight, white blood cell (WBC), lymphocytes, neutrophils, hemoglobin (HB),
platelets, alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin, creatinine (CREA). Nutritional indices were calculated as follows: (1) GNRI = 14.89 × Alb (g/dL) + 41.7 × (body weight/ideal body weight) [6]. The ideal body weight was defined as (height [m])² × 22. (2) PNI = 10 × albumin (g/dL) + 0.005 × lymphocytes (× 10⁹/L) [7].

### Statistical methods

Categorical variables and continuous variables are presented as frequencies and percentages (n, %) or median with inter-quartile range (IQR). Student's t test or Mann–Whitney U test was used for comparisons of continuous data with or without normal distribution, while the chi-square test was used for comparisons of categorical variables. Bivariate and multivariable analyses were used to assess the relationship between variables and in-hospital mortality. IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp.Armonk, NY, USA) were used for statistical analyses.

### Results

#### Patient characteristics

A total of 145 patients were included in this survey. Sixty (41.4%) patients died in the hospital before discharging. There were 94 males (64.8%) and 51 females (35.2%); respiratory diseases (72.1%) was the most common syndromes at admission, followed by hypertension (38.6%), renal disease (22.6%) and diabetes mellitus (21.4%). Compared with survivor group, the median age (71 [25–96] vs. 67 [23–91]), the levels of ALT (20.4 [2.30–4,102.10] vs. 25.2 [2.20–317.60]) and CREA (123.51 ± 105.32 vs. 82.24 ± 49.57) were higher and the levels of PAB (0.118 ± 0.082 vs. 0.167 ± 0.088) were lower in the non-survivor group (p<0.038; p=0.023; p<0.002 and p<0.001, respectively). There were no significant differences in the levels of WBC, lymphocytes, neutrophils, HB, platelets, AST, albumin, CREA, BMI, GNRI and PNI between the two groups (all p>0.05) (Table 1).

### Univariate and multivariate analyses of risk factors

Continuous variables were transformed into binary variables with the value of clinically recognized or calculated with ROC. Table 2 showed the results of the analysis. In the univariate analysis, age, lymphocytes, albumin, CREA, BMI, GNRI, PNI and PAB were associated with in-hospital mortality (all p<0.1). Multivariate analysis was adopt to select independent factors, the results expressed that only age (HR: 5.584, 95% CI 1.373–22.706, p=0.016), CREA

### Table 1: Baseline patients’ characteristics.

| Variable        | Survival group n=85 | Non-survival group n=60 | p-Value |
|-----------------|----------------------|--------------------------|---------|
| Gender, %       | Gender male          | 52 (63.41%)              | 42 (70.00%) | 0.276 |
| Median age (range), year | 67 (23–91)         | 71 (25–96)               | 0.038   |
| Body weight, kg | 60.73 ± 13.27        | 62.00 ± 11.64            | 0.548   |
| WBC, ×10⁹/L     | 11.56 ± 6.17         | 11.59 ± 6.06             | 0.977   |
| Lymphocytes, ×10⁹/L | 1.04 ± 0.56       | 0.88 ± 0.64              | 0.113   |
| Neutrophils, ×10⁹/L | 9.85 ± 5.81       | 10.11 ± 5.88             | 0.778   |
| HB, g/L         | 109.62 ± 24.56       | 112.00 ± 24.51           | 0.567   |
| Platelets, ×10⁹/L | 174.89 ± 96.21      | 161.43 ± 96.98           | 0.410   |
| ALT, U/L        | 25.2                 | 20.4                     | 0.023   |
| AST, U/L        | (2.20–317.60)        | (2.30–4,102.10)          |         |
| ALB, g/L        | 32.4                 | 36.4                     | 0.079   |
| CREA, µmol/L    | 31.17 ± 7.20         | 29.50 ± 5.64             | 0.131   |
| BMI, kg/m²      | 82.24 ± 49.57        | 123.51 ± 105.32          | 0.002   |
| GNRI            | 21.89 ± 4.34         | 22.49 ± 3.84             | 0.390   |
| Platelets, ×10⁹/L | 505.58 ± 110.69     | 481.81 ± 80.57           | 0.158   |
| ALT, U/L        | 316.86 ± 72.46       | 299.34 ± 54.45           | 0.115   |
| AST, U/L        | 1,067 ± 0.088        | 0.118 ± 0.082            | 0.001   |

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CREA, creatinine; CI, confidence interval; GNRI, geriatric nutritional risk index; HB, hemoglobin; PAB, pre-albumin; PNI, prognostic nutritional index; WBC, white blood cell.

### Table 2: Univariate and multivariate analyses of in-hospital mortality in critically unites patients.

| Variable | Univariate analysis | Multivariate analysis |
|----------|---------------------|-----------------------|
|          | HR                  | p                     | HR                  | p         |
| Gender   | 1.481               | 0.294                 | 5.584               | 0.016     |
| Age      | 6.234               | 0.001                 |                      |           |
| Body weight | 1.686               | 0.162                 |                      |           |
| WBC      | 1.012               | 1.000                 |                      |           |
| Lymphocytes | 2.299               | 0.032                 |                      |           |
| Neutrophils | 1.422               | 0.441                 |                      |           |
| HB       | 1.651               | 0.177                 |                      |           |
| Platelets | 1.984               | 0.056                 |                      |           |
| ALT      | 1.052               | 1.000                 |                      |           |
| AST      | 1.203               | 0.616                 |                      |           |
| Albumin  | 9.708               | 0.015                 |                      |           |
| CREA     | 2.374               | 0.041                 | 3.301               | 0.018     |
| BMI      | 2.000               | 0.075                 | 2.799               | 0.021     |
| GNRI     | 4.082               | 0.005                 |                      |           |
| PNI      | 3.086               | 0.008                 |                      |           |
| PAB      | 4.386               | <0.001                | 6.329               | <0.001    |

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CREA, creatinine; CI, confidence interval; GNRI, geriatric nutritional risk index; HB, hemoglobin; HR, hazard ratio; PAB, pre-albumin; PNI, prognostic nutritional index; WBC, white blood cell.
(HR: 3.301, 95% CI 1.229–8.862, p=0.018), BMI (HR: 2.799, 95% CI 1.167–6.715, p=0.021) and PAB (HR: 6.329, 95% CI 2.660–15.151, p<0.001) were independent factors (Table 2).

Performance of different nutritional factors

Receiver operating characteristic (ROC) was selected to calculate the predictive values of in-hospital mortality for different nutritional elements. The results showed that the area under the curve (AUC) of PAB was 0.696 (95% CI 0.607–0.785, p=0.045) (Figure 1) (Table 3), which was obviously superior than those of PNI, GNRI, BMI and albumin in cohort (PNI: AUC 0.571, 95% CI 0.478–0.664, p=0.047; GNRI: AUC 0.561, 95% CI 0.468–0.654, p=0.047; BMI: AUC 0.639, 95% CI 0.545–0.732, p=0.005; albumin: AUC 0.568, 95% CI 0.475–0.660, p=0.047).

Discussion

The results of this investigation suggest that the levels of PAB in the survivor group were higher than that in non-survivor group. In addition, PAB is an independent and best biomarker to predict in-hospital mortality among various nutritional indices.

There is a relationship between PAB and inflammation/nutrition to nutrition support therapy in adult critically ill patients [8]. Previous studies exhibited that a decline in serum PAB was independently associated with increased death risk in hemodialysis patients and critically ill patients [5, 9]. This was consistent with our results. Thus, PAB can not only be used as an indicator of the nutritional status and inflammation, but also as an indicator of in-hospital of mortality. That is to say, to ICU patients, physicians should pay more attention to patients with low PAB when patients are admitted to the hospital. For inpatients, PAB can also be used for treatment monitoring. Physicians can use PAB to evaluate treatment effect through a single measurement or series measurements: when the single value is low or a decrease of PAB during hospital stay, it is necessary to consider whether the treatment plan is suitable for the patient.

Currently, BMI is commonly used as an international standard to measure the degree of body weight and health and is associated with a risk of death in diseases such as heart failure (HF) and COVID-19 Infection [10–12]. But none of these studies included PAB and made a comparison with BMI.

In this study, we first compared the predictive effects of different nutritional indexes on the in-hospital mortality of ICU patients. The results showed that lymphocyte, albumin, BMI, GNRI, PNI and PAB were related to patients’ in-hospital mortality. Then multivariate analysis found that only BMI and PAB can be independent risk factors without interference from other factors. At last, we did ROC analysis, and the prediction effect of PAB was significantly better than other nutritional indexes. Therefore, PAB should be used as a predictor of in-hospital mortality in ICU patients and the predictive value of PAB is the best among many nutritional indexes.

There are several limitations of our study. Because of the retrospective design, there are numerous confounding variables that affect nutritional indexes that it was infeasible to control, such as premorbid malnutrition and medicine use. C-reactive protein or other markers of inflammation (interleukin-6) are not included as these markers are not routinely gained in ICU patients. Furthermore, we did not

Table 3: Performance of independent factors.

| Variable   | AUC   | 95%CI          | p-Value |
|------------|-------|----------------|---------|
| Albumin    | 0.568 | 0.475–0.660    | 0.047   |
| BMI        | 0.561 | 0.467–0.656    | 0.048   |
| GNRI       | 0.561 | 0.468–0.654    | 0.047   |
| PNI        | 0.571 | 0.478–0.664    | 0.047   |
| PAB        | 0.696 | 0.607–0.785    | 0.045   |

AUC, area under the curve; BMI, body mass index; CI, confidence interval; GNRI, geriatric nutritional risk index; PAB, pre-albumin; PNI, prognostic nutritional index.
verify our conclusion in another cohort. Therefore, we look forward to a prospective, large-scale study to verify our conclusions.

Conclusions

Our study suggests that PAB, the best marker, could be useful for comprehensive clinical evaluation and prediction of in-hospital mortality in ICU patients. Especially, low PAB could independently predict worse prognosis.

Research funding: None declared.

Author contributions: All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Competing interests: Authors state no conflict of interest.

Informed consent: Informed consent was obtained from all individuals included in this study.

Ethical approval: Research involving human subjects complied with all relevant national regulations, institutional policies and is in accordance with the tenets of the Helsinki Declaration (as revised in 2013), and has been approved by the authors’ Institutional Review Board.

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