Determinants of prognosis in geriatric patients followed in respiratory ICU; either infection or malnutrition

Guler Eraslan Doganay, MD, Mustafa Ozgur Cirik, MD

Abstract
Severity of illness, age, malnutrition, and infection are the important factors determining intensive care unit (ICU) survival.

The aim of the study is to determine the relations between Geriatric Nutritional Risk Index (GNRI), C-reactive protein/albumin (CAR), and prognosis-mortality of geriatric patients (age of ≥65 years) admitted to intensive care unit.

The study with 10/15/2020, 697 approval date, and number retrospectively registered. Between January 1, 2018 and December 31, 2019, 413 geriatric patients admitted to ICU. The patients were divided into three groups according to their age.

The age group, gender, Charlson comorbidity index, intensive care scores (Acute Physiology And Chronic Health Evaluation II and Sequential Organ Failure Assessment), the infection markers (white blood cell, procalcitonin, CAR levels), malnutrition tools for each patient (body mass index, Nutrition Risk in Critically ill score, and GNRI scores) were analyzed retrospectively. Also length of stay (LOS) ICU, length of stay hospital, and 30-day mortality were recorded.

Geriatric patients number of 403 was included in the study. Forty-nine (12.3%) patients had a history of malignancy, 272 (67.5%) patients had Chronic Obstructive Pulmonary Disease comorbidity. There was no difference in mortality between age groups.

In patients with mortality, body mass index, had being Chronic Obstructive Pulmonary Disease history, GNRI, length of stay hospital, and albumin were significantly lower; malignancy comorbidity rate, inotrope use, modified Nutrition Risk in Critically Ill score, mechanical ventilation duration, LOS ICU, Sequential Organ Failure Assessment, Acute Physiology And Chronic Health Evaluation II, Charlson comorbidity index, C-reactive protein, procalcitonin, and CAR were significantly higher. Both malnutrition and infection affect mortality in geriatric patients in intensive care. The GNRI is better than CAR at predicting mortality.

Abbreviations: APACHE II = Acute Physiology And Chronic Health Evaluation II, BMI = body mass index, CAR = CRP/albumin ratio, CCI = Charlson comorbidity index, COPD = Chronic Obstructive Pulmonary Disease, CRP = C-reactive protein, GNRI = Geriatric Nutritional Risk Index, ICU = intensive care unit, LOS H = length of stay hospital, LOS ICU = length of stay ICU, mNUTRIC score = modified Nutrition Risk in Critically Ill score, MV = mechanical ventilation, NUTRIC score = Nutrition Risk in Critically Ill score, SOFA = Sequential Organ Failure Assessment.

Keywords: CAR, geriatric patients, GNRI, ICU, infection, nutrition
1. Introduction

Nowadays with the increase in average life expectancy and decrease in birth rates, the elderly population in the society increases and also the rate of geriatric patients in intensive care units is increasing day by day. It is reported that the number of persons aged 60 or over is expected to more than twice by 2050 compared to 2017.[1] In our country, the rate of elderly people was 5.3% in 2000.[2]

Severity of illness, age, malnutrition, and infection are the important factors determining intensive care unit (ICU) survival. There are many comorbidities that increase the mortality rate in the geriatric population.[3] Additionally, the incidence of sepsis increases with age, the ages over than 80 is associated with extremely high mortality rates.[4]

C-reactive protein (CRP) is an acute phase reactant and indicates inflammation due to infection. Albumin is an indicator of malnutrition and the ratio of CRP/albumin (CAR) has recently been evaluated as a prognostic marker for mortality in sepsis.[5,6] Elderly patients are vulnerable to infection, and nutritional condition is very important predictive factor.

While elderly patients hospitalized in intensive care are treated for primary disease, malnutrition may be overlooked. In evaluating the nutritional status of patients, all clinical findings should be taken into consideration; both anthropometric methods and screening tools should be used. The Geriatric Nutritional Risk Index (GNRI) is a tool to determine the nutritional status of elderly people based on their albumin level, current weight, and ideal weight.[7]

Although it is known that malnutrition and infection adversely affect the prognosis of geriatric patients [8], it has not been reported which one has more effect. In this study, we aimed to determine the possible relations between GNRI, CAR, and prognosis-mortality of geriatric patients admitted to intensive care unit.

2. Materials and methods

The study was designed retrospectively and initiated after approval from the Medical Specialization Training Board of Ataturk Chest Diseases and Thoracic Surgery Training and Research Hospital (approval date and number: 15/10/2020, 697). Between January 1, 2018 and December 31, 2019; consecutive 561 patients admitted to respiratory ICU. Four hundred thirteen of them were geriatric patients (age of 65 years). Patients with hyponatremia (135 mmol/L), hypernatremia (145 mmol/L), severe liver disease, and severe kidney failure (creatinine clearance < 15 mL/min) were excluded from the study to rule out albumin changes not related to malnutrition (n: 7). Also the patients had missing data (n: 3) were excluded from the study (Fig. 1). The number of patients were 403 included in the study.

The patients were divided into three groups according to their age; 65 to 74 early elderly, 75 to 84 advanced elderly, and 85 and over very advanced elderly.

The age group, gender, Charlson comorbidity index (CCI), Intensive care scores (Acute Physiology And Chronic Health Evaluation II [APACHE II] and Sequential Organ Failure Assessment [SOFA]), the infection markers (white blood cell, procalcitonin, CAR levels), malnutrition tools for each patient (body mass index [BMI], Nutrition Risk in Critically ill score [NUTRIC], and GNRI scores) were analyzed retrospectively.

Also length of stay (LOS) ICU, length of stay hospital (LOS H), and 30-day mortality were recorded.

We calculated GNRI values according to Bouillanne et al[9];
\[ \text{GNRI} = \frac{1.489 \times \text{serum albumin level (g/L)} + 41.7 \times (\text{actual bodyweight/ideal bodyweight})}{\text{actual bodyweight/ideal bodyweight}} \]

If the actual body weight is higher than ideal bodyweight, the ratio (actual bodyweight/ideal bodyweight) is taken as 1.

We evaluate GNRI values as severe risk (GNRI < 82), moderate risk (GNRI 82–92), low risk (GNRI 92–98), and no risk (GNRI > 98).

2.1. Statistical analysis

Data analyses were performed using SPSS for Windows, version 22.0 (SPSS Inc., Chicago, IL). Whether the distribution of continuous variables was normal or not was determined by Kolmogorov-Smirnov test. Levene test was used for the evaluation of homogeneity of variances. Unless specified otherwise, continuous data were described as mean ± standard deviation and median (minimum value–maximum value) or categorical data were described as number of cases (%). Categorical variables were compared using Pearson’s chi-square test or fisher’s exact test. Statistical analysis differences in not normally distributed variables between two independent groups were compared by Mann–Whitney U test. It was evaluated degrees of relation between variables with point biserial correlation and spearman correlation analysis. First of all it was used one variable multinomial logistic regression with risk factors that is thought to be related with mortality. Variables with a p value below 0.25 in univariate logistic regression analysis were included in multivariate logistic regression analysis. Whether every independent variables were significant on model was analyzed with Wald statistic. It was evaluated with Nagelkerke R² how much independent variable explained dependent variable. Besides, it was evaluated model adaptation of estimates with Hosmer and Lemosow model adaptation test. ROC curve analysis was used to determine the cut-off points for mortality. It was accepted P-value < .05 as significant level on all statistical analysis.

3. Results

Geriatric patients number of 403 was included the study. The males were 229 (56.8%), female were 174 (43.2) of them. Forty-nine (12.3%) patients had a history of malignancy, 272 (67.5%)
There is a statistically significant correlation between CAR and intrope use and MV duration in the same direction. As CAR increases, the duration of receiving introp support and MV increases. There is no statistically significant relation between CAR and LOS ICU or LOS H. There is a low statistically significant correlation between procalcitonin and introp use, MV duration, and LOS ICU. As procalcitonin increases, intrope use, MV duration, and LOS ICU increase. There is no statistically significant relation between white blood cell and the prognostic parameters (Table 2).

There is a statistically significant correlation between ICU severity scores (APACHE II, SOFA) and intrope use, MV duration, and LOS H in the same direction (Table 2).

To determine the factors affecting mortality, firstly, single variables logistic regression analysis was applied (Univariate Analyze). Variables with P < .25 in univariate logistic regression analysis were included in multivariate logistic regression analysis. The backward LR method was used for multivariate logistic regression analysis. The results of Step 11, which is the last step of the analysis, are given in the table. According to the results, it was understood that CAR, SOFA, CCI, procalcitonin, length of hospital stay, MV, and COPD affect mortality. The increase in CAR, SOFA and CCI, procalcitonin and decrease in hospital stay and MV, and not having COPD increase mortality (Table 3).

A ROC curve analysis was applied in order to provide a cut-off value for the success of GNRI and CAR values in predicting
mortality. It is observed that GNRI can differentiate in determining the mortality risk, that is, it can classify the patients correctly at a rate of 68.9% (medium level). In order to answer the question of which value should be taken as the cut-off value for this test, each sensitivity and specificity values given as a result of the analysis were examined and the optimum point was chosen. While the sensitivity value was 71% and the specificity value was 61.3%, the cut-off value was found to be 85.79. As a result, the risk of mortality was higher in cases with GNRI 85.79 and below (Fig. 3).

It shows that CAR can differentiate in determining the risk of mortality in cases, that is, it can classify patients correctly at a rate of 61.6% (moderate). In order to answer the question of which value should be taken as the cut-off value for this test, each sensitivity and specificity values given as a result of the analysis were examined and the optimum point was chosen. While the sensitivity value was 69.9% and the specificity value was 49.8%, the cut-off value was found to be 3.13. As a result, the risk of mortality was higher in cases with CAR 3.13 and above (Fig. 3).

In geriatric patients hospitalized in the intensive care unit, sepsis was most common in patients with malignancy comorbidity, followed by pneumonia, and least in those with both COPD and malignancy comorbidity, and this was statistically significant (Table 4).

4. Discussion
This study showed that while age and gender do not affect, both malnutrition and infection affect mortality in geriatric patients treated in respiratory intensive care. However, low GNRI significantly increases inotrope use, MV duration, LOS H, and LOS ICU, while high CAR levels only increase inotrope use and MV duration significantly and also at predicting mortality GNRI is better than CAR.

| Table 2 | Correlation between nutrition and infection parameters. |
|---------|--------------------------------------------------------|
|         | Inotrop Desteci | Mv Süresi | Yb Yaş Suesi | Hastane Yaş Süresi |
| GNRI    | r = -0.264     | -0.232    | -0.146       | -0.142             |
|         | p < .001       | < .001    | < .001       | < .001             |
| Nutric score | r = 0.334 | 0.420 | 0.132 | -0.036 |
|         | p < .001       | < .001    | .008         | .473               |
| CAR     | r = 0.141      | 0.111     | 0.022        | 0.050              |
|         | p = 0.005      | .026      | .659         | .312               |
| CCI     | r = 0.257      | 0.160     | 0.034        | -0.059             |
|         | p < .001       | .001      | .497         | .234               |
| APACHE II | r = 0.257 | 0.379 | 0.119 | -0.009 |
|         | p < .001       | < .001    | .017         | .849               |
| SOFA    | r = 0.412      | 0.508     | 0.117        | -0.087             |
|         | p < .001       | < .001    | .019         | .082               |
| WBC     | r = 0.014      | 0.074     | 0.047        | 0.037              |
|         | p = .783       | .138      | .343         | .457               |
| Procalcitonin | r = 0.233 | 0.273 | 0.166 | 0.046 |
|         | p < .001       | < .001    | .001         | .356               |

CAR = CRP/albumin ratio; CCI = Charlson comorbidity index; CRP = C-reactive protein; GNRI = Geriatric Nutritional Risk Index; NUTRIC score = Nutrition Risk in Critically Ill score; SOFA = Sequential Organ Failure Assessment; WBC = white blood cell.
Some studies have found that chronological age has an impact on morbidity and mortality, some have suggested that biological age and some other factors are effective.\(^{[10,11]}\) Brunner-Zeigler et al.\(^{[12]}\) determined that mortality increases with age, but the physiological condition of the patients is more effective on mortality. Contrary we evaluate that age do not affect the mortality in geriatric patients in ICU.

The CAR affect as a predictor of mortality is controversial. It has been stated that the CAR is more effective in predicting mortality compared to albumin and CRP alone.\(^{[13]}\) In a study by Cirik et al.\(^{[14]}\) evaluating the clinical benefit of the CAR in predicting 30-day mortality in critically ill patients, it was revealed that the CAR was independently associated with 30-day mortality but APACHE II and CCI predicted mortality more than CAR. Although it was shown in a study that increased CAR was associated with increased mortality in intensive care patients, it was concluded that its sensitivity and specificity were not sufficient to predict mortality.\(^{[15]}\)

Table 3

| Test variables | AUC | p  | 95% Confidence Interval | Cut-off | Sensitivity | Specificity |
|----------------|-----|----|------------------------|---------|-------------|-------------|
| GNRI           | 0.689 | <0.001 | 0.637 - 0.740 | 85.79% | 57% | 91.3% |
| CAR            | 0.615 | <0.001 | 0.541 - 0.687 | 53.33% | 50% | 90.8% |

AUC: area under the curve

Figure 3. ROC curve analysis for GNRI and CAR. GNRI = Geriatric Nutritional Risk Index.

Table 4

| COPD (n: 252) | Malignancy (n: 31) | COPD + Malignancy (n: 18) | Pneumonia (n: 99) |
|---------------|-------------------|---------------------------|------------------|
| Procalcitonin (≥ 0.5 ng/mL) | SEPSIS | 78 (31.0%) | 18 (58.1%) | 5 (27.8%) | 42 (42.4%) |

P = .009

COPD = Chronic Obstructive Pulmonary Disease; ICU = intensive care unit.

Multinominal Logistic Regression Nagelkerke $R^2 = 0.620$ (Hosmer ve Lemeshow P > .05). BMI = body mass index; CAR = CRP/albumin ratio; CCI = Charlson comorbidity index; COPD = Chronic Obstructive Pulmonary Disease; CRP = C-reactive protein; GNRI = Geriatric Nutritional Risk Index; LOS H = length of stay hospital; MV = mechanical ventilation; NUTRIC score = Nutrition Risk in Critically ill score; OR = odds ratio; SOFA = Sequential Organ Failure Assessment; WBC = white blood cell.
study, we determined that low GNRI and high mNUTRIC scores have a significant effect on mortality.

In this study we also found that had being malignancy history rather than COPD, and high CCI, APACHE II, SOFA scores were significantly increase mortality similar to Kao et al.\(^{22}\) They suggested that CCI and SOFA scores were correlated with mortality.

This study has several limitations to be considered. It has a retrospective design, and conducted at a single center. The sample size was relatively small.

5. Conclusion

Both malnutrition and infection affect mortality in geriatric patients in intensive care. However, low GNRI increases inotrope use, MV duration, LOS H, and ICU, while high CAR levels only increase inotrope use and MV duration significantly and also at predicting mortality GNRI is better than CAR.

Author contributions

Conceptualization: Guler Eraslan Doganay.

Data curation: Guler Eraslan Doganay, Mustafa Ozgur Cirik.

Formal analysis: Guler Eraslan Doganay.

Investigation: Guler Eraslan Doganay, Mustafa Ozgur Cirik.

Methodology: Guler Eraslan Doganay.

Project administration: Guler Eraslan Doganay.

Software: Mustafa Ozgur Cirik.

Supervision: Guler Eraslan Doganay.

Validation: Guler Eraslan Doganay.

Visualization: Mustafa Ozgur Cirik.

Writing – original draft: Guler Eraslan Doganay.

Writing – review & editing: Guler Eraslan Doganay, Mustafa Ozgur Cirik.

References

[1] World Population Prospects: The 2017 Revision. United Nations, Department of Economic and Social Affairs, United Nations.

[2] http://www.ceterisparibus.net/veritaban/1923_1990/nufus.ht. Date of access: 08/24/2008.

[3] Cirik MO, Yenibertiz D. What are the prognostic factors affecting 30-day mortality in geriatric patients with respiratory failure in the Intensive Care Unit? Pak J Med Sci 2021;37:15–20.

[4] Haas LE, van Dillen LS, de Lange DW, van Dijk D, Hamaker ME. Outcome of very old patients admitted to the ICU for sepsis: a systematic review. Eur Geriatr Med 2017;8:446–53.

[5] Llop-Talaveron J, Badia-Tahull MB, Leiva-Badosa E. An inflammation-based prognostic score, the C-reactive protein/albumin ratio predicts the morbidity and mortality of patients on parenteral nutrition. Clin Nutr 2018;37:1575–83.

[6] Oh J, Kim SH, Park KN, et al. High-sensitivity C-reactive protein/albumin ratio as a predictor of inhospital mortality in older adults admitted to the emergency department. Clin Exp Emerg Med 2017;4:19–24.

[7] Durán Alert P, Milà Villarroel R, Formiga F, Virgili Casas N, Vilarasau Farré C. Assessing risk screening methods of malnutrition in geriatric patients: Mini Nutritional Assessment (MNA) versus Geriatric Nutritional Risk Index (GNRI). Nutr Hosp 2012;27:590–8.

[8] Yamana I, Takeno S, Shimakoa H, et al. Geriatric Nutritional Risk Index as a prognostic factor in patients with esophageal squamous cell carcinoma – retrospective cohort study. Int J Surg 2018;56:44–8.

[9] Bouillanne O, Morineau G, Dupont C, et al. Geriatric Nutritional Risk Index: a new index for evaluating at-risk elderly medical patients. Am J Clin Nutr 2005;82:777e83.

[10] Vosylius S, Spylaite J, Ivaskevicius J. Determinants of outcome in elderly patients admitted to the intensive care unit. Age Agong 2005;34:157–62.

[11] Kleinpell RM, Ferrans CE. Factors influencing intensive care unit survival for critically ill elderly patients. Heart Lung 1998;27:337–43.

[12] Brunner-Zeigler S, Heinze G, Ryffel M, Kompatscher M, Slany J, Valentín A. “Oldest old” patients in intensive care: prognosis therapeic activity. Wien Klin Wochenschr 2007;119:14–9.

[13] Atalay E, Ergodu H, Tur BK, Balyen LSD, Karabag Y, Ardcı S. The relationship between C-reactive protein/albumin ratio and 1-year mortality in hospitalized elderly COPD patients with acute exacerbation. Turk J Geriatr 2019;22:9–17.

[14] Cirik M, Baldemir R, Doganay GE, Unver M, Avci S. The 30-day mortality predictor role of C-reactive protein/albumin ratio in critically ill COPD patients. Crit Care Innov 2020;5:1–12.

[15] Park JE, Chung KS, Song JH, Kim SY, Kim EY, Jung JY. The C-reactive protein/albumin ratio as a predictor of mortality in critically ill patients. J Clin Med 2018;7:333.

[16] Wang H, Hai S, Zhou Y, Liu P, Dong BR. The Geriatric Nutritional Risk Index predicts mortality in nonagenarians and centenarians receiving home care. Asia Pac J Clin Nutr 2018;27:78–83.

[17] Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA 2016;315:801–10.

[18] Tsai MT, Liu HC, Huang TP. The impact of malnutritional status on survival in elderly hemodialysis patients. J Chin Med Assoc 2016;79:309–13.

[19] Oral O, Ozgun G. Comparison of the course and prognosis of geriatric patients admitted to the intensive care unit according to BMI and albumin values. Anesthes Pain Med 2016;6:e32509.

[20] Kaysen GA. Malnutrition and the acute-phase reaction in dialysis patients-how to measure and how to distinguish. Nephrol Dial Transplant 2000;15:1521.e4.

[21] Bergstrom J, Lindholm BM. Malnutrition, cardiac disease, and mortality: an integrated point of view. Am J Kidney Dis 1998;32:834.e41.

[22] Kao KC, Hsieh MJ, Lin SW, et al. Survival predictors in elderly patients with acute respiratory distress syndrome: a prospective observational cohort study. Sci Rep 2018;8:13459.