Geriatric Nutritional Risk Index: a new index for evaluating at-risk elderly medical patients

Olivier Bouillanne, Gilles Morineau, Claire Dupont, Isabelle Coulombel, Jean-Pierre Vincent, Ioannis Nicolis, Simone Benazeth, Luc Cynober, and Christian Aussel

ABSTRACT

Background: Patients at risk of malnutrition and related morbidity and mortality can be identified with the Nutritional Risk Index (NRI). However, this index remains limited for elderly patients because of difficulties in establishing their normal weight.

Objective: Therefore, we replaced the usual weight in this formula by ideal weight according to the Lorentz formula (WLo), creating a new index called the Geriatric Nutritional Risk Index (GNRI).

Design: First, a prospective study enrolled 181 hospitalized elderly patients. Nutritional status [albumin, prealbumin, and body mass index (BMI)] and GNRI were assessed. GNRI correlated with a severity score taking into account complications (bedsores or infections) and 6-mo mortality. Second, the GNRI was measured prospectively in 2474 patients admitted to a geriatric rehabilitation care unit over a 3-y period.

Results: The severity score correlated with albumin and GNRI but not with BMI or weight:WLo. Risk of mortality (odds ratio) and risk of complications were, respectively, 29 (95% CI: 5.2, 161.4) and 4.4 (95% CI: 1.3, 14.9) for major nutrition-related risk (GNRI: 82 to <92), 6.6 (95% CI: 1.3, 33.0), 4.9 (95% CI: 1.9, 12.5) for moderate nutrition-related risk (GNRI: 82 to <92), and 5.6 (95% CI: 1.2, 26.6) and 3.3 (95% CI: 1.4, 8.0) for a low nutrition-related risk (GNRI: 92 to ≤98). Accordingly, 12.2%, 31.4%, 29.4%, and 27.0% of the 2474 patients had major, moderate, low, and no nutrition-related risk, respectively.

Conclusion: GNRI is a simple and accurate tool for predicting the risk of morbidity and mortality in hospitalized elderly patients and should be recorded systematically on admission. Am J Clin Nutr 2005;82:777–83.

KEY WORDS Weight loss, body mass index, albumin, Nutritional Risk Index, elderly, malnutrition

INTRODUCTION

Protein-energy malnutrition (PEM) is a common disorder in the elderly. Estimations of the prevalence of PEM vary (20–78% in elderly medical patients) significantly between studies because of a variety of indexes and cutoff values used for anthropometric and biological assessment (1–6). No single indicator is able to set PEM diagnosis, and various combinations of indicators have led to a range of scales and indexes. Consequently, no standard is currently available for the assessment of malnutrition and related risk in the elderly. In particular, despite frequent use, albuminemia remains an unreliable indicator of nutritional status because it may be more related to inflammation or hydration status than to malnutrition (7).

Both the European Society of Parenteral and Enteral Nutrition (ESPEN) guidelines and the French Programme National Nutrition Santé (PNNS) recommend using the Mini Nutritional Assessment (MNA) to detect the risk of undernutrition among elderly subjects aged ≥70 y (8, 9). The MNA, which is based on a questionnaire, does not use biological indicators. It is more adapted to the elderly at home or in a nursing home setting than during hospitalization, which by nature biases the questionnaire. For hospitalized adults of all ages, the ESPEN guidelines recommend using a combination of body mass index (BMI; in kg/m²) and weight loss (Malnutrition Universal Screening Tool, or MUST), whereas the PNNS recommends using the Nutritional Risk Index (NRI) (9). The NRI index was first described by Buzby et al (10, 11) to score the severity of postoperative complications. It combines 2 nutritional indicators (albumin and weight loss). By extension, it has been used as an index of malnutrition in hospitalized adults (12). However, usual weight is often impossible to obtain in elderly patients (13). Indeed, only half of the elderly can remember their usual weight, and even under professional care they are rarely weighed (14). Faced with the difficulty in identifying the usual body weight of elderly patients, we hypothesized that usual body weight could be replaced by ideal body weight in the NRI formula. We named the resulting index the Geriatric Nutritional Risk Index (GNRI). Ideal body weight was calculated according to the Lorentz formula that takes into account a patient’s height and sex. Height is difficult to obtain in hospitalized patients because they are often unable to stand, and declared height has no value. We therefore preferred to use the estimated standing height, calculated by using the equation by Chumlea et al (15), which is based on knee height (KH).

The main aim of this study was to validate our adaptation of the NRI (ie, GNRI) to elderly patients. For validation, we compared...
the GNRI with malnutrition-related risks of mortality and morbidity, including infection and bedsores. The second aim of this study was to estimate the prevalence of nutrition-related risks of complications in elderly hospitalized patients with the use of the GNRI.

SUBJECTS AND METHODS

Subjects

In the first phase of the study, subjects admitted into a geriatric rehabilitation care unit were enrolled consecutively over a 6-mo period. The inclusion criterion was age ≥65 y. Exclusion criteria were hyponatremia (<135 mmol/L) and hypernatremia (>145 mmol/L), severe hepatic disease, and severe renal insufficiency (creatinine clearance calculated from the Cockroft and Gault formula at <15 mL/min) to rule out non-malnutrition-related modifications in albuminemia. The included patients were evaluated for their nutritional status at admission and for their severity score 6 mo later (n = 181).

In the second phase of the study, GNRI was calculated at patient admission over a period of 3 y in a consecutive series of patients aged ≥65 y and admitted into the same geriatric rehabilitation care hospital (n = 2474). This study was carried out according to French ethical guidelines for medicine (Law No. 88-1138 of 20 December 1988 and amendments) and the Declaration of Helsinki (1996).

Procedures

Baseline nutritional assessment, which is part of the routine admission assessment in use for 3 y in our hospital, was performed for all patients within 48 h after their admission. Nutritional status was assessed by body weight and KH. All subjects were weighed without clothing with the use of a validated seated weight scale (ARJO, Roncq, France) recalibrated every year by an approved metrology company. In a recent article, Ritz (16) showed that KH is a sufficiently accurate substitute for standing height in French elderly patients. Estimated height was derived from KH and age by using the following equations taken from Chumlea et al (15):

For men:

$$H (\text{cm}) = [2.02 \times \text{KH (cm)}] - \left[0.04 \times \text{age (y)}\right] + 64.19 \quad (1)$$

For women:

$$H (\text{cm}) = [1.83 \times \text{KH (cm)}] - \left[0.24 \times \text{age (y)}\right] + 84.88 \quad (2)$$

The personnel were trained in KH measurements by using a pediatric height gauge.

BMI was calculated. Ideal weight was calculated from the Lorentz equations (WLo) as follows:

For men:

$$H = 100 - \left[\frac{(H - 150)}{4}\right] \quad (3)$$

For women:

$$H = 100 - \left[\frac{(H - 150)}{2.5}\right] \quad (4)$$

Subjects were fasted from 2030. A venous blood sample was drawn at 0830 and analyzed for albumin, prealbumin, and C-reactive protein (CRP).

The GNRI formula is as follows:

$$\text{GNRI} = \left[1.489 \times \text{albumin (g/L)}\right] + \left[41.7 \times \text{(weight/WLo)}\right] \quad (5)$$

The GNRI formula results from the replacement of ideal weight in the NRI formula by usual weight as calculated from the Lorentz formula. In line with Buzby et al (11), we set weight: WLo = 1 when weight exceeded WLo (note: Buzby used usual weight instead of WLo). GNRI cutoff values were calculated by using the cutoff values for albumin and weight loss in the elderly (when GNRI = 82, albumin = 30 g/L and weight:WLo = 0.9; when GNRI = 92, albumin = 35 g/L and weight:WLo = 0.95; when GNRI = 98, albumin = 38 g/L and weight:WLo = 1, respectively). From these GNRI values, we defined 4 grades of nutrition-related risk: major risk (GNRI: <82), moderate risk (GNRI: 82 to <92), low risk (GNRI: 92 to ≤98), and no risk (GNRI: >98).

The GNRI cutoff values were determined according to weight losses of 5% or 10% and abnormal albumin concentrations of 38, 35, and 30 g/L. Indeed, it seems that a clinically significant weight loss for the elderly is ≥5%/y (17). The weight loss norms of 5% and 10% were also used in the ESPEN Guidelines for Nutrition Screening (8). The normal concentration of albumin is usually considered to range from 38 to 50 g/L. Reuben et al (18) found that older persons with albumin <38 g/L are at risk of high hospital resource use. In terms of risk of mortality, albumin <35 g/L is associated with a significant increased risk in older persons (19, 20). A critical threshold of 30 g/L is associated with a high risk of mortality (9).

Patients were followed for 6 mo for the occurrence of complications: infectious complications (pneumonia, urinary tract infection except cystitis, septicemia, erysipelas, mucus enteritis, infectious arthritis, and bedsores) and bedsores. Definitions of infections were those routinely used in elderly patients: diagnosis of pneumonia requires fever >38 °C, a clinical sign, and radiographic confirmation; urinary tract infection requires fever >38 °C, a clinical sign, and bacteriologic confirmation of >10^3 organisms/mL urine; septicemia requires either fever >38 °C or hypothermia <36 °C and ≥1 positive blood culture for pathogenic organisms; diagnosis of infectious arthritis requires bacteriologic confirmation in the articular fluid; mucus enteritis requires diarrhea and the presence of Clostridium difficile toxin in the feces.

We used the severity score described by Buzby et al (11) which grades patient outcome as 1 if death, 2 if alive with complications (infectious complications described earlier in our study, bedsores, or both), and 3 if alive without complications. In addition to complications, data relevant to patient ethnic origin, diagnoses on admission, discharge, or transfer to another unit were also recorded during hospitalization.

Assays

Serum albumin was measured by colorimetry. Serum prealbumin and CRP were measured by immunoturbidimetry with the use of a Hitachi 911 analyzer (Paris, France). Reagents were obtained from Roche Diagnostic (Meylan, France) for albumin and prealbumin measurements and from Randox (Montpellier Fréjorgues, France) for CRP.
The admission unit. Mean hospital stay was 71.2 days for long-term care and 8% to a long-term care unit, and 16% were still in the unit. 15% patients had died, 4% had been transferred to an acute care unit. The chi-square test or the Fisher’s exact test was used to determine risk of death and of infectious complications or bedsores according to the 3 GNRI grades (0.01–0.04). The relations between severity score and the anthropometric measurements. The partial correlation coefficient between severity score and GNRI as if CRP was kept constant was 0.21 (P = 0.001).

The risk of death or complications was calculated as an odds ratio calculation, the 3 measurements of BMI (1.83 ± 0.9 y for GNRI 98, and 80.5 ± 0.9 y for GNRI > 98 (P < 0.001, ANOVA). Mean albumin, prealbumin, CRP, weight, and BMI differed among GNRI classes but not WLo (Table 1).

The relations between severity score and the nutrition variables were as follows (Table 2): albumin and GNRI correlated positively to severity score (P < 0.001); prealbumin and CRP, respectively, were also positively and negatively correlated to severity score (P = 0.02 and P = 0.001, respectively) but to a lesser degree. No significant correlation was observed between severity score and the anthropometric measurements. The partial correlation coefficient between severity score and GNRI as if CRP was kept constant was 0.21 (P = 0.004).

The risk of death or complications was calculated as an odds ratio after the patient population was stratified according to the GNRI (Table 3). The risk of mortality and morbidity was significant in cases of major, moderate, or low nutrition-related risks. The risk of death was strongly significant in cases of major nutrition-related risk.

### TABLE 1

<table>
<thead>
<tr>
<th>GNRI</th>
<th>Total (n = 181)</th>
<th>&lt;82 (n = 16)</th>
<th>82 to &lt;92 (n = 43)</th>
<th>92 to ≤98 (n = 62)</th>
<th>&gt;98 (n = 60)</th>
<th>P (ANOVA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin (g/L)</td>
<td>36.0 ± 0.3</td>
<td>27.2 ± 0.8</td>
<td>32.6 ± 0.3</td>
<td>35.9 ± 0.2</td>
<td>40.9 ± 0.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prealbumin (g/L)</td>
<td>0.23 ± 0.01</td>
<td>0.13 ± 0.01</td>
<td>0.21 ± 0.01</td>
<td>0.24 ± 0.01</td>
<td>0.26 ± 0.01</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>26.7 ± 3.3</td>
<td>75.9 ± 16.1</td>
<td>25.6 ± 6.2</td>
<td>28.6 ± 6.4</td>
<td>12.1 ± 1.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>59.8 ± 0.9</td>
<td>47.8 ± 2.3</td>
<td>55.1 ± 2.0</td>
<td>62.7 ± 1.4</td>
<td>63.5 ± 1.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WLo (kg/height)</td>
<td>53.4 ± 0.5</td>
<td>53.4 ± 1.6</td>
<td>51.8 ± 0.9</td>
<td>52.7 ± 0.8</td>
<td>54.9 ± 0.8</td>
<td>0.06</td>
</tr>
<tr>
<td>Weight:WLo</td>
<td>0.97 ± 0.01</td>
<td>0.86 ± 0.04</td>
<td>0.95 ± 0.01</td>
<td>0.99 ± 0.01</td>
<td>0.99 ± 0.01</td>
<td>—</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.0 ± 0.3</td>
<td>20.2 ± 1.1</td>
<td>23.6 ± 0.7</td>
<td>26.5 ± 0.5</td>
<td>25.7 ± 0.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

1. CRP, C-reactive protein; WLo, weight determined according to the Lorentz formula; H, height; KH, knee height.
2. Weight was calculated with the equations of Lorentz: WLo = H - 100 - [(H - 150)/4] for men and H - 100 - [(H - 150)/2.5] for women, where H = (2.02 × KH) - (0.04 × age) + 64.19 for men and H = (1.83 × KH) - (0.24 × age) + 84.88 for women.
3. Where weight:WLo = 1 when weight exceeded WLo; no ANOVA was performed on this variable.

### Statistics

Computerized statistical calculations were performed with the use of STATVIEW for Windows (version 4.57; Abacus Concepts Inc, Berkeley, CA). All values were expressed as mean and SEM of individual variables, unless stated otherwise. One-way analysis of variance (ANOVA) was performed to study independence between qualitative and quantitative variables. Simple linear correlations were used to assess the relation between outcome score and quantitative nutritional variables. Partial correlation coefficients were computed from the variance covariance matrix applied to the quantitative study variables; these partial coefficients can be used to calculate the correlation between 2 variables as if the third variable was kept constant. Odds ratios were calculated to determine risk of death and of infectious complications or bedsores according to the 3 GNRI grades (<82, 82 to <92, 92 to ≤98), the 3 concentrations of albumin (<30, 30 to <35, 35 to <38), and the 3 measurements of BMI (<19, 19 to <22, 22 to <24); for each of these odds ratio calculations, the unexposed patients were patients with GNRI > 98, albumin ≥38, and BMI ≥24. The chi-square test or the Fisher’s exact test (2-tailed) for expected values of <5 was applied to study the independence between qualitative variables. The two-tailed significance level of type 1 error was set at 0.05.

### RESULTS

Mean age of the 181 patients was 83.8 ± 0.6 y (range: 68–103 y). Patients included 144 women and 37 men, all of whom were white; 79% came from the setting of an acute care unit and 21% from a home setting. After 6 mo, 57% of the patients had returned home, 15% patients had died, 4% had been transferred to an acute care unit and 8% to a long-term care unit, and 16% were still in the admission unit. Mean hospital stay was 71.2 ± 3.7 d for patients who were no longer hospitalized at 6 mo (because mortality rate covered a 6-mo period). The main patient diagnoses on admission were rehabilitation after fractures (28%), neurologic diseases (27%), cardiovascular diseases (13%), postinfectious diseases (8%), and other medical diseases (24%).

Twenty-eight (15%) of the 181 patients died. Of these 28 patients, 12 (43%) died of infectious complications. Of the total 181 patients, 59 (32.6%) had infectious complications, bedsores, or both. Infectious complications were pneumonia (n = 24), pneumonia and urinary tract infection (n = 14), urinary tract infection (n = 5), septicemia (n = 3), erysipelas (n = 3), mucus enteritis (n = 2), infectious arthritis (n = 1), and parotitis (n = 1). During hospitalization, 14 patients developed a bedsore, including 8 associated with infectious complications.

Mean age was 86.1 ± 2.1 y for GNRI < 82, 87.2 ± 1.1 y for GNRI 82 to <92, 83.9 ± 0.9 y for GNRI 92 to ≤98, and 80.5 ± 0.9 y for GNRI > 98 (P < 0.001, ANOVA). Mean albumin, prealbumin, CRP, weight, and BMI differed among GNRI classes but not WLo (Table 1).

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The risk of death or complications was calculated as an odds ratio after the patient population was stratified according to the GNRI (Table 3). The risk of mortality and morbidity was significant in cases of major, moderate, or low nutrition-related risks. The risk of death was strongly significant in cases of major nutrition-related risk.
After stratification according to albuminemia (Table 4), compared with Table 3 for GNRI, the odds ratios for albumin were lower, and the increased risk of death was only significant in cases of severe malnutrition. Conversely, BMI showed no statistically significant increase in risk of death or complications (data not shown).

In the second part of the study, we showed the prevalence of nutrition-related risk of complications according to GNRI cutoff values (Table 5). Mean age was 83.1 ± 0.2 y (range: 67–107 y). There were 1785 women and 689 men; all were white except for 8 Asians and 15 of African origin. Major or moderate nutrition-related risks were present in 44% of patients.

The overlap between different patient groups with major nutrition-related risk and severe malnutrition (n = 541) according to GNRI, albumin, and BMI cutoff values, respectively, among the 2474 patients is shown in Figure 1. Of the 541 patients who were scored as having severe nutrition-related risk (GNRI < 82) or severe malnutrition (albumin < 30 g/L or BMI < 19), 17 patients (3%) had only 1 index below the cutoff for GNRI compared with 82 (15%) for albumin and 157 (29%) for BMI.

### DISCUSSION

This is the first study that describes a prognostic nutritional index, the GNRI, which enables quantitative determination of the risk of nutrition-related morbidity and mortality in elderly patients at admission into a geriatric hospital. The GNRI is a clinical biological index derived from the NRI, which was developed by Buzby et al (10, 11) in young adult surgical patients but which is not applicable to the elderly because of difficulties in determining usual weight. Naber et al (12) used the Buzby index as an index of malnutrition but only validated it with a severity score and not a nutritional criterion such as lean body mass [in Naber et al (12), the prevalence of malnutrition in apparently healthy elderly volunteers was 3.8% according to the NRI]. There is clearly confusion between a nutrition-related risk index and an index of malnutrition. GNRI is not an index of malnutrition, but it is a “nutrition-related” risk index because GNRI scores are correlated to a severity score that takes into account nutritional status-related complications (bedsores and infections).

### Table 3

Risk of death or infectious complications after nutritional status based on the Geriatric Nutritional Risk Index (GNRI)^

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<td>Absent, ≥98 GNRI (n = 60)</td>
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1 CRP, C-reactive protein.
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1 CRP, C-reactive protein.
2 Chi-square test or Fisher’s exact test (2-tailed) used when expected values were <5; the unexposed patients were patients with GNRI > 98.
The normal GNRI cutoff of 98 used in the present study is slightly lower than that used by Buzby et al (10) who chose a normal threshold of 100 for NRI, corresponding to the lowest 40th percentile of albumin (38.3 g/L) and a weight:WLo of 0.95 in a population of malnourished surgical patients (10). Given that our cutoff values of 98, 92, and 82 are based on threshold values established with larger populations (albumin of 38, 35, or 30 g/L and weight loss of 5% or 10%) (8, 9, 18–20), we consider these values to be better grounded than the NRI values of 100, 97.5, and 83.5 used by Naber et al (12) who gave no details on how their norms were determined.

In the GNRI formula, the weight:WLo is set as equal to 1 if weight was higher than WLo, as described by Buzby. Otherwise, malnourished patients with overweight would not have been diagnosed. This leads to a higher weighting for albumin than for weight. This does not mean that obesity in older persons is not associated with increased risk of mortality, but that this risk is lower than in patients with low BMI (21).

The complications taken into account in our study were infections and bedsores, which were not the postoperative complications used in Buzby’s score. Malnutrition is clearly associated with an increased incidence of death as a result of infection (22). Infectious complications were more common in our patients than were bedsores. GNRI is based on measurements of serum albumin and weight loss, which are strong independent risk factors for morbidity in older persons (4, 6, 19, 23, 24). Our findings are consistent with previous studies reporting that low albumin or weight loss was correlated with increased mortality in older persons (4, 19, 24).

After nutritional stratification according to albumin values, the increased risk of death was only significant in cases of severe malnutrition. Serum albumin is negatively correlated with increased extracellular fluid volume (25). Weight is also affected by hydration status, but variations in hydration status contrast strongly with variations in albumin concentrations. The utilization of both indicators in the GNRI minimizes confounding variables such as hydration status.

In the same way, albumin values are related to comorbidities associated with malnutrition. In the lowest category score of the GNRI, low albumin and high CRP may be more closely related to active disease and inflammation than to malnutrition. Indeed, aging is associated with increased production of catabolic cytokines correlated with increased production of CRP (26, 27). In the liver, inflammatory cytokines (tumor necrosis factor α, interleukin 1, interleukin 2, and interleukin 6) promote the synthesis of acute-phase proteins and repress the synthesis of albumin. Furthermore, proinflammatory cytokines increase the breakdown and capillary escape of albumin (7, 28, 29). Elevated plasma concentrations of these cytokines may be clinically relevant. Thus, a reduction in serum albumin concentrations may reflect inflammatory conditions rather than nutritional status. Whether related to cytokine concentrations or nutritional status, serum albumin concentrations can still be used to identify subjects at risk, but it clearly becomes essential to use serum albumin in association with a more stable indicator such as body weight, as is the case in the GNRI.

This elderly population with multiple pathologies comprised a large number of patients presenting a low GNRI associated with a strong risk of morbidity and mortality without an underlying

![FIGURE 1. Prevalence of severe nutrition-related risk and severe malnutrition (n = 541) according to Geriatric Nutritional Risk Index (GNRI), albumin, and BMI cutoff values among the 2474 patients.](https://academic.oup.com/ajcn/article-abstract/82/4/777/4607473/776740743)
inflammatory process. Indeed, the severity score still correlated with GNRI, independently of CRP values.

No significant correlation was observed between severity score and anthropometric measurements. This observation conflicts with the results of Buzby et al (10, 11) who found a correlation between severity score and both BMI and weight loss. In adult patients in the intensive care unit, a BMI < 18.5 was also reported as being independently associated with higher mortality (30), but this population was quite different from ours (only 5% of our patients had a BMI < 19). One study conducted in hospitalized elderly patients did find that a BMI ≤ 20 was strongly associated with mortality but only after adjusting for illness severity and functional status (31). An important feature of our study was that patients were not selected for malnutrition (all admitted patients were consecutively enrolled), in contrast with Buzby’s study. This may explain the lack of correlation between severity score and anthropometric measurements in our study.

In the second part of the study, we determined the prevalence of nutrition-related risk according to GNRI cutoff values. Even though the prevalence of severe malnutrition calculated by using albumin or BMI (11.3% for albumin < 30 g/L, 12.0% for BMI < 19) was quite similar to the prevalence of a major nutrition-related risk (12.2% for GNRI < 82), the tools identified different populations, as shown in Figure 1. In the first part of the study, we showed that GNRI is a better nutrition-related risk index compared with albumin or BMI alone. We have observed that there is often confusion in published reports between the use of albumin and BMI as a nutrition-related risk index and as an index of malnutrition, which, in fact, are 2 different concepts. Had the prevalence of major nutrition-related risk been determined according to just albumin or BMI, only 65% and 46%, respectively, of the patients identified by using the GNRI would have been screened.

In conclusion, GNRI is a nutrition-related risk index that makes it possible to classify patients according to a risk of morbidity and mortality in relation to pathologies in elderly patients that are often associated with malnutrition. The GNRI is a more reliable prognostic indicator of morbidity and mortality in hospitalized elderly patients than are indexes that use albumin or BMI alone. The GNRI is a simple and accurate tool; it requires only routine measurement of albumin, weight, and KH at admission. The systematic use of GNRI would allow clinicians to identify suitable patients for nutritional support. In our study, 44% of the hospitalized elderly patients had major or moderate nutrition-related risk and were suitable for nutritional supplementation.

OB and CA designed the experiment and drafted the manuscript. GM, CD, and IC collected the data. IN and SB analyzed the data. LC and J-PV provided significant advice. None of the authors had any financial or personal relations with people or organizations that could have inappropriately influenced their work. The corresponding author states that he had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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