Geriatric Nutritional Risk Index, a simplified nutritional screening index, is a significant predictor of mortality in chronic dialysis patients

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Abstract

Background. Malnutrition is a common complication in haemodialysis patients. Recently, the Geriatric Nutritional Risk Index (GNRI) has been reported as a simple and accurate tool to assess nutritional status of haemodialysis patients. Our objective was to examine the association between GNRI and mortality in chronic haemodialysis patients.

Methods. We examined the GNRI of 490 maintenance haemodialysis patients (60 ± 12 years, 293 males and 197 females) and followed up these patients for 60 months. Predictors for all-cause death were examined using Kaplan–Meier analysis and Cox proportional analyses.

Results. The GNRI was 98.0 ± 6.0, and was significantly and negatively correlated with age and haemodialysis duration. During the 60-month follow-up period, 129 patients died. According to the highest positive likelihood and risk ratios, the cutoff value of GNRI for mortality was set at 90. Kaplan–Meier analysis revealed that patients with a GNRI <90 (n = 50) had a significantly lower survival rate, compared to those with GNRI ≥90 (n = 440) (log-rank test, P < 0.0001). Multivariate Cox proportional hazards analyses demonstrated that GNRI was a significant predictor for mortality [hazard ratio (HR) 0.962, 95% confidence interval (CI) 0.931–0.995, P < 0.05], after adjustment for age, gender, C-reactive protein, presence of diabetes and haemodialysis duration.

Conclusions. These results demonstrated that GNRI is a significant predictor for mortality in haemodialysis patients. The simple method of GNRI is considered to be a clinically useful marker for the assessment of nutritional status in haemodialysis patients.

Keywords: Geriatric Nutritional Risk Index; haemodialysis; malnutrition; mortality

Introduction

Protein–energy wasting (PEW), or malnutrition, is highly prevalent in maintenance haemodialysis patients [1], and is associated with increasing risk of mortality [2]. Malnutrition and nutritional management is important for patients on maintenance haemodialysis, and regular nutritional assessment is recommended for all dialysis patients [1,2,3]. For the assessment of the nutritional status of haemodialysis patients, there are several methods, including objective global assessment (SGA) [4,5] and malnutrition–inflammation score [6]. However, since these methods utilize several subjective assessments and judgements, assessment by a well-trained staff is necessary to obtain consistent results between different examiners and institutions. Furthermore, these methods are somewhat time-consuming and cumbersome.

Without the use of several subjective assessments, there are some simpler, more objective nutritional assessments that have been developed for use in various patients, such as hospitalized, post-operative and elderly patients. These methods include the Mini Nutritional Assessment-Short Form (MNA-SF) [7], Nutrition Risk Score (NRS) [8], Malnutrition Universal Screening Tool (MUST) [9], Malnutrition Screening Tool (MST) [10] and Geriatric Nutritional Risk Index (GNRI) [11]. The GNRI was developed as a simple method to assess nutritional condition, which utilizes only three objective parameters of body weight, height...
and serum albumin. Recently, Yamada et al. compared the validity of several nutritional tools and reported that GNRI was a useful tool for the assessment of nutritional status, not only for elderly patients but also for chronic haemodialysis patients [12]. To date, there have been few longitudinal studies, in which GNRI was used to assess the effect of GNRI on mortality [13]. In the present study, we examined whether GNRI could be a useful clinical predictor for mortality in chronic haemodialysis patients.

Materials and methods

Subjects

In the present study, 490 patients on stable, maintenance haemodialysis with haemodialysis duration of more than 6 months at Shirasagi Hospital (Osaka, Japan) were enrolled. Patients with acute illness, significant infection or malignancy were excluded. All patients underwent maintenance haemodialysis sessions three times a week, using conventional bicarbonate-buffered dialysate containing 100 mg/dL glucose and 30 mEq/L bicarbonate. Data collection and GNRI

At enrolment of the study, the clinical data of the patients, i.e. sex, age, body mass index, presence of diabetes and laboratory data, were recorded from each patient’s chart. Blood laboratory tests were performed twice a month, and the data from 3 months were averaged. The body weight (dry weight) was measured after each dialysis session, and BMI (kilogram per square metre) was calculated from the dry weight.

The GNRI was calculated by modifying the Nutritional Risk Index for elderly patients [11], as reported by Yamada et al. [12], as follows:

\[
\text{GNRI} = \frac{14.89 \times \text{albumin (g/dL)}}{+ 41.7 \times (\text{body weight/ideal body weight})}
\]

BGNI = 22, because of its validity [14], instead of the value calculated using the Lorentz formula in the original GNRI equation [11]. Ideal body weight of BMI 22 was also reported to be associated with lowest morbidity in a Japanese population [15,16], in whom appropriate BMI and obesity criteria may be different from Caucasians [17,18].

Statistical analysis

Data are expressed as the mean ± SD. C-reactive protein (CRP) was logarithmically transformed, since it exhibited a skewed distribution. Unpaired t-tests and chi-square tests were performed for comparisons between the two groups. A simple regression analysis was used to examine the relationship between variables. Survival curves were calculated by the Kaplan–Meier method. The P-values for comparison of survival curves were determined by the log-rank test. The relative risk of mortality for different parameters was estimated using Cox proportional hazards models. Hazard ratios (HR) and their 95% confidence intervals (CI) were calculated using the estimated regression coefficients and their standard errors in Cox regression analysis. P-values <0.05 were considered to be statistically significant. Statistical analysis was performed using the Stat-View V system for Windows (SAS Institute Inc., Cary, NC, USA).

To determine the GNRI cutoff value, the positive likelihood and risk ratios were calculated as follows:

\[
\text{Sensitivity} = \frac{\text{true positive}}{\text{true positive} + \text{false negative}}
\]

\[
\text{Specificity} = \frac{\text{true negative}}{\text{true negative} + \text{false positive}}
\]

\[
\text{Positive likelihood ratio} = \frac{\text{sensitivity}}{1 - \text{specificity}}
\]

\[
\text{Risk ratio} = \frac{\text{true positive}}{\text{true positive} + \text{false positive}}
\]

\[
\frac{\text{false negative}/(\text{false negative} + \text{true negative})}
\]

The surviving and dead patients were divided into two categories according to the GNRI cutoff values.

Fig. 1. Distribution of the GNRI of the 490 haemodialysis patients. GNRI presented normal distribution.

CRP, C-reactive protein; GNRI, Geriatric Nutritional Risk Index; n.s., not significant.

Table 1. Clinical characteristics of 490 chronic dialysis patients

<table>
<thead>
<tr>
<th></th>
<th>Total patients</th>
<th>Patients with GNRI &lt;90</th>
<th>Patients with GNRI &gt;90</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>60 ± 12</td>
<td>70 ± 11</td>
<td>59 ± 11</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male/female</td>
<td>293/197</td>
<td>21/29</td>
<td>272/168</td>
<td>n.s.</td>
</tr>
<tr>
<td>Haemodialysis duration (month)</td>
<td>88 ± 76</td>
<td>92 ± 89</td>
<td>88 ± 74</td>
<td>0.0106</td>
</tr>
<tr>
<td>Diabetes (+/−)</td>
<td>367/123</td>
<td>39/11</td>
<td>328/112</td>
<td>n.s.</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>53.2 ± 9.9</td>
<td>42.8 ± 7.2</td>
<td>54.4 ± 9.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Body mass index</td>
<td>20.7 ± 2.8</td>
<td>17.8 ± 1.9</td>
<td>21.0 ± 2.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>4.0 ± 0.3</td>
<td>3.6 ± 0.3</td>
<td>4.1 ± 0.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Blood urea nitrogen (mg/dL)</td>
<td>72 ± 12</td>
<td>64 ± 11</td>
<td>73 ± 12</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>11.0 ± 2.4</td>
<td>8.7 ± 1.6</td>
<td>11.3 ± 2.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Log CRP (log mg/dL)</td>
<td>−0.74 ± 0.56</td>
<td>−0.44 ± 0.60</td>
<td>−0.80 ± 0.52</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CRP (mg/dL)</td>
<td>(0.43 ± 0.88)</td>
<td>(0.79 ± 1.06)</td>
<td>(0.36 ± 0.71)</td>
<td></td>
</tr>
<tr>
<td>GNIR</td>
<td>98.0 ± 6.0</td>
<td>86.6 ± 3.2</td>
<td>99.3 ± 4.7</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Results

Patient characteristics and GNRI

The clinical characteristics of the patients are shown in Table 1. GNRI exhibited a normal distribution (Figure 1), and the mean GNRI (± SD) was 98.0 (± 6.0). The GNRI was significantly negatively correlated with age (r = −0.436, P < 0.0001, Figure 2). GNRI was significantly negatively correlated with the duration of dialysis (r = −0.111, P = 0.0144, Figure 2). The GNRI value in males was significantly higher than the GNRI value in females (99.1 ± 5.9 vs. 96.4 ± 5.7, P < 0.0001). There were no significant differences in GNRI between patients with and without diabetes (98.1 ± 6.0 vs. 98.0 ± 6.0).

Survival rate and GNRI

During the 60-month follow-up period, 129 patients died. The GNRI values of the surviving patients were significantly greater than those who died (99.0 ± 5.6 vs. 95.3 ± 6.2, P < 0.0001).

To determine a possible cutoff GNRI value for survival, the sensitivity, specificity, positive likelihood and risk ratios were examined for the outcome of survival of patients. As shown in Table 2, a GNRI value of 90 was shown to indicate the highest values for the positive likelihood and risk ratios (4.20 and 2.67, respectively). According to the highest positive likelihood and risk ratios, the cutoff value of GNRI for mortality was set at 90. Patients with GNRI <90 exhibited significantly higher age and log CRP, longer haemodialysis duration, and significantly lower body weight, body mass index, serum albumin, blood urea nitrogen (BUN), and creatinine (Table 1).

Influence of GNRI on 5-year survival

Kaplan–Meier analysis revealed that patients with GNRI <90 (n = 50) had a significantly lower survival rate, compared to those with GNRI ≥90 (log-rank test, P < 0.0001) (Figure 3).

Univariate Cox proportional hazards analysis for mortality showed that GNRI was a significant predictor for mortality (HR 0.916, 95% CI 0.891–0.941, P < 0.0001, Table 3). Multivariate Cox proportional hazards analysis demonstrated that GNRI was a significant predictor for mortality (HR 0.962, 95% CI 0.931–0.995, P < 0.05, Table 4), after adjustment for age, gender, log CRP, presence of diabetes and haemodialysis duration.

Table 2. Sensitivity, specificity, positive likelihood ratio and risk ratio for the outcome of survival, according to each GNRI value

<table>
<thead>
<tr>
<th>GNRI</th>
<th>88</th>
<th>89</th>
<th>90</th>
<th>91</th>
<th>92</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>0.12</td>
<td>0.17</td>
<td>0.23</td>
<td>0.26</td>
<td>0.30</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.97</td>
<td>0.96</td>
<td>0.94</td>
<td>0.93</td>
<td>0.90</td>
</tr>
<tr>
<td>Positive likelihood ratio</td>
<td>4.07</td>
<td>3.85</td>
<td>4.20</td>
<td>3.25</td>
<td>2.95</td>
</tr>
<tr>
<td>Risk ratio</td>
<td>2.43</td>
<td>2.45</td>
<td>2.67</td>
<td>2.52</td>
<td>2.36</td>
</tr>
</tbody>
</table>

Fig. 2. Relationship between age and GNRI, and between haemodialysis duration and GNRI. There was a significant negative correlation between age and GNRI (r = −0.436, P < 0.0001), and between haemodialysis duration and GNRI (r = −0.111, P = 0.0144).

Fig. 3. GNRI and 60-month survival of haemodialysis patients. Patients with GNRI <90 had a significant lower survival rate during the follow-up period, compared with those with GNRI ≥90 (Kaplan–Meier analysis).
pared to those with GNRI lower BMI, serum albumin, BUN and creatinine, com-
positive likelihood and risk ratios. Patients with GNRI <90
GNRI cutoff value was set at 90 according to the highest

Recently, Yamada
in hospitalized and home-cared elderly patients [11,19,20].
The GNRI was shown to be a simple
to predict mortality and hospitalization, which are components of the GNRI; GNRI <82, ma-

Kaplan-Meier analysis showed that the former exhibited
increased chronic inflammation, as represented by a sig-
ificantly increased log CRP, compared to the latter.
Kaplan-Meier analysis showed that the former exhibited a
significantly poorer outcome, compared to the latter.
Furthermore, GNRI was a significant predictor for mor-
ality, after adjustment for several confounders.

GNRI was originally proposed by Bouillanne et al., for the assessment of the nutritional status of elderly hospitalized patients [11]. The GNRI was shown to be a simple and accurate tool for predicting morbidity and mortality in hospitalized and home-cared elderly patients [11,19,20].
Recently, Yamada et al. reported that GNRI was a useful tool for the assessment of nutritional status of chronic haemodialysis patients [12]. In their study [12], of the five simple reliable nutritional tools (MNA-SF, NRS, MUST, MST and GNRI), GNRI was shown to be the most accurate in identifying haemodialysis patients at nutritional risk, because the area under the receiver operating characteristic curve generated with the malnutrition–inflammation score value [6] was the largest. In the present study of 490 chronic haemodialysis patients, we showed that GNRI was a significant predictor for mortality, not only in univariate Cox proportional hazards analysis (Table 3) but also in multivariate Cox proportional hazards analysis after adjustment for several confounders (Table 4). Since malnutrition has been shown to be a significant predictor of mortality in haemodialysis patients [1,5], our study indicates that GNRI is clinically relevant to the nutritional assessment of chronic haemodialysis patients. Since the calculation of GNRI utilizes three simple, definite parameters of serum albumin, height and body weight, instead of the subjective assessments utilized in subjective global assessment [4] and the malnutrition–inflammation score [6], which are possibly affected by the examiner’s skill or uncertain subjective complaints by the patient, GNRI is considered to be a clinically useful, simple tool for the assessment of nutritional status of chronic haemodialysis patients.

As for the cutoff values of GNRI for elderly hospitalized patients, Bouillanne et al. determined four GNRI cutoff values according to weight loss and albumin concentrations, which are components of the GNRI; GNRI <82, major nutrition-related risk; GNRI 82 to <92, moderate nutrition-related risk; GNRI 92 to ≤98, low nutrition-related risk; GNRI >98, no risk [11]. In the study by Yamada et al. on chronic haemodialysis patients [12], the most accurate GNRI cutoff value to identify malnourished patients was determined to be <91.2, based on the malnutrition–inflammation score [6]. In the present study, the cutoff value of GNRI for mortality was set at 90, according to the highest positive likelihood and risk ratios. Although the ideal cutoff value could be determined, i.e. to minimize the rate of both false-negative errors and false-positive errors, we considered that reducing the false-positive rate might be more important than reducing the false-negative rate for severe and high-mortality diseases, such as chronic renal failure. Therefore, we made the best attempt to increase the positive likelihood ratio. The cutoff value of 90 for GNRI in our study, in which the outcome of survival of haemodialysis patients was examined, is close to the cutoff value of 91.2 determined by Yamada et al. [12], who examined malnutrition in haemodialysis patients, although the study aims are different between the two. In the present study, patients with GNRI <90 are suggested to be at a poorer nutritional status in view of lower body weight, BMI, serum albumin, BUN and creatinine, compared to those with GNRI ≥90, although body weight, BMI, serum albumin, BUN and creatinine could not fully represent definite criteria for malnutrition. The former showed increased chronic inflammation, in view of significantly increased log CRP and significantly lower serum albumin, compared to the latter. The former showed greater age and longer duration of haemodialysis. The results in the present study are similar to those reported by Yamada et al., who set the cutoff values at 91.2 [12]. In the present study, we further showed that patients with GNRI <90 demonstrated significantly increased mortality, compared to those with GNRI ≥90 (Figure 3).

In conclusion, our study suggests that GNRI is a simple but useful tool to assess nutritional status in chronic haemodialysis patients. Our study demonstrates that lower GNRI is a significant predictor for mortality in these patients.

Discussion
In the present study, we examined the nutritional status of haemodialysis patients using the GNRI, as reported by Yamada et al. [12]. GNRI was distributed normally. The GNRI cutoff value was set at 90 according to the highest positive likelihood and risk ratios. Patients with GNRI <90 exhibited a poorer nutritional status, as represented by lower BMI, serum albumin, BUN and creatinine, compared to those with GNRI ≥90. The former showed increased chronic inflammation, as represented by a significantly increased log CRP, compared to the latter. Kaplan-Meier analysis showed that the former exhibited a significantly poorer outcome, compared to the latter. Furthermore, GNRI was a significant predictor for mortality, after adjustment for several confounders.

GNRI was originally proposed by Bouillanne et al., for the assessment of the nutritional status of elderly hospitalized patients [11]. The GNRI was shown to be a simple and accurate tool for predicting morbidity and mortality in hospitalized and home-cared elderly patients [11,19,20]. Recently, Yamada et al. reported that GNRI was a useful tool for the assessment of nutritional status of chronic haemodialysis patients [12]. In their study [12], of the five simple reliable nutritional tools (MNA-SF, NRS, MUST, MST and GNRI), GNRI was shown to be the most accurate in identifying haemodialysis patients at nutritional risk, because the area under the receiver operating characteristic curve generated with the malnutrition–inflammation score value [6] was the largest. In the present study of 490 chronic haemodialysis patients, we showed that GNRI was a significant predictor for mortality, not only in univariate Cox proportional hazards analysis (Table 3) but also in multivariate Cox proportional hazards analysis after adjustment for several confounders (Table 4). Since malnutrition has been shown to be a significant predictor of mortality in haemodialysis patients [1,5], our study indicates that GNRI is clinically relevant to the nutritional assessment of chronic haemodialysis patients. Since the calculation of GNRI utilizes three simple, definite parameters of serum albumin, height and body weight, instead of the subjective assessments utilized in subjective global assessment [4] and the malnutrition–inflammation score [6], which are possibly affected by the examiner’s skill or uncertain subjective complaints by the patient, GNRI is considered to be a clinically useful, simple tool for the assessment of nutritional status of chronic haemodialysis patients.

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In conclusion, our study suggests that GNRI is a simple but useful tool to assess nutritional status in chronic haemodialysis patients. Our study demonstrates that lower GNRI is a significant predictor for mortality in these patients.

Acknowledgements. The authors have received no funding for research on this article.

Conflict of interest statement. None declared.

Table 3. Univariate Cox proportional hazards analysis of mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unit increase</th>
<th>Hazard ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Year</td>
<td>1.083 (1.061–1.103)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Haemodialysis duration</td>
<td>Month</td>
<td>0.998 (0.995–1.000)</td>
<td>0.0638</td>
</tr>
<tr>
<td>Gender</td>
<td>vs. male</td>
<td>1.179 (0.833–1.670)</td>
<td>0.3521</td>
</tr>
<tr>
<td>Diabetes</td>
<td>vs. absence</td>
<td>2.100 (1.468–3.006)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Log CRP</td>
<td>log (1 mg/dL)</td>
<td>2.108 (1.563–2.844)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>GNRI</td>
<td>1</td>
<td>0.916 (0.891–0.941)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Table 4. Multivariate Cox proportional hazards analysis of mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unit increase</th>
<th>Hazard ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Year</td>
<td>1.074 (1.051–1.098)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Haemodialysis duration</td>
<td>Month</td>
<td>1.000 (0.997–1.003)</td>
<td>0.9466</td>
</tr>
<tr>
<td>Gender</td>
<td>vs. male</td>
<td>0.865 (0.690–1.248)</td>
<td>0.4393</td>
</tr>
<tr>
<td>Diabetes</td>
<td>vs. absence</td>
<td>2.111 (1.438–3.098)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Log CRP</td>
<td>log (1 mg/dL)</td>
<td>1.618 (1.180–2.219)</td>
<td>0.0028</td>
</tr>
<tr>
<td>GNRI</td>
<td>1</td>
<td>0.962 (0.931–0.995)</td>
<td>0.0232</td>
</tr>
</tbody>
</table>
**Insulinogenic index during haemodialysis**

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**Abstract**

**Background.** The aim of this study was to analyse whether the insulin to glucose relationship following an intravenous glucose load in non-diabetic patients delivered during haemodialysis was affected by extracorporeal clearance and whether this relationship could be determined by an abridged sampling protocol.

**Methods.** Studies were done during routine haemodialysis following the infusion of 0.5 g glucose per kilogram body mass. Extracorporeal effects were measured by online clearance (\(K_{OCM}\)) and insulin clearance (\(K_I\)). The insulin to glucose relationship was examined for a period of 1 h following the infusion of glucose. The integral response measured as the insulinogenic index (\(I_g\)) was compared...