Relationship between geriatric nutritional risk index and subpopulation lymphocyte counts in patients undergoing hemodialysis and peritoneal dialysis

Gyong Hoon Kang, Ye Na Kim and Ho Sik Shin
Department of Internal Medicine, Kosin University College of Medicine, Busan, Korea

ABSTRACT
We investigated the relationship between geriatric nutritional risk index (GNRI) and subpopulation lymphocyte counts (SLCs) in hemodialysis (HD) and peritoneal dialysis (PD) patients and evaluated whether they can be helpful in the diagnosis of malnutrition in these patients. We examined the GNRI and SLCs of 50 HD patients (mean: 55.8 ± 12.7 years; 28 men and 22 women) and 16 Continuous Ambulatory Peritoneal Dialysis (CAPD) patients (mean: 49.8 ± 14.5 years; 10 men and six women). The GNRI is calculated based on the serum albumin level, dry weight, and ideal body weight and uses the following equation: GNRI = [14.89 × albumin (g/dL)] + [41.7 × (weight/ideal body weight)]. SLCs were evaluated using flow cytometry. T-tests and χ² tests were performed to compare the two groups. Logistic regression analysis was performed for predicting malnutrition in dialysis patients. The average GNRI value was 100.1 ± 8.4 in HD patients and 99.2 ± 8.1 in PD patients, and no significant differences in GNRI or SLC were observed between the two groups. SLCs were higher in patients with higher GNRI (GNRI ≥ 100) although there was no statistical difference. Logistic regression for predicting malnutrition according to GNRI revealed that age, female sex, and CD19 counts predicted malnutrition in HD and PD patients. These results suggest that GNRI and SLCs (especially CD19 count) may be significant nutritional markers in these patients.

ARTICLE HISTORY
Received 22 June 2015
Revised 26 October 2015
Accepted 22 November 2015

KEYWORDS
Geriatric nutritional risk index; subpopulation lymphocyte counts; dialysis

Introduction
Malnutrition is highly prevalent in maintenance dialysis patients and is associated with an increased risk of mortality.1,2 Thus, regular nutritional assessment is recommended for all dialysis patients. Serial assessment of nutritional status for detection and management of protein energy wasting (PEW) is recommended using old and new scoring tools, including the subjective global assessment, malnutrition-inflammation score, geriatric nutritional risk index (GNRI), and PEW definition criteria.1,2

To the best of our knowledge, no study has examined the relationship between GNRI and subpopulation lymphocyte counts (SLCs) in hemodialysis (HD) and peritoneal dialysis (PD) patients.

The GNRI is a simple and accurate method to assess nutritional condition using only three parameters: body weight, height, and serum albumin levels.1,3 Recently, the GNRI was found to be a reliable screening tool for malnutrition in HD and PD patients.3,4

Quantities of ingested nutrients influence circulating lymphocyte counts in PD patients.5 Thus, total lymphocyte count (TLC) and SLCs could be helpful in monitoring the nutritional status of PD patients.

There is some controversy regarding the use of TLC as a marker for protein-calorie malnutrition;6,7 however, evaluation of TLC has been shown to be helpful in monitoring nutritional status and assessing prognosis in PD patients.5,8–10

Among SLCs, CD19 counts were reported to decrease over the course of PD11, and higher CD19 counts were associated with better clinical and laboratory scores, indicating an adequate PD treatment.5

In the present study, we investigated the relationship between GNRI and SLCs in HD and PD patients and evaluated whether they can be helpful in the diagnosis of malnutrition in these patients.

Methods

Patients
We enrolled 66 patients (50 HD and 16 CAPD patients) receiving stable maintenance dialysis at the Kosin University Gospel Hospital. The study inclusion criteria...
were ongoing HD or PD therapy for more than 6 months and stable condition. Exclusion criteria included cardiovascular disease, respiratory disease, gastrointestinal disease, neurologic disease, malignancy, severe infection, or use of medications (corticosteroids, cyclosporine, or other major immunosuppressive drugs) affecting TLC. HD patients underwent maintenance HD three times a week using conventional bicarbonate-buffered dialysate. PD patients were dialyzed using glucose PD solutions and the twin-bag connection system.

The study protocol was approved by the ethics committee of our hospital.

**Data collection**

Clinical and laboratory data from the enrolled patients were gathered from medical records. We collected clinical data, such as sex, age, body mass index (BMI), and the presence of diabetes mellitus (DM), and laboratory results. Blood laboratory tests including SLCs were performed once a month and averaged over 2 months. SLCs were evaluated using flow cytometry. The analyses included CD3 cells (T lymphocytes), CD4 cells (helper lymphocytes), CD8 cells (cytotoxic suppressor lymphocytes), and CD19 cells (B lymphocytes).

Body weight was measured after each dialysis session and averaged over 1 month.

BMI (kg/m²) was calculated using dry weight. Serum albumin levels were measured by bromocresol green. We calculated GNRI using serum albumin values, dry weight, and ideal body weight. GNRI was calculated by modifying the nutritional risk index for elderly subjects, as reported by Yamada et al.³:

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

Note that body weight/ideal body weight was greater than 1 when a subject’s body weight exceeded his ideal body weight. Ideal body weight was calculated using height and a BMI of 22, which is reportedly associated with the lowest morbidity rate in the Asian population. GNRI was calculated twice at the first and second month of observation.

Subjects were divided into two groups according to dialysis method (HD or PD), GNRI (≥ 100 or < 100), and CD19 counts (≥ 100/mm³ or < 100/mm³).

To determine a possible GNRI cutoff value, patients were divided into two groups on the basis of serum albumin level. The malnutrition group was defined as patients with serum albumin under 3.0 g/dL because of our patient’s malnutrition.

**Statistical analysis**

Data are expressed as a mean ± standard deviation. T-tests and \( \chi^2 \) tests were performed for comparisons between the two groups. The odds ratios (OR) were calculated using a logistic regression model. \( p \)-values < 0.05 were considered statistically significant. All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS), version 18.0 (SPSS Inc., Chicago, IL).

To determine the GNRI cutoff value, positive likelihood ratio was calculated as follows:

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

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

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

**Results**

**Subject characteristics**

The clinical characteristics of the patients according to dialysis method are shown in Table 1. GNRI data represented a normal distribution, and the average GNRI value was 100.1 ± 8.4 in HD patients and 99.2 ± 8.1 in PD patients. No significant differences in GNRI and SLC were observed between the two groups. The levels of potassium and albumin were higher in HD patients. Patient clinical characteristics according to GNRI are shown in Table 2. No significant differences in age, sex, or presence of DM were observed between the two groups. SLCs were higher in patients with higher GNRI although there was no statistical difference. The levels of BUN and albumin were higher in patients with higher GNRI.

**Factors for predicting malnutrition**

Logistic regression analysis was performed for investigating the causal relationship between independent variables and GNRI. The results of the logistic regression for predicting malnutrition according to GNRI are shown in Table 3. The results showed that age > 60 years (OR: 10.783, 95% CI: 1.936–60.059, \( p = 0.007 \)), female sex (OR: 6.643, 95% CI: 1.269–34.788, \( p = 0.025 \)), and CD19 count < 100 (OR: 9.202, 95% CI: 1.481–57.191, \( p = 0.017 \)) predicted malnutrition in HD and PD patients.

Patient clinical characteristics according to CD19 count are shown in Table 4. Duration of dialysis was shorter, and SLC and albumin levels were higher, in the group with higher CD19 counts.

**Discussion**

In this study, we examined the relationship between GNRI and SLC in HD and PD patients using logistic regression.
Several studies have suggested that GNRI is the simplest and most accurate index to assess malnutrition in HD patients.\(^3\)\(^a\)\(^\ce{12\text{-}14}\) Similarly, a recent study of 486 PD patients over 14 years showed that GNRI is also able to predict nutritional status and prognosis in PD patients, although the role of GNRI in PD patients had been unclear previously. According to this study, GNRI is significantly associated with creatinine, albumin, BMI, arm circumference, fat mass index, and comorbidity.\(^4\)

Yamada et al. suggested that the most accurate GNRI cutoff value to identify malnutrition in HD patients was less than 91.2 based on the malnutrition-inflammation score.\(^5\) In a study of 753 HD patients, Panichi et al. demonstrated that GNRI less than 92, the lowest quartile, was strongly associated with creatinine, albumin, BMI, arm circumference, fat mass index, and comorbidity.\(^4\)

In addition, a GNRI cutoff value of 96.4 is associated with significant reduction of lean mass index according to Kang et al.\(^4\)

In this study, to determine a possible GNRI cutoff value for malnutrition, the sensitivity, specificity, and positive likelihood ratio were examined. A GNRI value of 100 was shown to indicate the highest value of positive likelihood ratio (data not shown).

It appears that dietary intake influences circulating lymphocyte counts in PD patients. In a study of 55 uremic patients, Grzegorzewska and Leander proposed that effectiveness of nutrition can be monitored by evaluating TLC and SLC.\(^5\)

TLC has been used as an index to represent nutritional status, but its role in assessing malnutrition and prognosis in HD and PD patients is debatable.\(^8\)\(^\text{15}\) Atesç et al. reported that volume status is more closely related to TLC than nutritional status in PD patients.\(^8\)

Among the SLCs in the present study, CD19 count, a marker of B lymphocytes, is associated with GNRI. These cells play an important role in initiating the immune response through antigen-independent and immunoglobulin-induced activation of B cells.\(^16\)

Palop et al. measured changes in cell immunity during a 3-year follow-up of PD patients. TLC, CD8, and CD19 cell counts were significantly decreased over time.\(^11\)

Grzegorzewska and Leander reported that CD19 cell count is positively correlated with intake of potassium,
Table 3. Logistic regression for predicting malnutrition according to GNRI at the start of the study.

| Variable                      | OR (95% CI)  | p     |
|-------------------------------|--------------|-------|
| Age > 60 years                | 10.783 (1.936–60.059) | 0.007 |
| Female                        | 6.643 (1.269–34.788)  | 0.025 |
| PD                            | 3.159 (0.338–29.533)  | 0.313 |
| Duration of dialysis (> 60)   | 0.705 (0.136–3.657)  | 0.677 |
| DM                            | 1.507 (0.342–6.633)  | 0.588 |
| Total lymphocyte count (×10³) | 0.473 (0.113–1.972)  | 0.304 |
| CD8 count (×10³) < 1500        | 0.598 (0.040–8.996)  | 0.711 |
| CD4 count (×10³) < 600         | 0.969 (0.176–5.329)  | 0.971 |
| CD8 count (×10³) < 350         | 3.509 (0.331–37.193) | 0.297 |
| CD19 count (×10³) < 100        | 9.202 (1.481–57.191) | 0.017 |

DM: diabetes mellitus; PD: peritoneal dialysis.

Table 4. Clinical characteristics of 66 dialysis patients according to CD19 count at the start of the study.

| Variables                      | CD19 > 100 | CD19 < 100 | p-values |
|-------------------------------|------------|------------|----------|
| Age (years)                   | 55.1 ± 13.7| 53.1 ± 12.7| 0.565    |
| Sex (male/female)             | 21/20      | 17/8       | 0.208    |
| DM                            | 15 (36.6%) | 10 (40%)   | 0.799    |
| HD/ PD                        | 32/9       | 18/7       | 0.768    |
| Duration of dialysis (months) | 50.6 ± 37.7| 78.8 ± 17.6| 0.022    |
| Body mass index               | 21.4 ± 2.9 | 22.3 ± 3.5 | 0.511    |
| GNRI                          | 101.2 ± 8.0| 97.9 ± 8.4 | 0.121    |
| Systolic blood pressure (mmHg)| 131.8 ± 30.6| 145.4 ± 26.5| 0.062    |
| Diastolic blood pressure (mmHg)| 78.2 ± 17.6| 84.7 ± 10.2| 0.065    |
| Kt/V                          | 1.7 ± 0.29 | 1.7 ± 0.22 | 0.504    |
| Neutrophil lymphocyte ratio   | 0.42 ± 0.15| 0.41 ± 0.15| 0.931    |
| Total lymphocyte count (×10³) | 1525 ± 586 | 1537 ± 513 | 0.933    |
| CD3 count (×10³)              | 1129 ± 406 | 796 ± 256  | 0.001    |
| CD4 count (×10³)              | 701 ± 262  | 488 ± 169  | 0.001    |
| CD8 count (×10³)              | 426 ± 177  | 302 ± 127  | 0.002    |
| CD19 count (×10³)             | 176 ± 74   | 57 ± 26    | 0.001    |
| CD4/CD8 ratio                 | 1.7 ± 0.7  | 1.7 ± 0.7  | 0.905    |
| Hemoglobin (g/dL)             | 11.1 ± 0.7 | 10.8 ± 0.9 | 0.145    |
| Iron (µg/dL)                  | 96.9 ± 35.9| 83.7 ± 38.0| 0.173    |
| TIBC (µg/dL)                  | 247.2 ± 38.2| 249.7 ± 40.6| 0.805    |
| TSAT (%)                      | 40.5 ± 17.5| 33.5 ± 15.6| 0.111    |
| Ferritin (µg/mL)              | 366.4 ± 241.3| 337.5 ± 295.4| 0.672    |
| BUN (µg/dL)                   | 63.1 ± 17.1| 66.1 ± 21.0| 0.534    |
| Cr (µg/dL)                    | 9.9 ± 2.6  | 10.3 ± 2.2 | 0.472    |
| Sodium (mEq/L)                | 137.8 ± 2.1| 137.3 ± 4.0| 0.487    |
| Potassium (mEq/L)             | 5.1 ± 0.8  | 5.1 ± 0.8  | 0.987    |
| Calcium (mg/dL)               | 8.9 ± 0.5  | 8.8 ± 0.5  | 0.656    |
| Phosphorus (mg/dL)            | 5.1 ± 1.3  | 5.4 ± 1.5  | 0.282    |
| Parathyroid hormone (pg/mL)   | 277.6 ± 251.4| 171.6 ± 216.6| 0.077    |
| Albumin (g/dL)                | 3.9 ± 0.3  | 3.6 ± 0.4  | 0.022    |
| Total cholesterol (mg/dL)     | 154.8 ± 37.0| 176.1 ± 54.0| 0.071    |
| High density lipid (mg/dL)    | 44.4 ± 19.0| 50.7 ± 14.6| 0.163    |
| Low density lipid (mg/dL)     | 67.8 ± 24.8| 81.7 ± 33.1| 0.064    |
| Uric acid (mg/dL)             | 7.6 ± 1.6  | 7.4 ± 1.4  | 0.748    |

DM: diabetes mellitus; HD: hemodialysis; PD: peritoneal dialysis; GNRI: geriatric nutritional risk index; TIBC: total iron binding capacity; TSAT: transferrin saturation.

copper, vitamin A, and beta-carotene, and its increase improves insomnia, weakness, and clinical symptoms (i.e., dysgeusia, anorexia, nausea, vomiting) and other indicators (i.e., serum albumin, hematocrit, Lean Body Mass (LBM)) that reflect nutritional status.5

In uremic patients, the relationship between malnutrition and immune function has been known for some time. Glasscock postulated that cellular immune dysfunction observed in these patients may be the consequence of nutritional deficiency rather than uremic toxins or endogenous factors.17 More research is needed to assess the nutritional function of immune cells in these patients.

Our study has several limitations. It is a prospective study, but the observational period was only 2 months, and the sample size was too small. A well-constructed study with a larger sample size and a longer follow-up period is needed.

In addition, it may be controversial that malnutrition is defined as serum albumin under 3.0 g/dL in the process of obtaining the GNRI cutoff value; however, the absence of a precise definition of malnutrition in dialysis patients led to our use of serum albumin level.

Finally, further studies on the relationship between SLC and mortality are needed.

Conclusions

These results suggest that GNRI and SLCs (especially CD19 count) may be significant nutritional markers in HD and PD patients.

Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

Funding

This study was supported by a grant from the Kosin University College of Medicine (2014).

References

1. 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;82:777–783.
2. de Mutsert R, Grootendorst DC, Axelsson J, et al. Excess mortality due to interaction between protein-energy wasting, inflammation and cardiovascular disease in chronic dialysis patients. Nephrol Dial Transplant. 2008;23:2957–2964.
3. Yamada K, Furuya R, Takita T, et al. Simplified nutritional screening tools for patients on maintenance hemodialysis. Am J Clin Nutr. 2008;87:106–113.
4. Kang SH, Cho KH, Park JW, Yoon KW, Do JY. Geriatric Nutritional Risk Index as a prognostic factor in peritoneal dialysis patients. Perit Dial Int. 2012;33:405–410.
5. Grzegorzewska, AE, Leander M. Total lymphocyte count in relation to dietary intake and nutritional status of peritoneal dialysis patients. Adv Perit Dial. 2005;21:35–40.
6. Forse RA, Rompre C, Crosilla P, O-Tuitt D, Rhode B, Shizgal HM. Reliability of the total lymphocyte count as a parameter of nutrition. Can J Surg. 1985;28:216–219.
7. Kuzuya M, Kanda S, Koike T, Suzuki Y, Iguchi A. Lack of correlation between total lymphocyte count and nutritional status in the elderly. *Clin Nutr*. 2005;24:427–432.

8. Ateş K, Ateş A, Kutlay S, Nergizoglu G, Karatan O. Total lymphocyte count in peripheral blood of peritoneal dialysis patients: Relationship to clinical parameters and outcome. *J Nephrol*. 2004;17:246–252.

9. Carvounis CP, Manis T, Coritsidis G, Dubinsky M, Serpente P. Total lymphocyte count: A promising prognostic index of mortality in patients on CAPD. *Perit Dial Int*. 2000;20:33–38.

10. Grzegorzewska AE, Leander M. Total lymphocyte count and subpopulation lymphocyte count in relation to blood bicarbonate concentration in peritoneal dialysis patients. *Adv Perit Dial*. 2005;21: 31–34.

11. Palop L, Vega N, Rodriguez T, et al. Nutritional status of CAPD patients at three years. *Perit Dial Int*. 1996;16(Suppl 1):S195–S202.

12. Kobayashi I, Ishimura E, Kato Y, et al. Geriatric Nutritional Risk Index, a simplified nutritional screening index, is a significant predictor of mortality in chronic dialysis patients. *Nephrol Dial Transplant*. 2010;25:3361–3365.

13. Panichi V, Cupisti A, Rosati A, et al. Geriatric nutritional risk index is a strong predictor of mortality in hemodialysis patients: Data from the Riscavid cohort. *J Nephrol*. 2014;27:193–201.

14. Park JH, Kim SB, Shin HS, Jung YS, Rim H. Geriatric nutritional risk index may be a significant predictor of mortality in Korean hemodialysis patients: A single center study. *Ther Apher Dial*. 2012;16: 121–126.

15. Jung YS, You G, Shin HS, Rim H. Relationship between geriatric nutritional risk index and total lymphocyte count and mortality of hemodialysis patients. *Hemodial Int*. 2014;18:104–112.

16. Wang K, Wei G, Liu D. CD19: A biomarker for B cell development, lymphoma diagnosis and therapy. *Exp Hematol Oncol*. 2012;1:36. doi: 10.1186/2162-3619-1-36.

17. Glassock RJ. Nutrition, immunology, and renal disease. *Kidney Int Suppl*. 1983;16:S194–S198.