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Relationship between probable sarcopenia and nutritional disorders as evaluated using the Geriatric Nutritional Risk Index and serum phosphorus concentration in maintenance dialysis patients: A cross-sectional study

Kenichi KONO (kohno1209@gmail.com)
International University of Health and Welfare
Yoshihumi MORIYAMA
Department Wellness center, Kaikoukai Nagoya Kyoritsu Hospital
Ayaka HARA
Dialysis division at Shizuoka, Kaishokai
Hiroki YABE
School of Rehabilitation, Seirei Christoper University
Yusuke NISHIDA
Department Physical Therapy, International University of Health and Welfare Graduate School
Tetsuya YAMADA
Dialysis division, Kaikoukai healthcare group

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Abstract

Background To explore the relationship between sarcopenia and nutritional disorders, as evaluated using the Geriatric Nutritional Risk Index (GNRI) and serum phosphorus concentration (P).

Methods: This cross-sectional study analyzed 909 Japanese maintenance hemodialysis patients from a multicenter hemodialysis unit. The nutritional indices (GNRI and P) and sarcopenia indices [grip strength and Short Physical Performance Battery (SPPB)] were evaluated in all patients. Multiple logistic regression analysis was performed with the sarcopenia indices as dependent variables and GNRI only, P only, and combined GNRI and P as independent variables adjusted for patient attributes. The odds ratio (OR) and 95% confidence interval (95% CI) for the reference value were calculated by setting the category reference value to GNRI ≥90 and P to 3.6-5.0 mg/dL. The main outcome measure was presence of probable sarcopenia.

Results: Grip strength was associated with decreased GNRI only (OR: 2.27, 95% CI: 1.64-3.16) and decreased GNRI and P (OR: 3.77, 95% CI: 1.49-9.53). In addition, SPPB was associated with decreased GNRI only (OR: 1.78, 95% CI: 1.30-2.44) and decreased GNRI and P (OR: 8.82, 95% CI: 3.52-22.12).

Conclusions: Nutritional disorders, in which both GNRI and P are decreased, are strongly related to sarcopenia compared with nutritional disorders in which only GNRI or only P is decreased.

Background

Protein energy wasting syndrome (PEW), which causes adverse changes in nutrition and body composition, is highly prevalent in patients with chronic kidney disease, especially in those undergoing dialysis, and is associated with high morbidity and mortality.[1] It has been reported that PEW is related to appetite ratings.[2] In addition, it has been pointed out that malnutrition accelerates aortic calcification and is closely related to cardiovascular disease onset and mortality.[3,4] In these studies, nutritional status was assessed using the Geriatric Nutritional Risk Index (GNRI). GNRI is used to assess serum albumin kinetics and physical condition and has been utilized as a nutritional assessment index in Japanese dialysis patients; the clinical usefulness of GNRI has also been reported.[3,5,6]

Moreover, serum phosphorus concentration (P) is used as another clinical evaluation index to assess the nutritional status of patients undergoing dialysis treatment. P is influenced by phosphorus intake and absorption. Therefore, as the specificity of malnutrition assessment is considered to be different between P and GNRI, it is necessary to investigate these two indicators in order to know their impact on epidemic sarcopenia. A previous study on the relationship between GNRI and P and mortality showed that higher GNRI and lower P were not significantly associated with patient mortality.[7] On the other hand, even if P is high or low, when GNRI is low, the mortality rate is significantly high.[7] In addition, malnutrition is reported to lead not only to death but also to sarcopenia.[8] Therefore, it is clinically useful to clarify the relationship between sarcopenia and nutritional status evaluated by GNRI and P. However, only a few studies have

evaluated nutritional status by combining GNRI and P and investigated the relationship between GNRI and P and sarcopenia.

We hypothesized that nutritional disorders can be likely more detected when evaluating GNRI and P together rather than when evaluating GNRI and P separately. The purpose of this study was to explore the relationship between sarcopenia and nutritional disorders evaluated using GNRI and P in patients undergoing maintenance dialysis.

Methods

Study population and design

This cross-sectional study included clinically stable Japanese outpatients in multicenter hemodialysis unit from April 2012 to April 2018. Exclusion criteria included age <18 years, dialysis vintage <6 months, and refusal to participate. This study was approved by the Ethical Committee of International University of Health and Welfare (Approval number. 17-Io–95).

Demographic and clinical laboratory findings

Patients' demographics, such as age, dialysis vintage, and body mass index (BMI) were investigated. Laboratory values of serum albumin, serum hemoglobin, C reactive protein, serum intact parathyroid hormone, standardized dialysis volume (Kt/V), and normalized protein catabolic rate (nPCR) were also collected.

Assessment of nutritional status and classification of malnutrition by GNRI and P

GNRI was calculated using the formula described elsewhere: *GNRI = [1.489×serum albumin (g/L)] + [41.7×(body weight/ideal body weight)].*[5,9] Ideal body weight was defined as weight with a BMI value of 22 kg/m^2.[10] Malnutrition was defined as a GNRI <90 according to previous studies.[3,11]

P was classified into three categories according to the guidelines of the Japanese Society of Dialysis Therapy[12]: a P of 3.5–6.0 mg/dL was considered the reference range, P <3.5 mg/dL was considered decreased, and P >6.0 mg/dL was considered abnormally high.[12]

In addition, GNRI and P were categorized together as follows: the reference category was set as GNRI ≥90 and 3.5≤ P ≤6.0, whereas six other categories, including 2 GNRI categories and 3 P categories were also formed.

Measurement of indicators related to sarcopenia

The diagnosis and definition of sarcopenia have been revised in 2018.[13] In its 2018 definition, low muscle strength was pointed out as the primary parameter of sarcopenia; presently, muscle strength is considered the most reliable measure of muscle function.[13] In addition, physical performance was formerly considered part of the core definition of sarcopenia.[13] In the definition of 2018, physical performance was regarded as an index for determining severity. According to this new algorithm,[13] we evaluated muscle strength by using grip strength test and physical performance by using Short Physical Performance Battery (SPPB) to determine probable sarcopenia. The cut-off value of grip strength was 26 kg for men and 18 kg for women from an Asian consensus[14] and that of SPPB was 8 points. Grip strength was measured using a Smedley-spring type dynamometer (101A HATS, Tokyo).

Statistics

All values are expressed as mean ± standard deviation (SD) or percentage, whenever appropriate. Descriptive statistics of nutrition and sarcopenia index were calculated by age group and were compared by one-way analysis of variance (ANOVA) and post hoc multiple comparisons. To analyze the relationship between probable sarcopenia and nutritional disorder, multiple logistic regression analyses were performed with grip strength and SPPB as dependent variables, and GNRI only, P only, and 6 categories of combined GNRI and P as independent variables. Results from logistic regression analyses were presented as odds ratios (OR) with 95% confidence intervals. A P value < 0.05 was considered statistically significant. Statistical analyses were performed using SPSS (version 24, IBM, Tokyo).

Results

Patient demographic, nutritional status, and sarcopenia index by age group

A total of 1141 Japanese patients were registered. 232 patients in whom GNRI and P data could not be obtained were excluded. Finally, 909 patients were analyzed.

Table 1 shows the patient's demographic, nutritional status, and sarcopenia index.

Table 2 shows the nutritional status and sarcopenia index according to 5 age groups. The patients' mean (±SD) age was 69.4 (±11.4) years. As shown in Table 2, 462 patients (56%) were elderly (age >70 years). Regarding nutritional status, the mean GNRI was 91.5, which decreased significantly with increasing age. In particular, the mean GNRI value in patients aged >80 years was 87.9, indicating malnutrition. In addition, grip strength and SPPB scores as sarcopenia indices decreased significantly with increasing

age. In elderly patients aged ≥80 years, grip strength and SPPB scores were lower than the diagnostic criteria for probable sarcopenia.

Relationship between nutritional status and grip strength as sarcopenia indices

Table 3 shows the relationship between GNRI and P (nutritional indices) and grip strength (probable sarcopenia index). When analyzing GNRI and P separately, the GNRI of <90 showed a significant association with grip strength as a probable sarcopenia index (OR 2.272, 95% CI 1.636–3.155), but P did not show a significant association with grip strength. Furthermore, when GNRI and P were analyzed together, grip strength was significantly lower regardless of P in GNRI<90. In particular, when P was <3.5 mg/dL, the OR of the decreasing grip strength as probable sarcopenia was 3.77 (95% CI 1.491–9.533).

Relationship between nutritional status and SPPB as sarcopenia indices

Table 3 shows the relationship between GNRI and P (nutritional indices) and SPPB (probable sarcopenia index). When analyzing GNRI and P separately, the GNRI of <90 showed a significant association with SPPB (OR 1.782, 95% CI 1.303–2.437) as a probable sarcopenia index, but P did not show a significant association with grip strength. Furthermore, when GNRI and P were analyzed together, SPPB was significantly lower in P <6.0 mg/dL and GNRI <90. In particular, when P <3.5 mg/dL, the OR of the decreasing SPPB as a sarcopenia index was 6.77 (95% CI 2.658–17.243).

Discussion

In this observational study, we showed the relationship between sarcopenia and malnutrition status as evaluated by GNRI and P. It was revealed that both decreased GNRI and P lead to the presence of sarcopenia. When predicting sarcopenia using GNRI, obtained by evaluating the physique and serum albumin kinetics, and P, patients with GNRI <90 and P <3.5 mg/dL had the highest OR for lower grip strength and SPPB score.

Recently, GNRI has been used to screen the nutritional status of patients with various diseases. A report on the usefulness of GNRI in dialysis patients was published in 2008.[5] In addition, it has been reported that GNRI has a higher sensitivity and specificity than the Mini Nutritional Assessment Short Form (MNA-SF) for predicting the cut-off value of the Malnutrition-Inflammation Score (MIS)[5,15]; the cut-off value was 91.2.[5] Moreover, if the outcome is mortality, the cut-off value of GNRI has been reported to be 90.5 in Japanese dialysis patients.[16] However, the value of GNRI for predicting sarcopenia has not been fully reported. Referring to the previous study investigating the relationship between sarcopenia and GNRI,

muscle strength and muscle mass were found to be related to GNRI,[17] and the cut-off value of GNRI for maintaining gait ability on their own was 86.7.[18] To estimate sarcopenia, we considered that the findings of the previous studies support the results in our present study, which are useful to investigate whether the value GNRI should be <90 in assessing nutritional status. Furthermore, in the analysis by age group, we should note that GNRI decreases along with increasing age; nearly half of all patients aged >70 years had GNRI of <90.

In addition, the effect of age was also observed in P. P in dialysis treatment is a general management index of chronic kidney disease mineral bone disorder (CKD-MBD). Hyperphosphatemia is a risk factor for ectopic calcification and mortality.[19–21] Patients with hypophosphatemia, which is closely associated with restriction of protein intake, are known to have increased mortality risk.[22,23] Recently, hemodialysis and medications were considered as management options for these patients to increase their protein intake. Moreover, the validity of P for assessing nutrition status has been reported. In our study findings, P > 3.5 mg/dL was shown to be not related to grip strength and SPPB in the adjusted model. It was indicated that assessing malnutrition using only P for predicting sarcopenia should be done cautiously. The absence of relationship between probable sarcopenia and P, unlike GNRI, may be due to the fact that P could be altered by medications based on the result of regular blood testing in a short period of time. In the management of CKD-MBD, it was suggested that P should be strictly maintained within the normal range (3.5–6.0 mg/dL) compared to calcium concentration and that of intact parathyroid hormone.[12] It has been reported that the phosphate binder improves the life prognosis[24] of patients with P >5.2 mg/dL.[25] However, in patients with P <3.7 mg/dL at baseline, it has been known that it is difficult to obtain the effect of improving life prognosis even if patients were treated by a phosphate binder.[24] The reason why life prognosis is less likely to improve in patients with low phosphorus is considered to be due to the involvement of malnutrition. Therefore, it is important to evaluate protein uptake by GNRI as well as phosphorus.

This study has several limitations. First, we could not investigate detailed complications affecting feeding and metabolism and nutritional states, such as diabetes, stroke, and gastrointestinal cancer, as well as conduct an analysis adjusted for these factors. Second, we were not able to obtain detailed dosing data, such as phosphorus adsorbent and activated vitamin D preparation affecting serum phosphorus concentration. Moreover, the dialysis membranes affecting serum albumin kinetics were also not investigated. Finally, we could not show the causal association between aging, malnutrition, and probable sarcopenia, because the study had a retrospective cross-sectional design.

Conclusion

A nutritional disorders, presenting with a decreased in both GNRI and P, are strongly related to sarcopenia compared with nutrition disorders showing only abnormalities in only GNRI or only P. Multilateral observation of protein uptake kinetics, physique, and P is useful in predicting sarcopenia in dialysis patients. Our findings provide additional data for identifying patients with a high risk of sarcopenia using

two nutritional indicators, such as GNRI and P. Moreover, these data will determine patients who require exercise interventions to reduce their sarcopenia risk. As part of the management of dialysis patients, it is necessary to recognize that their nutritional status and physical function decrease with age. When estimating the physical function deterioration related to sarcopenia by nutritional status, it is useful to not only analyze GNRI or phosphorus separately but also both indices together.

Abbreviations

GNRI: Geriatric Nutritional Risk Index; P: phosphorus; SPPB: Short Physical Performance Battery; OR: odds ratio; 95% CI: 95% confidence interval; PEW: Protein energy wasting syndrome; BMI: body mass index; Kt/V; standardized dialysis volume; nPCR: normalized protein catabolic rate; SD: standard deviation; CKD-MBD: chronic kidney disease mineral bone disorder

Declarations

Ethics approval and consent to participate

The study protocol complied with the Helsinki Declaration standards and was approved by the Ethical Committee of International University of Health and Welfare (Approval number 17-Io–95). The requirement of written informed consent was waived as this study used retrospective data.

Consent for publication

Not Applicable.

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interest.

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Authors' contributions

KK, YM, AH, HY, YN, and TY contributed to the conception and design of the work, the acquisition, analysis and interpretation of data, drafting or revision of the manuscript, and final approval of the version to be submitted.

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Tables

Table 1. Patients' demographic data, nutritional status, and sarcopenia index

Age (years)	69.4 (11.4)
Sex (male/female)	498 / 411
Dialysis vintage (month)	82.3 (91.2)
BMI (kg/m^2)	22.0 (4.22)
Serum albumin (g/dL)	3.55 (0.33)
GNRI	91.5 (6.56)
Serum hemoglobin (g/dL)	10.9 (1.07)
CRP (mg/dL)	0.38 (0.83)
Serum phosphorus (mg/dL)	5.15 (1.25)
Serum calcium (mg/dL)	8.98 (5.15)
Serum intact-PTH (pg/dL)	158.3 (169.0)
Grip (kg)	23.6 (8.68)
SPPB (point)	8.79 (3.43)

GNRI, Geriatric Nutritional Risk Index; CRP, C-reactive protein; SPPB, Short Physical Performance Battery; PTH, parathyroid hormone; BMI, body mass index

Table 2. Nutritional status and sarcopenia index by age group

	≤49 years (n=60)	50-59 years (n=88)	60-69 years (n=249)	70-79 years (n=350)	≥80 (n=162)	P value
GNRI	95.8 (5.11)	94.2 (4.85)	92.9 (6.11)	90.7 (6.71)	87.9 (6.05)	<0.01
Serum phosphorus (mg/dL)	5.76 (1.44)	5.43 (1.35)	5.26 (1.27)	5.04 (1.17)	4.84 (1.17)	<0.01
Grip strength	32.0 (8.68)	27.1 (7.59)	24.8 (8.69)	22.6 (8.03)	18.8 (7.06)	<0.01
SPPB	10.6 (250)	9.71 (3.10)	9.19 (3.21)	8.74 (3.32)	7.13 (3.80)	<0.01

Data are expressed mean ± SD

GNRI, Geriatric Nutritional Risk Index; SPPB, Short Physical Performance Battery

Table 3. Interrelationship between nutritional status and probable sarcopenia index

	Multivariate model			
	Loss of grip strength (man<26 kg, woman<18 kg)		Loss of SPPB (<8 points)	
	OR (95% CI)	P value	OR (95% CI)	P value
GNRI≥90	Reference		Reference	
GNRI<90	2.272 (1.636–3.155)	<0.001	1.782 (1.303–2.437)	< 0.001
3.5≤P≤6.0 (mg/dL)	Reference		Reference	
P<3.5 (mg/dL)	1.400 (0.790–2.481)	0.25	1.430 (0.840–2.435)	0.19
P>6.0 (mg/dL)	1.143 (0.760–1.719)	0.52	0.632 (0.419–0.952)	0.03
GNRI≥90 and 3.5≤P≤6.0 (mg/dL)	Reference		Reference	
GNRI≥90 and P<3.5 (mg/dL)	0.844 (0.357–1.997)	0.70	0.588 (0.242–1.426)	0.24
GNRI≥90 and P>6.0 (mg/dL)	1.099 (0.668–1.807)	0.71	0.815 (0.503–1.322)	0.41
GNRI<90 and 3.5≤P≤6.0 (mg/dL)	2.005 (1.345–2.988)	0.001	1.690 (1.161–2.459)	0.006
GNRI<90 and P<3.5 (mg/dL)	3.770 (1.491–9.533)	0.005	6.770 (2.658–17.243)	< 0.001
GNRI<90 and P>6.0 (mg/dL)	2.764 (1.309–5.836)	0.008	0.663 (0.307–1.432)	0.30

The multivariate model was adjusted for sex, dialysis vintage, and age.

SPPB, Short Physical Performance Battery; GNRI, Geriatric Nutritional Risk Index; P, serum phosphorus; OR, Odds ratio; 95% CI, 95% confidence interval

Supplementary Files

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