Association between the Ankle-Brachial Pressure Index and Geriatric Nutrition Risk Index in Hemodialysis Patients

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Abstract

Objective: The development of atherosclerosis in hemodialysis (HD) patients is associated with malnutrition. However, the relation between the ankle-brachial pressure index (ABI), as a diagnostic assessment tool for atherosclerosis obliterans (ASO), and nutritional indicators has not been well studied. The present study was performed to identify nutritional factors related to atherosclerosis by investigating the relationship between the ABI and various parameters, including the Geriatric Nutrition Risk Index (GNRI) as a nutritional indicator, in HD patients.

Methods: We measured the ABI of 47 HD patients and compared its relationship to patient characteristics (sex, age, and history of diabetes), laboratory parameters (white blood cell count, low-density lipoprotein cholesterol [LDL-C], and C-reactive protein [CRP]), and the GNRI. The patients were categorized into two groups according to whether their ABI value was above or below 0.9, with a low ABI being a diagnostic marker for ASO. The results from the two groups were then analyzed and compared.

Results: The percentage of patients with an ABI <0.9 was 66%. Linear regression analysis revealed that a low ABI was significantly associated with a low GNRI, low hematocrit, hemoglobin, and LDL-C levels, high levels of inflammatory parameters (CRP level and white blood cell count); and a high platelet count. Among the factors having significant association with ABI in linear regression analysis, those related to nutritional status and inflammation were selected and used as explanatory variables in multiple logistic regression analysis, where the dependent variables were the two groups. We found only GNRI was a significant predictive factor for ABI.

Conclusion: The ABI in HD patients was associated with indicators of the nutritional status. In the multivariate analysis, a low GNRI was a significant predictive indicator for a low ABI.

Keywords: Ankle-brachial pressure index; Geriatric nutritional risk index; Hemodialysis; Atherosclerosis; Peripheral arterial disease; Cardiovascular disease; Malnutrition inflammation atherosclerosis syndrome

Introduction

Hemodialysis (HD) patients have a high prevalence of peripheral arterial disease (PAD) [1], such as arteriosclerosis obliterans (ASO), which is known to have a significant impact on patient morbidity and mortality.

The effectiveness of measuring the ankle-brachial pressure index (ABI) for diagnosing ASO has been well documented, and the guidelines recommend annual measurement of ABI for HD patients. A low ABI is associated with an increased risk of atherosclerosis and is known to predict morbidity and mortality due to cardiovascular disease (CVD) [2]. Many patients with an ABI of less than 0.9 have been observed to have malnutrition-inflammation-atherosclerosis syndrome (MIA syndrome) [1,3], in which malnutrition, inflammation and atherosclerosis are closely related and influence each other. This suggests there is a strong relation between atherosclerosis and malnutrition. The GNRI was developed by Bouillanne et al. [4] as a tool for predicting the risk of malnutrition-related morbidity and mortality. Yamada et al. [5] showed the GNRI was a very simple indicator of malnutrition in HD patients that can be calculated using serum albumin, height, and present body weight (dry weight) [5].

Although the relation between ABI and MIA syndrome in HD patients is recognized, there are few reports analyzing the relationship between ABI and nutritional indicators. Therefore, we measured various parameters including the nutritional indicator, GNRI, in HD patients and analyzed the relationship between ABI and each parameter. The ultimate aim of our study was to identify nutritional factors that are related to atherosclerosis in HD patients.

Methods

This study was approved by the Ethics Review Committee of Fukuoka Sanno Hospital. This study was a retrospective study using samples and clinical information of patients that were collected during past regular medical examinations. The research objective and other information were fully disclosed on the hospital website. We took care to protect personal patient information.
In this study, we enrolled 47 patients undergoing maintenance HD whose ABI was measured from April 2014 to April 2018 at Fukuoka Sanno Hospital in Japan. Patients with a history of lower limb amputation, an abnormally high ABI (≥ 1.40), and low cardiac function (left ventricular ejection fraction of <40%) were excluded. The ABI of each patient was measured in the supine position using the VS-1500N vascular screening system (Fukuda Denso Co., Ltd, Tokyo, Japan). The ABI was measured on both lower limbs, and the lower value was used as the ABI value for each patient. We analyzed whether an association was present between the ABI and patient characteristics (sex, age, history of diabetes, time on HD, heart rate, and history of treatment for dyslipidemia [hydroxymethylglutaryl-CoA reductase inhibitors, fibrate drugs, eicosapentaenoic acid]), the GNRI as a nutritional indicator, and several laboratory parameters (blood urea nitrogen, creatinine, triglycerides, low-density lipoprotein cholesterol [LDL-C], hematocrit, hemoglobin, white blood cell [WBC] count, total protein level, C-reactive protein [CRP] level, and platelet [plt] count). The GNRI was calculated using patient present body weight (dry weight) and height measured at the time of ABI measurement. The laboratory test results were obtained a few days before or after the ABI measurement prior to dialysis. In addition, the patients were analyzed by group (ABI ≥ 0.9 and ABI<0.9), where an ABI<0.9 was considered a nutritional indicator, and several laboratory parameters (blood urea nitrogen, creatinine, triglycerides, low-density lipoprotein cholesterol [LDL-C], hematocrit, hemoglobin, white blood cell [WBC] count, total protein level, C-reactive protein [CRP] level, and platelet [plt] count). The GNRI was calculated using patient present body weight (dry weight) and height measured at the time of ABI measurement. The laboratory test results were obtained a few days before or after the ABI measurement prior to dialysis. In addition, the patients were analyzed by group (ABI ≥ 0.9 and ABI<0.9), where an ABI<0.9 was considered a diagnostic marker for ASO. The GNRI was calculated according to the formula proposed by Yamada et al. as shown below [5].

$$\text{GNRI}=14.89 \times \text{serum albumin (g/dL)} + 41.7 \times (\text{present body weight (kg)} / \text{ideal body weight (kg)})$$

where ideal body weight (kg) = $\left(\text{height (m)} \times 22\right)$. In cases where the current body weight exceeded the ideal body weight, it was considered that the present body weight/ideal body weight = 1. A GNRI<91.2 was considered a risk for malnutrition [5].

The normality of the sampling distribution was tested using standard skewness and kurtosis. For normally distributed data, the mean ± standard deviation was used whereas the median was used for the non-normally distributed data. Continuous variables were compared using a t-test (normal distribution) or Wilcoxon signed-rank sum test (non-normal distribution) according to the normality of the sampling distribution. Categorical variables were compared using the chi-squared test. A multivariate logistic regression analysis was carried out using the predictive factors found to have a significant association with the ABI in univariate analysis using Kendall’s rank correlation and the dependent variables were the two groups, ABI<0.9 and ABI ≥ 0.9. The statistical analysis software, StatMateV (version 5.01), was used for all analyses. A p-value <0.05 was considered statistically significant.

**Results**

**Patient background**

The characteristics of the 47 enrolled patients were as follows: Mean age, 71.0 ± 10.7 years (range, 48–96 years; 74.5% men); median time on HD for the first to third quartile, 67.0 months (range, 27.0–129.0 months); and patients with a history of diabetes, 68.1%.

**Distribution of ABI and LDL-C level**

The frequency distribution chart for the ABI and LDL-C level of all patients is shown in Figures 1 and 2. The sample had a non-normal distribution (p=0.05; skewness, 0.445; kurtosis, 1.997), and the median ABI of the first to third quartiles was 0.71 (range, 0.64–0.99). The number of patients in the low ABI group (ABI<0.9) was 31 (66%) (Figure 1). The sample had a normal distribution (p=NS; skewness, 0.067; kurtosis, 2.552), and the mean LDL-C level was 90.6 ± 27.2 mg/dL (Figure 2).

![Figure 1: Bar graph showing frequency distribution of the ABI. ABI: Ankle-Brachial Index.](image)

![Figure 2: Bar graph showing frequency distribution of the LDL-C level. LDL-C: Low-Density Lipoprotein Cholesterol.](image)

**ABI and patient background**

The ABI was significantly different between male and female patients, between patients with and without diabetes, and between patients with and without treatment of dyslipidemia. The ABI value of the group with a GNRI<91.2 was significantly lower than that of the group with a GNRI ≥ 91.2 (Table 1). A significant negative correlation was observed between the ABI and heart rate. However, no correlation was found between the ABI and age or dialysis history (Table 2).

**ABI and laboratory values**

A significant positive correlation was observed between the ABI and serum blood urea nitrogen, creatinine, triglyceride, LDL-C, hematocrit, and hemoglobin levels. A significant negative correlation was observed between ABI and serum total protein, CRP, WBC, and plt levels (Table 2). Multiple logistic regression analysis was conducted to determine factors that predict an ABI<0.9, where explanatory variables were LDL-C, GNRI, and CPR, all of which were found to have significant differences as shown in Tables 1 and 2. They are also all related to nutritional status and inflammation. It revealed that a lower GNRI (<91.2) is associated with a lower ABI (<0.9). The LDL-C
and CRP had no predictive value when analyzed separately. As a result, a low GNRI value remained as a significant indicator (Table 3).

### Table 1: Characteristics of the studied population according to in hospital ABI data availability.

| Parameter | Total, n(%) | ABI | P-Value |
|-----------|-------------|-----|---------|
| Overall   | 47 (100)    | 0.71 (0.64-1.02) | -       |
| Sex       |             |     | <0.01  |
| Male      | 35 (74.5)   | 0.73 (0.64-1.02) |         |
| Female    | 12 (25.5)   | 0.69 (0.63-0.84) |         |
| Diabetes  |             |     | <0.01  |
| No        | 15 (31.9)   | 0.81 (0.67-1.05) |         |
| Yes       | 32 (68.1)   | 0.69 (0.64-0.93) |         |
| GNRI      |             |     | <0.01  |
| <91.2     | 24 (51.1)   | 0.65 (0.61-0.77) |         |
| ≥ 91.2    | 23 (48.9)   | 0.92 (0.70-1.09) |         |
| Treatment of dyslipidemia | | | <0.05 |
| No        | 28 (59.6)   | 0.77 (0.67-1.04) |         |
| Yes       | 19 (40.4)   | 0.66 (0.64-0.87) |         |

ABI: Ankle Brachial Index; GNRI: Geriatric Nutritional Risk Index.

### Table 2: Relationship between the ABI and clinical parameters.

| Parameter                  | OR (95% CI)          | P-Value |
|----------------------------|----------------------|---------|
| LDL-C (mg/dL)              | 1.007 (0.982-1.033)  | 0.573   |
| GNRI (≥91.2)               | 4.477 (1.105-18.141) | 0.036   |

ABI: Ankle Brachial Index; LDL-C: Low-Density Lipoprotein Cholesterol; Hct: Hematocrit; Plt: Platelets; NS: Not Significant.
**Discussion**

A low ABI in HD patients was found to be associated with a low GNRI. In addition, linear regression analysis revealed that a low ABI was significantly associated with a low GNRI; low levels of LDL-C, hematocrit, and hemoglobin; high levels of inflammatory parameters (CRP level and WBC count); and a high plt count. These findings are consistent with the concept of MIA syndrome, in which malnutrition, inflammation, and atherosclerosis are closely related and influence each other as described in a previous study [3]. Multiple logistic regression analysis showed an association between the ABI and LDL-C (one of the classic risk factors for atherosclerosis), GNRI (a nutritional indicator), and CRP (an inflammation indicator). The results showed that GNRI was an independent positive related factor of ABI and that low ABI value was related to worsening of nutritional status.

It has been shown that GNRI is a suitable and effective indicator of malnutrition in HD patients. GNRI was reported to be less affected by body fluid volume than Alb or BMI and to have a clear association with patient morbidity and mortality [4,5]. HD patients can be malnourished for various reasons, such as metabolic acidosis, protein-energy wasting and overexpression of the muscle protein synthesis inhibitor, myostatin [6,7]. Previous reports showed that GNRI correlated with the brachial-ankle pulse wave velocity in HD patients with ABI values in the normal range [8]. This suggests that the GNRI is related to atherosclerosis and may be associated with patient morbidity and mortality. However, the relationship between the GNRI and ABI in HD patients has not been reported. To our knowledge, our study is the first to show an association between them.

It is known that in HD patients ABI decreases with elevated CRP, and inflammation is related to atherosclerosis [9-11]. In this study, the relationship between ABI and inflammation indicators (CRP and WBC) were observed. Some HD patients were reported to have micro-inflammation, and it is thought that inflammation is related to CVD and patient morbidity and mortality [12]. Although the mechanism of micro-inflammation in HD patients is not yet known, stimulation caused by dialyzer membranes and dialysate is believed to be at least a part of it [13,14]. This study revealed that, at a minimum, inflammation in HD patients were related to atherosclerosis.

In HD patients as well as in non-HD patients, there is a possibility that malnutrition affects the progression of atherosclerosis. It was reported that malnutrition induces inflammation, and dialysis patients often show symptoms of inflammation, such as endothelial dysfunction (decrease in the vasodilatation response), increased plt aggregation, and a decrease in aortic calcification inhibitory factor [15]. Malnutrition in HD patients causes a loss of body protein (muscle) and a decrease in an energy source (fat). In association with inflammation and atherosclerosis, the result is the progression of CVD and worsening morbidity and mortality [3,6].

This study revealed a relationship between a low ABI and low GNRI, and the GNRI was considered to be an effective indicator of atherosclerosis. In addition, this study showed that in the target observational group, the indicators of atherosclerosis were related to the indicators of malnutrition and inflammation, which reconfirmed the concept of MIA syndrome in HD patients.

Lastly, the study has some limitations. This was an observational study performed at a single hospital facility and the sample size was small. Some blood test parameters were excluded because the ABI and laboratory results were not obtained at the same time, such as at the beginning of the week or before dialysis. In addition, sufficient confounding factors were not eliminated by the multivariate analysis. These limitations should be addressed in future studies. Furthermore, in this study, only the GNRI was identified as a predictive factor for ABI. Further prospective observational studies using a larger sample size are needed to investigate in detail the relationship between atherosclerosis, nutritional indicators, and development of CVD.

**Conclusion**

A low ABI in HD patients was associated with nutritional indicators. Multivariate analysis found a low GNRI to be a significant predictive factor for a low ABI. This suggests that the GNRI may be an indicator for the development of atherosclerosis.

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**Conflicts of Interest**

None

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