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Low urine pH associated with sarcopenia in the elderly

A multi-center observational study

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Abstract

The pathophysiology of sarcopenia is complex and must be further explored. While metabolic acidosis may be a risk factor for sarcopenia, it remains unclear whether acidic urine is related to sarcopenia. The purpose of the present study was to investigate the association between sarcopenia and urine pH in the elderly.

An elderly population (n = 123 [male = 46]; mean age = 81.7 years) was classified into 2 groups based on the sarcopenia status according to their strength, requirement of assistance in walking, their ability to rise from a chair their ability to climb stairs, and their history of falls. Urinalysis was measured using dipstick tests.

The sarcopenia group (n = 32) was significantly older, had less exercise habit and showed a lower urine pH (mean pH = 5.5) in comparison to the nonsarcopenia group (mean pH = 6.2, $P < .01$). A multivariate analysis that was adjusted for age, male sex, body mass index, uro-renal variables and exercise habit revealed that urine pH (odds ratio, 0.43; 95% confidence interval, 0.22–0.85, $P = .02$), age and less exercise habit were independently and significantly associated with sarcopenia.

The findings of the present study suggest a potential association between metabolic acidosis and the pathophysiology of sarcopenia in the elderly. As urine pH is a simple biomarker that can be obtained using dipstick tests, it is therefore expected to be helpful for detecting sarcopenia in the clinical setting.

Abbreviations: BMI = body mass index, GFR = glomerular filtration rate, SARC-F = strength, assistance in walking, rising from a chair, climbing stairs, and falls.

Keywords: aciduria, aging, rural district, sarcopenia, urine dipstick test

1. Introduction

Sarcopenia is the age-related loss of muscle mass, strength, and/or performance.[1–3] The prevalence of sarcopenia in the elderly is high (10%–50%).[4–7] With aging trends worldwide, the population of individuals with sarcopenia is rapidly increasing. Sarcopenia is thus a serious public issue as it is associated with an increased risk of falls and fractures,[8] reduced activities of daily living,[9] reduced quality of life,[10] and increased mortality.[11]

The aging process is characterized by a progressive decline in the intrinsic physiologic function of all organs.[12] For instance, the kidney is one of the best organs related to aging, and a reduced glomerular filtration rate (GFR) with albuminuria and/or proteinuria is suggested to the presence of sarcopenia even in the population without chronic kidney disease.[13,14] The early detection of such an aging process is important; however, this is so difficult in individuals with sarcopenia due to its asymptomatic situations and a lack of easily measured biomarkers.[15]

Of interest, previous studies have demonstrated that chronic kidney diseases,[16,17] chronic heart failure,[18] and metabolic abnormalities such as obesity and metabolic syndrome[19,20] can show a low level of urine pH. Additionally, these diseases and syndromes were indicated to be associated with aging and sarcopenia.[21,22] Given the phenomenon, the relationship between metabolic acidosis and biological aging may be hypothesized.[23] The pathophysiology of sarcopenia is complex and must still be explored, while urine pH may be related to the presence of sarcopenic conditions. The present study therefore aimed to investigate the association between sarcopenia and urine pH easily measured using urine dipstick tests.

Editor: Sorush Niknamian.

This work was supported in part by Scientific Research from the Foundation for Development of Community.

This study was approved by the Ethics Committee of the Jichi Medical University (number: 18–149).

The authors have no conflicts of interests to disclose.

The datasets analyzed in this study are available from the corresponding author on reasonable request.

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How to cite this article: Saitsu A, Iwazu Y, Matsushita H, Hayashi H, Mizuhashi Y, Kotani K. Low urine pH associated with sarcopenia in the elderly: a multi-center observational study. Medicine 2021;100:21(e26114).

Received: 17 December 2020 / Received in final form: 8 May 2021 / Accepted: 10 May 2021

http://dx.doi.org/10.1097/MD.0000000000026114

2. Methods

2.1. Study population

A multicenter, cross-sectional study was conducted from August 2018 to February 2019 in the patients with common diseases who attended 3 clinics in Japan. A total of 123 patients (mean age, 81.7 years) were interviewed to investigate their strength, requirement for assistance in walking, ability to rise from a chair, ability to climb stairs, and history falls using strength, assistance in walking, rising from a chair, climbing stairs, and falls (SARC-F),[24,25] which is a screening tool for sarcopenia. The following exclusion criteria were applied: subjects without sufficient urinalysis, with <70 years of age,[7] and with serum creatinine >2.0 mg/dl meaning kidney dysfunction. The present study protocol was approved by the institutional Ethics Committee of Jichi Medical University (approval number: 18–149). The study was conducted in accordance with the Helsinki Declaration.

2.2. Assessment of sarcopenia

The SARC-F has 5 items that assess the patient's perception of their limitations in strength, ability to walk, rise from a chair, and climb stairs, and their experience of falls.[24,25] The scores range from 0 to 10 (0–2 points for each component, with 0 indicating the best result and 10 indicating the worst result). The patients were classified, according to these scores, into the nonsarcopenia (0–3 points) group and the sarcopenia (≥4 points) group.

2.3. Clinical and laboratory variables

Clinical information, such as the existence of hypertension, diabetes mellitus, and hyperlipidemia, was simultaneously obtained from medical records when the SARC-F was performed. These diseases were extracted from the medical history and/or based on the medicines that the patients took. The information of exercise habit (≥1 time per week regularly [26,27]) was also obtained on self-report. The body mass index (BMI) was calculated as the weight in kilograms divided by height in meters squared. After an overnight fast, venous blood was collected for the measurement of serum creatinine. The GFR was estimated using the Japanese Society of Nephrology equation: estimated GFR = 194 × serum-creatinine$^{-1.094}$ × age $^{-0.287}$ (mL/min/1.73 m^2).[28] For women, the estimated GFR was multiplied by a correction factor of 0.739.[28] Urine pH, proteinuria, occult blood and glycosuria were determined in fasting morning urine using standardized dipstick tests. Urine pH is typically measured with a reagent test strip in which methyl red and bromothymol blue for a range of colors at different pH values.[27,29] In dipping the strip into the spot urine obtained from midstream urine, pH based on the colors is judged in 30 to 60 seconds.

2.4. Statistical analyses

Data were expressed as the mean and standard deviation for continuous variables, and proportions were used for categorical variables. Comparisons were made between 2 groups using the Chi-Squared test for categorical variables and the *t* test for continuous variables. We used a multiple logistic regression analysis adjusted for measured variables (selected to avoid an over-adjustment). Data were analyzed using IBM SPSS, Version 25.0 (Tokyo, Japan). In all analyses, *P* values of <.05 were considered a statistical significance.

3. Results

As shown in Table 1, all patients were divided, based onto the results of SARC-F, into the non-sarcopenia group (n = 91) and the sarcopenia group (n = 32). The patients in the sarcopenia group were significantly older than those in the nonsarcopenia group. There were significantly less exercise habit in the sarcopenia group than in the nonsarcopenia group. There were no significant differences in sex, BMI, estimated GFR, or hypertension, diabetes mellitus, and hyperlipidemia between the sarcopenia and non-sarcopenia groups. The urine pH levels of the sarcopenia group were significantly lower in comparison to the nonsarcopenia group. There were no marked differences between the groups in the proportion of proteinuria, occult blood, and glycosuria.

The factors associated with sarcopenia are shown in Table 2. Low pH levels, older age, and less exercise habit were significantly associated with sarcopenia. After adjustment for age, male sex, BMI, serum creatinine, urine pH, proteinuria, occult blood, glycosuria and exercise habit, urine pH (odds ratio,

Table 1

Baseline characteristics of the study patients.

Variables	All patients (n = 123)	Nonsarcopenia (n = 91)	Sarcopenia (n = 32)	*P* value
Age (yr)	81.7 ± 6.5	80.0 ± 5.6	86.3 ± 6.8	<.01
Men, n (%)	46 (37)	37 (41)	9 (28)	.21
Body mass index (kg/m^2)	24.2 ± 3.7	24.3 ± 3.6	22.9 ± 4.0	.49
Hypertension, n (%)	108 (88)	79 (87)	29 (91)	.42
Diabetes mellitus, n (%)	32 (26)	23 (25)	9 (28)	.75
Hyperlipidemia, n (%)	58 (47)	42 (46)	16 (50)	.71
Serum creatinine (mg/dL)	0.83 ± 0.26	0.83 ± 0.24	0.84 ± 0.30	.84
estimated GFR (mL/min/1.73m^2)	59.7 ± 17.5	60.2 ± 16.7	58.4 ± 19.7	.56
Urine pH	6.0 ± 0.9	6.2 ± 1.0	5.5 ± 0.6	<.01
Proteinuria, n (%)	57 (46)	39 (43)	18 (56)	.19
Occult blood, n (%)	65 (53)	48 (53)	17 (53)	.97
Glycosuria, n (%)	9 (7)	6 (7)	3 (9)	.70
Exercise habit, n (%)	64 (52)	53 (58)	11 (34)	.02

Continuous variables are reported as the mean ± standard deviation; categorical variables are reported as the frequency (percentage).
P values were obtained using *t* test for continuous variables and Chi-Squared test for categorical variables.
GFR = glomerular filtration rate.

Table 2

Factors associated with sarcopenia.

Variables	Crude OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
Age	1.21 (1.11–1.32)	<.01	1.18 (1.07–1.30)	.01
Male sex	0.57 (0.24–1.37)	.21	0.44 (0.14–1.40)	.16
Body mass index	0.97 (0.87–1.09)	.62	1.01 (0.87–1.16)	.95
Serum creatinine	1.17 (0.25–5.50)	.85	0.49 (0.07–3.74)	.50
Urine pH	0.39 (0.22–0.70)	<.01	0.43 (0.22–0.85)	.02
Proteinuria	1.71 (0.76–3.86)	.19	1.81 (0.66 – 4.98)	.25
Occult blood	1.02 (0.45–2.28)	.97	1.23 (0.44–3.38)	.70
Glycosuria	1.47 (0.34–6.24)	.61	6.14 (0.71–53.21)	.10
Exercise habit	0.38 (0.16–0.87)	.02	0.31 (0.11–0.87)	.03

CI = confidence interval, OR = odds ratio.

0.43; 95% confidence interval, 0.22–0.85, $P=.02$), age (odds ratio, 1.18; 95% confidence interval, 1.07–1.30, $P=.01$), and exercise habit (odds ratio, 0.31; 95% confidence interval, 0.11–0.87, $P=.03$) were found to be independently and significantly associated with sarcopenia.

4. Discussion

In the present study, lower urine pH levels, older age, and less exercise habit showed a significant association with sarcopenia. Chronological age and physical inactivity are respectively established risk factors for sarcopenia.[2–7,11,30,31] On the other hand, since further investigations into the pathophysiology of sarcopenia (a complex disorder) are still required, the new finding of a potential association between the urine pH level and sarcopenia may promote our overall understanding of the pathophysiology of sarcopenia. Additionally, the possible detection of sarcopenia using urine dipstick tests would be expected to be useful in the clinical setting as such tests are easy to perform.

In general, biological aging can cause metabolic acidosis.[23] This induces a negative balance of protein by blunting synthesis of protein[32] as well as degradation of protein,[33] which presents the decline of muscle mass, with the use of nitrogen as a buffer. Metabolic acidosis consumes ammonia (NH_3), which contains nitrogen, and the conversion to ammonium (NH^{4+}) alleviates the acidosis by accepting H^+ ions.[34] In this process, the muscles are broken down to provide nitrogen and then the excretion of nitrogen to the urine increases,[35,36] leading to aciduria. Since sarcopenic conditions of muscle declines are hard to provide nitrogen, with the development of acidosis.[37] Also, additional evidence exists; for instance, a potassium bicarbonate supplementation revises metabolic acidosis, while alkali supplementation serves a nitrogen-sparing role[38,39] and can protect muscle declines.[40] These may partly explain aciduria, low pH, in patients with sarcopenia, as was observed in the present study.

An aged society is in progress worldwide and is facing a serious problem due to the increase in patients with sarcopenia.[4–7] Thus, there is a need for objective biomarkers that can be easily applied in the detection of sarcopenia. As demonstrated in the present study, the use of urine dipstick tests, a simple method, appears to be a good idea. Dipstick test strips are reported to produce reliable results when the data are compared to data obtained using electrochemical pH meters.[41]

The strength of the present study was that it was conducted in multiple centers. Nevertheless, this study was associated with several limitations. First, the number of patients with sarcopenia was relatively small. Second, since the study was based on the cross-sectional design in nature, it is insufficient to mention any causality. The change of urine pH should be further examined by not only pharmacological interventions [38–40] but also non-pharmacological treatments including exercise (even at a low-intensity resistance level).[30,31] Third, exercise habit was self-reported and the report did not include the intensity and duration of exercise. Finally, we used the SARC-F to define sarcopenia. The European Working Group on sarcopenia in Older People recommends the measurement of muscle mass, strength, and performance for the diagnosis of sarcopenia,[2,5] while the SARC-F is considered to be adequately correlated with sarcopenia.[9,42] These limitations to confirmation of the study findings will be addressed in future research.

5. Conclusions

The present study showed a significant association between lower urine pH and sarcopenia in the elderly, which might provide a new insight into the pathophysiology of sarcopenia. Urine pH is able to be measured using urine dipstick tests, which are available everywhere; accordingly, this might be useful for the early detection of sarcopenia in the clinical setting. The present study findings should be validated in further studies.

Author contributions

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