Factors Associated with Nutrition of Japanese Patients with Rheumatoid Arthritis Who Underwent the Mini Nutritional Assessment (MNA), Health Assessment Questionnaire Disability Index, and Body Composition Assessment by Bioelectrical Impedance Analysis

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Summary The aim of this study is to identify the factors associated with nutrition in Japanese patients with rheumatoid arthritis (RA). Overall, 409 patients with RA who underwent the Mini Nutritional Assessment (MNA), bone mineral density determination, and body composition assessment by bioelectrical impedance analysis were enrolled. The analysis of factors associated with malnutrition was performed by comparing groups categorized by MNA score (≥24, 17–23.5, and <17). Moreover, correlation analysis for MNA score and variables was performed. The factors associated with malnutrition were the Health Assessment Questionnaire Disability Index (HAQ-DI) (p = 0.005; odds ratio, 1.98), fat-free mass index (FFMI) (p = 0.002; odds ratio, 0.59), and fat mass index (FMI) (p = 0.022; odds ratio, 0.75). Statistical correlations of the MNA score with the following variables were observed: HAQ-DI (correlation coefficient [R], −0.261; p < 0.001), FFMI (R, 0.371; p < 0.001), and FMI (R, 0.272; p < 0.001). This study identified nutrition-associated factors in Japanese patients with RA. The nutrition-associated factors were HAQ-DI, FFMI, and FMI. Therefore, physicians should evaluate nutrition of patients with RA.

Key Words daily clinical practice, fat mass, fat-free mass, malnutrition, physical function

Rheumatoid arthritis (RA) is an inflammatory autoimmune disease that causes pain, swelling, stiffness, and loss of function in joints throughout the body. The disease results in progressive joint destruction and deformity, with varying degrees of deterioration in quality of life and limitations in daily activities and work (1–3). Moreover, rheumatoid cachexia is recognized as a state of advanced malnutrition and wasting and is defined as the loss of fat-free mass (FFM), predominantly skeletal muscle, in patients with RA (4, 5). The prevalence of malnutrition as rheumatoid cachexia is higher than that in the general population, and malnutrition is a recognized common symptom of RA. Malnutrition affects body condition and physical function (6–8). Moreover, compared with patients who are well nourished, patients with malnutrition have been shown to have longer hospital stays and to more often require readmission (9).

In RA treatment, we hypothesized that understanding the patients’ nutritional status may lead to understanding their physical condition. However, how RA influences malnutrition is not well known. The aim of this study is to identify the factors associated with nutrition in Japanese patients with RA.

MATERIALS AND METHODS

This clinical study investigated the clinical course and background variables of patients with RA who fulfilled the American College of Rheumatology (ACR) classification criteria (1987) and/or the ACR/European League Against Rheumatism criteria (10, 11). A total of 428 patients were enrolled. Patients with a pacemaker and/or joint arthroplasty using metallic implants were excluded. For various reasons, only 409 patients were included in the statistical analysis (Fig. 1). The clinical data that were collected were age, sex, disease duration, body mass index (BMI), anti-cyclic citrullinated peptide antibody positivity, biological disease-modifying antirheumatic drugs (DMARDs) or targeted synthetic DMARDs use, methotrexate use, glucocorticoid use, serum albumin level (Alb), C-reactive protein level, disease activity score in 28 joints (DAS28)–erythrocyte sedimentation rate (ESR), and Health Assessment Questionnaire Disability Index (HAQ-DI). The HAQ-DI is a standard assessment and a patient-reported measure of physical disability that consists of questions related to 20 activities of daily living, such as dressing, grooming, arising, eating, walking, maintaining hygiene, reaching objects, maintaining grip, opening things, and performing daily activities. In the HAQ-DI, questions are scored from 0 to 3, with higher scores indicating greater disability (0, without any difficulty; 1, with some difficulty; 2, with much difficulty; and 3, unable to do). The scores are then averaged into an overall HAQ-DI of 0–3 (12, 13).

This study was conducted according to the principles
of the Declaration of Helsinki, and informed consent was obtained from all patients. The Ethics Committee for Clinical Research of Kamagaya General Hospital approved this study (approval number: TGE00870-064).

Nutritional assessment. The Mini Nutritional Assessment (MNA) is a simple and noninvasive clinical scale for the evaluation of the nutritional status in elderly patients (14, 15). Therefore, the MNA has been used as a screening tool for malnutrition (15, 16). In this study, the MNA was used for malnutrition, because many of the patients enrolled in this study were elderly. The MNA consists of 18 dietary questionnaires, including change in meal amounts, weight loss, lifestyle, food and fluid intake, self-assessment of nutritional status, and anthropometric measurements. The maximum MNA screening score is 14. The maximum MNA assessment score is 16. Therefore, the maximum MNA score is 30. The MNA scores are categorized as follows: adequate nutritional status, MNA ≥24 points; risk for malnutrition, MNA 17–23.5 points; and malnutrition, MNA <17 points (15).

Bone mineral density assessment. The bone mineral density (BMD) of the lumbar spine and total hip was measured using a dual energy X-ray absorptiometry machine (PRODIGY system; GE Healthcare, Madison, WI, USA), and the results were evaluated using T-scores.

Body composition assessment by bioelectrical impedance analysis. Body muscle mass and basal metabolic rate were acquired by bioelectrical impedance analysis (BIA) using an MC-780A instrument (TANITA, Tokyo, Japan). The MC-780A is a body composition analyzer that estimates segmental body composition (trunk, arms and legs) according to several factors, including FFM and fat mass (FM). The use of MC-780A BIA instrument involves passing a multifrequency alternating current through the body and measuring the resulting impedance consisting of resistance, capacitive reactance, and phase angle. These variables were measured in the patients while they stood on the footplate and grasped the handles of the analyzer electrodes. The patients were lightly clothed and advised to remove their shoes during the measurement. The appendicular skeletal mass (ASM) was assessed using the sum of skeletal muscle mass in the arms and legs. The ASM index (ASMI), FFM index (FFMI), and FM index (FMI) were calculated from the ASM, FFM, and FM divided by the square of the patient’s height (kg/m²), respectively.

Statistical analysis. Statistical analysis was performed to investigate factors associated with malnutrition in patients with RA. The analysis of factors associated with malnutrition was performed by comparing groups categorized by MNA score (≥24, 17–23.5, and <17). Variables were analyzed by univariate analysis using ANOVA and Fisher’s test. A multivariate logistic regression analysis was performed using the variables with a p-value of <0.1 identified in the univariate analysis. Moreover, correlation analysis for MNA score and variables was performed using Spearman’s rank correlation. A p-value of <0.05 was considered to be indicative of statistical significance. All analyses were performed using the R Statistical Package, version 3.3.2 (http://www.r-project.org/).

RESULTS

The demographic and clinical characteristics were disaggregated by the MNA score ≥24 group, 17–23.5 group, and <17 group. The results of univariate analysis comparing the groups are shown in Table 1. The univariate analysis identified the following factors as significant: sex, BMI, Alb, DAS28-ESR, HAQ-DI, lumbar BMD, hip BMD, ASMI, FFMI, and FMI. Moreover, multivariate analysis showed that HAQ-DI (p=0.005; odds ratio, 1.98), FFMI (p=0.002; odds ratio, 0.59), and FMI (p=0.022; odds ratio, 0.75) were significant factors (Table 2). The HAQ-DI, FFMI, and FMI were significantly associated with malnutrition.

Statistical correlations of MNA score were observed for the following variables: HAQ-DI (correlation coefficient [R], -0.261; 95% confidence interval [CI], -0.349 to -0.168; p<0.001), FFMI (R, 0.371; 95% CI, 0.284 to 0.451; p<0.001), and FMI (R, 0.272; 95% CI, 0.180 to 0.360; p<0.001) (Table 3).

DISCUSSION

In this study, we investigated the factors associated with nutrition in Japanese patients with RA. The prevalence rate of malnutrition (MNA ≤23.5 points) was 43.5%. In a previous report, the prevalence rate of malnutrition (MNA ≤23.5 points) was 33.8% in 2009 (17). The mean BMI scores in the previous report were 25.0 for women and 27.0 for men. The difference in the prevalence rates between ours and that of the earlier study...
can be attributed to the BMI, which was a significant factor by univariate analysis in the present study. Moreover, our study identified FFMI and FMI as nutrition-associated factors. The MNA score was weak positively correlated with FFMI and FMI. Similar to these results, FFMI and FMI have already been reported as nutritional statuses (18). On the other hand, comparison with standard value is necessary to show the relationship between a nutritional status and body composition. The FFMI and FMI had lower values than standard values in previous reports (19, 20). Therefore, we believe that low FFMI and FMI were associated with malnutrition. Rheumatoid cachexia is defined as the loss of FFM with minimal or no weight loss, which leads to muscle weakness.

Table 1. Patient demographic and clinical characteristics and univariate analysis results comparison between groups categorized by MNA score.

| MNA score | p value |
|-----------|---------|
| ≥24 group (n=231) | 17–23.5 group (n=163) | <17 group (n=15) |
| Age, y | 66.6 (12.5) | 66.3 (13.9) | 73.5 (12.0) | 0.123 |
| Median (IQR) | 70 (59.76) | 68 (57.76) | 79 (67.83) | |
| Sex, female, n (%) | 173 (74.9) | 142 (87.1) | 13 (86.7) | 0.007 |
| Disease duration, y | 13.8 (11.1) | 13.6 (11.7) | 13.9 (8.9) | |
| Median (IQR) | 10 (6.18) | 9 (5.18) | 13 (8.23) | |
| BMI, kg/m² | 23.7 (3.6) | 21.0 (4.4) | 19.2 (3.4) | <0.001 |
| Mean (SD) | 23.3 (21.2, 25.1) | 19.9 (18.2, 22.5) | 18.6 (17.1, 22.3) | |
| Median (IQR) | 165 (71.4) | 124 (76.1) | 9 (60.0) | 0.291 |
| Anti-CCP Ab positive, n (%) | 113 (48.9) | 95 (58.3) | 8 (53.3) | 0.161 |
| bDMARDs or tsDMARDs use, n (%) | 155 (67.1) | 98 (60.1) | 9 (60.0) | 0.313 |
| MTX use, % | 45 (19.5) | 44 (27.0) | 6 (40.0) | 0.066 |
| Glucocorticoid use, % | 3.9 (0.6) | 4.1 (0.4) | 3.9 (0.6) | 0.014 |
| Alb. g/L | 4.1 (0.3) | 4.1 (0.4) | 3.9 (0.6) | 0.845 |
| Mean (SD) | 4.1 (3.9, 4.3) | 4.1 (3.9, 4.3) | 4.0 (3.6, 4.3) | |
| CRP, mg/dL | 0.40 (0.85) | 0.37 (0.59) | 0.29 (0.62) | 0.014 |
| Mean (SD) | 0.10 (0.04, 0.40) | 0.13 (0.04, 0.41) | 0.03 (0.02, 0.10) | |
| Median (IQR) | 2.49 (1.08) | 2.77 (1.12) | 2.50 (1.55) | 0.048 |
| DAS28-ESR | 2.46 (1.80, 3.24) | 2.61 (1.95, 3.52) | 2.69 (1.17, 3.73) | |
| Mean (SD) | 0.26 (0.43) | 0.48 (0.62) | 0.51 (0.64) | <0.001 |
| Lumbar BMD, T-score | 0 (0, 0.375) | 0.250 (0, 0.750) | 0.375 (0, 0.875) | |
| Mean (SD) | 0 (0.5) | 0 (1.4) | 0 (1.4) | 0.001 |
| Median (IQR) | 0.7 (−1.6, 0.5) | 1.1 (−1.9, −0.1) | 1.8 (−2.7, −1.1) | |
| Hip BMD, T-score | 0.11 (0.11) | 1.6 (1.0) | 2.1 (1.2) | 0.001 |
| Mean (SD) | −1.3 (−1.9, −0.5) | −1.8 (−2.3, −0.8) | −2.0 (−2.8, −1.5) | |
| Median (IQR) | 5.9 (1.5) | 5.7 (1.5) | 5.9 (1.1) | 0.021 |
| ASMI, kg/m² | 6.0 (5.3, 6.6) | 5.9 (5.2, 6.5) | 5.7 (4.9, 6.5) | |
| Mean (SD) | 16.4 (2.1) | 15.1 (1.7) | 14.5 (2.2) | <0.001 |
| Median (IQR) | 15.8 (15.2, 17.3) | 14.8 (13.9, 15.9) | 14.2 (13.0, 15.5) | |
| FMI, kg/m² | 7.4 (3.2) | 5.7 (3.7) | 4.7 (2.5) | <0.001 |
| Mean (SD) | 7.1 (5.2, 8.8) | 5.0 (3.9, 6.8) | 3.8 (2.7, 6.5) | |

MNA, Mini Nutritional Assessment; Normal, MNA ≥24 points; pre malnutrition, MNA: 17 to 23.5 points; malnutrition, MNA <17 points; SD, standard deviation; IQR, interquartile range; BMI, body mass index; Anti-CCP Ab, anti-cyclic citrullinated peptide antibody; bDMARDs, biological disease-modifying antirheumatic drugs; tsDMARDs, targeted synthetic disease-modifying antirheumatic drugs; MTX, methotrexate; Alb, albumin; CRP, C-reactive protein; DAS, disease activity score; ESR, erythrocyte sedimentation rate; HAQ-DI, Health Assessment Questionnaire Disability Index; BMD, bone mineral density; ASMI, appendicular skeletal muscle mass index; FFMI, fat-free mass index; FMI, fat mass index.
and a loss of functional capacity, that occurs in RA (21). An earlier study found that 18% of the patients with RA (mean age 58 y, mean disease duration 7 y) with moderate disease activity in DAS28 had low FFMI (22). In RA, inflammatory cytokines such as tumor necrosis factor (TNF)-α, interleukin (IL)-6, and IL-1β are increased. The inflammatory cytokines are associated with muscle protein loss and muscle damage (4, 23). Moreover, in RA, loss of body cell mass is likely to occur because of the presence of inflammatory cytokines such as TNF-α and IL-1β. Loss of body cell mass has been found to be associated with starvation and muscle mass decline (24). In RA, although inflammatory cytokines affect body composition, the results of the present study showed that FFMI and nutrition were correlated. Our study suggests that improved nutrition may contribute to the increase in FFMI, apart from inflammation. On the other hand, ASMI was not associated with MNA score by multivariate analysis. These results suggest that the effect of nutrition is large on the trunk in patients with RA. In previous reports, patients with RA were likely to gain truncal fat, such as central obesity (17, 25). Moreover, in RA patients with increased FFMI, use of the BMI score was not able to detect malnutrition in a previous study (26). Therefore, we believe that it is important to assess the trunk as well as the nutritional assessment. Moreover, in this study, the HAQ-DI was weakly correlated with the MNA score and was associated with nutrition. Based on these results, HAQ-DI may affect not only nutrition but also joint damage, which could not be examined in this study. In a previous report, FFMI and HAQ-DI were negatively correlated. Additionally, HAQ-DI was previously found to be independently associated with low MNA score (17). Similarly, the results of our study showed that low FFMI may also affect dysfunction. In Japanese elderly patients, MNA score was correlated age, BMI, and Alb (27). In our univariate analysis, BMI and Alb were associated with MNA score, but age was not associated. We believe that malnourishment occurs in younger and elderly RA patients. Therefore, all patients with RA should be monitored for nutritional status.

This study had several limitations. First, the sample size was small, particularly for the MNA score (<17 group. Therefore, the results might change if the number of cases increases. Second, 13 patients could not undergo BIA because they had received joint arthroplasty with metallic implants. These patients often have dysfunction related to RA. We concluded that those results did not affect the overall results of this study because the HAQ-DI was a significant factor. Moreover, this was a cross-sectional study. In the future, we think that a longitudinal study with a large sample size is necessary to clarify and further characterize the factors associated with malnutrition.

In conclusion, this study identified nutrition-associated factors in Japanese patients with RA. The nutrition-associated factors were HAQ-DI, FFMI, and FMI. Although it is important to know body composition, BIA measurements are limited in daily clinical practice in Japan. Therefore, physicians should evaluate nutrition of patients with RA. Improvement of nutrition may lead to improvements in physical function and body composition.

**Table 2. Odds ratio of malnutrition-associated factors by logistic regression analysis.**

| Variables        | Odds ratio (95% CI) | p value |
|------------------|---------------------|---------|
| Sex, male        | 0.99 (0.42–2.37)    | 0.988   |
| BMI              | 1.12 (0.88–1.44)    | 0.346   |
| Glucocorticoid use | 1.14 (0.67–1.95) | 0.632   |
| Alb              | 0.90 (0.45–1.81)    | 0.765   |
| DAS28-ESR        | 1.10 (0.87–1.37)    | 0.429   |
| HAQ-DI           | 1.98 (1.22–3.20)    | 0.005   |
| Lumbar BMD       | 1.07 (0.87–1.31)    | 0.542   |
| T-score          | 0.90 (0.68–1.19)    | 0.458   |
| Hip BMD, T-score | 1.13 (0.94–1.34)    | 0.187   |
| ASMI             | 0.59 (0.43–0.83)    | 0.002   |
| FFMI             | 0.75 (0.59–0.96)    | 0.022   |
| FMI              | 1.07 (0.87–1.31)    | 0.542   |

BMI, body mass index; Alb, albumin; DAS, disease activity score; ESR, erythrocyte sedimentation rate; HAQ-DI, Health Assessment Questionnaire Disability Index; BMD, bone mineral density; ASMI, appendicular skeletal muscle mass index; FFMI, fat-free mass index; FMI, fat mass index.

**Table 3. Pearson’s correlation analysis of MNA score and variables.**

| Variables | Correlation coefficient | 95% CI | p value |
|-----------|------------------------|--------|---------|
| HAQ-DI    | −0.261                 | −0.349 to −0.168 | <0.001   |
| FFMI      | 0.371                  | 0.284 to 0.451  | <0.001   |
| FMI       | 0.272                  | 0.180 to 0.360  | <0.001   |

MNA, Mini Nutritional Assessment; CI, confidence interval; HAQ-DI, Health Assessment Questionnaire Disability Index; FFMI, fat-free mass index; FMI, fat mass index.

**Authorship**

Study concept and design: T. Mochizuki, K. Ikari and K. Okazaki. Acquisition of subjects and/or data: T. Mochizuki. Analysis and interpretation of data: K. Ikari and K. Yano. Preparation of manuscript: T. Mochizuki, K. Ikari, and K. Okazaki.

**Disclosure of state of COI**

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interpretation of data; writing of the paper; and/or decision to submit the results for publication.

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