Aging of the population (the proportion >65 years) is occurring worldwide; it was estimated that this older population represented about 8.5% of the world's total population in 2016 [1]. In Japan, which has one of the world's fastest growing aging population, the proportion of people >65 years was 26.7% in 2015, and it is estimated that in 2060, this group will represent 40% of the population [2].

Aging is associated with various health issues, and recently sarcopenia has been gaining increasing attention, as people often experience a loss in muscle mass with aging. Low muscle mass is one of the criteria for sarcopenia [3–5]. Thus the prevalence of sarcopenia will increase as the population ages [6]. Sarcopenia is associated with high medical costs and mortality rates [7–9].

Elderly people with low muscle mass and high body fat mass are considered to have sarcopenic obesity [10]. Lim et al. [11] and Kim et al. [12] noted that sarcopenic obesity was associated with metabolic syndrome. Park et al. [13] reported that sarcopenic obesity and lifestyle-related disease are associated with sedentary lifestyle and eating habits [14].

Several tools are available to measure muscle mass, although many of them are cumbersome and costly. Bioelectrical impedance analysis (BIA) is noninvasive, does not use radiation, and can be performed quickly and easily in a clinical setting. As a result, BIA is becoming a more common way to measure muscle mass. However, there are few studies to assess the correlation between imbalance of muscle mass to body weight and lifestyle-related diseases using BIA among Japanese population.

Aim of the present study is to investigate the correlation between imbalance of muscle mass to body weight and lifestyle-related diseases using bioelectrical impedance analysis (BIA) among Japanese population.

Methods: This was a retrospective, cross-sectional study conducted at Juntendo University Hospital in Tokyo, Japan, from May 2015 to November 2017. Their muscle-to-weight ratio were stratified into “muscle-to-weight ratio” quartiles as follows: men, Q1 (<0.79), Q2 (0.79 to <0.79), Q3 (0.72 to <0.75), and Q4 (<0.72); women, Q1 (<0.73), Q2 (0.68 to <0.73), Q3 (0.63 to <0.68), and Q4 (<0.63). The primary outcome was prevalence of ≥2 lifestyle-related diseases, including hypertension, dyslipidemia, type 2 diabetes mellitus, and hyperuricemia.

Results: Data from 2009 individuals (men, 55%; mean age, 62 years) were analyzed. Compared to the lowest quartile, risk for the presence of ≥2 lifestyle-related diseases, in a multivariable regression model for men was as follows: Q2 (odds ratio [OR], 1.93; 95% confidence interval [CI], 1.31–2.87), Q3 (OR, 2.85; 95% CI, 1.89–4.29), and Q4 (OR, 6.00; 95% CI, 4.07–8.84). For women, an increased risk was seen in Q2 (OR, 2.31; 95% CI, 1.20–4.46), Q3 (OR, 4.45; 95% CI, 2.40–8.26), and Q4 (OR, 12.6; 95% CI, 6.80–23.5).

Conclusions: Our results showed that an imbalance of muscle mass to body weight confers an independent and stepwise increased risk for lifestyle-related diseases.

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related diseases using BIA among Japanese population.

2. Methods

2.1. Participants

This pilot, cross-sectional study was conducted at the Juntendo University Hospital, Tokyo, from May 2015 to November 2017. Participants of the present study were those who had undergone voluntary medical health checkup at Juntendo University Hospital and had BIA assessed.

Initially, data were available for 3622 participants (mean age, 62 years). Subjects with missing data (n = 144) and those for with duplicate cases during the study period (n = 1469) were excluded. Thus, 2009 subjects were included in the study (inclusion rate: 55.4%) (Fig. 1).

2.2. Ethics

Participants' clinical data were retrospectively retrieved from an institutional database. All examinations included in this study were performed as a customary part of the voluntary health checkup. The participants' records/information were anonymized prior to the analysis. The institutional ethics committee of Juntendo University Hospital approved the study protocol (No. 17-177). We posted consent form on the website and obtained consent from all participants.

2.3. Percent muscle mass

Total muscle mass was measured by BIA (MC-780A Body Composition Analyzer; Tanita Co., Tokyo, Japan). The BIA method requires subjects to stand in place on the BIA machine for approximately 30 seconds. BIA is used in this health checkup because it is low cost, simple, easy, and suitable for obtaining measurements in a large number of people. BIA is typically used to assess body composition in the clinical setting, and useful to measure muscle mass and fat mass, also calculate muscle-to-weight ratio.

Muscle-to-weight ratio was calculated as muscle mass (kg)/body weight (kg) in the study. Subjects with low muscle mass and high weight show a small muscle-to-weight ratio. We believe that subjects with smaller muscle-to-weight ratio have a muscle mass to body weight imbalance.

2.4. Variables

We reviewed data from medical examinations, including blood tests, electrocardiograms, computed tomography scans. All examinations had been performed by trained staff at a single institution.

As part of their routine checkup, subjects had completed a self-administered questionnaire regarding medical history (HT, dyslipidemia, diabetes mellitus, and hyperuricemia/gout), and then well-trained staff obtained data from any subjects who had failed to complete their forms. Weight and height were measured after removing shoes and clothing. Blood pressure (BP) was measured in the sitting position with a monitor. Serum and urine tests were collected from each subject after an overnight fast and immediately subjected to biochemical analysis. Blood was used to determine the fasting cholesterol, serum uric acid, fasting plasma glucose (FPG), and serum creatinine levels.

Lifestyle-related diseases included the following: HT, defined as a systolic BP level ≥ 140 mmHg or a diastolic BP level of ≥ 90 mmHg [15], or receiving treatment with an antihypertensive medication; type 2 diabetes mellitus, defined as a FPG level ≥ 126 mg/dL, glycosylated hemoglobin (HbA1c) level of ≥ 6.5% [15], or receiving treatment with a hypoglycemic agent; and dyslipidemia, defined as triglyceride (TG) level ≥ 150 mg/dL, high-density lipoprotein cholesterol (HDL-C) level < 40 mg/dL, low-density lipoprotein cholesterol (LDL-C) level ≥ 140 mg/dL [15], or receiving treatment for dyslipidemia. In addition, hyperuricemia was considered a lifestyle-related disease. In men, hyperuricemia was defined as a uric acid level > 7 mg/dL based on the Japanese Society of Gout and Nucleic Acid Metabolism criteria [16]. Because few women had a uric acid level > 7 mg/dL, we defined hyperuricemia in women as a uric acid level > 6 mg/dL, based on a previous study [17]. And, we used the presence of ≥2 lifestyle-related diseases based on the average number of lifestyle-related diseases were 1.6 ± 1.0 and 1.0 ± 1.0 (men and women).

2.5. Statistical analysis

Results are presented as mean ± standard deviation for continuous variables or prevalence (%) for categorical variables. We
analyzed data for each sex separately. Subjects were stratified into quartiles according to their muscle-to-weight ratio as follows: men, Q1 (≥0.79), Q2 (0.75 to <0.79), Q3 (0.72 to <0.75), and Q4 (<0.72); women; Q1 (≥0.73), Q2 (0.68 to <0.73), Q3 (0.63 to <0.68), and Q4 (<0.63). Trend in P-values was calculated using the Cochran-Armitage test for categorical data and linear regression analysis for continuous variables between quartiles. Analysis of covariance was adjusted by age and creatinine for continuous variables, and Levine test was used for the homogeneity assumption. Logistic regression analysis was used adjusting by age and creatinine for categorical variables, and Hosmer-Lemeshow test was used for goodness of fit.

Factors associated with the percent muscle mass then determined using multivariable logistic regression analysis. The covariates examined in the multivariable analysis were age, presence of ≥2 lifestyle-related diseases, and creatinine level. Receiver operating characteristic curve analysis was used to assess appropriate cutoff values of percent muscle mass, and we estimated areas under the curves (AUC), and measure the sensitivity and specificity of lifestyle-related diseases (≥2) associated with percent muscle mass in both sexes.

All calculations were performed using JMP PRO software, ver. 13.0 (SAS Institute, Cary, NC, USA) and the IBM SPSS Statistics ver. 22.0 (IBM Co., Armonk, NY, USA). P-values <0.05 were considered statistically significant.

3. Results

A total of 2009 individuals were included in this study (males, 55.2%; mean age, 62 ± 12 years). Table 1 shows baseline characteristics of the 1105 men included in this study. Mean muscle mass was 52.0 ± 5.9 kg and mean body weight was 69.8 ± 10.9 kg. For the 904 women in this study (Table 2), mean muscle mass was 35.8 ± 5.3 kg and mean body weight was 53.7 ± 9.5 kg. Mean muscle-to-weight ratio for men and women was 0.75 ± 0.05 and 0.68 ± 0.07, respectively. Among men and women, 543 (49.1%) and 239 (26.4%) had ≥2 lifestyle-related diseases, respectively. Tables 1 and 2 show summarized results according to muscle-to-weight ratio in each sex. For both men and women, muscle-to-weight ratio quartile was inversely associated with the presence of ≥2 lifestyle-related diseases. Lower muscle-to-weight ratios (group 1 to group 4) were associated with significantly higher BP, TG, and LDL-C, as well as lower HDL-C levels. Similarly, lower muscle-to-weight ratios were associated with significantly higher FPG and HbA1c levels (P <0.01). Lower muscle-to-weight ratios were also associated with significantly higher serum uric acid levels (P <0.01). Similar significant findings for all variables were seen in women.

Table 3 shows factors that were significantly associated with ≥2 lifestyle-related diseases. For both men and women, compared to those with the highest percent muscle mass (Q1), decreasing muscle-to-weight ratio conferred a stepwise increase in risk for multiple lifestyle-related diseases. For men, the risk was as follows: Q2 (odds ratio [OR], 1.93; 95% confidence interval [CI], 1.31–2.87), Q3 (OR, 2.85; 95% CI, 1.89–4.29), and Q4 (OR, 6.00; 95% CI, 4.07–8.84). For women, increase in risk was even more pronounced: Q2 (OR, 2.31; 95% CI, 1.20–4.46), Q3 (OR, 4.45; 95% CI, 2.40–8.26), and Q4 (OR, 12.6; 95% CI, 6.80–23.5).

Appropriate cutoff value, sensitivity, specificity, and AUC were 0.76, 0.59, 0.68, and 0.69, respectively in men (Fig. 2). Those were 0.68, 0.78, 0.54, and 0.72 respectively in women (Fig. 3).

4. Discussion

Our findings showed that in both sexes, muscle-to-weight ratio was significantly associated with all lifestyle-related diseases after

| Variable | Overall | Q1 | Q2 | Q3 | Q4 | P-value<sup>a</sup> | P-value<sup>b</sup> |
|----------|---------|----|----|----|----|----------------|----------------|
| No. of participants | 1105 | 213 | 304 | 234 | 354 | | |
| Age, yr | 62 ± 12 | 61 ± 13 | 62 ± 12 | 62 ± 12 | 62 ± 12 | 0.39 | |
| Body height, m | 1.69 ± 0.07 | 1.69 ± 0.06 | 1.69 ± 0.06 | 1.70 ± 0.07 | 1.69 ± 0.07 | 0.09 | 0.31 |
| Body weight, kg | 69.8 ± 10.9 | 59.8 ± 6.7 | 65.7 ± 6.6 | 72.7 ± 7.8 | 77.3 ± 11.4 | <0.01 | <0.01 |
| Waist circumference, cm | 87.0 ± 8.7 | 77.4 ± 5.9 | 83.7 ± 4.5 | 89.5 ± 5.1 | 93.9 ± 8.0 | <0.01 | <0.01 |
| Muscle mass, kg | 52.0 ± 5.9 | 49.5 ± 5.0 | 50.9 ± 5.0 | 53.1 ± 5.7 | 53.8 ± 6.4 | <0.01 | 0.01 |
| Muscle-to-weight ratio | 0.75 ± 0.05 | 0.83 ± 0.03 | 0.77 ± 0.01 | 0.73 ± 0.01 | 0.70 ± 0.04 | <0.01 | <0.01 |
| Blood pressure related measurements | | | | | | | |
| Systolic blood pressure, mmHg | 124 ± 14 | 120 ± 15 | 123 ± 14 | 125 ± 13 | 128 ± 13 | <0.01 | 0.38 |
| Diastolic blood pressure, mmHg | 76 ± 10 | 74 ± 11 | 75 ± 10 | 77 ± 10 | 77 ± 10 | <0.01 | 0.78 |
| Hypertension | 532 (48) | 70 (33) | 134 (44) | 116 (50) | 212 (60) | <0.01 | 0.55 |
| Lipid-metabolic related measurements | | | | | | | |
| High-density lipoprotein cholesterol, mg/dL | 56 ± 14 | 62 ± 15 | 57 ± 13 | 55 ± 15 | 52 ± 13 | <0.01 | 0.01 |
| Triglycerides, mg/dL | 126 ± 91 | 100 ± 77 | 121 ± 98 | 134 ± 75 | 141 ± 99 | <0.01 | 0.30 |
| Low-density lipoprotein cholesterol, mg/dL | 112 ± 28 | 106 ± 26 | 113 ± 28 | 113 ± 27 | 114 ± 30 | <0.01 | 0.24 |
| Dyslipidemia | 618 (56) | 85 (39) | 159 (52) | 140 (60) | 234 (66) | <0.01 | <0.01 |
| Glucose-metabolic related measurements | | | | | | | |
| Fasting plasma glucose, mg/dL | 106 ± 20 | 100 ± 14 | 104 ± 19 | 107 ± 22 | 110 ± 22 | <0.01 | <0.01 |
| Hemoglobin A1c (% NGSP) | 5.9 ± 0.7 | 5.8 ± 0.6 | 5.9 ± 0.6 | 6.0 ± 0.8 | 6.0 ± 0.7 | <0.01 | <0.01 |
| Diabetes mellitus | 217 (20) | 32 (15) | 51 (17) | 44 (19) | 88 (25) | <0.01 | <0.01 |
| Uric acid-metabolic related measurements | | | | | | | |
| Uric acid, mg/dL | 6.0 ± 12 | 5.7 ± 12 | 6.0 ± 11 | 6.1 ± 13 | 6.2 ± 12 | <0.01 | 0.28 |
| Hyperuricemia/Gout | 344 (31) | 41 (19) | 86 (28) | 80 (34) | 137 (39) | <0.01 | 0.98 |
| No. of lifestyle-related diseases | 1.6 ± 1.1 | 1.1 ± 1.0 | 1.4 ± 1.0 | 1.6 ± 1.0 | 1.9 ± 1.0 | <0.01 | 0.55 |

Values are presented as mean ± standard deviation or number (%). Percent muscle mass=muscle mass [kg]/body weight [kg]. NGSP, National Glycohemoglobin Standardization Program.

Trend in P-values were calculated using the Cochran-Armitage test for categorical data and linear regression analysis for continuous variables.

<sup>a</sup> Analysis of covariance was used adjusting by age and creatinine for continuous variables. Multivariable Logistic regression analysis was used adjusting by age and creatinine for categorical variables.

<sup>b</sup> Levine test was used for the homogeneity assumption. Hosmer-Lemeshow test was used for goodness of fit.
Trend in P-values were calculated using the Cochran-Armitage test for categorical data and linear regression analysis for continuous variables.

NGSP, National Glycohemoglobin Standardization Program.

Values are presented as mean ± standard deviation or number (%).

Percent muscle mass = (muscle mass [kg]/body weight [kg]).

Table 2
Demographic and baseline characteristics in women.

| Variable                                      | Overall | Q1     | Q2     | Q3     | Q4     | P-value | P-value |
|----------------------------------------------|---------|--------|--------|--------|--------|---------|---------|
| No. of participants                          | 904     | 185    | 227    | 261    | 231    |         |         |
| Age, yr                                      | 62 ± 13 | 60 ± 13| 61 ± 13| 63 ± 13| 63 ± 13| 0.03    |         |
| Body height, m                               | 1.56 ± 0.06| 1.57 ± 0.06| 1.57 ± 0.06| 1.56 ± 0.06| 1.57 ± 0.07| 0.11    | 0.19    |
| Body weight, kg                              | 53.7 ± 9.5| 44.5 ± 4.7| 49.7 ± 4.4| 54.4 ± 5.5| 64.2 ± 9.5| <0.01   | <0.01   |
| Waist circumference, cm                      | 81.3 ± 10.0| 70.7 ± 5.6| 77.1 ± 5.6| 82.5 ± 5.2| 92.7 ± 8.1| <0.01   | <0.01   |
| Muscle mass, kg                              | 35.8 ± 3.5| 34.5 ± 2.9| 35.2 ± 3.1| 35.9 ± 3.4| 37.4 ± 3.8| <0.01   | <0.01   |
| Muscle-to-weight ratio                        | 0.68 ± 0.07| 0.78 ± 0.04| 0.71 ± 0.01| 0.66 ± 0.01| 0.59 ± 0.04| <0.01   | <0.01   |
| Blood pressure related measurements          |         |        |        |        |        |         |         |
| Systolic blood pressure, mmHg                | 119 ± 16 | 112 ± 16| 116 ± 16| 120 ± 16| 125 ± 15| <0.01   | 0.68    |
| Diastolic blood pressure, mmHg               | 72 ± 11  | 69 ± 10 | 70 ± 11 | 73 ± 10 | 75 ± 10 | <0.01   | 0.77    |
| Hypertension                                 | 264 (29) | 26 (14) | 52 (23) | 77 (30) | 109 (47) | <0.01   | 0.29    |
| Lipid-metabolic related measurements         |         |        |        |        |        |         |         |
| High-density lipoprotein cholesterol, mg/dL  | 68 ± 16  | 76 ± 14 | 71 ± 16 | 67 ± 15 | 59 ± 12 | <0.01   | 0.02    |
| Triglycerides, mg/dL                         | 94 ± 28  | 70 ± 28 | 83 ± 38 | 102 ± 79| 114 ± 57| <0.01   | <0.01   |
| Low-density lipoprotein cholesterol, mg/dL   | 118 ± 29 | 113 ± 26| 116 ± 28| 118 ± 31| 123 ± 29| <0.01   | 0.04    |
| Dyslipidemia                                  | 417 (46)| 47 (25) | 89 (39) | 137 (52)| 144 (62)| <0.01   | 0.01    |
| Glucose-metabolic related measurements       |         |        |        |        |        |         |         |
| Fasting plasma glucose, mg/dL                | 97 ± 15  | 94 ± 19 | 94 ± 11 | 98 ± 14 | 102 ± 16| <0.01   | 0.06    |
| Hemoglobin A1c (NGSP), %                     | 5.8 ± 0.6| 5.7 ± 0.8| 5.7 ± 0.4| 5.8 ± 0.4| 5.9 ± 0.6| <0.01   | <0.01   |
| Diabetes mellitus                            | 75 (8)   | 10 (5)  | 9 (4)   | 21 (8)  | 35 (15) | <0.01   | 0.12    |
| Uric acid, mg/dL                             | 4.7 ± 1.0| 4.4 ± 0.9| 4.5 ± 1.0| 4.7 ± 1.0| 5.2 ± 1.1| <0.01   | 0.20    |
| Hyperuricemia/Gout                           | 129 (14)| 10 (5)  | 19 (8)  | 25 (10) | 65 (28) | <0.01   | 0.45    |
| No. of lifestyle-related diseases             | 1.0 ± 1.0| 0.5 ± 0.7| 0.7 ± 0.8| 1.0 ± 1.0| 1.5 ± 1.0| <0.01   | <0.01   |
| >2 Lifestyle-related diseases                | 239 (26)| 15 (8)  | 36 (17) | 73 (28) | 113 (49)| <0.01   | 0.98    |

Values in women were also shown that sarcopenia is related to adjusting for age and creatinine level. Thus, it may be necessary to consider an imbalance of muscle mass to body weight for lifestyle-related diseases management. Previous in vitro studies showed that type II fibers (fast muscle fibers) selectively decrease with age [18]. Type II fibers are related to glycolysis and insulin resistance [19]. Most of the storage sites of glucose in the body are skeletal muscles, and it is thought that a decrease in muscle mass directly affects glucose metabolism. Similarly, another human study showed that serum leptin levels were related to sarcopenic obesity [20]. In addition, high serum leptin levels were positively correlated with visceral fat and negatively correlated with muscle mass [20]. Thus it is possible that leptin levels may be associated with the occurrence of sarcopenic obesity. Human studies have also shown that sarcopenia is related to insulin resistance and diabetes mellitus [21–23]. Furthermore, slow metabolism, which causes an accumulation of visceral fat, may also be associated with sarcopenia [24]. It is well known that obesity leads to insulin resistance and is a risk factor for lifestyle-related diseases [25,26]. Based on these findings, as well as the findings of the current study, it appears that an imbalance in muscle mass and body mass index may be associated with the occurrence of lifestyle-related diseases.

As noted, several tools are available to evaluate muscle mass. We used BIA for its convenience. In addition, it has been reported that findings on BIA are closely associated with findings on magnetic

Table 3
Factors associated with the presence of >2 lifestyle-related diseases.

| Muscle-to-weight ratio | Univariate analysis | Multivariate analysis | P-value |
|------------------------|---------------------|-----------------------|---------|
| Men                    |                     |                       |         |
| Q1                     | Reference            | Reference             |         |
| Q2                     | 1.96 (1.34–2.87)     | 1.93 (1.31–2.87)      |         |
| Q3                     | 2.88 (1.94–4.29)     | 2.85 (1.89–4.29)      |         |
| Q4                     | 5.69 (3.90–8.29)     | 6.00 (4.07–8.84)      | 0.55    |
| Women                  |                     |                       |         |
| Q1                     | Reference            | Reference             |         |
| Q2                     | 2.28 (1.21–4.29)     | 2.31 (1.20–4.46)      |         |
| Q3                     | 4.40 (2.43–7.96)     | 4.45 (2.40–8.26)      |         |
| Q4                     | 10.9 (6.03–19.5)     | 12.6 (6.80–23.5)      | 0.98    |

Values in women were also shown that sarcopenia is related to adjusting for age and creatinine level. Thus, it may be necessary to consider an imbalance of muscle mass to body weight for lifestyle-related diseases management.

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Adjusting for creatinine was used adjusting by age and creatinine for continuous variables. Multivariable Logistic regression analysis was used adjusting by age and creatinine for categorical variables.

b) Levine test was used for the homogeneity assumption. Hosmer-Lemeshow test was used for goodness of fit.

Fig. 2. Receiver operating characteristic curve analysis of muscle-to-weight ratio for lifestyle-related diseases in men. AUC, area under the curve.
resonance imaging [27]. The prevalence of sarcopenia assessed with BIA was higher than that assessed with dual-energy X-ray absorptiometry [28,29]. Second, we evaluated muscle mass adjusted for weight. Some studies have suggested that adjusted height is more likely to be underestimated that adjusted weight, especially in Asian populations [8,30]. Another study indicated that adjusted height is not useful in the evaluation of body fat [31]. To our knowledge, few studies have assessed muscle mass evaluated by BIA for adjusted. In addition, to the best of our knowledge, this is the first study to stratify muscle mass into quartiles.

Our study has several limitations. First, it is a cross-sectional observational study based on data from a single institution, and the results are therefore limited in their applicability to other populations. In addition, no causal relationships can be established. Second, our study did not evaluate muscle strength. The European Working Group on Sarcopenia in Older People suggested that an investigation of muscle mass alone is inadequate, and muscle strength should also be assessed. However, another study showed that muscle mass and muscle strength were not directly related [3]. We were unable to examine muscle strength in our study. However, as a decrease of muscle mass is associated with decreased insulin sensitivity, we believe there is an association between muscle mass and lifestyle-related diseases.

Third, there is a limitation regarding with accuracy when using BIA. Water, food, and exercise can affect the measurement of BIA and give inaccurate readings of muscle mass and fat mass [32]. Our study was the single measurement of BIA and future multiple measurement studies including longitudinal studies may be required.

5. Conclusions

This study showed that an imbalance between muscle mass and body weight may be a risk factor for lifestyle-related diseases. It may be necessary to consider an imbalance of muscle mass to body weight for lifestyle-related diseases management.

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

CRediT authorship contribution statement

Taiju Miyagami: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data curation, Writing - original draft. Hirohide Yokokawa: Formal analysis, Investigation, Data curation, Writing - original draft. Kazutoshi Fujibayashi: Formal analysis, Investigation, Data curation, Writing - original draft. Hiroshi Fukuda: Supervision, Project administration. Teruhiko Hisaoka: Supervision, Project administration. Toshio Naito: Supervision, Project administration.

Acknowledgments

We thank the participants of the study and the staff at Juntendo University Hospital for their assistance in data collection. ORCID Hiroaki Okamoto: 0000-0003-3110-5545. Nayumi Shibasaki: 0000-0001-8433-6107. Takeshi Yoshimura: 0000-0001-7395-8840. Toyoonobu Uzawa: 0000-0002-0242-6051. Toshitsugu Sugimoto: 0000-0003-0627-1816.

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