RESEARCH ARTICLE

Sex-related differences in the effects of nutritional status and body composition on functional disability in the elderly

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Abstract

Background
The aim of our study was to evaluate the influence of changes of nutritional status and body composition on the results of comprehensive geriatric assessment (CGA) in inpatients of a geriatric ward. Sex differences in these relationships were also investigated.

Methods
A total of 212 elderly patients (>65 years old) admitted to the geriatric ward at the University of Tokyo hospital between 2012 and 2019 were enrolled in this study. CGA (ADL, IADL, MMSE, GDS, Vitality Index) was performed, along with assessment of body compositions (appendicular muscle mass, abdominal muscle mass, body fat mass) and blood malnutrition biomarkers (serum albumin, pre-albumin, 25-hydroxy vitamin D, zinc, hemoglobin concentrations).

Results
Multiple linear regression analysis showed that upper, lower limbs and abdominal muscle masses were significantly associated with the score on ADL in men. On the other hand, abdominal muscle mass was negatively associated with the scores on GDS. Body fat mass was also negatively associated with the score on IADL. In contrast, in women, multiple linear regression analysis failed to show any significant associations between body composition parameters and scores on any domains of CGA. Unlike in men, however, blood malnutrition biomarkers were significantly associated with ADL, IADL, MMSE, and Vitality Index in women.

Conclusions
Our study findings revealed that the association of the nutritional status and body composition with the functional status in the elderly differs by sex. These results suggest that
intensification of exercise in men and improvement of the nutritional status in women are particularly useful to maintain the functional status.

**Introduction**

With the aging of the world population, over the next three decades, the global population of older persons is projected to more than double, exceeding 1.5 billion, by 2050 [1]. In particular, aging of population is occurring most rapidly in Asia, where more than half of the elderly in the world are concentrated, representing an important issue that should be addressed urgently.

The elderly tend to exhibit multimorbidity and functional decline, which are believed to be correlated with each other [2–4]. It is important not only to provide appropriate treatment for the multimorbidity but also to perform a comprehensive functional assessment of the elderly. These functions can be evaluated with comprehensive geriatric assessment (CGA), which is defined as a multidimensional interdisciplinary diagnostic process focused on medical, psychological and functional capabilities of frail elderly in order to develop a coordinated plan for treatment and long-term care [5]. In practice, CGA involves evaluation of physical, cognitive and environmental functions including activities of daily living (ADL), instrumental activities of daily living (IADL), cognitive impairment, depression, and vitality, respectively [6], leading to improvement of the survival and functioning of the elderly [7–9].

Malnutrition is one of the critical factors that could be related to poor outcomes among the elderly population. Evaluation of elderly malnutrition includes assessment of blood biomarkers and body composition [10]. Albumin, pre-albumin, and hemoglobin have been widely used as representative markers of nutritional status, and lower serum albumin, pre-albumin, and hemoglobin levels are also known to be associated with malnutrition and impairment of ADL. Recently, both vitamin D and zinc levels have been highlighted as additional nutritional makers related to cognitive impairment and functional decline [11–13].

In addition, body composition alters with age, represented by a decrease in lean body mass together with an increase in body fat [14]. Previous studies have suggested that while an age-related increase in the body fat area was observed in both men and women [15], the decrease in skeletal muscle mass with advancing age was significantly more pronounced in men than in women [16,17]. These age-related changes of body composition were also reported to be associated with higher risk of hip fracture and mortality [18–20], further suggesting that age-related alterations of malnutrition biomarkers and body composition might be associated with functional disability and poorer prognosis. Nevertheless, it appears that sex-differences of the nutritional status, including biomarker levels and body composition data, on the domains of CGA have not been focused so much thus far.

Taken together, the aim of our study was to evaluate the association of the nutritional status, as assessed from biomarker levels and body composition data, with domains of the CGA, including physical and cognitive function, in elderly inpatients.

**Materials and methods**

**Participants**

This study was carried out in 212 elderly patients (>65 years old) admitted to a geriatric ward at the University of Tokyo hospital between 2012 and 2019. Major aim of the admission was to assess cognitive function, examine dizziness and gait disturbance, and/or control glycermia.
We excluded patients who were admitted to hospital because of heart failure, edema or dehydration, since body composition as assessed by bioelectrical impedance analysis (BIA) system is affected by the hydration status. We also excluded patients who needed treatment in specialized units and/or with serum C-reactive protein (CRP) levels of >3 mg/l, because these may also be associated with significant alterations of nutritional status. Written informed consent was obtained from all the participants and/or their immediate family members, and the study was conducted with the approval of the Research Ethics Committee of the University of Tokyo Hospital (3811, 11707), in accordance with the principles of the Declaration of Helsinki; every effort was made to ensure patient anonymity.

**CGA assessment**

CGA included the following five evaluations. Functional status in terms of ADL was assessed by Barthel index [21], where a score of 100 indicated the patient was independent with no need for assistance from others [22]. IADL was assessed by Lawton & Brody scale [22], where IADL score ranged from 0–5 points in men and 0–8 points in women [23]. Cognition was assessed by Mini Mental State Examination (MMSE), with scores of $\leq 23$ denoting mild cognitive impairment [24,25]. Mood was assessed by geriatric depression scale-15 (GDS-15), with scores of $\geq 6$ denoting depression [26,27]. ADL-related vitality was assessed by Vitality Index, with scores of $\leq 7$ implying lower survival rates [28]. CGA assessment was performed by senior geriatricians.

**Body composition**

We used the BIA system (InBody S10, InBody Japan) to evaluate the appendicular muscle mass, abdominal muscle mass and body fat mass of the participants. The system separately measured the impedance in the subjects’ right arm, left arm, trunk, right leg, and left leg at six different frequencies (1, 5, 50, 250, 500 and 1000 kHz) for each body segment. Body composition analysis was performed at ambient temperature in accordance with the recommended BIA measurement conditions, as follows; (1) fasting for 4 hours and no alcohol for 8 hours prior to the measurements; (2) bladder voided prior to the measurements; (3) no exercise for 8 hours prior to the measurements [29]. BIA assessment was carried out between 4 pm and 6 pm. We use the absolute values of muscle and fat mass, since recent studies demonstrated that the absolute values of muscle and fat mass were associated with risk factors for cognitive impairment and cardiovascular disease or all-cause mortality in elderly people [30–32].

**Blood biomarkers**

Blood biochemical parameters of nutrition were analyzed, including serum albumin, pre-albumin, 25-hydroxy vitamin D (25(OH)D), zinc, and hemoglobin concentrations. Blood samples were collected from all participants at admission.

**Statistical analysis**

Results are expressed as means ± standard deviation (SD). Comparisons between groups were performed by Student’s t-test for two samples. Correlations between body composition parameters and scores on the CGA domains or between blood biomarkers and scores on the CGA domains were analyzed by calculation of Pearson correlation coefficients. Multiple linear regression analysis using CGA as the dependent variable was performed to identify the determinants of scores on the CGA domains among potential factors. Independent variables with a variance inflation factor of less than 2 were adopted to avoid the multicollinearity problem.
[33,34]. We also confirmed normality of residuals for each dependent variable through histograms [33,34]. P values of less than 0.05 were considered as being indicative of statistical significance. Data were analyzed using SPSS version 22 (IBM SPSS Statistic Version 22).

Results

Characteristics of the study participants according to sex

A total of 212 subjects were included in the study, including 98 men (46.2%) and 114 women (53.8%); average age of men was 80.4 ± 9.3 years, while that of women was 81.8 ± 6.4 years (Table 1). Average body mass index (BMI) was 22.1 ± 3.7 kg/m² in men and 21.9 ± 3.7 kg/m² in women. Consistent with previous reports [15,17], appendicular muscle mass was higher in men, while body fat percentage was higher in women.

Serum concentration of 25(OH) D was 57.6 ± 18.0 nmol/L in men and 53.3 ± 17.8 nmol/L in women on average, respectively. Mean serum zinc concentration was 70.3 ± 15.2 μg/dL in men and 64.5 ± 17.1 μg/dL in women, both of which, less than 80 μg/dL, were regarded as malnutrition-related zinc deficiency [35].

The overall mean ADL score was 87.4 ± 17.8, and almost half of the participants (n = 116) had functional limitations (ADL scores < 95). The mean IADL score was 3.8 ± 1.5 in men and 5.4 ± 2.3 in women, respectively, indicating that most of the participants (men: n = 48, women: n = 65) needed some assistance (IADL scores < 5 in men and < 8 in women). The mean MMSE score was 22.9 ± 5.2; almost half of the subjects (n = 100) had mild cognitive impairment (MMSE scores < 24). The mean score on GDS was 5.9 ± 3.8, and almost half of the participants (n = 101) had depression (GDS scores ≥ 6). The mean Vitality Index was

| Variable                        | All (n = 212) | Men (n = 98) | Women (n = 114) | P-value |
|---------------------------------|--------------|-------------|-----------------|---------|
| **Age (y)**                     | 81.2 ± 7.9   | 80.4 ± 9.3  | 81.8 ± 6.4      | 0.174   |
| **Body composition**            |              |             |                 |         |
| Body mass index (kg/m²)         | 22.0 ± 3.7   | 22.1 ± 3.7  | 21.9 ± 3.7      | 0.632   |
| Upper limb muscle mass (kg)     | 3.24 ± 1.06  | 4.06 ± 0.84 | 2.58 ± 0.69     |         |
| Lower limb muscle mass (kg)     | 12.4 ± 4.1   | 15.3 ± 3.3  | 9.8 ± 2.8       |         |
| Abdominal muscle mass (kg)      | 15.4 ± 3.5   | 18.2 ± 2.5  | 13.1 ± 2.2      |         |
| Body fat mass (kg)              | 14.7 ± 6.4   | 14.7 ± 6.3  | 14.8 ± 6.6      | 0.991   |
| Body fat percentage (%)         | 27.4 ± 9.2   | 24.2 ± 7.8  | 30.1 ± 9.4      | <0.01   |
| **Blood biomarkers**            |              |             |                 |         |
| Albumin (g/dl)                  | 3.8 ± 0.4    | 3.8 ± 0.4   | 3.7 ± 0.4       | 0.750   |
| Pre-Albumin (mg/dl)             | 21.7 ± 5.7   | 22.2 ± 6.2  | 21.2 ± 5.1      | 0.223   |
| 25-hydroxy vitamin D (nmol/L)   | 55.1 ± 17.9  | 57.6 ± 18.0 | 53.3 ± 17.8     | 0.173   |
| Zinc (μg/dL)                    | 66.8 ± 16.5  | 70.3 ± 15.2 | 64.5 ± 17.1     | 0.121   |
| Hemoglobin (g/dL)               | 12.2 ± 1.7   | 12.7 ± 1.9  | 11.8 ± 1.4      |         |
| **CGA**                         |              |             |                 |         |
| ADL (score)                     | 87.4 ± 17.8  | 88.4 ± 18.0 | 86.6 ± 17.7     | 0.485   |
| IADL (score)                    | 3.8 ± 1.5    | 5.4 ± 2.3   | 0.071           |
| MMSE (score)                    | 22.9 ± 5.2   | 23.6 ± 4.8  | 22.3 ± 5.5      |         |
| GDS (score)                     | 5.9 ± 3.8    | 5.4 ± 3.6   | 6.3 ± 4.0       | 0.079   |
| Vitality Index (score)          | 8.8 ± 1.5    | 8.9 ± 1.5   | 8.8 ± 1.5       | 0.818   |

Data are expressed as the means ± SD. CGA, Comprehensive Geriatric Assessment; ADL, activities of daily living; IADL, instrumental activities of daily living; MMSE, Mini Mental State Examination; GDS, geriatric depression scale-15. P-values were calculated by Student’s t-test for two-samples.

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8.8 ± 1.5, and almost 20% of the patients (n = 38) showed impaired ADL-related vitality (Vitality Index ≤ 7). There was no significant difference in the average score on the GDS or the Vitality Index between the men and women included in the study.

**Associations between body composition parameters and scores on the CGA domains in men and women**

In male patients, upper, lower limb and abdominal muscle masses were significantly positively associated with scores on ADL (P < 0.01), IADL (P < 0.05), and Vitality index (P < 0.01), whereas they were negatively associated with the score on GDS (P < 0.05) (S1 Table). Lower limb muscle mass was positively associated with MMSE score (P < 0.01) (S1 Table). These results suggest the associations of various body composition parameters with scores on the CGA domains in men. Multiple linear regression analysis in men demonstrated that upper, lower limb and abdominal muscle masses were significantly positively associated with the score on ADL (Table 2). On the other hand, body fat mass was negatively associated with the score on IADL. Abdominal muscle mass was also negatively associated with the score on GDS, suggesting that more abdominal muscle mass is associated with better psychological condition. In contrast, in women, correlation analysis revealed association of lower limb mass with the score on IADL (P < 0.01) (S1 Table), whereas multiple linear regression analysis failed to reveal any significant positive associations between the variables and any scores on the CGA domains (Table 2).

**Associations between blood malnutrition biomarkers and scores on the CGA domains in men and women**

In male subjects, higher serum albumin and 25(OH) D levels were significantly associated with higher scores on ADL respectively (P < 0.05) (S2 Table). Serum pre-albumin level was also positively associated with the score on IADL. Abdominal muscle mass was also negatively associated with the score on GDS, suggesting that more abdominal muscle mass is associated with better psychological condition. However, multiple linear regression analysis failed to reveal any such associations (Table 3). In women, serum levels of

| Table 2. Multiple linear regression analysis to identify unique associations between body composition parameters and scores on the CGA domains. |
|-----------------------------------------------|------------------|------------------|------------------|------------------|------------------|
| Variable                          | ADL† P-value | IADL‡ P-value | MMSE§ P-value | GDS|| P-value | Vitality Index¶ P-value |
|-----------------------------------------------|----------------|----------------|----------------|------------------|------------------|
| **Men**                                      |                |                |                |                  |                  |
| Upper limb muscle mass                    | 0.430*        | 0.005          | -0.193         | 0.166            | -1.24            | 0.294            | -0.165           | 0.109            | 0.227           | 0.076            |
| Lower limb muscle mass                    | 0.291*        | 0.034          | 0.233          | 0.071            | 0.129            | 0.242            | -0.047           | 0.672            | 0.031           | 0.787            |
| Abdominal muscle mass                     | 0.468**       | 0.002          | -0.197         | 0.154            | -0.076           | 0.520            | -0.219*          | 0.034            | 0.134           | 0.291            |
| Body fat mass                              | 0.010         | 0.948          | -0.324*        | 0.035            | -0.202           | 0.877            | -0.202           | 0.859            | 0.250           | 0.069            |
| **Women**                                   |                |                |                |                  |                  |
| Upper limb muscle mass                    | -0.021        | 0.875          | 0.035          | 0.828            | -0.001           | 0.993            | 0.005            | 0.965            | 0.125           | 0.342            |
| Lower limb muscle mass                    | -0.105        | 0.442          | 0.310          | 0.056            | 0.057            | 0.634            | -0.027           | 0.779            | -0.066         | 0.610            |
| Abdominal muscle mass                     | -0.055        | 0.687          | 0.103          | 0.516            | 0.013            | 0.913            | 0.008            | 0.941            | 0.115           | 0.378            |
| Body fat mass                              | -0.138        | 0.307          | -0.043         | 0.787            | 0.164            | 0.171            | 0.000            | 0.997            | -0.006         | 0.966            |

Multiple linear regression analysis was performed using CGA as the dependent variable, to identify the determinants of the scores on the CGA domains among potential factors.

*Significant at P < 0.05.
**Significant at P < 0.01.
\( \beta \) denotes standardized regression coefficient.
ADL, activities of daily living; IADL, instrumental activities of daily living; MMSE, Mini Mental State Examination; GDS, geriatric depression scale-15.

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albumin, pre-albumin, zinc, and hemoglobin showed positive associations with scores on ADL (P<0.01), IADL (P<0.01), and Vitality Index (P<0.05) (S2 Table). Serum levels of albumin and hemoglobin also significantly associated with MMSE score (P<0.05) (S2 Table). Multiple linear regression analysis revealed a significant association between serum levels of albumin and the score on ADL (Table 3). Serum levels of albumin and hemoglobin remained significant determinants of the score on IADL, while those of pre-albumin and zinc revealed no significant associations with the score on IADL. Significant association was also seen between serum hemoglobin levels and MMSE score. Higher serum albumin and pre-albumin levels were also associated with higher scores on Vitality Index. These results suggest that the associations between blood malnutrition biomarkers and scores on the CGA domains were stronger in women than in men.

**Discussion**

The objective of this study was to examine whether body composition and blood malnutrition biomarkers were associated with scores on the CGA domains in elderly subjects. While our results suggested the existence of an association between the body composition and physical functional status in men, blood malnutrition biomarkers were associated with all of the physical functional status, cognitive function, and ADL-related vitality in women.

In the present study, significant associations were observed in men, but not in women, between upper, lower limb and abdominal muscle masses and physical functions such as ADL and GDS. While the muscle mass is well-known to be relatively higher in men, the rate of age-related loss of muscle mass is also known to be higher in men than in women. In a previous study examining skeletal muscle mass and its distribution, the rate of decrease in upper and lower limb muscle masses with age was significantly greater in men than in women [16]. Similar results that more rapid decrease in muscle masses in men were also reported in Japanese,
where the absolute rates of change in both total and appendicular muscle masses were consistently larger in men compared with women during 20 to 79 years of age [36]. Thus, loss of muscle mass is likely to affect the physical functional status to a greater degree among elderly men compared with elderly women.

Upper limb, lower limb and abdominal muscles are known to play overlapping and distinct roles in physical activities. In this study, we also investigated the relationship between each of the three muscles and CGA domains, and found that all of them were associated with ADL in men, further indicating that abdominal muscle mass was significantly associated with depressive state (Table 2). These results suggest that keeping all these muscles might be important for the maintenance of both physical and psychological functions in elderly people. Further studies are expected to reveal underlying mechanism of the relationship between abdominal muscle mass and depression in elderly men.

Multiple linear regression analysis also revealed the existence of a significant association between blood hemoglobin level and scores on IADL and MMSE in women (Table 3). Consistent with this finding, a previous cohort study demonstrated an association between malnutrition-related anemia and impairment of IADL only in women, not in men [37]. It was also reported that malnutrition-related anemia is an independent risk factor for dementia [38] and that elderly women, but not men, with dementia had a higher prevalence of iron deficiency anemia [39]. Taken together, elderly women with low hemoglobin levels due to malnutrition are more likely to exhibit lower scores on MMSE and IADL.

It is also well known that prevalence of osteoporosis and dementia are higher in women compared with men, and that malnutrition are potential risk factors of both of the diseases [40,41]. In addition, decrease in ADL, IADL and MMSE scores are also known to be associated with risk of osteoporosis and dementia, respectively [40,42]. Taken together with our findings that malnutrition was associated with decrease in ADL, IADL and MMSE scores only in women, nutritional assessment and its improvement might play an important role in maintaining physical and cognitive function mostly in women. Verbrugge defined the contradiction of higher female morbidity but higher male mortality as "sex morbidity-mortality paradox" [43]. It is also suggested that sex differences found in this study where domains of the CGA were associated with body composition in men and nutritional status in women might contribute to the underlying background of the paradox.

There were some limitations of this study. First, due to its cross-sectional study design, we could not clarify the causal relationship between the changes in nutritional status/body composition and functional status of the subjects. Second, because of the relatively small sample size, our results may not well represent the general Japanese older adult population. Third, sensitivity of BIA used in the present study is not well validated and BIA system may not yield entirely accurate body composition parameters. In practice, abnormal hydration status or extremes of body weight might also influence the measurements [44]. Forth, due to a lack of information on sociodemographic factors such as education and marital status, multiple linear regression analysis was not adjusted for these variables. To clarify age-related changes of nutritional status and body composition together with its sex differences, further investigation using a larger sample size including populations of various ethnicities is expected.

In conclusion, our study suggest that there exist sex differences in the association of the nutritional status and body composition with the functional status in the elderly. While significant associations were observed between the body composition parameters and physical function in men, blood malnutrition biomarker levels were associated with all of the physical functional status, cognitive function, and ADL-related vitality in women. Physical exercise and appropriate nutrition are important measures in older people to reduce the incidence of comorbidities and prevent disability, further suggesting that intensification of exercise in men...
and improvement of the nutritional status in women are particularly useful to maintain the functional status.

Supporting information

S1 Table. Correlations between the body composition parameters and scores on the CGA domains.
(DOCX)

S2 Table. Correlations between blood biomarkers and scores on the CGA domains.
(DOCX)

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References

1. United Nations. World Population Ageing 2019 Report. https://www.un.org/en/development/desa/population/publications/pdf/ageing/WorldPopulationAgeing2019-Report.pdf.

2. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. Lancet. 2012; 380(9836):37–43. https://doi.org/10.1016/S0140-6736(12)60240-2 PMID: 22579043

3. Marengoni A, Angleman S, Melis R, Mangialasche F, Karp A, Garmen A, et al. Aging with multimorbidity: a systematic review of the literature. Ageing Res Rev. 2011; 10(4):430–9. https://doi.org/10.1016/j.arr.2011.03.005 PMID: 21402176

4. Kadam UT, Croft PR, Group NSGC. Clinical multimorbidity and physical function in older adults: a record and health status linkage study in general practice. Fam Pract. 2007; 24(5):412–9. https://doi.org/10.1093/fampra/cmm049 PMID: 17698977
5. Rubenstein LZ, Stuck AE, Siu AL, Wieland D. Impacts of geriatric evaluation and management programs on defined outcomes: overview of the evidence. J Am Geriatr Soc. 1991; 39(9 Pt 2):8S–16S; discussion 7S-8S. https://doi.org/10.1111/j.1532-5415.1991.tb05927.x PMID: 1832179

6. Palmer RM. Geriatric assessment. Med Clin North Am. 1999; 83(6):1503–23, vi-viii. https://doi.org/10.1016/s0025-7125(05)70177-2 PMID: 10584605

7. Rubenstein LZ, Josephson KR, Wieland GD, English PA, Sayre JA, Kane RL. Effectiveness of a geriatric evaluation unit. A randomized clinical trial. N Engl J Med. 1984; 311(26):1646–70. https://doi.org/10.1056/NEJM198412273112604 PMID: 6390207

8. Stuck AE, Siu AL, Wieland GD, Adams J, Rubenstein LZ. Comprehensive geriatric assessment: a meta-analysis of controlled trials. Lancet. 1993; 342(8878) :1032–6. https://doi.org/10.1016/0140-6736(93)92884-v PMID: 8105269

9. Ellis G, Whitehead MA, Robinson D, O’Neill D, Langhorne P. Comprehensive geriatric assessment for older adults admitted to hospital: meta-analysis of randomised controlled trials. BMJ. 2011; 343:d6553. https://doi.org/10.1136/bmj.d6553 PMID: 22034146

10. Zhang Z, Pereira SL, Luo M, Matheson EM. Evaluation of Blood Biomarkers Associated with Risk of Malnutrition in Older Adults: A Systematic Review and Meta-Analysis. Nutrients. 2017; 9(8). https://doi.org/10.3390/nu90829 PMID: 28771192

11. Byrn MA, Sheean PM. Serum 25(OH)D and Cognition : A Narrative Review of Current Evidence . Nutrients. 2019; 11(4). https://doi.org/10.3390/nu11040729 PMID: 30934861

12. Portbury SD, Adlard PA. Zinc Signal in Brain Diseases. Int J Mol Sci. 2017; 18(12). https://doi.org/10.3390/ijms18122506 PMID: 29168792

13. Gschwind YJ, Bischoff-Ferrari HA, Bridenbaugh SA, Härdi I, Kressig RW. Association between serum vitamin D status and functional mobility in memory clinic patients aged 65 years and older. Gerontology. 2014; 60(2):123–9. https://doi.org/10.1159/000355667 PMID: 24335110

14. He X, Li Z, Tang X, Zhang L, Wang L, He Y, et al. Age- and sex-related differences in body composition in healthy subjects aged 18 to 82 years. Medicine (Baltimore). 2018; 97: e11152. https://doi.org/10.1097/MD.0000000000011152 PMID: 29924020

15. Guo SS, Zeller C, Chumlea WC, Siervogel RM. Aging, body composition, and lifestyle: the Fels Longitudinal Study. Am J Clin Nutr. 1999; 70(3):405–11. https://doi.org/10.1093/ajcn/70.3 .405 PMID: 10479203

16. Gallagher D, Visser M, De Meersman RE, Sepúlveda D, Baumgartner RN, Pierson RN, et al. Appendicular skeletal muscle mass: effects of age, gender, and ethnicity. J Appl Physiol (1985). 1997; 83 (1):229–39.

17. Janssen I, Heymsfield SB, Wang ZM, Ross R. Skeletal muscle mass and distribution in 468 men and women aged 18–88 yr. J Appl Physiol (1985). 2000; 89(1):81–8. https://doi.org/10.1152/jappl.2000.89. 1.81 PMID: 10904038

18. Janssen I, Heymsfield SB, Ross R. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. J Am Geriatr Soc. 2002; 50(5):889–96. https://doi.org/10.1046/j.1532-5415.2002.50216.x PMID: 12082177

19. Oliveira A, Vaz C. The role of sarcopenia in the risk of osteoporotic hip fracture. Clin Rheumatol. 2015; 34(10):1673–80. https://doi.org/10.1007/s10067-015-2943-9 PMID: 25912213

20. Pasco JA, Mohebbi M, Holloway KL, Brenneman LS, Hyde NK, Kotowicz MA. Musculoskeletal decline and mortality: prospective data from the Geelong Osteoporosis Study. J Cachexia Sarcopenia Muscle. 2017; 8(3):482–9. https://doi.org/10.1002/jcsm.12177 PMID: 28025860

21. Mahoney FI, Barthel DW. Functional evaluation: The Barthel Index: A simple index of independence useful in scoring improvement in the rehabilitation of the chronically ill. Maryland State Medical Journal. 1965; 14: 61–65.

22. Shah S, Vanclay F, Cooper B. Improving the sensitivity of the Barthel Index for stroke rehabilitation. J Clin Epidemiol. 1989; 42(8):703–9. https://doi.org/10.1016/0895-4356(89)90065-6 PMID: 2760661

23. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist. 1969; 9(3):179–86. PMID: 5349366

24. Folstein MF, Folstein SE, McHugh PR. “Mini-mental state”. A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975; 12(3):189–98. https://doi.org/10.1016/0022- 3956(75)90026-6 PMID: 1202204

25. Tsoi KK, Chan JY, Hirai HW, Wong SY, Kwok TC. Cognitive Tests to Detect Dementia: A Systematic Review and Meta-analysis. JAMA Intern Med. 2015; 175(9):1450–8. https://doi.org/10.1001/jamainternmed.2015.2152 PMID: 26052687

26. Yesavage JA. Geriatric Depression Scale. Psychopharmacol Bull. 1988; 24(4):709–11. PMID: 3249773
27. Herrmann N, Mittmann N, Silver IL, Shulman KI, Busto UA, Shear NH, et al. A validation study of the Geriatric Depression Scale short form. International Journal of Geriatric Psychiatry. 1996; 11(5):457–460.

28. Toba K, Nakai R, Akishita M, Iijima S, Nishinaga M, Mizoguchi T, et al. Vitality Index as a useful tool to assess elderly with dementia. Geriatrics & gerontology international. 2002; 2(1):23–29.

29. Kyle UG, Bosaeus I, De Lorenzo AD, Deurenberg P, Elia M, Manuel Gómez J, et al. Bioelectrical impedance analysis-part II: utilization in clinical practice. Clin Nutr. 2004; 23(6):1430–53. https://doi.org/10.1016/j.clnu.2004.09.012 PMID: 15556267

30. Bagger YZ, Tankó LB, Alexandersen P, Qin G, Christiansen C. The implications of body fat mass and fat distribution for cognitive function in elderly women. Obes Res. 2004; 12(9):1519–26. https://doi.org/10.1038/oby.2004.189 PMID: 15483217

31. Minn YK, Suk SH. Higher skeletal muscle mass may protect against ischemic stroke in community-dwelling adults without stroke and dementia: The PRESENT project. BMC Geriatr. 2017; 17(1):45. https://doi.org/10.1186/s12877-017-0433-4 PMID: 28158989

32. Lee CG, Boyko EJ, Nielsen CM, Stefanick ML, Bauer DC, Hoffman AR, et al. Mortality risk in older men associated with changes in weight, lean mass, and fat mass. J Am Geriatr Soc. 2011; 59(2):233–40. https://doi.org/10.1111/j.1532-5415.2010.03245.x PMID: 21288234

33. Pedhazur EJ. Multiple regression in behavioral research: Explanation and prediction (3rd ed.). Stamford, CT: Thompson Learning; 1997.

34. Nathans Laura L., Frederick L. Oswald, and Nimon Kim. Interpreting multiple linear regression: A guidebook of variable importance. Practical Assessment, Research & Evaluation. 2012. 17.9.

35. Brown KH, Wuehler SE, Peerson JM. The importance of zinc in human nutrition and estimation of the global prevalence of zinc deficiency. Food and Nutrition Bulletin. 2001; 22(2):113–125.

36. Ito H, Ohshima A, Ohto N, Ogawarama M, Tsuzuki M, Takao K, et al. Relation between body composition and age in healthy Japanese subjects. Eur J Clin Nutr. 2001; 55(6):462–70. https://doi.org/10.1038/sj.ejcn.1601206 PMID: 11423923

37. Chung SD, Sheu JJ, Kao LT, Lin HC, Kang JH. Dementia is associated with iron-deficiency anemia in females: a population-based study. J Neurol Sci. 2014; 346(1–2):90–3. https://doi.org/10.1016/j.jns.2014.07.062 PMID: 25127441

38. Huffman FG, Vaccaro JA, Zarini GG, Vieira ER. Osteoporosis, Activities of Daily Living Skills, Quality of Life, and Dietary Adequacy of Congregate Meal Participants. Geriatrics (Basel). 2018; 3(2). https://doi.org/10.3390/geriatrics3020024 PMID: 31011062

39. Brodaty H, Connors MH, Loy C, Teixeira-Pinto A, Stocks N, Gunn J, et al. Screening for Dementia in Primary Care: A Comparison of the GPCOG and the MMSE. Dement Cognit Funct. 2013; 46(1–6):323–30. https://doi.org/10.1159/000350992 PMID: 27811463

40. Verbrugge LM. Sex differentials in health. Public Health Rep. 1982; 97(5):417–37. PMID: 6750677

41. Woodrow G. Body composition analysis techniques in the aged adult: indications and limitations. Curr Opin Clin Nutr Metab Care. 2009; 12(1):8–14. https://doi.org/10.1097/MCO.0b013e32831b9e5b PMID: 19057181