acknowledged that the obvious treatment for what he termed "Syndrome X" (Met.S) is weight maintenance and physical activity [47].

4.1. Frontal-subcortical syndrome, neurodegeneration, and the cerebrovascular hypothesis

A large body of evidence has been suggesting that AD [20,48,55,60,70,88], Parkinson disease (PD) [9,12,26,57] and late-onset depression [2,5,13,28,58,70] are strongly associated with vascular (pathological) aging as well as among themselves more than what it would simply be expected by probability. At instance, 70% of patients with PD develop dementia [9]. Moreover, often the presence of frontal-subcortical atrophy seems to be partially related to the coexistence of cognitive impairment, PD and late-onset depression [9,12,57,58,70]. These disorders, though clinically and neuropathologically distinct, seem to share a common risk profile [26]. Patients with AD, PD and hypertension exhibit similar ultrastructural breakdown of cerebral capillaries [26]. There is increasing evidence that this shared risk is accelerated vascular aging, which, in turn, is promoted by cardiovascular risk factors [26]. Cerebrovascular disease disproportionably affects frontal systems [44] and frontal system atrophy is also common to AD, vascular dementia (VaD), and late-onset depression [9].

While stroke reflects a dramatic disturbance of the cerebrovasculature, FSCS may be the consequence of insidious chronic changes in the microcirculation [82]. The frontal-subcortical network is particularly susceptible to suboptimal oxygen and glucose offer [44]. While atherosclerosis of these thin arterioles may cause lacunes, WML would be caused by chronic partial ischemia to the terminal, watershed zones [44]. These zones are located mainly in the frontal-subcortical region, are irrigated by long penetrating branches of the anterior and middle cerebral arteries, and are more susceptible to disturbances of generalized poor perfusion [44]. Additionally, there is a higher susceptibility of the cerebral microvascular endothelium to the mitogenic and metabolic effects of insulin compared with endothelium from other vessel territories [99]. Indeed, cerebrovascular endothelial cell proliferation, swelling and luminal narrowing are a feature of hyperinsulogenic states such as diabetes and Met.S, and also a common consequence of the oligoischemic brain [17,99]. Age-related alterations in energy metabolism contribute to an increased vulnerability of the aging brain to anoxic damage [79]. Besides neurodegeneration, mild chronic hypoperfusion (−30%) may lead also to a non-infarctional state with impaired neuronal function [79], in resemblance to what happens with the 'hibernating' myocardium. Atleast a part of the neurofunctional deficit in cerebral ischemic states may be related to the consequent 'transmission failure' (neurotransmitter deficits) [85].

It has been shown that the degree of WML and lacunar infarcts found in the MRI strongly correlates and predicts aspects of the FSCS [50,82]. In a very recent study, Met.S, but not conventional risk factors, was independently associated with intracranial atherosclerosis and lacunar stroke, both neuropathological correlates of FSCS [82]. Moreover, a study of identical elderly male twins showed that the most significant determinant of late life WML were glucose levels, HDL-c, and systolic blood pressure, all which are components of the Met.S [14].

Risk of AD was found to double among hyperinsulinemic elderly [60], and this effect seems to be independent of the apolipoprotein E4 phenotype [55]. Cognitive impairment with but not without subcortical features is also associated with features of insulin resistance syndrome [18]. Hyperinsulinemia was shown to independently increase the risk of WML [99]. A study evidenced that insulin levels are significantly higher in patients with lacunar stroke or subcortical atherosclerotic encephalopathy than in normal control subjects [99]. In older asymptomatic hypertensive subjects, hyperinsulinemia is associated with lacunar-type silent cerebral infarcts, particularly those located in the subcortical white matter [50]. It has been also shown that reduced glucose tolerance is associated with poor memory performance and hippocampal atrophy even among the non-diabetic elderly [16].

4.2. Metabolic syndrome and cerebral small-vessel disease in Latin America

Met.S is a virtually inexistent clinical entity in primitive societies and reflects well the overfeeding and sedentary environment to which modern societies are influenced. Because it agglutinates the major risk factors for atherosclerosis and cardiovascular diseases, it might appropriately be considered the most common chronic epidemic syndrome in modern western societies [62].

High BMI values explain the variance of roughly 37% of all strokes in both North and Latin America (highest PAR in the world) [45]. Latin American elderly have already one of the highest BMI among all the world regions [45]. At any given BMI point Hispanic older people seem to be at a higher risk for DM and Met.S than Blacks and non-Hispanic Whites [7]. Moreover, Hispanics have the highest rates of Met.S in the USA [30].

Besides Met.S impairment in cognition, a study has shown Met.S to be a risk factor for the development of functional disability among Mexican-American older people [73]. The SABE Study has found that in many Latin American countries functional dependence among the elderly is high, and that, among all surveyed countries, Brazil has one of the highest prevalences of functional disability [74].

There is a higher influence of DM in predicting both cognitive and functional decline among Hispanic-Americans than among both Blacks and Whites [7], and cerebral small-vessel disease/microangiopathy may be the immediate cause. Older Hispanic Americans are at almost three-fold higher risk for concomitant cognitive and functional decline than the other two ethnic groups. Besides, asymptomatic small-vessel (lacu-

nar) strokes seem to be more common among Hispanics living both in the USA and Latin America [87] than in non-Hispanic Whites.

In the NHANES III [69] Study, Met.S was associated with a two times higher chance of having stroke. Average age and Met.S criteria being similar to the one in the present study, a lower prevalence of Met.S (24%) was found as compared with the present study prevalence (36.3%). Moreover, in that study the prevalence of stroke was 2.9%, therefore substantially lower than the prevalence found (9.5%) among our Brazilian elderly. Because, in a give elderly population, prevalence of asymptomatic stroke is usually five-times higher than that of symptomatic ones [93], the above comparison points to a larger (in populational terms) association between Met.S and stroke, and possibly FSCS, in Brazil.

4.3. Frontal-subcortical syndrome: a conceptual framework for neuropathological aging

As a group, humans show a steeper decline in both cognitive and functional performances from the seventh decade on [75]. Leukoaraiosis and lacunes might be one of the pathological hallmarkers of this transition [75]. However, rates of cerebral degenerative and cognitive/functional changes differ widely from one person to another [82]. This difference has been shown to be related to cerebral small-vessel disease [70]. Indeed, age-related leukoaraiosis has been reported to be associated with lacunar strokes and selective cognitive, affective, executive, neuromotor, and sphincteric dysfunction, all known for having a role in the loss of independence at older ages [75]. The extreme manifestation of this process would lead to FSCS, but the elderly who experiences 'successfully' aging would decline much slower. Risk factors for cerebrovascular disease, including Met.S, may be the main modifiable determinants of pathological neuroaging.

FSCS may be a key element in explaining the concomitant and interrelated decline in cognitive, affective, executive and neuromotor functions among the elderly.

Our proposed criteria for FSCS can easily be accessed in a neurogeriatric consultation by FRR elicitation, by performing a simple MMSE test, diagnosing late-onset depression, evaluating the presence of 'fear of falling' or falls, and diagnosing urgency incontinence; excluded dementia and bedridden cases.

Features of the FSCS are often inadvertently attributed to normal aging and, therefore, considered to be not amenable to intervention. Moreover, because FSCS entails also a dysexecutive feature, these patients are often labeled as non-compliant, stubborn, or unmotivated [82]. Recognizing this syndrome as an age-associated disease that, like Alzheimer's disease, does dramatically increase in prevalence with age but does not necessarily affect all elderly (and therefore is not 'normal') is, hence, the first step in improving medical care for this large group of elderly people. A second step would involve a better control of cerebrovascular risk factors from early adulthood to late life, and preventing/managing Met.S may be a central goal. Besides, drugs which increase insulin sensitivity are a promise. There is already some evidence that some of these drugs may positively affect cognitive function in humans [95].

The vascular hypothesis for the FSCS is supported by: (1) the high rate of occurrence of FSCS and its individual components in patients with hypertension, diabetes, coronary disease, and now possibly also Met.S; (2) the high rate of the syndrome in patients with cerebral small-vessel disease; (3) the high prevalence of an advanced degree of WML and lacunes in patients with FSCS.

Clinically manifested stroke is the most common condition responsible for functional decline among older people in both western and eastern societies [15,35]. An equivalent but more insidious (and less perceptible) process is possibly happening with asymptomatic lacunar strokes, ischemic WML, and FSCS. In fact, according to recent projections, worldwide stroke-related disability is projected to increase during the following 15 years and this disability will grow even more among developing countries [66,67]. As FSCS is a cerebrovascular disease which is extremely prevalent among the oldest-old, its burden certainly should keep increasing with the worldwide populational aging. This would account for a large amount of not readily predictable burden due to cerebrovascular disease [66,67].

4.4. Limitations

This study has several limitations. Even though it is well known that frontal-subcortical structures are highly vulnerable to the aging process, firm separation between what is 'normal' aging and what represents 'disease' remains difficult [82]. For this reason we made an intermediary third group to account for the 'borderline pathological' cases, what might have minimized the (binomial) categorization problem. Since epidemiological studies cannot prove cause-and-effect when the end-point is an outcome of a chronic non-communicable condition, this epidemiological evidence can be cited only as being consistent with the hypothesis in question.

It is possible that more people have deceased precociously from cardiovascular causes in the Met.S group than in the control group. This would make the Met.S group appear to be healthier due to a survival effect. However, the consideration of such possible survival effect would tend to magnify, rather than decrease, the differences found between these two groups in this study.

For diagnose of FSCS we relied solely on the medical history, neurologic examination, and battery of neurofunctional tests. However, FSCS is not an image diagnosis but rather a clinical one [82], for frontal-subcortical lacunes and WML are of high sensibility but low specificity for FSCS [21,92,93]. Even so, further studies incorporating brain images are required for grading the extension of leukoaraiosis, measuring the degree of frontal lobe (and hippocampal) atrophy, as well as to look for the possible associations between the pro-

gression of these variables and baseline Met.S. The inclusion of brain image techniques would also provide a 'golden standard' method with which several clinical criteria for FSCS could be confronted to.

We relied also on FRR as a criterion for FSCS. In the elderly FRR are neither very sensitive nor specific [23]. Nonetheless, in the absence of dementia, coexistence of cognitive impairment, late-onset depression, and gait disturbance are considered to be highly specific of frontal-subcortical small-vessel disease and atrophy; indeed these characteristics are considered to be 'phenotypic' of FSCS [82]. Presence of the above three disorders coexisted in 88.1% of the cases classified as FSCS in this sample.

Some of our subjects might have normal-pressure hydrocephalus (NPH), which is also characterized by gait disturbance, cognitive impairment and urine incontinence [92]. However this 'classical' triad of Hakim and Adams is rarely found in patients with NPH, the most common presentation being gait disorder alone [92], idiopathic NPH is also often associated with leukoaraiosis [92]. In this case the differential diagnosis between NPH and FSCS becomes difficult and, even more often, blurred. Some studies have suggested that idiopathic NPH is of cerebrovascular cause [92]. However, NPH is a rare cause of dementia (1–5%), whereas FSCS is a very common pathology in the elderly [92]. In this study the 12 cases of dementia were excluded. Besides, 74% of our individuals with FSCS presented evidence of depression, a feature not typical in 'pure' NPH. Because the vast majority of patients presenting mental deterioration, gait disorder and bladder dysfunction has FSCS [92], we cogitate that if some 'pure' NPH case was still present in our sample, it did not interfered significantly with our results.

4.5. Final remarks

The results hereby presented are consistent with the above evidences that link metabolic syndrome, vascular disease, and subclinical inflammation to cognitive, affective, executive, neuromotor and functional decline. To our knowledge, this is the first study to comprehensively evaluate the association between Met.S and FSCS.

Both AD and PD may occur before one reaches old age. Though rarely, even VaD itself can also occur before old age in the case of multiple large strokes. FSCS, however, is a geriatric disease par excellence for it does not seem to occur before the seventh or eighth decade of life, being therefore of possible lesser genetic determinism. This suggests a high potential for prevention. More than 10 years ago, Hachinsk has alluded to the vascular dementias as "preventable senility" [37]. Now it is time to consider that FSCS itself may be the 'preventable senility' par excellence.

Vascular disease, especially small-vessel disease and microangiopathy, may be the most common pathway to FSCS dysfunction with aging. William Osler has once mentioned that "longevity is a vascular question; a man is as old as his arteries" [72]. In the case of the brain, however, it might be more appropriate to restate that as "a person's brain is as old as his/her arterioles and capillaries".

5. Conclusions

FSCS was strongly associated with Met.S (OR = 5.8; CI: 1.7–20.3; $P = 0.006$), independently of age, gender or presence of stroke. Features of the Met.S explained 30.7% of the variance in the number of FSCS components. Met.S was also significantly associated with lower cognitive, executive, and neuromotor functions, depressive symptoms, fear of falling, falls and urgency incontinence ($P < 0.05$ for all). Met.S' PAR for FSCS was 31.6%.

Since Hispanics are at high risk for Met.S and silent strokes, these associations should be replicate in other, non-Hispanic populations to be proved universal. Future researches should also confirm Met.S to be longitudinally related to the development of FSCS, if possible including also brain image techniques. Additionally, randomized trails on non-pharmacological (exercise, diet and weight loss) or pharmacological (enhancers of insulin sensitivity) management of Met.S, and their capacity to prevent the development of FSCS, would be welcomed.

Preventing and treating Met.S may be an important step in 'preventing senility' and promoting 'successful' (neuro)aging.

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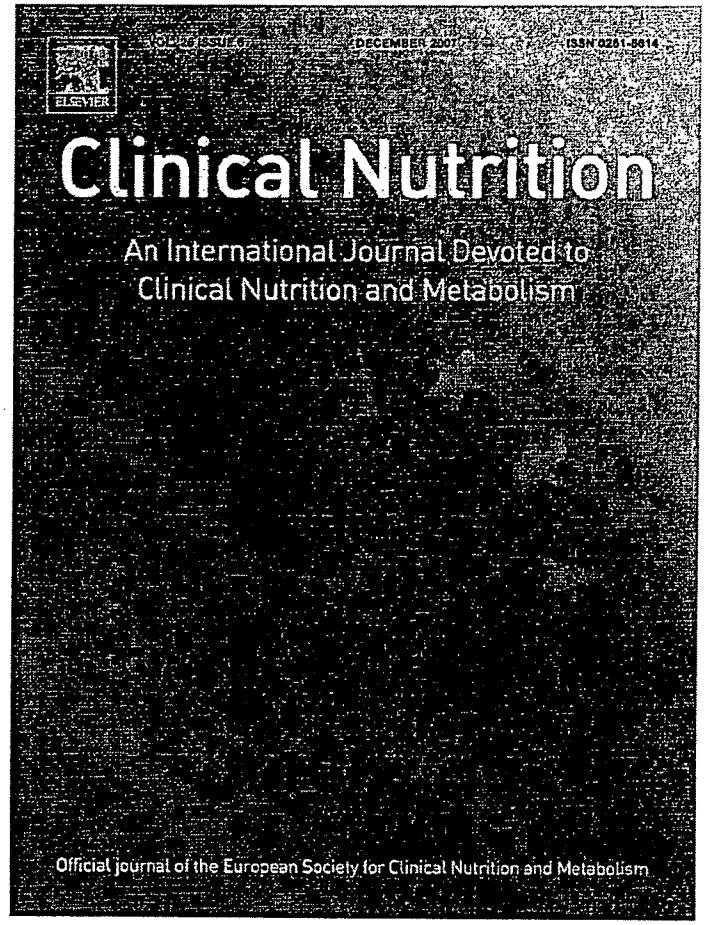

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ORIGINAL ARTICLE

Lack of body weight measurement is associated with mortality and hospitalization in community-dwelling frail elderly

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Summary
Background & aims: Although it is not uncommon for there to be frail older people living in the community, who do not know their weight and/or height, the health-related outcomes of those older remains unknown. We examined whether missing these anthropometries are a predictor of mortality or hospitalization during a 2-year follow-up period in community-dwelling older people using various community-based services.
Methods: This study was a prospective cohort analysis of 952 community-dwelling elderly. Data included the clients' demographic characteristics, basic activities of daily living (ADL), comorbidity, and anthropometric measurements at baseline. Analysis of mortality and hospitalization over the 2-year period was conducted using multivariate Cox proportional hazards models.
Results: Among the 952 participants, 342 and 292 had missing data for height and weight at baseline, respectively. Multivariate Cox proportional hazards models adjusting for potential confounders showed that the lack of data on weight was associated with 2-year mortality (hazard ratio, HR:1.54, 96% CI:1.09–1.79) as well as hospitalization (HR:1.34,

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95% CI:1.01–1.79) during the 2-year follow-up, although the lack of height measurement was not associated with these adverse outcomes.
Conclusions: Older people living in the community with unavailable weight data appear to be more likely to have a high risk of mortality and hospitalization.

Introduction

Height and weight are two of the most commonly used anthropometric measurements to assess nutritional status and overall health in clinical practice and research.[1–3] Changes in weight or body mass index (BMI), the most widely used anthropometric index, during certain periods are frequently used to determine whether nutritional status or overall health status has changed. In fact, a number of studies have demonstrated that weight loss or BMI reduction is an independent risk factor of adverse outcomes for older people, including high mortality and functional decline.[4–8]

In addition, low weight or low BMI levels themselves have been demonstrated to be a predictor of adverse outcomes including mortality or prolonged hospital stays in the older people.[9–11]

However, it is not uncommon for there to be frail and non-ambulatory older people, especially older people living in the community, who do not know their weight and/or height, or cannot be weighed or measured for height due to disabilities or postural changes. In fact, when subjects living at home have severe functional disabilities, it is essential to have special equipment such as beds or wheelchair scales to measure their weight. In addition to weight measurements, height measurements are also essential in the calculation of BMI levels. It is also not uncommon for it to be difficult to measure the height for the older people with postural changes, including muscle and arterial contracture and kyphosis. Thus, for older people with disabilities, data on anthropometry such as height and weight are likely to be missing, and therefore these individuals are likely to be under-represented in many comparisons. Whereas BMI that is generally regarded as the most widely used anthropometric index, in most previous studies those elderly with missing data for height, body weight, and BMI are excluded from the analysis. Analysis of only the available data leads to findings that apply only to a subgroup of the original population of interest, and that subgroup cannot be prospectively identified. However, the health-related outcomes of those people who cannot measure these essential anthropometries at home or do not know recent their anthropometries remains unknown.

In the present prospective cohort study we tried to determine whether lack of height or body weight measurement is a predictor of mortality or hospitalization during a 2-year follow-up period in community-dwelling older people using various community-based services.

Methods

Subjects

The present study employed baseline data of the subgroup of participants in the Nagoya Longitudinal Study for Frail Elderly (NLS-FE) and data on the mortality and hospitalization of these participants during the 2-year follow-up period. Details of participants and the NLS-FE have been published elsewhere.[12,13] The study population consisted of 952 community-dwelling frail elderly (355 men and 597 women, age 65 years or older) who were eligible for long-term care insurance (LTCI) program,[14–16] lived in Nagoya City, and were provided visiting nurse services from the Nagoya City Health Care Service Foundation for Older People, which has 17 visiting nursing stations associated with care-managing centers. The LTCI system covers care for both the elderly aged 65 and older. Under the LTCI program, care levels (levels 0–5) are determined according to eligibility criteria. The elderly in the community who are eligible for LTCI are disabled and chronically ill, have physical and mental problems, and are easy to admit acute hospital or institute care setting.[14–16] These NLS-FE participants, who were enrolled between 1 December 2003 and 31 January 2004, were scheduled to undergo comprehensive in-home assessments by trained nurses at the baseline, and at 6, 12, and 24 months. At 3-month intervals, data were collected about any important events in the lives of the participants, including admission to the hospital and mortality. Written informed consent for participation, according to procedures approved by the institutional review board of Nagoya University Graduate School of Medicine, was obtained from the patients or, for those with substantial cognitive impairment, from a surrogate (usually the closest relative or legal guardian).

Data collection

The data were collected at the clients' homes from standardized interviews with patients or surrogates and caregivers, and from care-managing center records taken by trained nurses. The data included clients' demographic characteristics, depressive symptoms as assessed by the short version of the Geriatric Depression Scale (GDS-15),[17] and a rating for 10 basic activities of daily living (ADL) (feeding, mobility on bed, bathing, grooming, dressing, using the toilet, walking inside and outside, transferring, and using stairs) using summary scores ranging from 0

(total disability) to 20 (no disability). The interview with participants also included questions about the utilization of care services, including the day-care service and home-help service programs, as well as medical services. Information obtained from care-managing center records included data on the following physician-diagnosed chronic conditions: ischemic heart disease, congestive heart failure, cerebrovascular disease, diabetes mellitus, dementia, cancer, neurodegenerative disorders including Parkinson's disease, and other diseases comprising the Charlson Comorbidity Index,[18] which represents the sum of weighted indexes, taking into account the number and seriousness of preexisting comorbid conditions. The data also included the number of prescribed medications. Of these 952 participants, 276 could not complete the GDS-15 because of severe cognitive impairment or communication impairment.

Height and weight data were generally measured at home and collected by nurses. The visiting nurses were asked to measure the height or weight of participants at home as much as possible. In the case that body weight measurements could not be taken at home for some reason, recorded or self-reported weight data obtained sometime within the last month was used. Weight was measured in light clothing without shoes using a portable weight scale at home. Height was generally measured in an upright position using a tape measure attached to the wall. However, when participants could not persist in an upright position, height measurements were obtained in a prone position. Height measurements were unavailable for subjects with severe kyphosis (defined as any subject whose kyphosis made it impossible for the visiting nurse to make a convenient or reliable height measurement) or severe muscle and arterial contracture.

Measurement of the triceps skin fold (TSF) thickness (to the nearest 0.1 mm) was made using skin-fold calipers and mid-upper arm circumference (AC) (to the nearest 0.1 cm) using a flexible measuring tape on the right side of the participant's body, unless affected by disability or disease. Arm area (AMA) was calculated using standard formulas: $AMA = (AC(cm) - 0.3142 \times TSF(mm))^2/4\pi$.

Of the 342 participants for whom height data were unavailable, 328 (95.9%) and 326 (95.3%) were available for their TSF and AC, respectively. Of the 292 participants for whom weight data were unavailable, 280 (95.9%) and 277 (94.9%) were available for their TSF and AC, respectively.

Statistical analysis

The Student's *t*-test and Chi-squared test were used to compare differences between participants with available and not available height data or between those with available and not available weight data. To evaluate the risk of participants with missing height or weight data, which was expressed as an odds ratio (OR) with a corresponding 95% confidence interval (CI), logistic regression models were used. The models included factors that differed significantly between participants with incomplete and complete anthropometric measurements.

Survival curves describing mortality and hospitalization over the 2 years after enrollment in participants with or without missing weight or height data at baseline were conducted using the Kaplan–Meier method and compared with the log-rank statistic. Cox proportional hazard models were used to assess the association of lack of height or weight measurement at baseline with 2-year mortality or hospitalization during a 2-year period. To create an ideal model for a multivariate Cox proportional hazards models, we selected covariates as follows. We first evaluated the univariate association between each covariate at baseline using the chi-square test for categorical and the *t*-test for continuous variables. Next, we evaluated the association between each covariate and 2-year mortality or hospitalization during the 2-year period using the univariate Cox proportional hazards model. We then sequentially evaluated the impact of each of the remaining covariates on the overall model fit through a series of Cox proportional hazards models. The risk of a variable was expressed as a hazard ratio (HR) with a corresponding 95% CI.

All analyses were performed using the Statistical Package for the Social Sciences (SPSS) Version 14.0. A probability value of 0.05 or less was considered significant.

Results

Baseline characteristics

Among the 952 participants, 342 (35.9%) and 292 (30.7%) had missing data for height and weight at baseline, respectively. Among the 610 participants with height data available, 96 (15.7%) had missing data for weight, and among the 660 participants with weight data available, 146 (22.1%) had missing data on height. As such, BMI was unavailable in 438 participants (46.0%).

Table 1 shows the comparisons of baseline characteristics of participants having or missing data for height or weight. Participants missing these anthropometric measurements were significantly more likely to be women, to be older, to have lower ADL scores, to have lower day-care service use, a lower rate to 3 and more regular prescribing medication, lower AC, and a higher prevalence of dementia and pressure sores compared with participants with anthropometric measurements at baseline. Participants with missing weight measurements were significantly more likely to have higher comorbidity, to have a lower rate of living alone, and to have lower AMA than those with available weight measurements.

Factors related to lack of measurement

To identify the factors associated with missing height and weight data, two different multivariate logistic regression models were conducted (Table 2). Model 1 is based on the inclusion of factors that differed significantly between participants with incomplete and complete anthropometric measurements. Model 2 includes the presence or absence of cerebrovascular disease, dementia, or pressure sores instead of the Charlson comorbidity index. We obtained comparable results with these two models, suggesting that age and ADL levels are determinants of the presence or absence of height and weight measurements: older and lower ADL function are associated with missing these anthropometric measurements. In addition, those utilizing

Table 1 Base line characteristics of the 952 care recipients.

	Total	Height		p	Weight		p
	$n = 952$	Available $n = 610$	Not available $n = 342$		Available $n = 660$	Not available $n = 292$	
Men/women, *n* (% of men/total)	355/597 (37.3)	254/356 (41.6)	101/241 (29.5)	<0.001	263/397 (39.8)	92/200 (31.5)	0.014
Age (years), mean (SD)*	80.5 (7.9)	79.8 (7.9)	81.6 (7.8)	<0.001	79.7 (7.8)	82.2 (8.1)	<0.001
Basic ADL (range, 0–20), mean (SD)*	10.3 (6.9)	11.4 (6.7)	8.3 (6.9)	<0.001	12.2 (6.2)	6.0 (6.6)	<0.001
GDS-15 (range, 0–15), mean (SD)†	7.1 (3.6)	7.1 (3.6)	6.9 (3.5)	0.400	7.0 (3.6)	7.2 (3.6)	0.655
Charlson comorbidity index, mean (SD)*	2.3 (1.6)	2.3 (1.6)	2.4 (1.6)	0.120	2.2 (1.7)	2.6 (1.5)	<0.001
Day-care (service) use (% of total)	35.6	33.0	40.4	0.022	38.9	28.1	0.001
Home help service use (% of total)	51.7	49.5	55.6	0.073	50.5	54.5	0.255
Regular medical checkups (% of total)	73.4	74.5	71.3	0.283	72.7	75.0	0.456
Three or more regular prescription medications (% of total)	79.9	82.0	76.2	0.035	84.7	69.1	<0.001
Living alone (% of total)	19.0	20.6	16.0	0.086	21.6	12.9	0.002
Mid arm circumference (cm), mean (SD)	23.5 (4.4)	23.7 (4.6)	23.1 (4.1)	0.031	23.9 (4.6)	22.6 (3.8)	<0.001
Triceps skin fold (cm), mean (SD)	1.4 (0.9)	1.5 (0.9)	1.4 (0.8)	0.067	1.5 (0.9)	1.4 (0.9)	0.590
Arm muscle area (cm^2), mean (SD)	29.6 (11.7)	29.9 (11.8)	29.1 (11.5)	0.280	30.7 (11.9)	27.1 (10.7)	<0.001
Chronic diseases (% of total)							
Ischemic heart disease	11.6	13.0	9.3	0.117	11.9	11.0	0.702
Congestive heart failure	11.2	10.9	11.7	0.719	11.7	9.7	0.401
Cerebrovascular disease	40.7	39.4	43.0	0.326	38.3	46.4	0.033
Diabetes mellitis	13.1	13.5	12.4	0.640	11.9	16.0	0.114
Dementia	38.1	33.7	46.0	<0.001	30.7	56.1	<0.001
Cancer	10.5	11.0	9.6	0.525	11.7	7.6	0.080
Hypertension	23.1	23.6	22.2	0.627	23.5	22.3	0.679
Pressure sore	11.6	9.2	15.8	0.002	7.0	21.9	<0.001

*Student *t*-test, others were analyzed by χ^2 test (user vs. nonuser).
†GDS-15: geriatric depression scale, total: $n = 676$.

day-care services were more likely to have their weight measurement but not height measurement. Furthermore, model 2 indicated that the presence of dementia or pressure sores is associated with missing weight measurement but not missing height.

Prospective study

Participants with missing weight measurement had a higher mortality rate (having: 18.0%; missing: 38.4%, $p<0.001$) and hospitalization (having: 32.6%; missing: 40.8%, $p = 0.015$) during the 2-year follow-up compared with those with available weight measurements. Participants with missing height measurement had higher mortality (having: 22.1%; missing: 28.1%, $p = 0.04$), but there was no difference in hospitalization (having: 33.3%; missing: 38.3%, $p = 0.119$).

Figure 1 shows the Kaplan–Meier curves describing mortality and hospitalization over the 2 years in participants with or without missing weight or height data at baseline. The missing weight and height data at baseline were significantly associated with lower survival rate during 2-years follow-up (Log rank test: $p<0.0001$ and $p = 0.030$, respectively) (Figure 1A and C). Although the missing weight data at the baseline was associated with higher hospitalization during 2-years follow-up, the missing height data was not (Log rank test: $p = 0.001$ and $p = 0.067$, respectively) (Figure B and D).

Table 3 provides the results of the series of Cox proportional hazards models to examine the HRs of missing height and weight data at baseline for 2-year mortality and hospitalization during 2-year follow-up. In the unadjusted models, missing data for height were significantly associated with an elevated risk for 2-year mortality, but not for hospitalization during the 2-year follow-up. For 2-year mortality, sequential adjustment for the covariates lost the association between participants with missing data on height and 2-year mortality. In unadjusted models, missing weight data were significantly associated with elevated risks for 2-year mortality and for hospitalization during follow-up periods. The sequential adjustment lowered the hazard for mortality associated with missing weight data, but the association remained statistically significant even after the fully adjusted model. For hospitalization, the rather constant HR associated with participants with missing weight data was observed even after full adjustment.

Discussion

In the present study we demonstrated that approximately one-third of elderly participants who are older people living

Table 2 Logistic regression analysis to identify independent predictors of lack of anthropometric measurements.

Base line variables	Model 1*				Model 2†			
	Height		Weight		Height		Weight	
	OR‡	95% CI	OR	95% CI	OR‡	95% CI	OR	95% CI
Men (vs. women)	0.74	0.53–1.02	0.86	0.59–1.26	0.74	0.53–1.03	0.87	0.59–1.27
Age (continous variable)	1.03	1.01–1.05	1.03	1.01–1.06	1.03	1.00–1.05	1.03	1.01–1.05
ADL score (continous variable, range, 0–20)	0.94	0.91–0.96	0.87	0.84–0.89	0.94	0.91–0.97	0.88	0.85–0.91
Living alone (vs. with others)	1.16	0.76–1.76	1.55	0.94–2.56	1.15	0.75–1.75	1.54	0.93–2.56
Day-car service use (vs. nonuse)	1.33	0.98–1.82	0.57	0.39–0.82	1.35	0.98–1.85	0.55	0.37–0.80
No of prescription medications (vs. <3)								
3–5	1.07	0.70–1.64	0.74	0.46–1.17	1.08	0.71–1.66	0.80	0.50–1.29
≧6	0.86	0.56–1.35	0.65	0.40–1.07	0.87	0.55–1.36	0.72	0.43–1.18
Charlson comorbidity index (continous variable)	1.00	0.90–1.10	1.03	0.92–1.16				
Presence of chronic diseases (vs. absence)								
Cerebrovascular disease					0.96	0.69–1.33	1.00	0.69–1.46
Dementia					1.01	0.72–1.42	1.48	1.01–2.18
Pressure sore					1.19	0.74–1.92	2.05	1.21–3.46

*Model 1 includes gender, age, ADL score, living arrangement at baseline, use or nonuse of day-care services, number of prescribed medication, and Charlson comorbidity index.
†Model 2 includes the presence or absence of cerebrovascular disease, dementia, or pressure sores instead of the Charlson comorbidity index.
‡Odds ratio (OR).

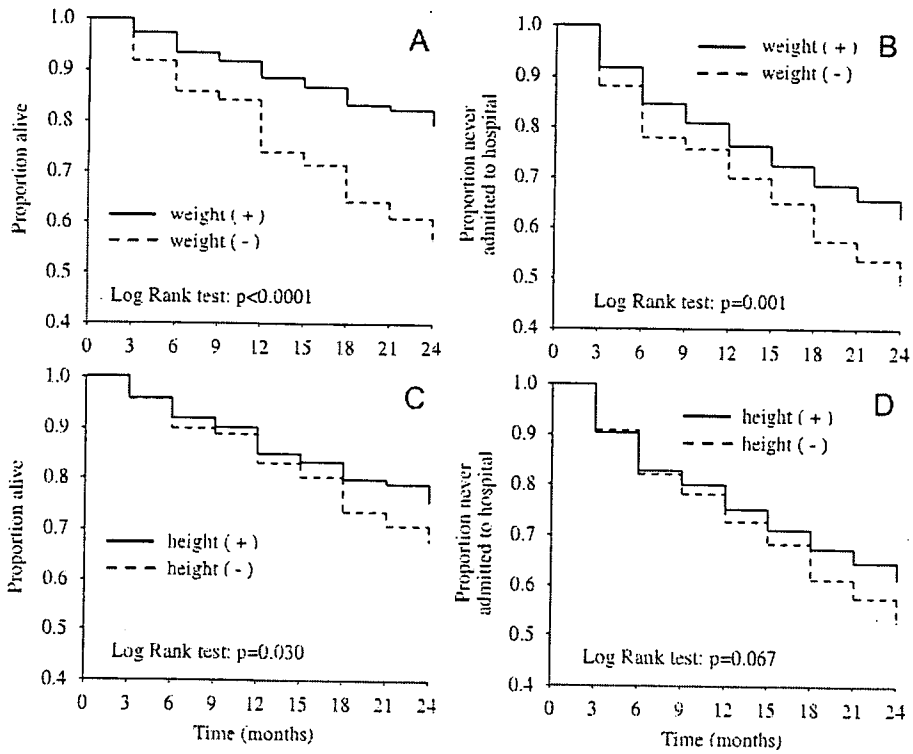

Figure 1 The Kaplan–Meier survival curves describing mortality (A, C) and hospitalization (B, D) over the 2-years after enrollment in participants with or without missing weight (A, B) or height (C, D) data at baseline.

at home and receiving informal or formal assistance under the LTCI program lack height or weight measurements. Among the 952 participants, 438 (46.0%) were missing data for height, weight, or both, indicating nearly half of the participants did not know their own BMI. Exact information regarding the reasons for the lack of height or weight

Table 3 Hazards risk of lack of anthropometric measurements according to Cox proportional hazard model to identify independent predictors of adverse events.

	Variable	Measurements			
		Height		Weight	
		HR*	95% CI	HR	95% CI
Mortality					
Unadjusted		1.33	1.02–1.72	2.38	1.84–3.08
Adjusted†	Model 1	1.31	1.01–1.71	2.29	1.76–2.98
	Model 2	1.00	0.73–1.35	1.55	1.10–2.19
	Model 3	0.97	0.71–1.32	1.54	1.09–2.18
Hospitalization					
Unadjusted		1.22	0.98–1.52	1.44	1.15–1.80
Adjusted‡	Model 1	1.27	1.02–1.59	1.53	1.22–1.92
	Model 2	1.18	0.92–1.52	1.34	1.00–1.78
	Model 3	1.17	0.90–1.51	1.34	1.01–1.79

*HR: hazard risk.

†Model 1 includes age and gender; Model 2 includes age, gender, ADL score, living arrangement at baseline, number of regular medical check per week, number of prescribed medication, use or nonuse of day-care services, and presence or absence of chronic diseases (dementia, cancer, hypertension, or pressure sore); Model 3 includes factors in Model 2 and mid arm circumference.

‡Model 1 includes age and gender; Model 2 includes age, gender, ADL score, number of regular medical check per week, number of prescribed medication, presence or absence of cancer or pressure sore; Model 3 includes factors used in Model 2 and mid arm circumference.

measurement or lack of knowledge of these values at the baseline is not available in the present study. However, the association between older age or lower ADL function, and missing either anthropometric data may suggest that the height and weight of older people with ADL impairment are more likely to not be measured at home or to not regularly be measured in the community. It should be noted that a lack of weight measurement is strongly associated with ADL functional status of the subjects compared with that of height measurement, suggesting that participants with missing weight measurement are more functionally dependent older people. In addition, we showed that the presence of dementia and pressure sores is associated with a lack of weight measurement but not of height measurement. In fact, it is not unusual for the frail elderly to be unable to be weighed at home without hoist or wheelchair scales due to severe ADL impairment or the presence of advanced dementia or pressure sore. In contrast, it seems that there are obviously individuals whose height cannot be measured because of the presence of kyphosis or other postural problems. Thus there are different groups of community-dwelling elderly for whom either height or weight or both cannot be measured.

We observed that those utilizing day-care services are more likely to have their weight measurement, suggesting that clients' weight is often measured at the day-care (service) center. It is well known that older people, especially those with functional limitations, are particularly vulnerable to undernutrition, which may further impair functional ability and increase the incidence of morbidity and mortality.[9,10] Nutritional screening is, therefore, crucial for not only hospitalized elderly people but also for those living in the community. However, the results regarding the unexpected high rate of older people with missing major anthropometric measurements in the community indicate that regular nutritional screening is not conducted for older people receiving community-based services under the LTCI program by health care professionals.

We observed that a lack of weight data is associated with 2-year mortality as well as hospitalization during the 2-year follow-up, even after adjusting for potential confounders, including age, ADL status, and comorbidity. A lack of height measurements is not associated with these adverse outcomes, suggesting again that there are different groups of community-dwelling elderly in the community for whom height and weight cannot be measured. The mechanisms underlying the association between lack of weight measurement and mortality and hospitalization are unclear in the present study, but could be related to several factors. A large number of studies have shown that lower levels of weight, BMI, or weight loss is an important predictor of mortality in elderly peoples.[4–11] Although we do not know whether their weight or BMI was lower than that of subjects who had been weighed at the baseline and whether they had weight loss during the study periods, it is possible that the association with adverse outcomes might be due to the undernutrition of participants with missing data on weight, since AC and AMA levels, potential markers of nutritional status, of the subjects with missing data on weight were significantly lower than those of the subjects who were weighed. However, we observed that the association between a lack of weight measurement and mortality or hospitalization persisted even after adjusting for AC, suggesting that undernutrition alone at baseline cannot explain this association. However, we cannot exclude the possibility that our participants lacking weight measurements might

have experienced weight change during the study period. Weight loss frequently goes unrecognized in older people and may lead to undernutrition and poor clinical outcomes.[4,19,20] The lack of weight measurement or a lack of knowledge of weight change by patients themselves, care givers, or health care professionals, including visiting nurses and physicians, results in a lost chance to detect early changes in patients' health conditions and nutritional status, and to respond appropriately to their weight changes.

The present study cannot reveal whether lack of knowledge of their own weight, weight change itself, or other background factors related to nonmeasurement of weight beyond what we could measure and control for may contribute to the 2-year mortality and hospitalization during a 2-year follow-up period. Future study is needed to examine whether measuring the weight of these older people with functional limitations and monitoring of weight changes in the community may have a positive effect on mortality and morbidity.

This study has important limitations. First, as described above the exact reasons for missing data on height or weight are not clear in the present study. Therefore, the exact cause of poor outcomes of participants with lack of weight measurement at baseline during the 2-year observation was not evaluated. As described in the methods, participants included in our present study were limited to those using visiting nurse services, which may have introduced a selection bias into the study. Because of the observational design of the present study, differences in unmeasured factors, including the severity of chronic diseases of patients, may account in part for the findings. In addition, these findings may not be generalizable to other populations, given the differing health practices, a variety of social and economic factors, and ethnic attitudes regarding caring for very old people.

In the present study we showed that there are many older people living in the community with functional disability whose weight or height is not measured for various reasons. Those subjects, especially those for whom weight data are unavailable, are more likely to have high risk for mortality and hospitalization.

Conflict of interest statement

None declared.

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ORIGINAL ARTICLE

Is serum albumin a good marker for malnutrition in the physically impaired elderly?

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Summary
Background and Aims: Although serum albumin is well known as a marker of nutritional status, it has remained unclear whether impaired physical function affects serum albumin concentrations in older people. We examined whether hypoalbuminemia can be used as a marker of malnutrition in elderly subjects with various levels of physical impairment.
Methods: A total of 262 elderly subjects without acute illness were enrolled from various geriatric settings. For the nutritional assessment, serum albumin, total cholesterol, anthropometric measurements, and subjective global assessment (SGA) were determined. Physical function was evaluated by rating score of activity of daily living (ADL).
Results: As a whole, participants' serum albumin levels correlated with various nutritional parameters including anthropometric measurements and levels of serum total cholesterol as well as the SGA evaluation. However, after adjusting for age and gender, serum albumin levels in participants with a low ADL function did not correlate with nutritional parameters. Approximately 80% participants with low ADL function who were evaluated as being well nourished according to SGA evaluation had serum albumin levels lower than 35 g/l.
Conclusions: The utility of serum albumin and the traditional cutoff (35 g/l) in older people with low ADL function is questionable even among those without inflammation.

Introduction

Malnutrition is a common finding in the elderly, not only in institutionalized populations but also in community-dwelling

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elderly, with prevalence rates ranging from 12% to 85%.[1,2] Malnutrition is associated with increased hospitalization, increased susceptibility to infection, decreased wound healing, reduced quality-of-life, and increased mortality in the elderly.[3,4]

Multidimensional screening tools such as subjective global assessment (SGA),[5] and anthropometry measurements such as body mass index (BMI), mid-arm circumference (MAC), calf circumference (CC), and skin-fold thickness are generally considered the most easily obtainable, inexpensive, and noninvasive method by which to assess nutritional state. Biochemical measurements such as serum albumin and total cholesterol are also well known as markers for protein energy malnutrition (PEM).[6,7] Among the biochemical parameters, serum albumin levels have long been considered a major measure of malnutrition. On the other hand, some reports have cautioned against using albumin as a measurement of nutritional status in hospitalized patients.[8–10] The criticism is based on the fact that albumin is inversely correlated with markers of inflammatory activity and can behave as an acute-phase reactant, with markedly reduced levels in the setting of acute illness. In addition, it remains unknown whether impaired physical function affects serum albumin concentrations in older people. Thus, we still do not know whether hypoalbuminemia can be used as a marker of malnutrition for elderly people at various levels of activities of daily living (ADL) impairment, especially in the absence of inflammation or acute illness.

In the present study we examined whether hypoalbuminemia defined by a serum albumin level lower than 35 g/l can be used as a marker of malnutrition in elderly subjects without inflammation or acute illness. In addition we also examined whether physical impairment may affect the serum albumin concentration among well-nourished older people.

Subjects and methods

Subjects

We enrolled 262 consecutive elderly subjects (86 males and 176 females, mean age $\pm$SD: 81.8 $\pm$ 7.5; range: 65–95 years) from our geriatric outpatient clinic ($n = 69$), a nursing home ($n = 56$), and geriatric hospitals ($n = 72$). Among 262 participants 55 participants were receiving tube feeding and there were no participants receiving parenteral nutrition. The participants from geriatric hospitals were transfers from the acute care setting or from nursing homes for the care of chronic diseases or for the rehabilitation. The nutritional assessments were conducted at the admission. Informed consent for participation, according to procedures approved by the institutional review board of Nagoya University Graduate School of Medicine, was obtained verbally from the patients, or, for those with substantial cognitive impairment, from a surrogate (usually the closest relative or legal guardian) and from caregivers. Subjects diagnosed with infection, inflammation, liver disorders, kidney disorders, cancer at least within 2 months, or serum C-reactive protein $\geqq$1.0 mg/dl were not included among the 262 participants to avoid the influence of inflammation on serum albumin levels.

Anthropometric measurements and biochemical markers

BMI is defined as weight in kg divided by height in meters squared. Triceps skin-fold (TSF) was measured with Harpenden calipers over the triceps muscle at the midway point between the acromion and the olecranon process. MAC and CC were measured on the left arm and calf with a tape measure. Arm muscle circumference (AMC = MAC(cm)-$\pi \times$ TSF(mm)/10) and arm muscle area (AMA) were calculated using the standard formula shown below: AMA $cm^2 = (AMC(cm^2))^2/4\pi$. Three repeat measurements were taken to the nearest 0.5 mm, with the mean taken as the true value. All anthropometric measurements were taken at least twice by two different investigators; the reported values are the means of the repeated measurements. Blood samples were collected after an overnight fast. Serum albumin and total cholesterol levels were determined using automated analyzers.

Nutritional status using SGA was conducted by trained dieticians who were blinded to the levels of serum albumin, total cholesterol, and hemoglobin. SGA consists of a brief nutritional history (weight loss during the last 6 months; dietary change; and a short physical examination of subcutaneous fat, muscle mass, and fluid balance).[5] SGA classifies patients as having PEM or moderate PEM or being well nourished; it focuses on medical issues and was constructed mostly from experience with surgical patients, but the use of SGA in older populations has also been validated.[11]

Each site's nursing staff assessed each patient's functional status which included a rating for seven basic ADL (feeding, bathing, grooming, dressing, using the toilet, walking, and transferring) using summary scores ranging from 0 (total disability) to 20 (no disability).[12] Information obtained from medical records included physician-diagnosed chronic conditions comprising the Charlson comorbidity index,[13] which represents the sum of a weighted index that takes into account the number and seriousness of preexisting comorbid conditions.

Definition of malnutrition

A BMI of less than 20 is widely accepted to indicate that the subject is underweight, particularly in well-developed countries, and 18.5 is recommended as a practical lower limit for most populations.[14] Therefore, a diagnosis of malnutrition was made when BMI was less than 18.5 kg/m^2. Serum albumin and total cholesterol levels were used as the biochemical markers of undernutrition: levels lower than 35 g/l of albumin or 3.88 mmol/l (1.5 g/l) of total cholesterol were taken to indicate malnutrition.[15,16]

Statistical analysis

The ADL score (range 0–20) was categorized into three groups with approximately equal number of participants in each group: high ADL function (ADL score $\geqslant$19), mid ADL function (ADL score 2–18), and low ADL function (ADL score $<$2). Differences between ADL function groups were determined by analysis of variance with a Bonferroni

correction, the χ^2 test, or the Kruskal–Wallis test, as appropriate. Partial rank correlation coefficients adjusted for age and gender were used to measure the relationships between serum albumin levels and anthropometric measurements, biochemical markers, and SGA evaluation. To examine the relationships between ADL scores and serum albumin levels, partial-rank correlation coefficients were used after adjusting for age, gender, and AMC or SGA evaluation. The sensitivity and specificity of 35 g/l of serum albumin as a cutoff point for predicting malnutrition based on the various nutritional markers were also calculated. The significance level was set at 0.05. Data evaluation was carried out using the SPSS software package (SPSS Inc., Chicago, USA).

Results

The age, ADL score, Charlson comorbidity index, anthropometric measurements, serum biochemicals (albumin and total cholesterol), and SGA assessment for total participants and groups categorized by ADL score are shown in Table 1.

The group of low ADL function had the highest comorbidity condition, lowest anthropometric measurements, and lowest levels of serum albumin and total cholesterol compared with the mid or high ADL-function group. Of the low, mid, and high ADL-function groups, 28%, 57.4%, and 87.2% were evaluated as being well nourished according to the SGA classification, respectively.

Among all participants, serum albumin levels were well correlated with various nutritional parameters including anthropometric measurements and the levels of serum total cholesterol as well as SGA classification after adjusting for age and gender (Table 2). Among high and mid ADL-function groups there was also good correlation between serum albumin levels and all nutritional makers tested except for AMA and AMC in the high ADL-function group. However, in the low ADL-function group no correlation was observed between serum albumin level and any nutritional marker tested. Among total participants after adjusting for age, gender and ADL score, serum albumin levels were correlated with BMI ($r = 0.202$, $P = 0.002$), MAC ($r = 0.213$, $P = 0.001$), TSF ($r = 0.265$, $P<0.0001$), CC ($r = 0.190$, $P = 0.003$), serum total cholesterol ($r = 0.275$, $P<0.0001$), and SGA classification ($r = 0.288$, $P<0.0001$) but not with

Table 1 ADL and nutritional characteristics.

	Total, $n = 262$		Low ADL function, ADL score ≦1, $n = 82$		Mid ADL function, ADL score = 2–18, $n = 94$		High ADL function, ADL score ≧19, $n = 86$		P
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Men/women (% of male)	86/176	32.8	29/53	35.4	25/69	26.6	32/54	37.2	0.2666*
Age	81.8	7.5	83.6	8.6	82.5	7.3	79.4	5.7	0.0006
Activities of daily living (ADL, range: 0–20)	10.2	8.7	0.2	0.4	10.3	6.1	19.8	0.4	<0.0001
Charlson index	2.1	1.8	2.6	1.5	2.5	1.9	1.3	1.5	<0.0001
Body mass index (BMI, kg/m^2)	19.7	3.9	17.4	2.8	19.5	3.4	22.2	3.9	<0.0001
Midarm circumference (MAC, cm)	22.2	3.7	20.2	3.3	21.9	3.4	24.6	3.1	<0.0001
Triceps skinfold (TSF, mm)	9.8	5.9	7.2	3.8	8.1	4.1	14.5	6.7	<0.0001
Arm muscle circumference (AMC, cm)	19.1	2.8	17.9	2.7	19.4	2.8	20.0	2.5	<0.0001
Arm muscle area (AMA, cm^2)	29.7	8.6	26.1	7.8	30.6	8.7	32.3	8.1	<0.0001
Calf circumference (CC, cm)	27.0	5.2	22.2	3.3	27.4	3.8	31.7	3.5	<0.0001
Albumin (g/l)	36.0	5.7	31.1	4.0	35.6	4.7	41.0	3.3	<0.0001
Total cholesterol (Tch, mmol/l)	4.8	1.1	4.2	0.9	4.8	1.1	5.3	0.9	<0.0001
Subjective global assessment (*n*, (*% of total*))									
Well nourished	152	(58.0)	23	(28.0)	54	(57.4)	75	(87.2)	
Moderatly malnourished	87	(33.2)	42	(51.2)	34	(36.2)	11	(12.8)	<0.0001**
Severely malnourished	23	(8.8)	17	(20.7)	6	(6.4)	0	(0.0)	

Age: high ADL vs. low ADL ($P = 0.0006$) or mid ADL ($P = 0.016$). Charlson index: high ADL vs. low ADL ($P<.0.0001$) or mid ADL ($P<.0.0001$).
BMI, MAC, CC: albumin: high ADL vs. low ADL ($P<0.0001$) or mid ADL ($P<0.0001$); mid ADL vs. low ADL ($P<0.0001$).
TSF: high ADL vs. low ADL ($P<0.0001$) or mid ADL ($P<0.0001$).
AMC; high ADL vs. low ADL ($P<0.0001$), mid ADL vs. low ADL ($P = 0.0012$).
AMA: high ADL vs. low ADL ($P<0.0001$), mid ADL vs. low ADL ($P = 0.0013$).
Tch: high ADL vs. low ADL ($P<0.0001$) or mid ADL ($P = 0.011$), mid ADL vs. low ADL ($P<0.0001$).
SD: Standard deviation.
*χ^2-test.
**Kruskal–Wallis test, others were determined by analysis of variance with a Bonferroni correction.

Table 2 Correlation between serum albumin and neutritional variables.

	Total, $n = 262$		Low ADL function, ADL score ≦1, $n = 82$		Mid ADL function, ADL score = 2–18, $n = 94$		High ADL function, ADL score ≧19, $n = 86$	
	r	P	r	P	r	P	r	P
Body mass index	0.482	<0.0001	0.135	0.2370	0.367	0.0010	0.2391	0.039
Midarm circumference	0.485	<0.0001	0.176	0.1230	0.395	<0.0001	0.2511	0.030
Triceps skinfold	0.501	<0.0001	−0.022	0.8500	0.417	<0.0001	0.3978	<0.0001
Arm muscle circumference	0.297	<0.0001	0.205	0.0710	0.285	0.0090	−0.0335	0.775
Arm muscle area	0.281	<0.0001	0.195	0.0870	0.265	0.0160	−0.0384	0.744
Calf circumference	0.636	<0.0001	0.096	0.4010	0.457	<0.0001	0.2957	0.010
Total cholesterol	0.469	<0.0001	0.194	0.0890	0.394	<0.0001	0.2525	0.029
Subjective global assessment (SGA)	0.499	<0.0001	0.199	0.0810	0.258	0.0190	0.5488	<0.0001

ADL: activities of daily living. Data were adjusted for age and gender.
SGA rating: 0, well nourished; 1, moderatly malnourished; 2, severely malnourished.

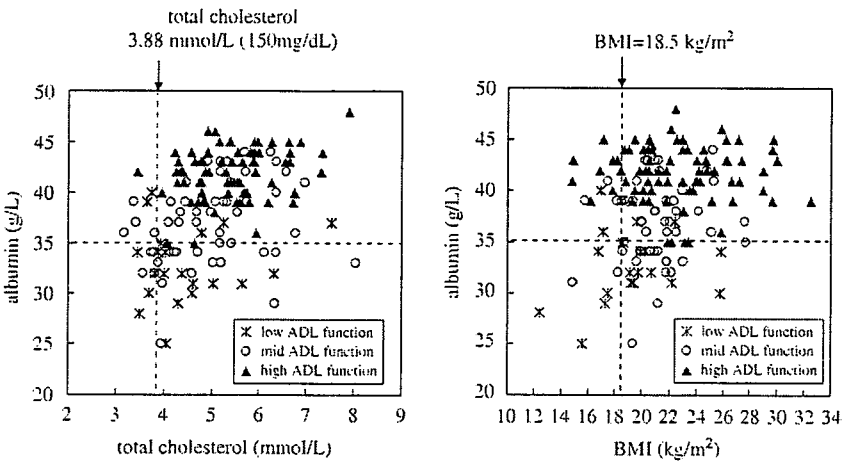

Figure 1 The relationship between levels of serum albumin and total cholesterol or BMI according to the three categories of ADL function among the well-nourished subjects as evaluated by SGA.

AMA ($r = 0.069$, $P = 0.285$) or AMC ($r = 0.086$, $P = 0.183$). Total ADL scores were well correlated with serum albumin concentration after adjusting for gender and age ($r = 0.726$, $P<0.0001$). This correlation persisted after adjusting for SGA classification ($r = 0.650$, $P<0.0001$) or AMC ($r = 0.699$, $P<0.0001$), or both ($r = 0.644$, $P<0.0001$).

Figure 1 shows the relationship between levels of serum albumin and total cholesterol or BMI according to the three categories of ADL function among the subjects evaluated as well nourished by SGA. There were no participants with albumin <35 g/l among the well-nourished high ADL-function group with total cholesterol ≧3.88 mmol/l (150 mg/dl) or BMI ≧18.5 kg/m^2. However, 13 out of 16 participants (81.3%) of the well-nourished low ADL-function group, and 13 out of 44 participants (29.5%) of well-nourished mid ADL-function group had albumin <35 g/l and total cholesterol ≧3.88 mmol/l (150 mg/dl). Furthermore, 12 out of 15 participants (80.0%) of the well-nourished low ADL-function group and 15 out of the 46 participants (32.6%) of the well-nourished mid ADL-function group had albumin <35 g/l and BMI≧18.5 kg/m^2.

In the low ADL-function group, 77.3% of the participants evaluated as being well-nourished according to SGA classification, 78.2% of the participants with serum total cholesterol concentration ≧3.88 mmol/l, and 82.1% of the participants with BMI≧18.5 kg/m^2 had a serum albumin level <35 g/l (Table 3). By contrast, among the high ADL-function group there were no participants with a serum albumin level <35 g/l among those evaluated as being well nourished. Furthermore, only 3.6% of participants with total cholesterol levels ≧3.88 mmol/l and 2.9% of participants with BMI≧18.5 kg/m^2 had serum albumin levels <35 g/l. The sensitivity and specificity of 35 g/l serum albumin as a cutoff point of malnutrition based on the various nutritional markers are presented in Table 3. Among low ADL-function participants with nutritional status based on either SGA evaluation, total cholesterol levels (<3.88 mmol/l), or BMI (<18.5 kg/m^2), the 35 g/l serum albumin cutoff point had

Table 3 Validity of cutoff point of serum albumin (<35 g/l) for malnutritional markers.

Nutritional markers		Serum albumin				P^*	Specificity	Sensitivity
		<35 g/l		≧35 g/l				
		n	%	*n*	%			
Total								
SGA	Well nourished	34	22.8	115	77.2		0.772	
	Moderatly malnourished	57	64.0	32	36.0	<0.0001		
	Severely malnourished	18	78.9	5	21.7			0.783
Tch	≧3.88 mmol/l	73	34.1	141	65.9	<0.0001	0.659	
	< 3.88 mmol/l	35	77.8	10	22.2			0.778
BMI	≧18.5 kg/m^2	45	28.7	112	71.3	<0.0001	0.713	
	< 18.5 kg/m^2	64	62.1	39	37.9			0.621
Low ADL function (*ADL socre:* ≦1)								
SGA	Well nourished	17	77.3	5	22.7	0.421	0.227	
	Moderatly malnourished	34	79.1	9	20.9			
	Severely malnourished	15	88.2	2	11.8			0.882
Tch	≧3.88 mmol/l	43	78.2	12	21.8	0.500	0.218	
	< 3.88 mmol/l	22	84.6	4	15.4			0.880
BMI	≧18.5 kg/m^2	23	82.1	5	17.9	0.787	0.179	
	< 18.5 kg/m^2	43	79.6	11	20.4			0.796
Mid ADL function (*ADL score:* 2–18)								
SGA	Well nourished	17	32.7	35	67.3	0.033	0.673	
	Moderatly malnourished	20	57.1	15	42.9			
	Severely malnourished	3	50.0	3	50.0			0.500
tch	≧3.88 mmol/l	27	36.0	48	64.0	0.003	0.640	
	< 3.88 mmol/l	13	76.5	4	23.5			0.765
BMI	≧18.5 kg/m^2	20	33.9	39	66.1	0.014	0.661	
	< 18.5 kg/m^2	20	60.6	13	39.4			0.606
High ADL function (*ADL socre:* ≧19)								
SGA	Well nourished	0	0.0	75	100.0	<0.0001	1.000	
	Moderatly malnourished	3	27.3	8	72.7			
	Severely malnourished	0		0				
tch	≧3.88 mmol/l	3	3.6	81	96.4	0.947	0.964	
	< 3.88 mmol/l	0	0.0	2	100.0			
BMI	≧18.5 kg/m^2	2	2.9	68	97.1	0.672	0.971	
	< 18.5 kg/m^2	1	6.3	15	93.8			0.063

SGA: subjective global assessment, tch: total cholesterol, BMI: body mass index,
ADL: activities of daily living.
*χ^2 test.

high sensitivity (0.882, 0.880, or 0.796, respectively) but low specificity (0.227, 0.218, or 0.179, respectively) as an indicator of malnutrition. Among low ADL-function participants with nutritional status based on SGA evaluation, the 3.88 mmol/l serum total cholesterol as a cutoff point had high specificity (0.727) but low sensitivity (0.500) as an indicator of malnutrition.

Discussion

In the present study we demonstrated that the serum albumin cutoff point of 35 g/l as an indicator malnutrition is not suitable for the elderly with low ADL function. In older people with low ADL function serum albumin levels were not correlated with various nutritional parameters including anthropometric measurements, levels of serum total cholesterol, and SGA evaluation after adjusting for age and gender. Using a serum albumin level <35 g/l as a malnutrition indicator for the ADL-impaired elderly, about 80% of older people without malnutrition would be classified as malnourished (low specificity) while 11–20% of elderly persons with malnutrition would be missed (sensitivity). These results suggest that the use of a serum albumin level <35 g/l as a marker of malnutrition for elderly with low ADL function leads to over-diagnosis of malnutrition. It should be noted that we also observed that the use of a serum total cholesterol level <3.88 mmol/l as a marker of malnutrition would miss the half of the ADL-impaired elderly person with malnutrition.

The observation that serum albumin is a negative acute-phase protein suggests that serum albumin concentration could be a marker of inflammation. In fact, serum levels of albumin decrease in response to acute or chronic inflammation by altering the normal hepatic protein metabolism and inducing capillary leak.[8–10] This concept is responsible for the reports that albumin is not a good marker for the nutritional status of the hospitalized elderly with illness.[17] However, in this study we excluded patients having high C-reactive protein levels or acute illness within the past 2 months. It has been reported that serum albumin levels and SGA, two possible measurements of nutritional status in hospitalized older people, are often discordant.[18] However, this previous interesting report did not address the interaction between serum albumin and the presence of inflammation or ADL status among hospitalized older people.

It has been reported that posture affects serum albumin levels; 1 h in the sitting position after resting in the supine posture during an overnight sleep increases serum albumin by 6.3%.[19] Simply standing upright or sitting increases hydrostatic pressure, and this shift in balance between hydrostatic and oncotic pressures leads to a net movement of fluid from intravascular to interstitial spaces.[20] Most participants with low ADL function in the present study were hospitalized patients, and most of these were bed-ridden elderly. Blood specimens were drawn from low ADL-function participants lying in bed and from high ADL-function ambulatory participants in a sitting position. These postural differences may have affected the serum levels of albumin in both types of participants. However, it has been reported that there is an increase from the lying to the sitting position of about 6.5–7.7% in serum concentrations, not only of proteins but also of lipids including cholesterol.[21,22] Therefore, the posture at the collection of blood samples may not explain our results.

We have demonstrated that ADL function is well correlated with serum albumin levels. One study has demonstrated that severe disability in ADL is strongly associated with anthropometric and biohumoral parameters including serum albumin levels suggesting the presence of malnutrition.[23] However, this is not the case here, since the association between serum albumin and ADL status persists after adjusting for SGA classification, suggesting that this association is not mediated through nutritional status. It is possible that the correlation of serum albumin with ADL function may be mediated by muscle mass, since physical disability is well known to be related with muscle atrophy[24] A cross-sectional study found an association between lower serum albumin concentration and lower muscle mass in the elderly.[25] It is known that several inflammatory cytokines down-regulate serum albumin concentration and increase muscle protein breakdown, which could potentially explain the association of low serum albumin with low muscle mass.[8,26] One study has demonstrated that a low serum albumin concentration in older persons was associated with a greater loss of muscle mass during a 5-year follow-up even after adjusting for the effect of inflammation, although no association was detected between albumin levels and muscle mass at the baseline.[27] In the present study we demonstrated that albumin levels were well correlated with AMC or AMA, markers of muscle mass, among older people without acute illness and inflammation, indicating that inflammation is not involved in the correlation between serum albumin levels and muscle mass, at least in the present study. However, after adjusting for ADL levels there was no correlation between serum albumin and the markers of muscle mass. In addition, the ADL score was well correlated with serum albumin levels after adjusting for muscle mass, suggesting that serum albumin levels might be associated with muscle mass through ADL function rather than with muscle mass directly among older people without acute illness or inflammation. Previous observation has demonstrated that physical exercise increases hepatic synthesis of albumin, resulting in the elevation of plasma albumin content.[28] It is possible that physical activity may be involved in the maintenance of serum albumin concentration through an increase in hepatic synthesis of albumin. Further studies will be required to determine the exact mechanism of the correlation of serum albumin concentration and ADL impairment in well-nourished older people. Since it has been reported that lower serum albumin is independently associated with weaker muscle strength,[29] further research is needed to clarify the exact interactions among serum albumin concentration, ADL status, and not only muscle mass but also muscle strength.

There are limitations in the present study. The distribution of ADL scores of our participants was not the normal distribution. Therefore, no line could be drawn separating the older people with poorer ADL function from those with better ADL function using <35 g/l of serum albumin as the cutoff point of malnutrition. A limitation included the relative small sample size in each categorized ADL subgroup which may affect the correlation between serum albumin and other nutritional parameters. Another potential limitation of this study was the reliance on self-reported past dietary change and past weight change which are included in SGA in subjects with potential for impaired cognition. We used only anthropometric measurements, AMC and AMC, for assessment of muscle mass; upper arm muscle mass might not reflect the full range of muscle mass.

In the present study we demonstrated that impaired physical function reduced serum albumin concentration even in well-nourished older people. The use of <35 g/l serum albumin as a marker of malnutrition for the elderly with low ADL function leads to over-diagnosis of malnutrition. Although the exact mechanism of the association between low albumin concentration and disability of ADL function remains unknown, lower muscle mass or decreased physical activity may be involved in this association. Therefore, when nutritional assessment is conducted for older people with impaired ADL function, special attention should be given to the interpretation of results of anthropometric measurements and serum albumin.

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