Risk factors for cardiovascular events appear to change with advancing age.[12] The importance of HDL-C is different for each age-group. The present study on diabetic individuals with type IIb dyslipidemia was small in size, so a larger study will be required. However, HDL-C might help prevent cardiovascular events diabetic patients with type IIb dyslipidemia who are aged <75 years.

With regard to antihypertensive agents, approximately half of the participants used antihypertensive agents. There were no significant relationships between CVD and antihypertensive agents. Although we did not focus on antihypertensive agents in the present study, investigation of antihypertensive agents is important, and further study will be required in the future.

In conclusion, the present study showed that lower HDL-C was an important risk factor for cardiovascular events in diabetic individuals with type IIb dyslipidemia who are aged <75 years. If HDL-C is well controlled in elderly diabetic individuals who are aged <75 years with type IIb dyslipidemia, then IHD and CVA might be decreased to the levels found in diabetic patients of middle-aged cohorts.

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Disclosure statement

All authors have no conflict of interests.

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ORIGINAL ARTICLE: EPIDEMIOLOGY, CLINICAL PRACTICE AND HEALTH

Relationship between small cerebral white matter lesions and cognitive function in patients with Alzheimer's disease and amnestic mild cognitive impairment

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Aim: The main purpose of the present study was to investigate the influence of small cerebral white matter lesions on cognitive functions, and its difference by clinical stage.

Methods: A total of 160 patients with Alzheimer's disease and 40 older adults with amnestic mild cognitive impairment were enrolled in the present study. The Fazekas rating scale was used for the semi-quantitative measurement of white matter lesions. Participants whose scales were more than grade 2 were excluded. Associations between the degree of small white matter lesions and cognitive functions including memory, verbal fluency, working memory, processing speed, and executive function were examined.

Results: We found that small white matter lesions influenced the performances of neuropsychological tests differently between Alzheimer's disease and amnestic mild cognitive impairment. Analysis of covariance showed significant effects of interaction on a test that assessed categorical verbal fluency. In the amnestic mild cognitive impairment group, small periventricular white matter hyperintensities were significantly associated with poor performances in categorical verbal fluency; whereas in the Alzheimer's disease group, such associations were not observed. Deep white matter hyperintensities did not influence any cognitive functions examined in both groups.

Conclusions: The results suggested the involvement of periventricular small white matter lesions on impairment in verbal fluency, and such influence might be different depending on an individual's clinical stage. **Geriatr Gerontol Int 2014; 14: 819–826.**

Keywords: Alzheimer's disease, cognitive function, mild cognitive impairment, verbal fluency, white matter lesions.

Introduction

Cerebral white matter lesions (WML) are identified as white matter hyperintensities, areas with high signal intensities on T2-weighed magnetic resonance imaging (MRI). The pathogenesis of WML has not been fully clarified, and the clinical relevance of WML also remains ambiguous. Several histopathological correlates have been reported: enlarged WML including myelin pallor, tissue rarefaction associated with loss of myelin and axons, and mild gliosis.[1,2] The occurrence of WML has been shown to increase with advancing age,[3,4] and the progression of WML has been associated with vascular risk factors.[5] In a meta-analysis, WML predicted an increased risk of stroke, dementia and death.[6]

In some non-demented population-based studies, WML predicted a higher rate of cognitive decline,[4,7–10] especially when located in the periventricular regions.[11–14] In some studies of Alzheimer's disease (AD) patients, it has been suggested that AD patients with WML had worse cognitive performances than those without WML,[15–17] whereas other studies did not find any association between WML and cognitive decline in AD patients.[18,19] Diversities in study samples with varying clinical stages or different methods for the assessment of WML might explain the inconsistent results in those studies. Several studies have suggested that WML could influence cognitive performance in the

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early stages of AD, but not in the late stages.[18,20] If this is true, WML might have greater influence on cognitive profiles in amnestic mild cognitive impairment (aMCI) patients than AD patients, because aMCI has been considered a preclinical and prodromal stage of AD. In some studies of MCI patients, WML were associated with cognitive decline,[21] and predicted a higher rate of conversion to dementia.[22,23] Studies investigating the influence of WML on cognitive function both in AD and aMCI patients have been sparse to date.

In view of investigating the influence of small WML on cognitive profiles of AD pathology, one has to preclude with caution a possible contamination of mixed pathology, such as vascular dementia or vascular mild cognitive impairment, from analysis. Therefore, in the present study, we focused on investigating neuropsychological traits in patients with AD or aMCI, and examined their associations with the degree of small WML, assessed by a semi-quantitative method based on MRI findings after carefully excluding patients with diffuse or extensive WML. If any difference was observed between the groups, the finding might suggest temporal profiles regarding the influence of small WML on cognitive performances during the progression of this neurocognitive disorder.

Methods

Participants

The present study was carried out among outpatients attending the Nagoya University Hospital department of geriatrics in Nagoya, Japan, between January 2010 and March 2012. Among 641 consecutive patients aged 60 years or older, 268 patients who were diagnosed with neither AD nor aMCI, and 109 patients who could not complete the relevant cognitive tasks were excluded. Regarding methods for objectively assessing the degree of WML, the Fazekas rating scale[24] was used in the present study. It is a visual semi-quantitative rating scale of WML volume, and this scale is one of the most widely-used and well-validated. This scoring system is a four-point scale, rated on a 0- to 3-point scale of increasing severity. As explained in the Introduction, in order to eliminate a possible contamination of mixed pathology, those who were graded more than 2 on the Fazekas rating scale (64 patients) were not included in the study, and only those who were graded either 0 or 1 on the scale were included, eventually leaving 200 patients subjected for analyses.

Of the participants, 160 patients were diagnosed as probable or possible AD according to the criteria of the National Institute of Neurological and Communicative Disorders and Stroke and Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA),[25] and 40 cases were diagnosed as aMCI according to the Mayo Clinic Criteria.[26] The patients with aMCI all met the criteria for single-domain amnestic MCI or multiple-domain amnestic MCI proposed by Petersen.[27] All of them had the complaint of memory impairment. Patients with single-domain amnestic MCI had impaired performance (more than 1.5 SD below controls) on one or more of the memory tests used in the neuropsychological battery, but not on the other tests. Patients with multiple-domain amnestic MCI had impaired performance on one or more of the memory tests, and impaired performance on one or more of the other tests. None of them had dementia according to the clinical assessment. Hereafter, aMCI includes both the single- and multiple-domain subtypes.

The evaluation procedure consisted of a detailed medical history, cognitive assessment, laboratory tests and cerebral MRI. The patients also underwent a clinical examination to exclude other etiologies. Patients who had a history of cerebrovascular disorders or the presence of significant vascular risk factors were excluded, as well as patients who had previously received an actual diagnosis of major depression.[28] Japanese was the primary language for all participants.

Cognitive assessment

All participants underwent a battery of neuropsychological tests. The battery of neuropsychological tests included the following tests: the Mini-Mental State Examination (MMSE)[29] for general cognitive function; the Logical Memory I and II subtests of the Wechsler Memory Scale-revised (WMS-R)[30] for memory; the category fluency test (participants were required to generate as many animal names as possible within 1 min) and the letter fluency test (participants were required to generate as many words beginning with the syllable "ka" (the Japanese version of the phonemic fluency task) as possible within 1 min for verbal fluency; the Digit Span Forward and Backward subtests of the Wechsler Adult Intelligence Scale Revised (WAIS-R)[31] for working memory; the Digit Symbol subtests of WAIS-R[31] for processing speed; and the Stroop colored word test for executive functions (controlled inhibition). All patients were also assessed for depressive mood using the Geriatric Depression Scale-15 (GDS-15).[32]

Testing and scoring of the neuropsychological tests were carried out by a trained clinical psychologist with a Master's degree in clinical psychology. Participants were tested individually in a single session. Written informed consent was obtained at the start of the evaluation from all participants or their closest relative.

White matter assessment

The MRI scans were carried out on a 1.5T machine. Ratings of WML on MRI images were carried out on a

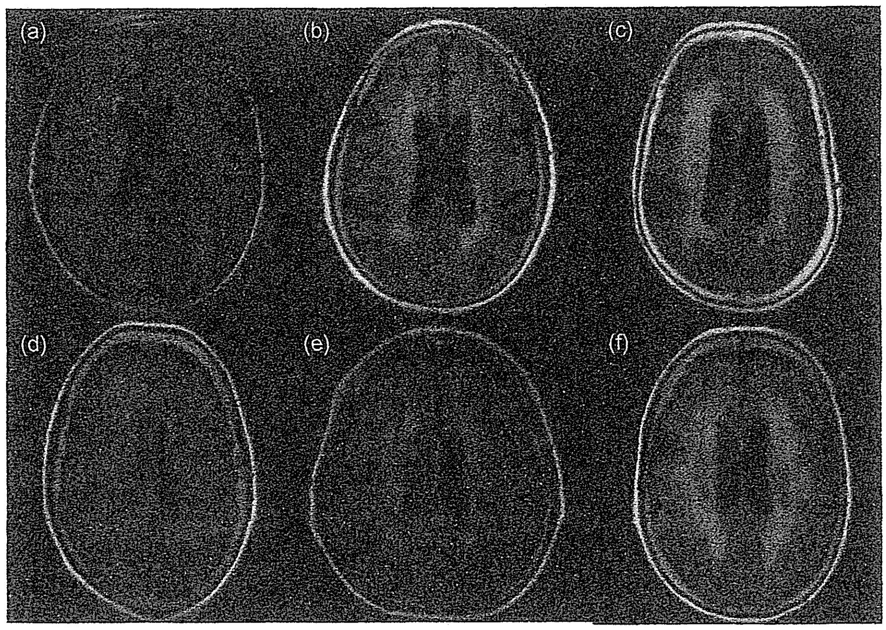

Figure 1 Examples of Fazekas scale ratings. (a) Periventricular hyperintensities (PVH) score = 1. (b) PVH score = 2. (c) PVH score = 3. (d) Deep white matter hyperintensities (DWMH) score = 1. (e) DWMH score = 2. (f) DWMH score = 3.

Table 1 Numbers of patients for Fazekas scale ratings

		AD (n = 160) DWMH Grade 0	AD (n = 160) DWMH Grade 1			aMCI (n = 40) DWMH Grade 0	aMCI (n = 40) DWMH Grade 1
PVH	Grade 0	30	14	PVH	Grade 0	5	4
	Grade 1	21	95		Grade 1	7	24

Definitions of rating scores of periventricular white matter hyperintensity (PVH): grade 0, absence; grade 1, caps or pencil-thin lining. Definitions of rating scores of deep subcortical white matter hyperintensity (DWMH): grade 0, absence; grade 1, punctate.
AD, Alzheimer's disease; aMCI, amnestic mild cognitive impairment.

computer screen with axial fluid-attenuated inversion recovery (FLAIR) images. The visual semi-quantitative rating scale of WML volume described by Fazekas *et al.*[24] was used. This scoring system is a four-point scale for separately assessing the increasing severity of periventricular white matter hyperintensity (PVH) and deep subcortical white matter hyperintensity (DWMH). PVH severity was scored according to the following categories: absence (grade 0); caps or pencil-thin lining (grade 1); smooth halo (grade 2) and irregular PVH extending into the deep white matter (grade 3). DWMH severity was scored according to the following categories: absence (grade 0); punctate (grade 1); beginning confluence (grade 2) and large confluence (grade 3). Examples of PVH and DWMH severities are shown in Figure 1. Participants who were graded more than grade 2 of PVH or DWMH were excluded from the present study. Table 1 shows the numbers of patients for the Fazekas rating scale included in this study. All ratings were carried out by two raters (the second and third authors). Each rater rated each case individually and then consulted with each other to reach a consensus.

Statistical analysis

The statistical analyses were carried out using IBM SPSS Statistics version 19 for Windows (SPSS Japan, Tokyo, Japan). A value of $P < 0.05$ was used in all analyses to show statistical significance.

First, we carried out descriptive analyses of sociodemographic and clinical characteristics. Table 2 shows the mean and standard deviations, and the frequency and percentage. We used the χ^2-test for the comparison of categorical data, and we applied Student's t-test for continuous data.

Analysis of covariance (ANCOVA) was used to determine the correlation of WML and cognitive data between AD and aMCI. It is well known that age and

Table 2 Clinical characteristics and cognitive performance of Alzheimer's disease and amnestic mild cognitive impairment patients

	AD (n = 160)				aMCI (n = 40)				
Sex (male/female)	66/94				15/25				
Diabetes mellitus (%)	29 (18.13%)				7 (17.50%)				
Hypertension (%)	70 (43.75%)				20 (50.00%)				
Hyperlipidemia (%)	70 (43.75%)				20 (50.00%)				
aMCI subtype (single domain/multiple domain)					19/21				
	MEAN	SD	MIN	MAX	MEAN	SD	MIN	MAX	*P*-value
Age (years)	77.01	6.87	61	92	76.08	6.56	60	90	0.440
Education (years)	11.40	2.78	6	20	12.26	2.95	8	18	0.084
GDS15	4.33	3.37	0	14	3.83	2.94	0	13	0.390
MMSE	21.94	3.69	11	29	27.13	1.49	24	30	<0.001
WMS-R Logical Memory I	6.26	4.30	0	22	10.05	4.65	1	22	<0.001
WMS-R Logical Memory I	1.16	2.40	0	12	3.20	2.83	0	9	<0.001
Category Fluency Test	11.67	3.72	2	23	14.90	4.02	6	24	<0.001
Letter Fluency Test	7.76	3.15	2	20	9.18	3.40	0	15	0.013
WAIS-R Digit-Span Forward	5.63	1.89	2	10	6.20	1.68	3	9	0.084
WAIS-R Digit-Span Backward	4.34	1.45	1	8	5.05	1.38	2	8	0.006
WAIS-R Digit-Symbol	33.22	11.73	3	77	38.38	12.01	9	68	0.014
Stroop Test Color	21.86	10.03	9.56	78.09	17.67	3.94	8.85	30.79	<0.001
Stroop Test Colored Word	46.75	20.04	15.40	134.19	40.08	18.03	20.32	113.21	0.056

P-values were calculated by Student's *t*-tests. AD, Alzheimer's disease; aMCI, amnestic mild cognitive impairment; Education, total number of years of schooling; GDS15, 15-item version of the Geriatric Depression Scale; MAX, maximum score; MIN, minimum score; MMSE, Mini-Mental State Examination; SD, standard deviation; WAIS-R, Wechsler Adult Intelligence Scale-Revised; WMS-R, Wechsler Memory Scale-Revised.

education level influence cognitive function, so these two variables were considered to be covariables in the analysis carried out later. As a post-hoc analysis, pairwise multiple comparisons of the cognitive data were tested with Bonferroni test after ANCOVA.

Results

Table 2 presents the sociodemographic and clinical characteristics of the participants, and the raw neuropsychological test results for both AD and aMCI. The means and standard deviations, and maximal and minimal values are shown.

The groups with different diagnoses were not statistically different in terms of the following variables: distribution of sex, clinical comorbidity (diabetes mellitus, hypertension, hyperlipidemia), age, years of education and depressive mood (GDS-15). Likewise, the MCI subtypes were similar in their distributions of the variables. Regarding the comparison of cognitive performances between the two groups, AD group performed significantly worse than did the aMCI group in tests as follows: MMSE (t [158.87] = 13.84, $P < 0.001$), logical memory I (t [198] = 4.91, $P < 0.001$), logical memory II (t [198] = 4.63, $P < 0.001$), category fluency (t [198] = 4.83, $P < 0.001$), letter fluency (t [198] = 2.51, $P < 0.05$), digit span backward (t [198] = 2.80, $P < 0.01$), digit symbol (t [198] = 2.47, $P < 0.05$) and Stroop color test (t [162.81] = 2.59, $P < 0.001$).

Table 3 shows the influence diagnosis and PVH had on participants' performances in the neuropsychological tests, as well as the interaction between the two factors. We found that diagnosis significantly influenced the results of the following tests: MMSE (F [1,194] = 49.43, $P < 0.001$), logical memory I (F [1,194] = 16.81, $P < 0.001$), logical memory II (F [1,194] = 14.68, $P < 0.001$), category fluency (F [1,194] = 29.43, $P < 0.001$), letter fluency (F [1,194] = 8.02, $P < 0.01$), digit symbol (F [1,194] = 4.86, $P < 0.05$) and Stroop colored word test (F [1,194] = 4.06, $P < 0.05$). PVH had a significant influence on the results of the tests that assess the following variables: category fluency (F [1,194] = 8.11, $P < 0.01$) and letter fluency (F [1,194] = 5.47, $P < 0.05$). Individuals having small PVH, independent of their diagnosis, performed worse than those having no PVH in terms of verbal fluency. We found significant effects of interaction on the results of the category fluency test (F [1,194] = 7.01, $P < 0.01$). The

Table 3 Cognitive performance according to periventricular hyperintensities

	AD PVH grade0 ($n = 44$)		AD PVH grade1 ($n = 116$)		aMCI PVH grade0 ($n = 9$)		aMCI PVH grade1 ($n = 31$)		P Diagnosis	P PVH	P Diagnosis × PVH
	MEAN	SD	MEAN	SD	MEAN	SD	MEAN	SD			
MMSE	22.82	3.04	21.60	3.86	27.67	1.22	26.97	1.54	<0.001	0.294	0.678
WMS-R Logical Memory-I	6.77	4.19	6.06	4.35	11.22	5.45	9.71	4.43	<0.001	0.500	0.651
WMS-R Logical Memory-II	1.09	2.61	1.19	2.32	3.44	3.32	3.13	2.73	<0.001	0.819	0.676
Category Fluency Test	12.25	3.11	11.45	3.92	18.44	3.68	13.87	3.55	<0.001	0.005	0.009
Letter Fluency Test	8.34	2.96	7.53	3.20	11.44	1.33	8.52	3.54	0.005	0.020	0.094
WAIS-R Digit-Span Forward	6.11	1.98	5.45	1.83	6.22	1.79	6.19	1.68	0.473	0.723	0.402
WAIS-R Digit-Span Backward	4.86	1.29	4.14	1.47	5.33	1.80	4.97	1.25	0.074	0.165	0.503
WAIS-R Digit-Symbol	36.11	12.24	32.12	11.40	44.78	11.97	36.52	11.55	0.029	0.105	0.304
Stroop Test Color	20.54	8.28	22.36	10.61	16.46	3.13	18.01	4.13	0.051	0.701	0.991
Stroop Test Colored Word	44.37	16.03	47.66	21.36	30.75	7.09	42.78	19.38	0.045	0.163	0.259

P-values were calculated by analysis of covariance and adjusted for age and education. AD, Alzheimer's disease; aMCI, amnestic mild cognitive impairment; MMSE, Mini-Mental State Examination; PVH, periventricular white matter hyperintensity; SD, standard deviation; WAIS-R, Wechsler Adult Intelligence Scale-Revised; WMS-R, Wechsler Memory Scale-Revised.

combination of aMCI and category fluency showed a significant negative influence (F [1,194] = 9.28, $P < 0.01$); whereas in the AD group, such an association was not observed.

Table 4 shows the influence that diagnosis and DWMH had on participants' performances on neuropsychological tests, as well as the interaction between the two factors. We found that diagnosis significantly influenced the results of the following tests: MMSE (F [1,194] = 56.00, $P < 0.001$), logical memory I (F [1,194] = 22.54, $P < 0.001$), logical memory II (F [1,194] = 21.09, $P < 0.001$), category fluency (F [1,194] = 16.06, $P < 0.001$), letter fluency (F [1,194] = 4.34, $P < 0.05$), digit span backward (F [1,194] = 4.02, $P < 0.05$). DWMH did not significantly influence any other neuropsychological tests. We did not find any other significant effects of the interaction between diagnosis and DWMH.

Discussion

The primary objective of the present study was to examine the association between small WML and cognitive function in older patients with AD or aMCI. To this end, two subgroups of patients with AD or aMCI differed regarding the influence of small WML on cognitive function.

Among aMCI participants, those without PVH had higher scores than those with PVH on the category fluency test. In contrast, the existence of small PVH did not significantly affect the score on the same test in AD patients. These findings might support a notion suggesting that WML could influence cognitive performance in the early stage of cognitive impairment, but not in the later stage of degenerative dementia.[18,20] Changes of relative involvement of WML on cognition by disease progression could explain the results obtained. It is well known that as AD pathology advances, cortical atrophy extends. Therefore, one could speculate that the relative influence of cortical atrophy on cognition compared with that of WML becomes increased in the later stage of AD. Further investigations focusing on patients with earlier stages of AD whose extent of cortical atrophy are considered minimal could address this speculation.

We found significant effects of interaction between diagnosis and PVH on the results of the category fluency test, whereas on the results of the letter fluency such interaction was not found. The category fluency task is associated with the ability to access semantic knowledge, whereas letter fluency is considered an index of frontal control function.[33] In a meta-analysis of verbal fluency in AD, it was suggested that impairment in category fluency rather than letter fluency might be among the early changes associated with AD.[34] A previous study has shown that the aMCI groups have

Table 4 Cognitive performance according to deep subcortical white matter hyperintensity

	AD				aMCI				*P*	*P*	*P*
	DWMH grade 0 (*n* = 51)		DWMH grade 1 (*n* = 109)		DWMH grade 0 (*n* = 12)		DWMH grade 1 (*n* = 28)		Diagnosis	DWMH	Diagnosis × DWMH
	MEAN	SD	MEAN	SD	MEAN	SD	MEAN	SD			
MMSE	22.53	3.48	21.66	3.76	27.00	1.48	27.18	1.52	<0.001	0.756	0.444
WMS-R Logical Memory-I	6.45	3.98	6.17	4.46	11.75	4.58	9.32	4.56	<0.001	0.213	0.161
WMS-R Logical Memory-II	1.16	2.41	1.17	2.40	4.17	2.98	2.79	2.71	<0.001	0.254	0.126
Category Fluency Test	11.96	3.65	11.53	3.76	14.67	4.96	15.00	3.65	<0.001	0.590	0.670
Letter Fluency Test	8.24	3.62	7.53	2.89	9.75	3.14	8.93	3.53	0.038	0.394	0.856
WAIS-R Digit-Span Forward	5.94	2.01	5.49	1.82	6.75	1.42	5.96	1.75	0.147	0.170	0.569
WAIS-R Digit-Span Backward	4.39	1.36	4.31	1.50	5.08	1.51	5.04	1.35	0.032	0.874	0.975
WAIS-R Digit-Symbol	36.96	12.60	31.47	10.93	40.33	12.22	37.54	12.04	0.112	0.221	0.621
Stroop Test Color	20.13	6.60	22.67	11.22	17.43	3.74	17.77	4.09	0.056	0.656	0.574
Stroop Test Colored Word	46.58	16.92	46.84	21.42	40.89	26.01	39.73	13.92	0.158	0.606	0.913

P-values were calculated by analysis of covariance and adjusted for age and education. AD, Alzheimer's disease; aMCI, amnestic mild cognitive impairment; DWMH, deep subcortical white matter hyperintensity; MMSE, Mini-Mental State Examination; SD, standard deviation; WAIS-R, Wechsler Adult Intelligence Scale-Revised; WMS-R, Wechsler Memory Scale-Revised.

greater impairment in category fluency performance than in letter fluency performance relative to healthy controls.[35] Neuroanatomically, category fluency relies on the medial temporal lobe regions, whereas letter fluency has been found to correlate with prefrontal lobe functioning.[36] Differences in the anatomical substrates for each verbal fluency task might explain the present results. Because of advanced medial temporal lobe atrophy, WML might not influence category fluency in the later stage of AD.

When diagnosis was not added, associations between the small PVH and low verbal fluency performance were shown in the present study. Several studies found that WML was particularly associated with a decline in mental processing speed, executive functions, but not with a decline in memory functions,[10,37–39] which could suggest that WML have an influence on frontal lobe functions. Memory decline is particularly related to medial temporal lobe atrophy, and might be less affected by WML.[17,40] The disruption of long associating fibers by PVH might be particularly deleterious for frontal lobe domain functions.[21] In the present results, small PVH contributed to cognitive decline in verbal fluency, but not in any other domains of cognitive function. It remains unclear why small PVH was correlated only with verbal fluency.

Our results are in line with several population-based studies[11–14] in which PVH and not are associated with different clinical conditions. It is also suggested that the pathology presenting PVH might impair cognitive functioning more easily than that affecting the subcortical area. Anatomically, the periventricular regions have a high density of long associating fibers, which connect the cortex with the subcortical nuclei and other distant brain territories, whereas the subcortical area has a high density of short-looped U fibers connecting adjacent gyri.[11] The mechanism underlying the present results requires further substantiation.

The main limitation of the present study was the rating system of WML. Regarding the semi-quantitative rating of white matter lesions used in our study, it could be argued that it is not sufficiently accurate, but this rating system has been shown to correlate well with quantitative volumetric measurements.[41] The present study showed that small amounts of WML were correlated with cognitive impairment. We assumed that greater degrees of WML correspond to different patterns of cognitive decline. WML could trigger or enhance neurodegenerative processes when the lesion load reaches a certain threshold.[19]

Because of the smaller sample size of aMCI patients, the statistical power of the study might have been insufficient to detect an association between cognitive deficit and small WML. Our sample size was also inadequate to examine the association of cognitive decline with the different locations of DWMH, which might have some importance. Some studies have shown that cognitive dysfunction differs according to where WML are present.[42] It would therefore be important to assess the specific roles of WML depending on their frontal, parietal or temporal locations.

In summary, the present study found that small PVH were significantly associated with cognitive decline, in particular with a deficit of verbal fluency, in aMCI patients. Furthermore, a category fluency deficit, not a letter fluency deficit, was found to show an interaction with small PVH. Further studies are required to confirm these results and to improve our understanding of the underlying mechanisms.

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Disclosure statement

The authors declare no conflict of interest.

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FACTORS ASSOCIATED WITH DETERIORATION OF MINI NUTRITIONAL ASSESSMENT-SHORT FORM STATUS OF NURSING HOME RESIDENTS DURING A 2-YEAR PERIOD

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Abstract: *Objective:* A number of other studies have been conducted to verify the Mini Nutritional Assessment (MNA) or the MNA short form (MNA-SF) as a nutritional assessment/screening tool in various clinical settings or communities. However, there are few longitudinal studies using these tools to analyze which factors affect the incidence of deteriorating nutritional status. We tried to identify the factors associated with deterioration of MNA-SF status of nursing home residents during a 2-year period. *Methods:* Participants were 392 people with a mean age of 84.3 in 12 nursing homes in Japan. The factors associated with deterioration in MNA-SF categories during the study period compared to stable/improved MNA-SF categories were identified. *Results:* At baseline, 19.9% of the participants were malnourished and 60.2% were at risk of malnutrition, according to the MNA-SF classification. After 2 years, 66.3% participants maintained and 6.1% participants improved their nutritional status according to the MNA-SF classification, while 27.6% showed deterioration in MNA-SF status. Stepwise logistic-regression procedure indicated that basic ADL impairment and hospitalization during the follow-up period were associated with declining MNA-SF status. *Conclusions:* Poor basic ADL status and hospitalization during the follow-up period were associated with malnutrition and risk of malnutrition as assessed by MNA-SF of nursing homes residents during a 2-year period.

Key words: The factors associated with deterioration of Mini Nutritional Assessment-Short Form stage, frail elderly, nursing home.

Introduction

Japan has the most rapidly aging population in the world and soon will have the largest percentages of elderly and very elderly in its population. In 2011, the rate of the population over age sixty-five was 23.3%. Elderly persons 100 years or older numbered 47,756 and 87.1% of these were women. The numbers of frail elderly people living in the community or institutions for the aged are increasing, along with their hospital admissions.

The nutritional status of older people is an important determinant of quality of life, morbidity and mortality (1-3). The relationship between poor nutritional status and impaired immune functions, the development of pressure sores, and impaired muscle function is well established (4-6). Therefore, it is quite important for the elderly to maintain good nutritional status.

The Mini-Nutritional Assessment (MNA) is a simple clinical scale for the evaluation of the nutritional status of frail elderly subjects (4, 7, 8). We evaluated the MNA test as a screening tool for malnutrition in the Japanese elderly population and concluded that the MNA full test is a useful screening tool for identifying Japanese elderly with malnutrition or a risk of malnutrition (9). A number of other studies have been conducted to verify the MNA or the MNA short form (MNA-SF) as a nutritional assessment/screening tool in various clinical settings or communities. However, there are few longitudinal studies using these tools to analyze which factors affect the incidence of deteriorating nutritional status.

In the present prospective study we tried to identify the factors associated with deterioration of MNA-SF status of residents of nursing homes during a 2-year period.

Methods

Subjects

The study population consisted of 649 residents of 12 nursing homes located in Nagoya City (116 men and 533 women, age 65 years or older). Twelve nursing homes belonged to a single social welfare corporation and staffs of nursing homes received the same education training. The dietitians carry out the nutritional assessment of the nursing home residents according to the Long-Term Care Insurance (LTCI) program. These participants, who were enrolled between May 1 and June 30, 2009, were scheduled to undergo comprehensive assessments by trained nursing home staff at baseline, and at 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 residents or, for those with substantial cognitive

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impairment, from a surrogate (usually the closest relative or legal guardian).

Data collection

The data were collected at the nursing homes using structured interviews with residents and nursing home staff, and from nursing home records taken by trained nurses. The data included clients' demographic characteristics and a rating for ten basic Activities of Daily Living (ADL: getting out of bed, transferring, walking, bathing, grooming, dressing, putting on and taking off pants, feeding, bowel and bladder management). For each ADL task, nurses rated residents as independent (a score of 10, able to perform the activity without help), partially dependent (a score of 5, requiring some assistance), or completely dependent (a score of 0, needing help for the entire activity). The sum of these scores theoretically range from 0 (total disability) to 100 (no disability). Nurse ratings were based on direct observation, interviews with residents, and information from staff. Information obtained from nursing homes 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 (10), which represents the sum of weighted indexes taking into account the number and seriousness of preexisting comorbid conditions. Chewing ability was categorized into three groups: difficulty chewing even soft food items such as boiled rice, tuna sashimi, and grilled eel (poor), difficulty chewing harder foods such as hard rice crackers, peanuts, and yellow pickled radish (fair), and no difficulty chewing harder foods (good). Dietitian ratings were based on direct observation and information from other staff.

Anthropometry

Height and weight data were generally measured at the nursing homes and collected by trained staff. Weight was measured in light clothing without shoes using a portable weight scale at the nursing homes. Height was generally measured in an upright position using a tape measure attached to the wall. However, when participants could not maintain an upright position, height measurements were obtained in a prone position.

Nutritional Assessment

The MNA-SF is composed of a combination of six questions taken from the full MNA about appetite loss, weight loss, mobility, stress/acute disease, dementia/depression, and body mass index (BMI). The score of the MNA-SF was used to classify subjects' nutritional status as well-nourished (a score of 12-14), at-risk for malnutrition (a score of 8-11), or malnourished (a score of 0-7). The MNA-SF was administered by dietitians, except for the mental state questionnaire which was obtained from nursing staff members or medical records at baseline, at 1 year later and at 2 years later.

Study participants

Among 450 survivors, the participants who stayed in the nursing home and were re-assessed at both baseline and at 2 years later were 392. The 60 participants who were assessed as malnourished according to the MNA-SF at both baseline and at 2 years later were excluded from our analysis to identify the factors associated with becoming malnourished or at risk of malnutrition.

Statistical analysis

The Student's t-test and Chi-squared test were used to compare differences between participants with the MNA-SF stage decline and those without decline (improved or stable MNA-SF stage). The 392 study participants were divided into tertiles according to the basic ADL score at baseline (first, 55-100; second, 20-50; third, 0-15). The significance level was set at $P< 0.05$ and quoted are two-sided.

Univariate and multivariate logistic regression models were used to identify independent predictors of declining MNA-SF status. The following baseline data were used in univariate analysis: gender, age, basic ADL, ability of chewing, and hospitalization during the 2-year period. The covariates included in the multivariate analysis were those variables associated with dependent variables at a level of $P< 0.05$ in univariate analysis. Stepwise logistic-regression procedure was conducted. The risk of a variable was expressed as an odds ratio (OR) with a corresponding 95% confidence interval (CI).

All analyses were performed using the Statistical Package for the Social Sciences (SPSS) Version 20.0. A probability value of 0.05 or less was considered significant.

Results

Among the 649 participants, 199 subjects died during the 2-year study period. It should be noted that mean MNA-SF score of 199 at the base line was significantly lower than that of 450 survivors (8.2 (SD 2.0) vs 9.3 (SD 2.4), $P<0.001$).

Table 1 shows the characteristics of the 392 participants at baseline. The mean age was 84.3 (SD 7.21) years, with 49.7% of the subjects 85 years or older and 82.9% of them women. The mean BMI, MNA-SF score and basic ADL score were 20.3 (SD 3.7) kg/m^2, 9.3 (SD 2.3) points, and 37.3 (SD 29.7) points, respectively. The participants had a high prevalence of dementia (56.9%), cerebrovascular disease (49.9%) and hypertension (46.4%). Among the 392 participants, 20.1% participants had poor chewing ability.

At baseline, 19.9% of the participants were malnourished and 60.2% were at risk of malnutrition, according to the MNA-SF classification (Table 1). As shown in table 2, after 2 years, 37.2% of the participants were classified as malnourished and 49.2% were at risk of malnutrition, according to the MNA-SF classification. Among the 392 participants, 260 (66.3%)

Table 1
Baseline characteristics of the 392 frail elderly

	total (n 392)			
	n	% of total	mean	SD
Age (years)	392		84,3	7,2
Body Mass Index (kg/m²)	392		20,3	3,7
MNA-SF score (max. 14 points)	392		9,3	2,3
MNA-SF classification				
malnourished	78	19,9		
at risk of malnutrition	236	60,2		
well-nourished	78	19,9		
Charlson comorbidity index (range, 0-19)	392		2,3	1,6
Chronic diseases				
dementia	223	56,9		
cerebrovascular disease	195	49,9		
hypertension	182	46,4		
heart failure	61	15,6		
ischemic heart disease	62	15,8		
diabetes mellitus	60	15,3		
Parkinson's disease	24	6,1		
Basic ADL (range, 0-100)	392		37,3	29,7
Chewing ability				
good	129	33,2		
fair	181	46,6		
poor	78	20,1		

Table 2
Mini Nutritional Assessment Short Form status at baseline and at 2-year follow-up

	MNA-SF status at 2-yr follow-up			
Baseline MNA-SF	**Malnourished**	**At risk of malnutriton**	**Well-nourished**	**Total**
Malnourished				
number of participants	60	18	0	78
% of baseline	76,9%	23,1%	0,0%	100,0%
% of at 2-year	41,1%	9,3%	0,0%	19,9%
At risk of malnutrition				
number of participants	77	153	6	236
% of baseline	32,6%	64,8%	2,5%	100,0%
% of at 2-year	52,7%	79,3%	11,3%	60,2%
Well-nourished				
number of participants	9	22	47	78
% of baseline	11,5%	28,2%	60,3%	100,0%
% of at 2-year	6,2%	11,4%	88,7%	19,9%
Total				
number of participants	146	193	53	392
% of baseline	37,2%	49,2%	13,5%	100,0%
% of at 2-year	100,0%	100,0%	100,0%	100,0%

participants maintained and 24 (6.1%) participants improved their nutritional status according to the MNA-SF classification (18 moved from "malnutrition" to "at risk of malnutrition"; 6 from "at risk" to "normal nutrition"), while 108 (27.6%) showed deterioration of MNA-SF categories during the study period (9 from normal nutrition to malnutrition, 22 from normal nutrition to at-risk status, and 77 from at-risk to malnutrition). Sixty (15.3%) participants were assessed as malnourished at both baseline and at 2 years later (Table 2). Therefore, the number of participants with improved/stable and deteriorating status according to MNA-SF classification, after excluding participants with malnutrition at both baseline and follow-up, were 224 and 108, respectively.

Table 3 compares the baseline characteristics of participants whose MNA-SF status deteriorated and remained stable/improved during the 2-year period. No differences were

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Table 3
Baseline and 2-yr follow-up characteristics of participants with improved/stable or deteriorating MNA-SF status

	MNA-SF change during 2-year period								
	improved/stable status (n 224)				deteriorating status (n 108)				
	n	% of total	mean	SD	n	% of total	mean	SD	P value
Men/Women	50/174	22.3/77.7			11/97	10.2/89.8			0.007†
Age (years)	224		83,9	7,3	108		85,0	7,3	0.183*
Body Mass Index (kg/m2)	224		21,1	3,8	108		20,5	3,7	0.120*
Charlson Comorbidity Index	224		2,3	1,6	108		2,2	1,6	0.589*
Basic ADL (range, 0-100 points)	224		44,3	30,0	108		35,0	29,1	0.007*
first tertile (55-100points)	98	43,8			27	25,0			0.003†
second tertile (20-50points)	65	29,0			46	42,6			
third tertile (0-15 points)	61	27,2			35	32,4			
Chewing ability									
good	91	41,0			32	29,9			0.026†
fair	107	48,2			53	49,5			
poor	24	10,8			22	20,6			
MNA-SF score (max. 14 points)	224		10,0	2,0	108		9,8	1,9	0.523*
Hospitalization during the 2-year period	60	26,8			43	39,8			0.022†

* Student's t-test was used to compare differences between participants with the MNA-SF stage decline and those without decline; † Chi-square test was used to compare differences between participants with the MNA-SF stage decline and those without decline

Table 4
Stepwise logistic-regression procedure to identify independent predictors of deteriorating MNA-SF status

	crude			multivariate					
				model 1			model 2		
	OR*	95% CI	p	OR*	95% CI	p	OR*	95% CI	p
Women (vs men)	2,53	1,26 -5,10	0,009	2,54	1,25-5,17	0,010	2,41	1,18 -4,92	0,016
Age (continuous variable)	1,02	0,99 -1,06	0,183						
The score of basic ADL (range:0-100)									
first tertile (55-100points)	1,00			1,00			1,00		
second tertile (20-50points)	2,57	1,45 -4,54	0,001	2,60	1,46-4,63	0,001	2,62	1,47 - 4,69	0,001
third tertile (0-15 points)	2,08	1,15 -3,78	0,016	2,01	1,10 -3,68	0,024	2,02	1,10 -3,72	0,024
Chewing ability									
good	1,00								
fair	1,41	0,84 -2,37	0,197						
poor	2,61	1,29 -5,28	0,008						
Hospitalization during the 2-year period									
no	1,00						1,00		
yes	1,81	1,11 -2,94	0,017				1,80	1,09 -2,97	0,023

OR* Odds Ratio; P values ; logistic regression variables; model 1 using stepwise selection; adjusted includes gender, age,the score of ADL at baseline, and chewing ability at baseline; model 2 using stepwise selection; adjusted includes gender, age, the score of ADL at baseline, chewing ability at baseline, and hospitalization during the 2-year period

observed in age, Charlson Comorbidity Index score, BMI, or the MNA-SF score at baseline between participants in the two groups. The basic ADL score (range, 0-100) at baseline of the stable/improved MNA-SF group (44.3, SD 30.0) was significantly higher than that of the deteriorating MNA-SF group (35.0, SD 29.1) (P = 0.007). The prevalence rates of hospitalization during the 2-year period were significantly higher for those with decline in MNA-SF status (39.8%) than for those with improved/stable MNA-SF status (26.8%) (P = 0.022). There was also a significant difference in the chewing ability between two groups (P = 0.026).

To identify the factors associated with categorical decline of MNA-SF during the study compared to stable/improved MNA-SF status, stepwise logistic-regression procedure was conducted. As shown in Table 4, women, lowest basic ADL status, poor chewing ability, and hospitalization during the 2-year period were independent predictors of a decline in MNA-SF status in univariate analysis.

We used two different models to conduct multivariate analysis, in which the variables with $P < 0.05$ in univariate analysis were further examined. In model 1 the covariates included were gender, age, basic ADL status, and chewing ability. In model 2, hospitalization during the 2-year period was added in the analysis. Stepwise logistic- regression procedure indicated a lower and lowest basic ADL status in model 1, and a lower and lowest basic ADL status and hospitalization during the follow-up period in model 2 were associated with deteriorating MNA-SF status (OR 2.60, 95%CI 1.46, 4.63, OR 2.01, 95%CI 1.10, 3.68, OR 2.62, 95% CI 1.47, 4.69, OR 2.02, 95% CI 1.10, 3.72, OR 1.80, 95% CI 1.09, 2.97, respectively).

Discussion

The aim of the present study was to identify the factors associated with deterioration of MNA-SF status of nursing home residents during a 2-year period. We showed that 27.6% of subjects had deteriorating MNA-SF status during the 2-year period and that basic ADL impairment and hospitalization experience during the study period were associated with this decline. Severity of comorbidity was not related with deteriorating MNA-SF status in this study.

At the baseline of this study, 19.9% and 60.2% of the participants were categorized by MNA-SF as malnourished and at risk of malnutrition, respectively. One review article has summarized the 13 studies in which MNA has been used for nutritional assessment in nursing homes, and reported that malnutrition was observed in 2 to 38% and a risk of malnutrition in 37 to 62% of nursing home residents (11). The combined database providing information on 1586 nursing home residents from 7 countries demonstrated that 32.9%, 53.4%, and 13.8% of residents were well-nourished, at risk of malnutrition, and malnourished, respectively (12). Recent study in which MNA has been used for nutritional assessment in 286 nursing home residents reported, malnourished (18.2%)and at risk of malnutrition (42.0%) (13). There have been only few studies to assess nutritional status of nursing home residents using MNA-SF. One study reported that 39.9% nursing home residents were assessed as well-nourished, 41.9% at risk of malnutrition, and 18.1% malnourished (14). In another study reported 66% of the screened by MNA-SF individuals were at risk of malnutrition and the prevalence of malnutrition is higher in women, in nursing homes and in older age groups (15). From these observations the prevalence rates of malnutrition classified through MNA/MNA-SF vary among various nursing homes. Compared with previous observations from nursing homes, fewer malnourished residents and more at risk of malnutrition were observed in the present cohort.

Most of the prospective studies using MNA/MNA-SF have demonstrated the predictive values of these nutritional screening tools for mortality or functional decline in various geriatric settings (16-18). However, there was no prospective studies to identify the risk of deterioration of MNA/MNA-SF status during a follow-up period. In the present study, we demonstrated that 3 variables at baseline—female gender, basic ADL impairment, and hospitalization—were associated with deterioration in MNA-SF status during a 2-year period. We do not know why women were associated with nutritional decline compared with men. Although women in nursing homes are on average older than men, the association persisted even if when age was incorporated in the analysis. It is possible that unmeasured factors might mediate this gender difference.

The odds ratio of dereriorating MNA-SF scores for participants in the third tertile (worst function) was lower than those in the second tertile. In the present study, the participants of the third tertile contained lower levels of mobility including bed ridden situation. It was possible there were the lower total energy expenditure among participants with advanced dysfunction compared with those with mid dysfunction.

There have been a number of cross-sectional studies demonstrating an association between physical function impairment/ADL dependence and poor nutritional status as assessed by MNA/MNA-SF (19-21). Although these studies suggest that there is an interrelationship between the nutritional status of the elderly in various settings and reduced functional capacity (22-24), the exact causal relationships remain controversial. The prior studies demonstrated that weight loss predicts the development of disability in older people (22-24). However, it remains unknown whether physical function/ADL status may influence the development of malnutrition or risk of malnutrition (25). The present study clearly indicated that the lowest basic ADL status was associated with a decline in MNA-SF status. This association persisted after adjusting for gender, age, and hospitalization during study periods.

There have been several cross-sectional studies showing that chewing problems are associated with malnutrition (26-28). Again, these results did not reveal the causal relationships between chewing ability and poorer nutritional status in the older people. The present study showed that poor chewing ability at baseline was associated with declining MNA-SF status during the study period in the crude model, although the ability was not selected by stepwise regression procedure, indicating that more attention should be paid to the impact of oral health, which imposes dietary restrictions on older people with consequences for their nutritional status.

The present study showed that hospitalization during the 2-year period was associated with a decline in MNA-SF status. In consisted with the previous studies demonstrated an association between hospitalization and malnutrition (3, 29). It should be noted that there is one item asking about the presence or absence of psychological stress or acute disease in the past 3 months in MNA-SF. This may influence the association.

The present study has several limitations. The subjects of the present study were dependent elderly people who had chronic diseases and needed help in everyday life at the nursing home. The results of the present study cannot be transferred to community-dwelling independent elderly individuals. These findings may not be generalizable to other populations given that they may have been influenced by health practices and a variety of social and economic factors.

In conclusion, this study showed that poor basic ADL status and hospitalization of nursing home residents during a 2-year follow-up period were associated with malnutrition and risk of malnutrition as assessed by MNA-SF.

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サルコペニア肥満

葛谷雅文

サルコペニアとは「加齢に伴う筋力の低下，または老化に伴う骨格筋筋肉量の減少」を指し，Rosenbergにより提唱された比較的新しい造語である[1]．骨格筋筋肉量は二重エネルギーX線吸収測定法（DXA法）またはインピーダンス法で測定された四肢骨格筋量（kg）を身長（m）の2乗で除した骨格筋指数（skeletal muscle index；SMI）を指標としている．サルコペニアの定義は健康な18～40歳未満のSMIの2標準偏差(2SD)未満を用いる[1]．2010年にはサルコペニアを骨格筋筋肉量の低下を必須とし，それに加えて筋力(握力)または身体機能（歩行速度）低下を認める場合と定義されている[2]．

一方，サルコペニア肥満はBaumgartnerが2000年に提唱し，四肢骨格筋の萎縮と肥満を併せ持つケースを指す[3]．横断的疫学調査ではこのサルコペニア肥満の存在は身体機能障害と強い関連があることや，縦断調査ではサルコペニア肥満の存在はサルコペニア単独または肥満単独に比較し，心血管イベントや身体機能障害のリスクが高いことが報告されている．しかし，相反する報告も存在する．

サルコペニア肥満の問題は，世界的にもその定義が定まっておらず，そのため相反する結果報告につながっている可能性が指摘されている．サルコペニアの定義もさることながら，肥満の定義をどのように設定するかが難しい．報告によっては体脂肪率を使用したり，BMI，ウエスト周囲長やCTを使用して内臓脂肪量を用いたり，さらにはその基準値（カットオフ値）の設定もまちまちである（表1）．

欧米に比較し肥満が少ないわが国において，欧米でその重要性が指摘されているサルコペニア肥満の有病率がどれほどであり，またその将来の健康障害へのリスクがどれほどなのかは十分に検討されているわけではなく，今後の研究成果が待たれる．

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表1　サルコペニア肥満のさまざまな定義

		Baumgartner[3]	Davison[4]	Zoico[5]	Bouchard[6]	Levine[7]	Kim[8]	Ochi[9]
国		米国	米国	イタリア	カナダ	米国	韓国	日本
サルコペニア	筋量測定法	DXA	BIA	DXA	DXA	DXA	DXA	CT
	筋肉量指標	ASM/m²	総骨格筋/m²	総骨格筋/m²	ASM/m²	ASM×100/体重	ASM/m²	CSA/体重
	定義	ASM<2SD	5分位階級の最下位ならびに第II階級	5分位階級の最下位ならびに第II階級	ASM<2SD	ASM×100/体重<2SD	ASM<2SD	CSA/体重<1SD
	男性	<7.26kg/m²	<9.12kg/m²	—	<8.51kg/m²	<25.7%	<6.58kg/m²	—
	女性	<5.45kg/m²	<6.53kg/m²	<5.7kg/m²	<6.29kg/m²	<19.4%	<4.59kg/m²	—
肥満	定義	体脂肪率	体脂肪率	体脂肪率	体脂肪率	ウエスト周囲長	ウエスト周囲長	内臓脂肪面積
	男性	>27%	>37.16%	—	≧28%	>102cm	≧90cm	>100cm²
	女性	>38%	>40.01%	>42.9%	≧35%	>88cm	≧85cm	

ASM ; appendicular skeletal muscle mass, SD ; standard deviation (若年者～成人値), BIA ; bioelectrical impedance assay, CSA ; femoral quadriceps muscle cross-sectional area at the mid-thigh

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高齢者における低栄養とその対策

葛谷雅文（くずや まさふみ）

はじめに

平成に入り日本では高齢者の数ならびに割合が急増し、現在では六五歳以上の人口の占める割合が総人口の四分の一を占めるまでに至り、大きな人口構造の変動が起きている。もちろんそれより以前にも高齢者は存在していたが、その割合は少なくマイノリティーであった。しかし二〇二五年問題と言われるように、今後団塊の世代が七五歳以上の後期高齢者に到達する時点で高齢化率は三〇%を超し、さらに七五歳以上の後期高齢者層のみが人口が増加するという、超高齢社会に突入している背景がある。それに伴い医療のターゲットになる年齢層も上昇し、健康問題も生活習慣病予防だけではなく、寝たきり予防、健康寿命延伸、自立した生活の維持、介護予防などの重要度が増して来ている。

高度成長期以降、少なくとも日本での成人の栄養の問題は生活習慣病の視点から過栄養がクローズアップされてきた。しかし、今後超高齢社会における栄養の問題は、先の過栄養の問題だけではなく、健康寿命の延伸、介護予防の視点から後期高齢者が陥りやすい「低栄養」「栄養欠乏」の問題の重要性が高まっている。

低栄養の定義

「低栄養とは何か?」と、問われるとその回答には難渋する。一般的には全体的な摂取カロリー不足、またはある種の栄養素の摂取不足により、健康上何らかの支障がある状態を低栄養といい、栄養不良、栄養失調と同義である。

表1　低栄養指標

1）身体計測		
body mass index (BMI) = 体重(kg) ÷ [身長(m)]²		
18.5未満	やせ	
18.5〜25未満	標準	
25〜30未満	肥満	
30以上	高度肥満	
%usual body weight (%UBW) = 測定時体重 ÷ 平常時体重 × 100 (%)		
75%未満	高度栄養障害	
75〜85%未満	中等度栄養障害	
85〜95%未満	軽度栄養障害	
%loss of body weight = (平常時体重 − 現在の体重) ÷ 平常時体重 × 100 (%)		
6ヶ月以内の体重減少が10%以上	中等度以上の栄養障害	
一日の体重減少率が0.2%以上	中等度以上の栄養障害	
上腕三頭筋皮膚脂肪厚(TSF) 上腕周囲長（AC） 上腕三頭筋周囲長(AMC) = AC − π × TSF 上腕筋面積（AMA）= AMC² ÷ 4π	日本人年齢別標準値を基準とする[1]	
	標準値の60%未満	高度栄養障害
	60〜80%未満	中等度
	80〜90%未満	軽度
	90%以上	正常
2）血液データ		
血清アルブミン（半減期：17-23日）：3.5g/dl未満		
トランスサイレチン（半減期：1.9日）：10mg/dl未満		
トランスフェリン（半減期：7-10日）：200mg/dl未満		

[1]日本人の身体計測基準 JARD2001, 栄養評価と治療 Vol:19(suppl.), 2002

しかし、低栄養の診断は絶対的指標がなく、臨床の現場ではその判定に難渋することもある。**表1**によく使用される一般的な指標を提示した。臨床で使用される血清アルブミン値も低栄養、特に慢性の低栄養状態では確かに低下するが、それ以外に炎症の存在でも低下するために急性期状態の判定には使用しづらい。

高齢者の低栄養リスク

ヒトは一般的に加齢とともに徐々に食事量が減少してくる。高齢者では身体活動の低下、安静時基礎代謝量の減少、さらには除脂肪体重の減少があり、これらによって高齢者の必要摂取熱量は減少する。若年時と比較すると食物摂取量は減少するが、それが必ずしも低栄養につながるわけではない。しかし、加齢に伴う生理的、社会的、経済的問題は高齢者の栄養状態に大きな影響を与える。**表2**に高齢者の代表的低栄養要因を挙げ、以下にその解説を述べた。

㈠社会的な要因

独居高齢者はそれだけで栄養障害のリスクとなる。日常生活動作（activities of daily living: ADL）の障害がなくても、一人暮らしのため十分な食事量を摂取し

ていなかったり、食事内容が偏ったりする場合がある。ＡＤＬ障害がある高齢者は十分な介護力、適切な介護がなければ、摂取量は確実に減少する。経済的な問題があり満足に食事を取れない場合も低栄養の要因になるのは言うまでもない。

(二)精神心理的要因

認知機能障害により、食事をするのを忘れたり、空腹感を感じなかったりすることはまれではない。認知症が進行すると味覚、嗅覚の低下が進むことも、食事摂取量が減少する一つの原因である。「うつ」は「消化管の問題」、「悪性腫瘍」にならぶ高齢者の食欲不振・体重減少の原因として頻度が高い。明らかな食欲不振・体重減少の原因がない場合は「うつ」の存在を疑う必要がある。嚥下障害がある場合、誤嚥を恐れるため本人、介護者が食事摂取量を制限している場合がある。

表２　高齢者の様々な低栄養の要因

１．社会的要因 独居 介護力不足・ネグレクト 孤独感 貧困	**２．精神的心理的要因** 認知機能障害 うつ 誤嚥・窒息の恐怖
３．加齢の関与 嗅覚、味覚障害 食欲低下	**４．疾病要因** 臓器不全 炎症・悪性腫瘍 疼痛 義歯など口腔内の問題 薬物副作用 咀嚼・嚥下障害 日常生活動作障害 消化管の問題（下痢・便秘）
５．その他 不適切な食形態の問題 栄養に関する誤認識 医療者の誤った指導	

(三)加齢による影響

加齢自体によっても食欲は一般に低下しやすいと言われている。味覚、嗅覚は食欲に重要な役割を果たすが、高齢者では味覚機能が低下し（六五歳以上では約四〇％に味覚障害があるとの報告もある）、特に苦味に関する感覚が低下する。また嗅覚の低下も一般的に認められる。味覚の低下の原因は単に加齢の影響のみならず、亜鉛欠乏、鉄欠乏、口腔内カンジダ症、うつなどが起因となっているケースもまれではない。さらに種々の薬剤によっても味覚異常を引き起こす可能性がある。また、高齢者では体重を保つため働く食欲の調節機構が若年者と異なることが知られている（急激な体重減少に反応して若年者では体重をもどすため食欲増加が起こるが、高齢者ではその調節が起こらない）。

(四)疾病要因

悪性腫瘍ならびに感染症、慢性炎症性疾患の存在、さらには心不全、呼吸不全、肝、腎不全などは食欲低下の大きな誘引になる。さらにこれらの疾患は代謝性ストレスに直結し、必要エネルギー量は増大し、食欲低下と相まって低栄養につながる。腰痛、頭痛、膝関節痛などの疼痛は食欲低下の誘因になる。歯の問題は

咀嚼機能の低下を含め栄養障害を引き起こす重要な因子である。特に義歯の不調、口腔ケア不足による歯槽膿漏などは低栄養の誘因として重要である。薬剤が高齢者の食欲低下、体重減少に関わっているケースは想像以上に多く、高齢者の食思不振の三五％は医原病によるとの報告もある。咀嚼・嚥下障害があれば、当然十分な経口摂取は期待できず、放置すれば短期間で低栄養に陥る。

(五)その他

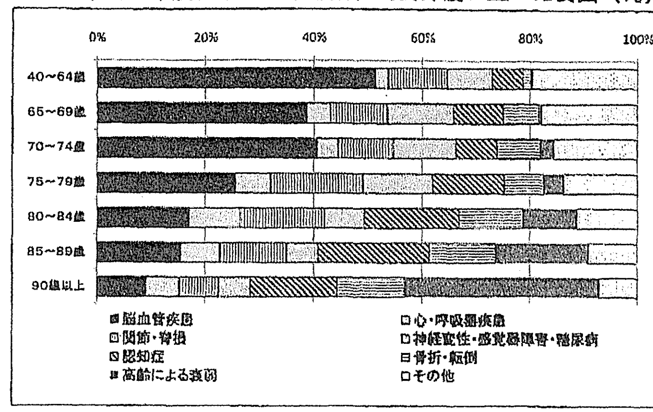
高齢者では咀嚼、嚥下障害を抱えるケースが多いが、それに対応した食形態が提供されていない場合がある。不適切な食形態の提供により、十分な食事が摂取できないばかりか、誤嚥の要因にもなっている。若い頃の過栄養に対する食事指導を体重減少が既に現れている高齢者になっても引きずっている場合がある。また医療者も後期高齢者を対象に若年者と同様の食事指導を行っている場合がある。

なぜ低栄養を改善する必要があるのか

低栄養状態が高齢者に及ぼす悪影響に関しては今まで多くの報告がある。低栄養の一つの指標である血清アルブミン値は重要な生命予後の指標であることは多くの論文で証明されている。低体重（低ＢＭＩ値）や体重減少は同様に生命予後の重要な予測因子である。実際、高齢者においてはＢＭＩ二五kg／m²以上の肥満に比較してもＢＭＩが一八・五kg／m²未満のヤセの状態では明らかに生命予後のリスクが高いことが欧米のみならず我が国においても報告されている。

ＢＭＩ低値また低栄養はＡＤＬの低下にも関与する

図1　平成22年度日本人の年齢階級別要介護に至った要因（%）



（平成22年度国民生活基礎調査より）

ことが明らかになっている。さらに、低栄養は免疫機能の低下を伴い、感染症を引き起こしやすくする。また褥瘡の形成に関与するのみならず、主要疾患の治癒を遅らせ、合併症を容易に引き起こすことが知られる。結果的に低栄養状態は入院期間の延長を引き起こし、医療費の高騰にもつながることが報告されている。

低栄養は要介護状態の原因である虚弱（フレイル）とも密接に関連している。超高齢社会の到来により、如何に要介護高齢者を増やさないかは、高齢者の生活の質を考えた上でも、医療経済上も喫緊の課題である。平成二二年度の要介護に至る原因をみると、前期高齢者（六五歳～七四歳）では脳血管障害が原因で要介護になる割合が圧倒的に高いが、八五歳以上の高齢者の集団では「高齢による衰弱」が多くなるのがわかる（図1）。この「高齢による衰弱」は老年医学で言う「虚弱（フレイル）」に相当するものである。フレイルとは〝老化に伴う種々の機能低下（予備能力の低下）を基盤とし、種々の健康障害に対する脆弱性 vulnerability）が増加している状態〟とされる。これは「機能障害」がある種の疾病（脳血管障害や骨折など）に起因するという「疾病モデル」ではなく、高齢者では老化に伴う予備能力の低下（恒常性低下）が「機能障害」につながるというシナリオを呈している。まさしく、老年医学での「フレイル」は「老衰」と同様な意味で使用される。

フレイルは（1）体重の減少（低栄養）、（2）身体機能の低下（歩行速度の低下）、（3）筋力の低下（握力の低下）、（4）主観的疲労感、（5）生活活動度の低下の五項目のうち三項目以上あてはまる場合とされ、一つ～二つあてはまる場合は前段階（前虚弱、プレフレイル）と評価する。この定義にあるように栄養障害の存在はフレイルの重要な要素であり、これからも低栄養が要介護に至るプロセスに重要な役割を果たしていることが理解できる。

表3　高齢者栄養障害に伴う病態

1. 免疫異常（感染症）
2. 褥瘡
3. 創傷治癒の遅延（手術後の回復遅延）
4. 貧血
5. 骨粗鬆症
6. 薬剤代謝の変動
7. 筋萎縮（sarcopenia）
8. 転倒
9. 骨折
10. 呼吸機能の低下
11. 疲労感
12. 浮腫

その他低栄養は加齢とともに出現する様々な老年症候群と密接に関わっている（表3）。したがって高齢者の低栄養を予防し、または低栄養を改善することは、高齢者にとって生命予後のみならず、ADL低下、老年症候群の予防、介護予防という面からも極めて重要である。

サルコペニアとたんぱく質

高齢者の栄養障害との関連で挙げておきたいのはサルコペニアである。サルコペニアとは「加齢に伴う筋力の低下、または老化に伴う筋肉量の減少」を指し、上記の「フレイル」や転倒との強い関連が指摘されている。一般的に七〇歳までに二〇歳台と比較すると骨格筋面積は二五～三〇％、筋力は三〇～四〇％減少し、五〇歳以降毎年一～二％程度筋肉量は減少する。加齢とともに骨格筋は筋線維数の減少だけではなく、一つ一つの筋線維自体も萎縮する。サルコペニアの要因は多因子によることが想定されているが、その中で栄養も大きく関連している。筋肉細胞自体の萎縮は筋たんぱく質の減少を伴っており、筋肉たんぱくの同化・異化バランスがこの病態に関わっている可能性が高い。高齢者では今まで動物性たんぱく質の摂取が少ない傾向にあり、これが骨格筋萎縮の一つの要因であるとも指摘されている。詳細は誌面の都合上省くが、たんぱく質摂取ならびに運動介入によりサルコペニアが改善するとの報告が蓄積されつつある。

さいごに

後期高齢者の増加により明らかに日本における医療のパラダイムシフトが起こっている。今後高齢者が一日でも要介護にならず自立した生活を継続するためには、栄養が果たす役割は大きく、今後のさらなる研究ならびに市民に向けた啓蒙が重要である。

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