Table 2. Adjusted hazard ratios (HRs) for all-cause mortality according to quartile of DSST score ($N = 811$)

Quartile	No.	Deceased (%)	Mean ± SD (range)	Model 1[a]		Model 2[b]		Model 3[c]	
				HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Fourth (reference)	200	26 (13.0)	50.1 ± 6.3 (43–73)	1		1		1	
Third	194	37 (19.1)	38.1 ± 2.1 (35–42)	1.84 (1.11–3.06)	0.018	1.59 (0.96–2.67)	0.073	1.62 (0.97–2.72)	0.068
Second	210	49 (23.3)	30.9 ± 1.9 (28–34)	2.02 (1.24–3.30)	0.005	1.74 (1.06–2.86)	0.029	1.73 (1.05–2.87)	0.033
First	207	70 (33.8)	22.4 ± 4.6 (5–27)	3.42 (2.09–5.58)	<0.001	2.76 (1.66–4.56)	<0.001	2.55 (1.51–4.29)	<0.001

[a]Adjusted for baseline characteristics, including age, sex, education level, and depressive symptoms.
[b]Adjusted for covariates in Model 1 plus chronic disease, sensory deficit, instrumental activities of daily living, and walking speed at baseline.
[c]Adjusted for covariates in Model 2 plus cognitive impairment at baseline.

than among higher-functioning individuals (log-rank test: $P < 0.001$).

Table 2 shows the association between DSST and mortality. By DSST quartile, the mean scores ± SD (score range) were 50.1 ± 6.3 (43–73), 38.1 ± 2.1 (35–42), 30.9 ± 1.9 (28–34), and 22.4 ± 4.6 (5–27), for the fourth, third, second, and first quartile quartiles, respectively.

In multivariate Cox regression analysis adjusted for the above-mentioned potential confounders, lower DSST score was associated with increased mortality risk in model 1 (hazard ratio [HR] = 1.84, 95% CI = 1.11–3.06; HR = 2.02, 95% CI = 1.24–3.30; HR = 3.42, 95% CI = 2.09–5.58, for the third, second, and first quartiles, respectively). In model 2, lower DSST score was associated with increased mortality risk (HR = 1.59, 95% CI = 0.96–2.67; HR = 1.74, 95% CI = 1.06–2.86; HR = 2.76, 95% CI = 1.66–4.56, for the third, second, and first quartiles, respectively). In model 3, as well, lower DSST score was associated with increased mortality risk (HR = 1.62, 95% CI = 0.97–2.72; HR = 1.73, 95% CI = 1.05–2.87; HR = 2.55, 95% CI = 1.51–4.29, for the third, second, and first quartiles, respectively).

DISCUSSION

In this study, we examined the relationship between information processing speed (as measured by DSST) and all-cause mortality among community-dwelling elderly Japanese during an 8-year follow-up period. Our results indicate that information processing speed at baseline predicted 8-year mortality. As in previous reports,[2,11,12] our findings suggest that slow information processing speed is a reliable predictor of mortality among community-dwelling older adults.

We additionally sought to understand and explain the mechanisms by which information processing speed is related to all-cause mortality. Two potential mechanisms were investigated. First, because of the possibility that individuals who have slower information processing speeds have shorter expected life spans as a consequence of poorer physical health,[13–16] we used multivariate analysis (model 2) to examine whether the relationship between information processing and mortality was independent of physical health status. In this model, we adjusted for confounders indicative of poor physical health, including presence of chronic disease, quality of sensory function, IADL, and walking speed. Multivariate analysis showed that DSST score was associated with mortality even after adjustment for these confounders. We therefore conclude that there is an independent relationship between information processing speed and mortality, regardless of physical health status.

Second, we examined if cognitive impairment explains the relationship between information processing speed and mortality. Older individuals with early dementia exhibit slower information processing speed.[7] Additionally, older individuals with dementia have shorter life spans than those who are cognitively intact,[17] which suggests that individuals with slower processing speeds may have shorter life spans because of cognitive impairment. To determine whether the relationship between information processing and mortality is independent of cognitive impairment, we performed additional multivariate analysis (model 3) in which we adjusted for cognitive impairment (defined as an MMSE score of ≤23). We found that DSST score was associated with mortality even after adjustment for this potential confounder, suggesting that the relationship between information processing speed and mortality is independent of cognitive impairment. Nevertheless, because dementia was not diagnosed by a specialist in the present study, we cannot eliminate the possibility that participants with dementia were accidentally included in the group with impaired DSST performance.

Although multivariate analysis largely excluded the possibility of confounding by physical health status and cognitive impairment, it is possible that the higher mortality among individuals with slower information processing speeds can be explained by mild cognitive impairment (MCI) in the

study population.[25] As compared with cognitively normal older adults, individuals with MCI reportedly exhibit slower processing speeds in performance-based measures of everyday functional activities.[26] Because individuals with MCI are prone to develop dementia,[27] they may be indirectly predisposed toward lower life expectancies. Additionally, recent studies have found that MCI may be a direct risk factor for shorter life spans,[28] perhaps because individuals with MCI tend to have diminished capabilities for performing everyday tasks (such as taking prescribed medications regularly and keeping medical appointments)[29] and lower levels of health literacy,[30] both of which are critical in maintaining health. Although we conducted additional analysis to exclude cognitive impairment (model 3), recent studies have reported that MMSE scores alone may be insufficient for identifying individuals with MCI.[31] Accordingly, some individuals who exhibited slower processing speeds in this study may have had MCI. Future studies should exclude individuals with MCI, perhaps by using tools that discriminate MCI, such as the Montreal Cognitive Assessment.[32] Excluding persons with MCI would allow a more direct examination of the relationship between information processing speed and mortality among elderly adults.

Recent studies have reported that interventions to improve information processing speed in elderly adults also transfer to activities instrumental to daily living, such as managing money, preparing meals, and driving.[9,10] These studies also suggest that information processing speed is a fundamental function that is closely associated with everyday activities in elderly adults, and that it is amenable to intervention strategies.[9,10] Therefore, early detection and treatment of older adults who exhibit slower information processing speed can improve cognitive performance in daily life and may contribute to the development of longevity-promoting strategies.

The representativeness of our study sample could potentially limit the external validity of our findings in 2 ways. First, the characteristics of the study participants were somewhat different from those of the general population. Specifically, the proportion of men in this study was relatively high and study participants were, on average, more educated than the general population (Itabashi ward, 2002; Cabinet office, Government of Japan, 1995). In Japan, education level is higher among elderly men than among elderly women.[33] Individuals who have higher levels of education are more likely to have good cognitive function during old age.[13] Therefore, the level of cognitive function in our study sample may be higher than that in the general population. Second, the participation rate at baseline (43.5%) was relatively low because we obtained our data by administering mass health checkups. It has been reported that participants in mass checkups are generally younger than nonparticipants and have higher education levels, fewer chronic diseases, less extensive histories of hospitalization, higher self-rated levels of health, better IADL scores, and better subjective well-being.[18] Therefore, as a consequence of self-selection bias, it is likely that the participants in our study had different health characteristics than those of nonparticipants.[18,34] To improve the representativeness of the study sample, future research should focus on increasing the rate of participation at baseline, which would limit the potential for self-selection bias. We suggest 2 principal methods of increasing baseline participation rates. First, the purpose of the survey should be explained in plain language to family members of potential participants, in addition to the potential participants themselves. This would allow older individuals to arrive at decisions concerning participation in full consultation with their families. Second, it may be necessary to transport participants to and from the checkups, so individuals who are physically frail can take part in the survey without inconvenience. However, this option might increase overall study costs.

For reasons of practicality, several covariates in our study were self-reported by the participants, namely, those related to history of chronic disease (stroke, heart disease, diabetes mellitus) and sensory deficits (hearing loss, eyesight problems). Self-reported evaluations of health status could be less accurate than objective evaluations, which might be obtained from medical records and clinical examinations. Therefore, future studies of the relationship between cognition and mortality should rely on more-objective measures of these covariates, which could eliminate any biases due to self-reporting and increase the precision of recorded data.

In conclusion, we examined the relationship between information processing speed and all-cause mortality among community-dwelling elderly adults in Japan and found that information processing speed (assessed using the DSST) predicted mortality. This suggests that older individuals with slower information processing speed are more likely to have shorter life spans as compared with higher-functioning elderly. Our results may help facilitate development of longevity-promoting strategies and underscore the importance of early detection and treatment of cognitive decline among elderly adults.

ONLINE ONLY MATERIALS

Abstract in Japanese.

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ORIGINAL ARTICLE: EPIDEMIOLOGY, CLINICAL PRACTICE AND HEALTH

Association of knee-extension strength with instrumental activities of daily living in community-dwelling older adults

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Aim: The purpose of the present study was to investigate the relationship between knee-extension (KE) strength and instrumental activities of daily living (IADL), and to examine the risk of IADL disability in relation to KE strength in community-dwelling older adults.

Methods: The participants were 1235 community-dwelling older adults (261 men and 974 women) in Tokyo who underwent a comprehensive health survey in 2009. The health survey included measurement of KE strength and a questionnaire on the Tokyo Metropolitan Institute of Gerontology (TMIG)-IADL. Pearson product-moment correlation coefficients and partial correlation coefficients were calculated separately for each sex for four parameters representing quadriceps muscle strength and TMIG-IADL. Pearson's χ^2-test of independence and the Cochran–Armitage test of trend were also carried out to determine the relationship between KE strength and IADL disability.

Results: In women, all correlations between the quadriceps muscle strength parameters and the TMIG-IADL score were statistically significant ($P < 0.0005$). The significance persisted remained even after factors regarding cognition or depression were taken into consideration. Furthermore, the percentage of female participants with IADL disability was dependent on KE strength; there was an inverse trend between KE strength and the percentage of people with IADL disability. In men, no significant relationship was found between KE strength and IADL.

Conclusions: KE strength and IADL correlated positively, and the percentage of people with IADL disability decreased with increasing KE strength in women. **Geriatr Gerontol Int 2014; 14: 674–680.**

Keywords: activities of daily living, aged, knee, muscle strength, quadriceps muscle.

Introduction

The instrumental activities of daily living (IADL) are the activities often carried out by a person who is living independently in a community setting during the course of a normal day, such as managing money, shopping, telephone use, travel in the community, housekeeping, preparing meals and taking medications correctly.[1] Declines in the ability to carry out these activities might result in the need for long-term care. Therefore, the unprecedented rate of aging seen in Japan today necessitates the identification of measures to prevent the decline of IADL in the elderly.

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Several studies have reported that hand muscle strength is related to IADL. For example, a meta-analysis of community-dwelling older participants by Judge *et al.* showed that handgrip strength was negatively related to the total number of IADL requiring assistance from others.[2] Sallinen *et al.* reported that handgrip strength below 37 kg for men and 21 kg for women increased the likelihood of mobility limitations, which are directly related to IADL disability.[3] A 3-year follow-up study by Ishizaki *et al.* also pointed out that weak handgrip strength was a significant predictor of functional decline in IADL performance.[4]

As most IADL involve walking, leg muscle strength might also greatly affect the performance of IADL. However, an association between lower-limb muscle strength and IADL cannot be assumed, as one could, for example, substitute a wheelchair for walking, to carry out each activity included in the IADL.

A multivariate analysis carried out by Uchida *et al.* showed that poor performance on the knee-raising test correlated strongly with decreased IADL performance.[5] A study by Azegami *et al.* involving 47 elderly people investigated the effect of lower-extremity muscle strength on IADL status in two ways: knee-extension (KE) in a single-joint task and total leg extension (TLE) in a multijoint task.[6] The authors found that there was a significant difference in TLE strength between participants with total and only partial IADL independence, whereas no such difference was found for KE strength in a single joint.

In many studies, the strength of lower-limb muscles has often been represented by KE strength,[7–9] as this measurement of the isometric strength of the quadriceps muscles in the sitting position is well established. The purpose of the present study was to examine the relationship between KE strength and IADL performance in a local elderly population.

Methods

Participants

The data were taken from a health survey carried out by Tokyo Metropolitan Institute of Gerontology (TMIG) for community-dwelling older adults in the Itabashi ward of Tokyo in 2009. The participants in the 2009 survey consisted of 1235 people (261 men and 974 women). This group of participants included two cohorts (2002 and 2006 cohorts). All the men ($n = 261$) and 405 of the women participated in a health survey carried out in 2002 (2002 cohort). Follow-up surveys were carried out for this cohort four times, including the survey in 2009. The remaining 569 women first participated in the health survey carried out in 2006 (2006 cohort). Follow-up surveys for this cohort were carried out once in 2007 and once in 2009.

A total of 15 men and 47 women whose IADL or KE data were not available were excluded from the study; the present study analyzed data from 246 men (age range, 77–91 years) and 927 women (age range, 72–91 years) (Table 1). The TMIG ethics committee approved this study. All participants gave their written consent.

Measurement of KE strength

KE strength was measured isometrically using a handheld dynamometer (μTas F-1; ANIMA, Tokyo, Japan). The participants were seated on a custom-made chair with their feet hanging. Participants practiced isometric knee extension by pushing against the tester's hand. The dynamometer was then placed 5 cm above the top of the lateral malleolus, and the chair was adjusted to ensure that the participant's knees were flexed at 90°. Voluntary maximal isometric knee extension effort was exerted twice on the dominant leg. Participants received consistent verbal encouragement as reinforcement. The greater value of two trials was used for analysis. The distance from the lateral knee joint space to the lateral point of the height of the dynamometer pad (F-L distance in Table 1) was measured to convert KE strength into KE torque. Those who were diagnosed with a serious medical problem (e.g. systolic blood pressure over 180 mmHg, diastolic blood pressure over 110 mmHg, or heart attack or cerebral stroke in the past 6 months) were excluded from the test for safety reasons.

Evaluation of IADL performance

IADL performance was assessed using a five-item list from the TMIG Index of Competence for instrumental self-maintenance,[10] which was developed for elderly Japanese participants and has been widely used in Japanese communities. The list assessed the following five activities: (i) using public transportation; (ii) shopping for daily necessities; (iii) preparing meals; (iv) paying bills; and (v) handling a bank account (Table 2). The response to each item was either "yes" (able to accomplish, 1 point) or "no" (unable to accomplish, 0 points). The IADL score (TMIG-IADL hereafter) was calculated as the total number of points.

Evaluation of other parameters potentially related to KE strength and IADL performance

To identify parameters that were related to both KE strength and IADL, which might result in a spurious correlation between the two, data on several other parameters were collected. Bodyweight was measured as a part of the body fat measurement. Cognitive function was evaluated using the Mini-Mental State Examination (MMSE), for which a higher score indicates better cognitive function.[11] Depression was assessed using the Mini-International Neuropsychiatric Interview (MINI);[12] those who gave a negative response to both of the first two questions were categorized as normal, and those who gave a positive response to either of these questions were categorized as depressed. A history of disease (hypertension, stroke, heart disease, diabetes mellitus, hyperlipidemia, osteoporosis, anemia, chronic kidney deficiency, asthma, chronic occlusive pulmonary disease [COPD], pneumonia, osteoarthritis of the hip, gonarthritis, or fracture occurring above the age of 60 years) and the use of drugs was assessed using yes/no questions. Family status was examined using one multiple-choice question, and the participants were categorized as "living alone" or "living with someone".

Data analysis

For quantitative variables, means and standard deviations were calculated. For qualitative variables assessed

Table 1 Basic participant characteristics

			Male (n = 246) Mean ± SD	Female (n = 927) Mean ± SD	Difference between sexes
Mean ± SD		Age (years)	82.2 ± 3.5	79.5 ± 4.2	‡
		Height (cm)	160.8 ± 5.8	147.8 ± 5.6	‡
		Weight (kg)	58.4 ± 8.6	48.8 ± 7.6	‡
		F-L Distance (cm)	27.1 ± 2.3	25.0 ± 2.0	‡
		KES (N)	292.4 ± 82.8	209.1 ± 58.5	‡
		TMIG-IADL	4.9 ± 0.4	4.9 ± 0.5	N.S.
		MMSE	27.7 ± 2.3	27.6 ± 2.3	N.S.
Percent Positive	History	Depression	4.9%	3.9%	N.S.
		Hypertension	58.1%	55.8%	N.S.
		Stroke	10.2%	6.6%	N.S.
		Heart disease	23.6%	22.0%	N.S.
		Diabetes mellitus	11.8%	8.5%	N.S.
		Hyperlipidemia	18.7%	36.1%	‡
		Osteoporosis	6.1%	34.1%	‡
		Anemia	2.8%	3.8%	N.S.
		CKD	2.0%	1.1%	N.S.
		Asthma	4.1%	3.2%	N.S.
		COPD	4.5%	1.5%	‡
		Pneumonia	11.0%	6.9%	†
		Osteoarthritis of hip	2.4%	4.0%	N.S.
		Gonarthritis	15.4%	28.0%	‡
		Fracture after 60 years	13.0%	23.5%	‡
	Drug use	Anti-inflammatory	6.5%	9.5%	N.S.
		Oral steroid	1.2%	1.3%	N.S.
		Anti-osteoporosis	4.9%	30.3%	‡
		Living alone	8.1%	37.2%	‡

†$P < 0.05$, ‡$P < 0.01$. CDK, chronic kidney deficiency; COPD, chronic occlusive pulmonary disease; F-L Distance, distance from fulcrum to the point of load in knee extension task; KES, knee extension strength; SD, standard deviation.

Table 2 English translation of the questions constituting the Tokyo Metropolitan Institute of Gerontology instrumental activities of daily living

Question	Answer
1. Can you use public transportation (bus or train) by yourself?	Yes/No
2. Are you able to shop for daily necessities?	Yes/No
3. Are you able to prepare meals by yourself?	Yes/No
4. Are you able to pay bills?	Yes/No
5. Can you handle your own banking?	Yes/No

by yes/no questions, the percentage of positive responses was calculated. Differences between sexes were analyzed using the t-test or the χ^2-test.

We carried out a preliminary analysis to determine potentially confounding factors for the relationship between KE strength and IADL; correlations between parameters, such as body weight, MMSE, MINI, medical conditions and diseases, medication use, family status, and KE strength or TMIG-IADL, were examined individually. The statistical significance of Pearson's or Spearman's correlation coefficients was tested.

Pearson's correlation coefficients between four parameters representing quadriceps muscle strength (KE strength, KE torque, bodyweight-adjusted KE strength and bodyweight-adjusted KE torque) and TMIG-IADL scores were examined. Partial correlation coefficients using MMSE and MINI as the controlling variables were also calculated. The statistical significance of the correlations was tested.

The participants were classified according to quintiles of KE strength into five categories, and were also classified into two categories according to the presence of IADL disability; participants with a TMIG-IADL score of 1–4 were defined as having IADL disability.[13,14] The χ^2-test was carried out to determine the relationship

between the percentage of participants with IADL disability and KE strength. Cochran–Armitage tests of trend were carried out to determine whether there were any trends in the prevalence of IADL disability according to the KE strength.

As the distribution of TMIG-IADL was very skewed (just 2% of men and 3% of women scored ≤3 points), the analyses were also applied to a subgroup of participants whose TMIG-IADL score was between 4 and 5. All of these analyses were carried out using PASW Statistics 18 (IBM Japan, Tokyo, Japan), except for Cochran–Armitage tests, which were carried out using an Excel program (Microsoft, Redmond, WA, USA). The level of significance was set at $P < 0.05$.

Results

Participant characteristics

The age, height, weight, F-L distance and KE strength were greater in men than in women. Hyperlipidemia, osteoporosis, gonarthritis, fracture after 60 years-of-age, use of anti-osteoporosis drugs and living alone were higher in women than in men. COPD and pneumonia were higher in men than in women. (Table 1).

Preliminary analysis of individual correlations

In men, statistically significant correlations with KE strength were observed for bodyweight ($r = 0.346$; $P < 0.0005$) and the MMSE score ($r = 0.230$; $P < 0.0005$). Statistically significant correlations with the TMIG-IADL score were observed for the MINI ($\rho = -0.134$; $P = 0.035$), stroke ($\rho = -0.145$; $P = 0.023$), heart disease ($\rho = -0.138$; $P = 0.030$) and asthma ($\rho = -0.159$; $P = 0.012$). No parameters correlated with both KE strength and the TMIG-IADL score.

In women, statistically significant correlations with KE strength were observed for bodyweight ($r = 0.343$; $P < 0.0005$), MMSE ($r = 0.160$; $P < 0.0005$), MINI ($r = -0.089$; $P = 0.007$), heart disease ($r = -0.105$; $P = 0.001$), osteoporosis ($r = -0.111$; $P = 0.001$), anemia ($r = -0.087$; $P = 0.008$) and the use of anti-osteoporosis drugs ($r = -0.084$; $P = 0.010$). Statistically significant correlations with the TMIG-IADL score were observed for the MMSE ($r = 0.302$; $P < 0.0005$), MINI ($\rho = -0.208$; $P < 0.0005$) and stroke ($\rho = -0.097$; $P = 0.003$). Thus, the MMSE and MINI correlated with both KE strength and the TMIG-IADL score. We therefore took these two parameters into consideration when we carried out the partial correlation analysis.

Correlation analysis

In men, all correlations between quadriceps muscle strength parameters and the TMIG-IADL score were statistically non-significant (Table 3). In women, all the correlations were weak (R 0.157–0.173), but statistically significant ($P < 0.0005$) (Table 3). These correlations remained significant for women even when the analysis

Table 3 Correlation coefficients between parameters related to quadriceps muscle strength and Tokyo Metropolitan Institute of Gerontology instrumental activities of daily living score

	Sex	Parameter	Correlation coefficient	Statistical significance
All participants	Male ($n = 246$)	KES	0.022	N.S.
		KET	0.030	N.S.
		WA-KES	0.066	N.S.
		WA-KET	0.072	N.S.
	Female ($n = 927$)	KES	0.173	‡
		KET	0.173	‡
		WA-KES	0.157	‡
		WA-KET	0.166	‡
Subgroup of TMIG-IADL ≥ 4	Male ($n = 241$)	KES	−0.005	N.S.
		KET	−0.001	N.S.
		WA-KES	0.010	N.S.
		WA-KET	0.012	N.S.
	Female ($n = 899$)	KES	0.109	‡
		KET	0.100	‡
		WA-KES	0.133	‡
		WA-KET	0.128	‡

†$P < 0.05$, ‡$P < 0.01$. KES, knee extension strength; KET, knee extension torque; TMIG-IADL, Tokyo Metropolitan Institute of Gerontology instrumental activities of daily living; WA-KES, weight-adjusted knee extension strength; WA-KET, weight-adjusted knee extension torque.

Table 4 Partial correlation coefficients, with Mini-Mental State examination and depression as the control variable, between parameters related to quadriceps muscle strength and Tokyo Metropolitan Institute of Gerontology instrumental activities of daily living score

	Sex	Parameter	Partial correlation coefficient	Statistical significance
All participants	Male (n = 234)	KES	0.009	NS
		KET	0.018	NS
		WA-KES	0.066	NS
		WA-KET	0.071	NS
	Female (n = 913)	KES	0.091	‡
		KET	0.091	‡
		WA-KES	0.085	†
		WA-KET	0.090	‡
Subgroup of TMIG-IADL ≥ 4	Male (n = 229)	KES	−0.017	NS
		KET	−0.011	NS
		WA-KES	0.014	NS
		WA-KET	0.017	NS
	Female (n = 879)	KES	0.088	‡
		KET	0.078	†
		WA-KES	0.115	‡
		WA-KET	0.108	‡

†$P < 0.05$, ‡$P < 0.01$. KES, knee extension strength; KET, knee extension torque; WA-KES, weight-adjusted knee extension strength; WA-KET, weight-adjusted knee extension torque.

included only those with TMIG-IADL scores of 4–5 (R 0.100–0.133; $P < 0.005$) (Table 3).

Using the MMSE and MINI as the controlling variables, all the partial correlations between the quadriceps muscle strength parameters and the TMIG-IADL score in men were statistically non-significant (Table 4). In women, all the partial correlations were weak (R 0.085–0.091), but statistically significant ($P < 0.05$; Table 4). These partial correlations for women remained significant even when analysis included only those with TMIG-IADL scores of 4–5 (R 0.078–0.115; $P < 0.05$) (Table 4).

Analysis of the ratio of IADL disability to KE strength

Male participants were classified by KE strength quintiles into the following five categories: very low, KE strength <229 N; low, KE strength 229–267 N; normal, 267–311 N; high, 311–355 N; and very high, KE strength >355N. The χ^2-test showed that IADL disability was independent of KE strength (Pearson's χ^2, 5.199; df, 4; $P = 0.267$) in men. The occurrence of IADL disability showed no trend related to KE strength (Cochran–Armitage test, $P = 0.828$) (Fig. 1). These results were also true for the subgroup of men whose TMIG-IADL scores were between 4 and 5.

Female participants were classified by KE strength quintiles into the following five categories: very low, KE strength <159 N; low, KE strength 159–192 N; normal, KE strength 192–221 N; high, KE strength 221–254 N; and very high, KE strength >254 N. IADL disability was dependent of KE strength (Pearson's χ^2, 23.685; df, 4; $P < 0.0005$). The occurrence of IADL disability decreased as KE strength increased; the percentage of participants with IADL disability was 12.9%, 6.5%, 6.3%, 4.3% and 1.1% for the grades very low, low, normal, high, and very high, respectively (Fig. 1), and this inverse trend was statistically significant (Cochran–Armitage test, $P < 0.0005$). These results were also true for the subgroup with TMIG-IADL scores between 4 and 5 (Pearson's χ^2, 11.811; df, 4; $P = 0.019$; Cochran–Armitage test, $P = 0.019$).

Discussion

The present study examined the relationship between KE strength and IADL in older adults living in a local area of Tokyo. In contrast to the study by Azegami *et al.*, the present results suggest that single-joint–task KE strength is significantly related to IADL in women.[6] In women, every KE strength parameter correlated with IADL. As partial correlations adjusted by cognitive function and depressive scale were also present, it is suggested that KE strength affects IADL independently. In women, KE strength was related to the prevalence of IADL disability. In men, no correlation between KE strength and IADL was observed. These results were the

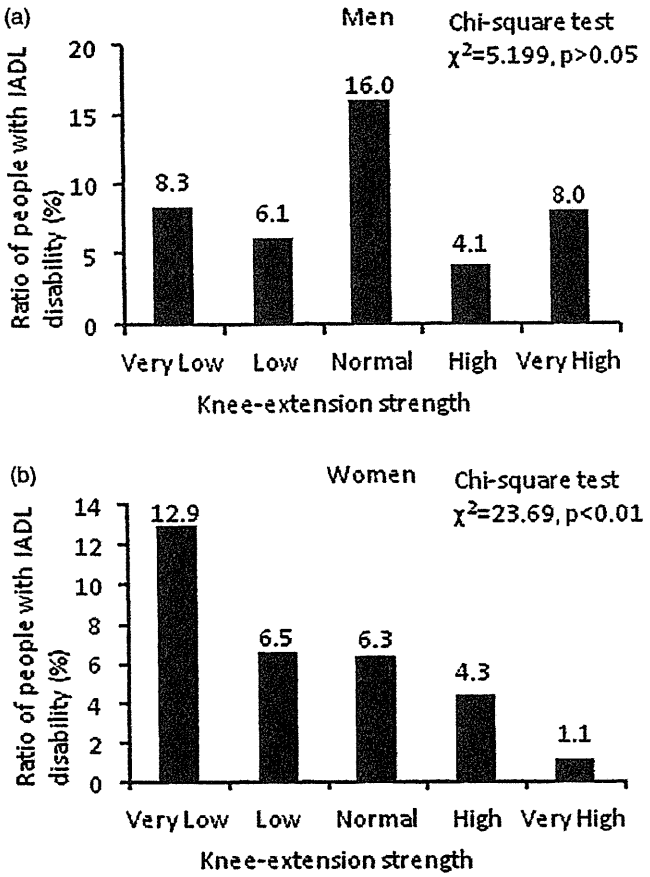

Figure 1 Prevalence of in instrumental activities of daily living (IADL) disability in relation to knee-extension strength (KES) in (a) men and (b) women. KES, men: very low, <229 N; low, 229–267 N; normal, 267–311 N; high, 311–355 N; very high, >355 N. KES, women: very low, <159 N; low, 159–192 N; normal, 192–221 N; high, 221–254 N; very high, >254 N. IADL, instrumental activities of daily living; KES, knee-extension strength.

same even when the subject population was limited to those who had relatively high TMIG-IADL scores (≥4).

Basic ADL has been reported to be affected by the knee extension strength; participants whose strength test scores were in the lowest tertile had two- to three-fold the risk of ADL dependence than those in the highest tertile.[15] Therefore, the present result for men, suggesting no relationship between KE strength and the degree of IADL disability, seems counterintuitive.

To determine whether any one question specifically affected the sex-based differences, we carried out Pearson's χ^2-tests to assess the relationship between KE strength and the answer to each specific question (Q1–Q5). This result showed that, in women, the KE strength and answers to specific questions were related for all items except Q3, with a same trend as total IADL. In men, KE strength and the responses to every specific question were independent. This result suggests that the sex-based difference was not due to any particular item.

One possible explanation for the lack of such a relationship in men is that men had a generally higher KE strength than women. The muscular strength threshold required to carry out IADL independently is 2.8 N/kg (force divided by bodyweight) in the Japanese elderly population.[16] A total of 95% of our male and 92% of female participants had a KE strength above this threshold. This suggests that based on KE strength, more men were able to carry out IADL independently than women. This factor could partly explain the lack of correlation in men.

Another possible explanation for the lack of a correlation between KE strength and IADL performance in men is that cognitive function might have contributed more to IADL performance in men than in women. IADL were reported to be associated with memory and executive functioning in patients with mild Alzheimer's disease.[17] The absence of a relationship between KE strength and IADL performance in men could be partly explained if one argued that cognitive function played a greater role in men, especially because the men were older than the women. As aforementioned, however, the MMSE was related to IADL in women only. The average MMSE score was not different between men and women. Thus, it seems unlikely that cognitive function played a greater role in men than in women in determining IADL performance.

Another possible explanation is that effects of diseases were overshadowing the effect of KE strength. IADL was associated with a history of stroke, heart disease and asthma in men, but only with stroke in women. It is conceivable that IADL in men was more affected by medical conditions than women. Conceptual tradition in Japan regarding family roles might result in the maintenance of IADL irrespective of diseases. According to an international social survey, 77.7% of Japanese married people stated that grocery shopping was usually done by the woman within a couple, compared with 34–57% in six other developed countries.[18] The same trend follows for doing laundry and preparing meals.[18] Our data also show that 37.2% of the women were living alone compared with 8.1% of the men. High dependency on the woman for household jobs and the high percentage of women living alone suggest that women were carrying out many daily physical activities, which might have prevented the deterioration of IADL in response to disease.

Relative dominance by women of household jobs could also suggest a limitation of using TMIG-IADL to evaluate the IADL, especially in Japanese men. At least two questions in TMIG-IADL (Table 2) are closely related to jobs mainly carried out by women in Japan. We might need an improved index of IADL that is more sensitive in healthier men.

The present study showed that in women, KE strength correlated positively with IADL score, and the

degree of IADL disability decreased with increasing KE strength. This correlation was not observed in men. We might need to study a frail population to identify a correlation in men. We conclude that elderly women need to take measures to prevent lower-limb muscles from declining to maintain IADL.

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No potential conflicts of interest were disclosed.

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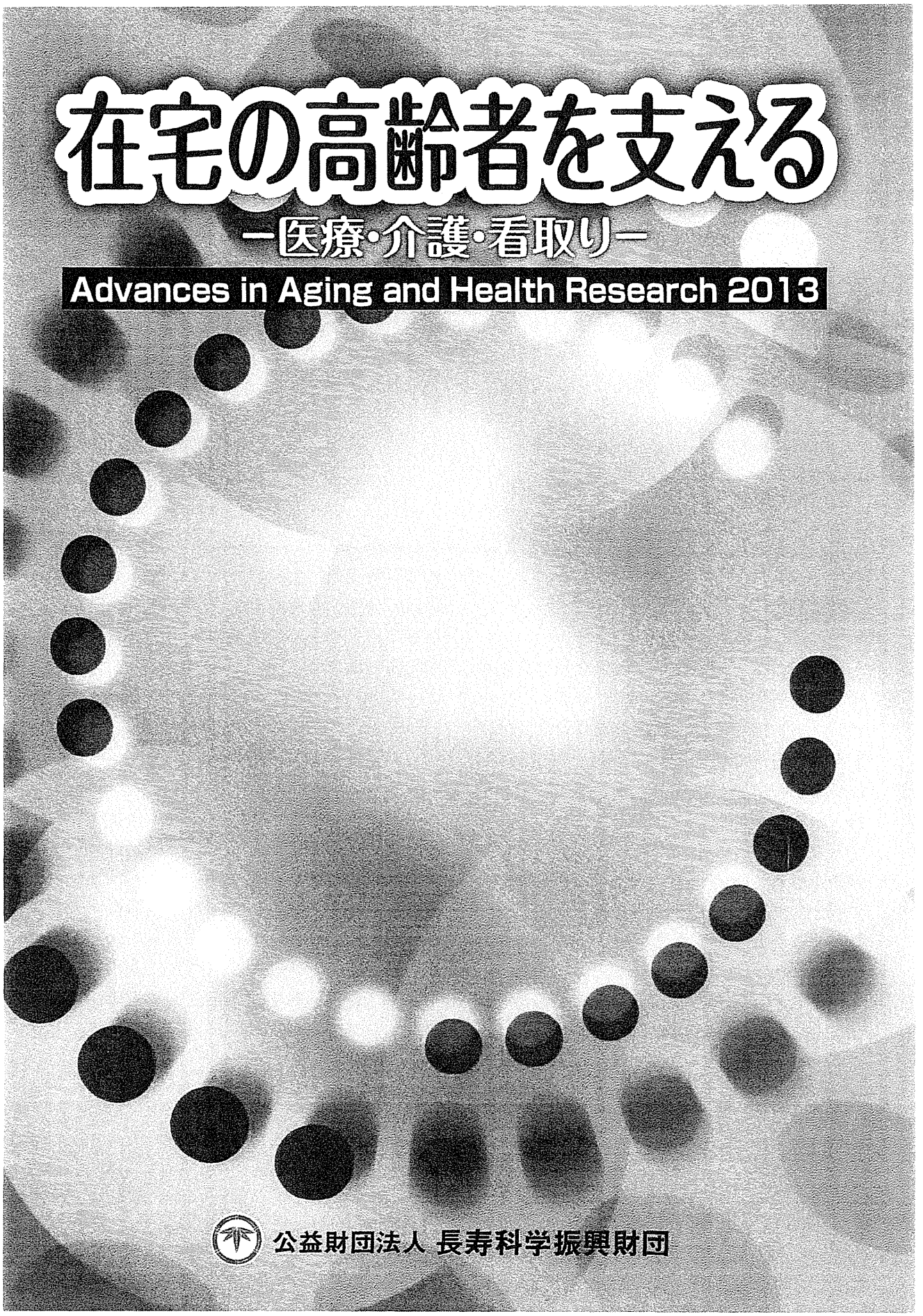
在宅の高齢者を支える
ー医療・介護・看取りー
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公益財団法人 長寿科学振興財団

地域在住高齢者における要介護化の危険因子

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はじめに

日本人の平均寿命は年々長くなり、高齢者、特に後期高齢者の人口が急増している[1]。しかし、高齢になるほど虚弱となり自立生活ができなくなって要支援・要介護となる者は増加する。一方で少子化が進み、今後は若い労働力が不足していくことが予想される。そのような状況で、介護のために若い人材の労力が費やされるようでは、日本の国が成り立って行かなくなってしまう。高齢化する日本の社会で、介護や支援を要するような高齢者を減らし、健康長寿を達成することは急務となっている[2]。本稿では、地域における悉皆調査での要支援・要介護リスクの解析と、地域住民の長期にわたるコホート追跡調査の解析からの結果を中心に、高齢者の自立障害の要因を明らかにし、その予防法を探る。

1. 東浦町介護予防研究

愛知県東浦町の平成21年４月１日現在の65歳以上全住民を対象として、３年半後の平成24年10月１日現在の要支援・要介護情報から、基本チェックリストの各項目や生活機能の評価がその後に要支援・要介護となるかどうかを予測できるかの検討を行った。基本チェックリストは厚生労働省地域支援事業実施要綱

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に基づくもので、65歳以上の高齢者を対象に要介護の原因となりやすい生活機能低下の危険性がないかどうかという視点で運動、口腔、栄養、物忘れ、うつ症状、閉じこもり等の全25項目について「はい」「いいえ」で記入する質問表である。東浦町では基本チェックリストは平成21年度には、65歳以上の人口9,374人のうち、すでに要支援・要介護となっている者を除く8,091人の69.6%にあたる5,631人に実施された。3年半後には死亡者、転出者を除いて603名が要支援・要介護となった。多重ロジスティック回帰により性別、年齢を調整して要支援・要介護となるリスクについて検討を行った。項目別の検討ではチェックリスト項目すべてで有意となった(表1)。オッズ比が2倍以上となった項目は、「日用品の買い

表1　地域住民における3年半の追跡による基本チェック各項目の要支援・要介護となるリスクのオッズ比

項目	オッズ比	95%信頼区間	p値
バスや電車で1人で外出をしていない	1.99	1.64 − 2.41	p<0.001
日用品の買い物をしていない	2.34	1.83 − 3.00	p<0.001
預貯金の出し入れをしていない	1.80	1.44 − 2.26	p<0.001
友人の家を訪ねていない	1.83	1.51 − 2.20	p<0.001
家族の相談にのっていない	1.66	1.34 − 2.04	p<0.001
階段をつたわらずに昇れない	2.17	1.79 − 2.63	p<0.001
つかまらずに立てない	2.51	2.04 − 3.08	p<0.001
15分続けて歩くことはない	2.07	1.67 − 2.56	p<0.001
1年間に転んだことがある	2.05	1.66 − 2.55	p<0.001
転倒の不安が大きい	1.97	1.62 − 2.38	p<0.001
6ヵ月で3kgの体重減少	1.71	1.34 − 2.17	p<0.001
BMIが18.5未満	1.66	1.25 − 2.20	p<0.001
固いものが食べにくい	1.33	1.09 − 1.62	p=0.005
お茶でむせる	1.28	1.02 − 1.61	p=0.031
口の渇きが気になる	1.50	1.22 − 1.83	p<0.001
週に1回以上外出ない	1.70	1.29 − 2.24	p<0.001
昨年より外出回数が減少	2.31	1.90 − 2.82	p<0.001
物忘れがある	1.60	1.29 − 2.00	p<0.001
電話番号を調べてかけることはしない	2.35	1.80 − 3.07	p<0.001
今日の日付がわからない	1.85	1.52 − 2.25	p<0.001
生活に充実感がない	2.20	1.75 − 2.76	p<0.001
楽しめなくなった	2.64	2.04 − 3.41	p<0.001
おっくうに感じる	2.70	2.21 − 3.29	p<0.001
役に立つ人間だと思えない	2.16	1.76 − 2.65	p<0.001
疲れたような感じがする	1.95	1.60 − 2.38	p<0.001

(性別・年齢を調整した多重ロジスティック回帰解析)

物をしていない」、「階段をつたわらずに昇れない」、「つかまらずに立てない」、「15分続けて歩くことはない」、「1年間に転んだことがある」、「電話番号を調べてかけることをしない」、「昨年より外出回数が減少」、「生活に充実感がない」、「楽しめなくなった」、「おっくうに感じる」、「役に立つ人間だと思えない」であった。運動機能や抑うつに関連する項目でリスクが大きいことが分かる。基本チェックリストからの生活機能評価結果では、生活機能全般の障害が要支援・要介護の最大のリスクであり、オッズ比は4倍近くとなった。次いで運動機能障害、うつ状態、栄養状態の不良の順でリスクが大きかった（表2）。

2. 国立長寿医療研究センター・老化に関する長期縦断疫学研究

私たちは平成9年の11月に「国立長寿医療研究センター・老化に関する長期縦断疫学研究（NILS-LSA）」を開始した[3～5]。一日の検査人数は7名で、毎日年間を通して詳細な老化に関連する検査を行ってきた。平成12年4月に2,267名の基礎集団が完成し、以後は2年ごとに検査を繰り返し実施し、平成24年7月に第7次調査を終了した。対象者は長寿医療研究センター周辺在住の観察開始時年齢が40歳から79歳までの男女であり、地方自治体（大府市および東浦町）の協力を得て、地域住民から年齢・性別に層化した無作為抽出を行った。抽出によって選定された者を説明会に招いて、検査の目的や方法などを十分に説明し、インフォームドコンセントを得た上で検査を実施してきた。追跡中の80歳未満のドロップアウトは新たに無作為抽出を行い、同じ年齢、性別で新たな補充を行った。また、どの時点でも若い世代との比較ができるように無作為抽出で40歳の男女を毎回新たに加えて、定常状態として約2,400人のダイナミックコホートを目指してきた。検査および調査はほとんどすべて施設内に設けた専用の検査センターで行った。朝9時から夕方4時までの間に分刻みでスケジュールを組み、頭部MRI検査や心臓および頸動脈超音波断層検査、骨密度測定、腹部CT検査などの最新の機器を利用した医学検査のみならず、詳細な生活調査、栄養調査、運動機能調査、心理検査など広汎

表2　地域住民における3年半の追跡による基本チェックからの生活機能障害項目の要支援・要介護となるリスクのオッズ比

項目	オッズ比	95%信頼区間	p値
生活機能障害	3.82	3.05 － 4.78	p<0.001
運動機能障害	2.70	2.20 － 3.33	p<0.001
栄養状態の不良	2.44	1.31 － 4.54	p=0.005
口腔機能障害	1.59	1.27 － 1.99	p<0.001
閉じこもり	1.70	1.29 － 2.24	p<0.001
認知機能障害	1.80	1.50 － 2.15	p<0.001
うつ状態	2.54	2.09 － 3.09	p<0.001

（性別・年齢を調整した多重ロジスティック回帰解析、オッズ比は各項目1点ごとの値）

で学際的な、しかも精度の高い調査・検査を実施した。

要支援・要介護化の危険因子について、NILS-LSAの第4次調査から第7調査までの6年間に調査に参加した40歳以上の地域在住中高年者3,126人（男性1,567人、女性1,559人）を対象とした。平均年齢は、男性58.4±13.2歳、女性58.9±13.5歳である。

今回の検討に用いた測定項目は以下の通りである。

①背景要因：喫煙習慣（調査時点での喫煙の有無）、高血圧症、心疾患、脂質異常症、糖尿病、脳卒中既往歴、自覚的健康度（「とても良い」、「良い」、「普通」、「悪い」、「とても悪い」の5段階）、血圧、抑うつ（Center for Epidemilogic Studies Depression Scale: CES-Dで16点以上を抑うつありとした）、認知機能（Mini Mental State Examination: MMSEで23点以下を認知機能障害ありとした）。

②身体活動：余暇身体活動量、総身体活動量、一日歩数。

③体格：BMI、大腿中部周囲長、下腿周囲長、上腕周囲長、体脂肪率（DXA法）。

④栄養摂取量：総エネルギー摂取量、たんぱく質、ビタミンD、イソロイシン、ロイシン、バリン、アルギニン（写真撮影を併用した3日間の秤量食事記録法により栄養素の摂取量を算出した）。

⑤体力：普通歩速度、速歩速度、上体起こし、膝伸展筋力、脚伸展パワー、握力、閉眼片足立ち、開眼片足立ち、全身反応時間。

⑥身体機能：SF36のphysical performance項目。具体的な項目は以下の通りである。軽度：体を前に曲げる、百メートル以上歩く、中等度：適度の運動、階段を1階上まで登る、数百メートル以上歩く、高度：階段を数階上まで登る、激しい運動、少し重い物を運ぶ、1キロ以上歩く。これらの項目による得点が75点以下は要支援・要介護となる程度のADLの障害があると判定される。physical performanceが75点以下となる6年間のリスクを各種要因について、一般推定方程式（GEE）で性別・年齢を調整して推定し、オッズ比を計算した。

①生活習慣・背景要因などとADLの低下との関連

喫煙はADLの低下とは有意な関連はみられなかった。高血圧症、心疾患、脂質異常症、糖尿病、脳卒中の有無は疾患を有する群でADLが低下するリスクは高かった。自覚的健康度は、「良い」群に比べ「悪い」、「普通」の群はADL低下のリスクが有意に高かった。オッズ比は3.2と高い値であった。血圧は有意な結果とならなかった。抑うつはある群に比べてない群で有意にADL低下のリスクが低くなっていた。認知機能は認知機能低下がない群でADL低下のリスクが下がっていた（表3）。

②身体活動量、体力とADLの低下との関連

余暇身体活動量、総身体活動量、一日の歩数の身体活動指標はいずれも高いほどADL低下のリスクを下げていた。体力の指標では、握力、開眼片足立ち、閉眼片足立ち、全身反応時間、脚伸展パワー、上体起こし、膝伸展筋力、普通歩速度、速歩速度と体力指標すべてで成績が悪いとADL低下のリスクとなっていた（表4）。

③体格、栄養とADLの低下との関連

BMIは高くなるほどADL低下のリスクを上げていた。DXAで測定した体脂肪率は高いほどADL低下のリスクが高かった。しかし、大腿中部周囲長、下腿周囲長、上腕周囲長は

ADL低下との関連が認められなかった。エネルギー摂取量、たんぱく質摂取量、ビタミンD摂取量、イソロイシン摂取量、ロイシン摂取量、バリン摂取量、アルギニン摂取量、血清アルブミンの栄養の指標はすべてADL低下に関連しており、数値が低いとADL低下のリスクとなっていた（表5）。

ADL低下や虚弱の予防には多くのアプローチがあるが、NILS-LSAの解析から慢性疾患や抑うつの予防、十分に運動して、歩行能力や、体力を保つことが重要であることを確認することができた。

表3　生活習慣、背景要因などとADLの低下との関連

	項目	オッズ比	95%信頼区間	p値
喫煙	吸う vs 吸わない	1.070	0.796 − 1.437	NS
高血圧症	あり vs なし	1.564	1.324 − 1.846	<0.0001
心疾患	あり vs なし	1.768	1.329 − 2.352	<0.0001
脂質異常症	あり vs なし	1.266	1.055 − 1.521	0.0014
糖尿病	あり vs なし	1.739	1.321 − 2.291	<0.0001
脳卒中	あり vs なし	2.428	1.702 − 3.463	<0.0001
自覚的健康	普通・悪い vs 良い	3.198	2.659 − 3.846	<0.0001
収縮期血圧	10mmHgごと	1.031	0.990 − 1.074	NS
拡張期血圧	10mmHgごと	1.008	0.939 − 1.081	NS
抑うつ	CES-D 15以下 vs 16以上	0.468	0.391 − 0.560	<0.0001
認知機能	MMSE 24以上 vs 23以下	0.702	0.530 − 0.930	0.0136

SF36 physical performanceが75点以下となる6年間のリスクを各種要因について、一般推定方程式（GEE）で性別・年齢を調整し全対象者で推定し、オッズ比を計算した。

表4　身体活動量、体力とADLの低下との関連

	項目	オッズ比	95%信頼区間	p値
余暇身体活動量	100,000METS*min/yごと	0.518	0.408 − 0.658	<0.0001
総身体活動量	100,000METS*min/yごと	0.569	0.467 − 0.693	<0.0001
歩数	1000歩ごと	0.812	0.783 − 0.843	<0.0001
握力	10kgごと	0.377	0.307 − 0.462	<0.0001
開眼片足立ち	10秒ごと	0.942	0.923 − 0.962	<0.0001
閉眼片足立ち	10秒ごと	0.815	0.721 − 0.923	0.0012
全身反応時間	0.1秒ごと	1.371	1.256 − 1.496	<0.0001
脚伸展パワー	10Wごと	0.947	0.937 − 0.957	<0.0001
上体起こし	1回/分ごと	0.926	0.904 − 0.948	<0.0001
膝伸展筋力	10kgごと	0.522	0.455 − 0.599	<0.0001
普通歩速度	1m/分ごと	0.019	0.011 − 0.031	<0.0001
速歩速度	1m/分ごと	0.944	0.937 − 0.951	<0.0001

SF36 physical performanceが75点以下となる6年間のリスクを各種要因について、一般推定方程式（GEE）で性別・年齢を調整し全対象者で推定し、オッズ比を計算した。

3. 性別、加齢と自立障害

要支援・要介護は男性よりも女性に多い。平成24年度介護給付費実態調査の概況によれば、平成25年4月審査分においては、認定者数575万人、受給者数463万人となっており、受給者を性別にみると、男性が29.6%、女性が70.4% と女性が圧倒的に多くなっている。日本では平均寿命は女性の方が男性よりも7歳近く長い。寝たきりの期間も女性の方が長く、支援や介護を要する女性の数は男性よりも多い。年齢を調整しても要支援・要介護のリスクは男性よりも女性の方が高い[6]。また介護を要する女性の死亡率は男性よりも高いという報告もある[7]。

介護を要するような高齢者の虚弱は定義にもよるが、75歳以上の20〜30%に認められ、高齢になるほどその割合は高くなる[8]。多くの研究で、加齢は要介護の最も強い危険因子のひとつにあげられている。しかし、加齢そのものが要介護となる要因なのか、加齢に伴って生じる様々な障害や疾病が要因であって、これらの要因をすべて除いても加齢が要介護の要因であるかどうかについては、まだ十分には明らかにされていない。

4. 生活習慣と要介護

高齢者では一般に身体活動量が減り、また歯の脱落、嗅覚や味覚の低下、消化機能の低下など生理学的な要因に加えて、抑うつなどの精神的な要因のため食欲が低下する。こうした生活習慣の変化が、高齢者が要介護となる要因である可能性が高い。要介護となる栄養学的要因として低栄養、痩せが重要である。特に摂取エネルギー、蛋白質や必須アミノ酸摂取の低下、ビタミンやミネラル、特にビタ

表5　体格、栄養とADLの低下との関連

	項目	オッズ比	95%信頼区間	p値
BMI	1m/kg^{2}ごと	1.080	1.045 − 1.116	<0.0001
大腿中部周囲長	1cmごと	0.999	0.995 − 1.002	NS
下腿周囲長	1cmごと	0.993	0.980 − 1.005	NS
上腕周囲長	1cmごと	1.004	0.985 − 1.023	NS
体脂肪率（DXA）	10%ごと	1.782	1.470 − 2.160	<0.0001
エネルギー摂取量	100kcal/日ごと	0.940	0.918 − 0.963	<0.0001
たんぱく質摂取量	10g/日ごと	0.870	0.824 − 0.919	<0.0001
ビタミンD摂取量	5μg/日ごと	0.943	0.891 − 0.997	0.0379
イソロイシン摂取量	1g/日ごと	0.763	0.678 − 0.858	<0.0001
ロイシン摂取量	1g/日ごと	0.854	0.797 − 0.915	<0.0001
バリン摂取量	1g/日ごと	0.790	0.714 − 0.873	<0.0001
アルギニン摂取量	1g/日ごと	0.827	0.756 − 0.904	<0.0001
血清アルブミン	1g/dlごと	0.725	0.604 − 0.869	0.0005

SF36 physical performanceが75点以下となる6年間のリスクを各種要因について、一般推定方程式（GEE）で性別・年齢を調整し全対象者で推定し、オッズ比を計算した。

ミンD、カロテン、ビタミンB12、葉酸の摂取不足は高齢者の要介護と関連が深いと言われている[9]。前述したように、NILS-LSAでの検討でもこれらの栄養素の摂取とADLの低下の関連が明らかとなった。またNILS-LSAでは、体力はほとんどの項目でADL低下の予防因子であり、筋力、柔軟性、持久力、平衡機能、歩行能力のいずれもが重要であった。さらに身体活動量は余暇身体活動量、総身体活動量、一日歩数のいずれもが多いほどADL低下を予防するという結果であり、運動の重要性が確認された。

要介護となるような虚弱の栄養の指標としてアルブミン、コレステロールが使われてきた。横断的な解析では、低アルブミン血症（血清アルブミン3.5g/dl未満）は地域在住高齢者の身体機能やADL障害に関連していた[10,11]。縦断的研究では、3.8g/dl以下の低アルブミン血症が3年後の身体機能低下と関連していたが、7年後の身体機能低下とは関連をしていなかった。170 mg/dl未満の低コレステロール血症は死亡のリスクにはなっていたが、ADL低下のリスクにはなっていなかった[12]。コレステロールとアルブミンを組み合わせた縦断的な検討では、血清総コレステロールが5.2mmol/l（201mg/dl）以下で女性でのADL低下の危険因子となっていたが、血清アルブミンが4.3g/dl以下での判定では男女ともADL低下の危険因子とはならなかった。しかし、コレステロールとアルブミンの両方を組み合わせたところ、男性でのADL低下の危険因子となった[13]。HDLコレステロールについても施設入所の高齢者の2年間の追跡で、身体機能低下の重要なリスクファクターになっていることが示されている[14]。ADL低下と関連する栄養指標は、単独では見逃してしまうこともある。いくつかの指標を組み合わせて判断することも重要であろう。

高齢者のADLの低下に関しての大規模な縦断研究として米国の40,657人の65歳から79歳の女性を対象とした3年間の追跡研究Women's Health Initiative Observational Study（WHI-OS）がある[15]。WHI-OSではベースライン調査で16.3%が虚弱と判断され、さらに3年間の追跡で14.8%が新たに虚弱となった。ADL低下の要因として生活習慣についても詳細な調査が行われているが、その結果では喫煙はADL低下の危険因子であるが、飲酒は少量ならばむしろ予防するという結果が出ている。また、体重は低体重も肥満もともに正常体重に比べてADL低下の要因となっていた。喫煙はさまざまな慢性疾患の要因ではあるが、NILS-LSAでの検討では喫煙はADLの低下要因とはならなかった。6年間でADLの低下をきたすような集団はすでに喫煙を止めている可能性がある。また体格は東浦町の調査では体重減少や痩せは要支援・要介護の要因であったが、NILS-LSAでは体格はBMIや体脂肪率が多いほどADL低下を来しやすいという結果であり、痩せよりも肥満予防の重要性が示された。

5. 慢性疾患と要介護

WHI-OSの報告では慢性疾患やうつ症状が要介護や虚弱の要因であり、一方、自覚的健康度が高いことは虚弱を防ぐ要因であった。虚弱との関連が認められた慢性疾患は、冠動脈疾患、脳血管障害、糖尿病、高血圧症、大腿骨頸部骨折、慢性閉塞性肺疾患（COPD）、転倒、抑うつ、関節炎であった[15]。さらに認知症や認知機能障害が、高齢者の虚弱と関連

しているとする報告もある[16,17]。NILS-LSAでの調査では、高血圧症、心疾患、脂質異常症、糖尿病、脳卒中のような慢性疾患は程度の差はあるが、すべてADL低下の要因となっていた。自覚的健康度は良い場合に比べて、普通あるいは悪い場合にはADLの低下の強い要因であった。自己判断による健康状態がその後のADL低下を予測する要因であることは興味深い。また抑うつもADL低下の強い要因であった。しかし認知機能低下は有意ではあったが、ADL低下への影響はそれほど大きくはなかった。

慢性の炎症も要介護や虚弱の要因となる。IL-6が3.8 g/mlを超える場合、CRPが2.65 mg/lを超える場合には、3年間の追跡で有意に身体機能が低下していた[12]。男性ホルモンの低下についても、高齢男性の虚弱の要因であるとの報告がある。米国での1,469名の65歳以上高齢男性の検討では、血清テストステロン濃度が低いほど虚弱の割合が多く、4年間の縦断的追跡でも血清テストステロン濃度が低いほど虚弱となるリスクが高かった[18]。男性高齢者の場合、アンドロポーズと呼ばれる加齢に伴う男性ホルモンの低下が虚弱の要因として重要である。副腎や性腺で産生される男性ホルモンの一種であるデヒドロエピアンドロステロン（DHEA）も低値であることが高齢男女で虚弱と関連していた[19]。これら様々な慢性疾患や病態が重積することでさらに要介護や虚弱の危険が増加する。

6. 社会経済的要因と高齢者の要介護、虚弱

同じ定義を用いても、要介護、虚弱高齢者の分布には地域差があるといわれている。ヨーロッパ10カ国の調査では、65歳以上の虚弱高齢者の割合はスイスの5.8%からスペインの27.3%までと異なっており、同じヨーロッパでも概して南欧は北欧よりも虚弱な高齢者が多いとの結果であった[20]。この地域差には教育など社会経済的な要因が関与しているという。

米国のWHI-OSでは社会経済的要因として、世帯年収が高いほど、教育が長いほど、白人に比べむしろ黒人やアジア人でリスクが低かった[15]。また一人暮らしは虚弱となるリスクを20%下げていた。一人暮らしは、他の家族に依存できず自立が必要なためと思われる。一方で、3年間にわたる縦断的研究で、外出頻度が少ない、いわゆる「閉じこもり」で虚弱の発生率が高かったとの報告もある[21]。

7. 虚弱高齢者への介入研究

要介護や虚弱の予防を目指しての介入研究が繰り返し行われている。1994年にNew England Journal of Medicineに掲載されたFiataroneらによる虚弱高齢者への古典的な介入研究がある[22]。施設入所中の高齢者に対する無作為割付研究で筋肉トレーニングにより、虚弱の有意な改善が認められている。運動による介入の虚弱の改善効果については他の良くデザインされた研究でも認められているが[23]、否定的な結果の研究もある[24]。

栄養での介入でも虚弱の改善効果ははっきりしない。Fiataroneらによる無作為割付研究でのビタミン、ミネラル、蛋白質、脂質、炭水化物による栄養介入では、虚弱の改善効果は認められなかった[17]。必須アミノ酸である、バリン、ロイシン、イソロイシンの3つを分岐鎖アミノ酸という。筋肉を構成している必須アミノ酸の約35－40%がこの分岐鎖ア