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August 2008, Volume 23, No. 8, pp.1309-1317

JOURNAL OF BONE AND MINERAL RESEARCH
Volume 23, Number 8, 2008
Published online on March 25, 2008; doi: 10.1359/JBMR.080328

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ABSTRACT: Previous studies have shown that low serum 25-hydroxyvitamin D [25(OH)D] level is a risk factor for falls among the elderly in European and North American populations. We used a cross-sectional community-based survey to study the association of serum 25(OH)D level and falls among Japanese community-dwelling elderly. A total of 2957 elderly persons (950 men and 2007 women) 65–92 yr of age who participated in mass health examinations for the prevention of geriatric syndrome for the elderly underwent an interview, blood analysis, and physical performance testing. Experience of falls over the previous year was assessed in an interview. Physical performance tests of handgrip strength, stork standing time with the eyes open, and normal waking speed as risk factors for falls among the elderly were conducted. Serum albumin and 25(OH)D concentrations were analyzed. Mean 25(OH)D concentration was significantly lower in women than in men ($p < 0.001$). Women showed a significant decline of 25(OH)D level with increased age ($p < 0.001$). There was also a significant difference in the prevalence of 25(OH)D insufficiency [25(OH)D level < 20 ng/ml] between the sexes ($p < 0.001$). The rate of falls was significantly higher in the lowest quartile of 25(OH)D level in women ($p = 0.02$) and in women with 25(OH)D insufficiency ($p = 0.001$). Women also showed significant declines in all three fall-related physical performance tests. Multiple logistic regression analysis showed significant and independent associations between 25(OH)D level and experience of falls in women only ($p = 0.01$). Low 25(OH)D level was significantly associated with a high prevalence of falls in Japanese elderly women because of their inferior physical performance. Low serum 25(OH)D levels appear preventable and easily treated; there is an evident need for greater awareness to screen and thus prevent this condition.
J Bone Miner Res 2008;23:1309–1317. Published online on March 25, 2008; doi: 10.1359/JBMR.080328

Key words: 25-hydroxyvitamin D, fall, physical performance, community elderly

INTRODUCTION

The importance of vitamin D for skeletal health is well known.[1,2] Through the regulation of calcium and phosphorus levels in the blood by promoting their absorption from food in the intestines, vitamin D promotes bone formation and mineralization for the development of a strong skeleton. Vitamin D deficiency, which can result from inadequate intake coupled with inadequate sunlight exposure, plays an important role in the development of osteoporosis because of the induction of a secondary hyperparathyroidism that mobilizes calcium from the bone.

Vitamin D deficiency results not only in impaired bone mineralization, but also in myopathy in the elderly.[3,4] It has also been shown recently to be associated with a decline of muscle strength,[5–8] sarcopenia,[7] and functional limitations and disability,[5,8] and probably because of these phenomena, with falls in the elderly.[9–11] We have studied and reported that concomitant low serum 25-hydroxyvitamin D [25(OH)D] and albumin were associated with decreased objective physical performance among Japanese community-dwelling elderly from a nutritional point of view.[12] However, falls were not taken into account in the previous study.

The aim of this study was to investigate the association between serum 25(OH)D levels and falls, and the associated physical performance among community-dwelling Japanese elderly who in some previous studies have been reported to have stronger muscle strength and lower fall rates than whites.[13,14] We hypothesized that low 25(OH)D levels (1) correlate with poor muscle strength, balance, and walking capability and (2) are consequently associated with the occurrences of falls among community-dwelling Japanese elderly.

MATERIALS AND METHODS

Subjects

The participants were 2957 residents (950 men and 2007 women) ≥65 yr of age living in Itabashi ward in Tokyo, Japan, who had participated in mass health checkups for the community elderly (Otasha-Kenshin) conducted in October/November 2004 and 2005. Otasha-Kenshin, which means "health checkups for successful aging" in Japanese, is a comprehensive mass health examination for commu-

The authors state that they have no conflicts of interest.

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nity-dwelling elderly that aims to prevent "geriatric syndrome" including falls and fractures, incontinence, poor oral health, mild cognitive impairment, depression, and undernutrition. The overall aim is to prevent the loss of independence and the need for long-term care in later life. Details of Otasha-Kenshin, including participant details, investigation methods, and its contents, have been described in our earlier papers.[15–17] None of the subjects analyzed in this study had a history of malignant diseases, current treatment of vitamin D, chronic renal failure, or other serious diseases affecting vitamin D regulation. All participants were essentially ambulatory, lived independently in their homes, and had sound functional capacity. Participants provided written informed consent to participate in the study, which was approved by the Institutional Review Board and Ethic Committee of the TMIG (Accepted No. 5, July 1, 2004).

Data collection

Interviews were conducted to assess the age, physical activity, and chronic disease conditions of subjects. History of chronic diseases was self-reported and included hypertension, stroke, heart disease, diabetes, and renal failure. Heart disease included angina pectoris, acute myocardial infarction, congestive heart failure, and various arrhythmias. Renal failure was defined as chronic renal failure under treatment including hemodialysis, which can affect the regulation and metabolism of serum vitamin D levels.

We also assessed fall experience over the previous year. A fall was defined as an unintentional change in position resulting in coming to rest at a lower level or on the ground. The subjects were asked about their falls in the same manner as in our previous study.[18] That is, they were asked the question, "Have you experienced any falls during the previous 12 months?" Those who reported one or more falls were asked about the circumstances and consequences of each fall (i.e., the time, reason and place of the fall, the presence or absence of injury, and whether they visited a doctor).

Previous population-based studies have confirmed that physical performance characteristics, including those based on handgrip strength, stork standing time with the eyes open, and normal walking speed, are risk factors for falls among the community elderly in Japan.[18–20] Moreover, these three variables have also been confirmed by a covariance structure model as the essential factors underlying physical performance measures for Japanese elderly living in a community.[21]

Handgrip strength

The peak handgrip force (kg) of each hand was measured by Smedley's hand dynamometer (Yagami, Tokyo, Japan). The test was performed twice, and the higher of the two measurements made on the dominant hand was recorded.

Stork standing

While standing on a square (0.4 × 0.4 m), each subject stood on one foot while watching a point set at eye level 1 m away and tried to maintain this posture. A stopwatch measured the duration in seconds, up to a maximum of 1 min, and the longer of two attempts was recorded.

Normal walking speed

A flat walking path of 11 m was marked with tape at the 3- and 8-m points. A stopwatch measured the time taken to walk 5m, from the time when a foot first touched the ground after the 3-m line to when a foot touched the ground after the 8-m line. The participants were asked to take the test by walking at their normal or preferable speed. The test was repeated and the faster speed recorded.

Because of the possibility of a high correlation among the three physical performance tests, after confirmation by Pearson's correlation coefficient (r), normal walking speed was selected as the representative independent variable for the multiple logistic regression model.

Measurement of serum levels of albumin and 25(OH)D

Blood samples were collected in a nonfasting state and in a sitting position. Analyses were carried out centrally in one laboratory (Special Reference Laboratories, Tokyo, Japan). Serum 25(OH)D levels are commonly used as a measure of vitamin D status,[22–24] and these were measured with an RIT 2 kit (Dia Sorin, Stillwater, MN, USA). The RIT 2 method is based on an antibody specific to 25(OH)D; using this method, the CV was <1%. We summarized the serum 25(OH)D levels of these subjects into quartiles, and used the 25 percentile cut-off to compare groups of subjects with higher and lower 25(OH)D. Lower serum 25(OH)D was defined as 25.0 ng/ml (62.5 nM) or below for men and 21.0 ng/ml (52.5 nM) or below for women. For a definition of vitamin D insufficiency, based on studies performed in the United States and Australia[25,26] showing that a serum 25(OH)D level of at least 15–20 ng/ml is needed to achieve optimum PTH levels, we defined a 25(OH)D level of <20 ng/ml as insufficiency.

Statistical analysis

All data were analyzed with SPSS software for Windows, version 13.0 (SPSS, Chicago, IL, USA); the level of significance was set at 5%.

Means and SDs (for continuous variables) along with proportions (for categorical variables) were calculated for all participants. Differences between men and women were assessed using t-tests for continuous variables and χ^2 tests for categorical data. Differences in serum 25(OH)D levels were analyzed among the four age groups by one-way ANOVA in both sexes. Furthermore, comparisons of fall-related variables by 25(OH)D level were performed using analysis of covariance (ANCOVA) controlled for age in continuous variables, and Mantel-Haenszel χ^2 tests were used to adjust for age in categorical variables in both sexes.

To analyze the association of serum albumin and 25(OH)D level with physical performance (i.e., handgrip strength, stork standing time with the eyes open, and normal walking speed), multiple regression analysis was conducted with age adjustment. To study the association of falls and 25(OH)D levels, logistic regression analysis was

TABLE 1. CHARACTERISTICS OF STUDY PARTICIPANTS

Characteristics	*Male (n = 950)*	*[Min–Max]*	*Female (n = 2007)*	*[Min–Max]*	*p*
Age (yr, mean ± SD)	74.5 ± 5.1	[65–89]	75.4 ± 4.7	[65–92]	<0.001*
Fall experience over the previous year (yes, %)	103 (10.8)		372 (18.5)		<0.001†
Hand grip strength (kg, mean ± SD)	31.4 ± 6.6	[10–52]	18.8 ± 4.6	[1–38]	<0.001*
Stork standing time with eyes open (s, mean ± SD)	37.1 ± 22.5	[1–95]	35.8 ± 23.3	[1–88]	0.152*
Normal walking speed (m/s, mean ± SD)	1.23 ± 0.26	[0.40–2.08]	1.18 ± 0.29	[0.15–2.00]	<0.001*
Serum albumin (g/dl, mean ± SD)	4.35 ± 0.23	[3.4–5.0]	4.31 ± 0.21	[3.3–5.0]	<0.001*
Serum 25(OH)D level (ng/ml, mean ± SD)	28.5 ± 5.0	[8–42]	24.2 ± 4.9	[9–38]	<0.001*
Age group	(n)		(n)		
65–69	(173) 28.4 ± 4.5		(163) 26.8 ± 3.8		
70–74	(314) 28.5 ± 5.3		(763) 24.2 ± 4.6		
75–79	(320) 28.6 ± 4.9		(675) 24.0 ± 5.1		
80+	(143) 28.4 ± 5.5	$p = 0.97$‡	(406) 23.6 ± 5.3	$p < 0.001$‡	
Quartile [cut-off value of 25(OH)D for each percentile]	(ng/ml)		(ng/ml)		
25 percentile	25.0		21.0		
50 percentile	29.0		24.0		
75 percentile	32.0		28.0		
Insufficient (<20 ng/ml, %)	4.8		17.7		<0.001†

* Student's *t*-test for continuous variables between males and females.
† χ^2 test for categorical variables between males and females.
‡ ANOVA in both males and females.

conducted using "fall experience over the previous year" as a dependent variable and other variables [age, physical performance test, serum albumin, and 25(OH)D levels] as independent variables.

RESULTS

The basic characteristics of the subjects, including age, handgrip strength, stork standing with the eyes open, normal walking speed, serum albumin level, and 25(OH)D level, are shown in Table 1. Mean ages were 74.5 ± 5.1 yr in men and 75.4 ± 4.7 yr in women ($p < 0.001$). Concerning fall experience, the numbers (percentage) of individuals who experienced a fall over the previous year were 103 (10.8%) in men and 372 (18.5%) in women. The prevalence of falls was significantly higher in women than men ($\chi^2 = 28.30$, $p < 0.0001$). The number of falls varied from one to five. Sixty-one men (59.2%) and 259 women (69.8%) had experienced only one fall, whereas 42 men and 113 women had recurrent falls of two or more times. The predominant cause of falling was "tripping" in both sexes, followed by "slipping" and "missing a step." The consequences of falling, that is, the conditions of injury, were clearly different between men and women. Although "bruise" (38.7%) and "scratch" (26.1%) were frequent among women, "no injury" accounted for nearly one half (44.7%) of men.

The mean 25(OH)D concentrations were 28.5 ± 5.0 ng/ml in men and 24.2 ± 4.9 ng/ml in women ($p < 0.001$). Only in women was there a significant decline of 25(OH)D concentration with increasing age by ANOVA ($p < 0.001$). Forty-six (4.8%) men and 356 (17.7%) women had a 25(OH)D level of <20 ng/ml (50 nM; $p < 0.001$).

Comparisons of the rate of fall experience over the previous year, average number of falls, physical performance tests, and serum albumin levels are shown in Table 2. Subjects who were judged as not appropriate for the tests because of high blood pressure, heart failure, lumbago, knee pain, etc., were excluded from the physical performance tests. Thus, the total number of subjects who underwent the physical performance tests was 2837 (917 men and 1921 women) in the handgrip strength test, 2519 (792 men and 1727 women) in the stork standing test, and 2044 (455 men and 1589 women) in the normal walking speed test. First, comparisons were conducted between the lowest quartile group (≤25.0 ng/ml in men and ≤21.0 ng/ml in women) and the higher groups. Both hand grip strength and stork standing time were significantly different in men, and all of the measurements were significantly different in women. Furthermore, for women only, the rate of fall experience and average number of falls were significantly higher in the lowest quartile group compared with the other groups ($p = 0.02$ for the rate and $p = 0.021$ for the number). Second, comparisons were conducted between the 25(OH)D insufficiency group (<20 ng/ml) and the normal group (≥20 ng/ml). Hand grip strength and serum albumin level in men, and all measurements except hand grip strength in women, were significantly different between these two groups. Stork standing time, normal walking speed, and serum albumin level were significantly lower in the 25(OH)D insufficiency group. As for rate of fall experience and average number of falls, only women showed that the 25(OH)D insufficiency group had a significantly higher rate ($p = 0.001$) and average number ($p = 0.006$) of falls than the normal group.

Table 3 shows the associations of serum concentrations of albumin and 25(OH)D with physical performance tests by multiple regression models adjusted for age. Serum 25(OH)D level showed significant association with all three variables in the physical performances of both men and women. However, serum albumin level showed significant association only with handgrip strength in both sexes.

Calculations of Pearson's correlation coefficient (r) were

TABLE 2. SERUM 25(OH)D LEVEL AND CHARACTERISTICS FOR MALES AND FEMALES

Characteristics	Male: Lower (≦25.0 ng/ml) (n = 249)	Male: Higher (≧26.0 ng/ml) (n = 701)	p	Female: Lower (≦21.0 ng/ml) (n = 576)	Female: Higher (≧22.0 ng/ml) (n = 1431)	p
Fall experience over the previous year (yes, n, %)	27 (10.8)	76 (10.8)	0.938*	129 (22.4)	243 (17.0)	0.020*
Average number of falls (times, mean ± SD)	2.1 ± 2.4	1.7 ± 1.1	0.422†	1.6 ± 1.2	1.4 ± 0.8	0.021[b]
Hand grip strength (kg, mean ± SD)	30.5 ± 6.7	31.7 ± 6.5	0.020[b]	17.9 ± 4.6	19.2 ± 4.6	0.002[b]
Stork standing time with eye open (s, mean ± SD)	34.6 ± 22.5	38.2 ± 22.5	0.046[b]	31.7 ± 23.5	37.7 ± 23.0	<0.001†
Normal walking speed (m/s, mean ± SD)	1.19 ± 0.26	1.25 ± 0.26	0.061†	1.12 ± 0.28	1.21 ± 0.27	<0.001†
Serum albumin (g/dl, mean ± SD)	4.34 ± 0.24	4.35 ± 0.26	0.616†	4.28 ± 0.23	4.33 ± 0.21	<0.001†
	Insufficiency (<20.0 ng/ml) (n = 46)	*Normal (≧20.0 ng/ml) (n = 904)*	*p*	*Insufficiency (<20.0 ng/ml) (n = 356)*	*Normal (≧20.0 ng/ml) (n = 1651)*	*p*
Fall experience over the previous year (yes, n, %)	3 (6.5)	100 (11.1)	0.454*	92 (25.8)	280 (17.0)	0.001*
Average number of falls (times, mean ± SD)	2.7 ± 0.6	1.8 ± 1.5	0.338†	1.7 ± 1.3	1.4 ± 1.5	0.006†
Hand grip strength (kg, mean ± SD)	28.5 ± 6.4	31.5 ± 6.5	0.003†	18.1 ± 4.7	19.0 ± 4.6	0.420[b]
Stork standing time with eye open (s, mean ± SD)	31.4 ± 22.9	37.5 ± 22.5	0.124†	29.8 ± 22.9	37.2 ± 23.2	<0.001†
Normal walking speed (m/s, mean ± SD)	1.16 ± 0.79	1.24 ± 0.26	0.138†	1.11 ± 0.29	1.20 ± 0.27	<0.001†
Serum albumin (g/dl, mean ± SD)	4.27 ± 0.26	4.35 ± 0.22	0.027†	4.27 ± 0.23	4.32 ± 0.21	<0.002†

* The Mantel-Haenszel χ^2 test adjusted for age.
† ANCOVA adjusted for age.

TABLE 3. ASSOCIATION OF SERUM ALBUMIN AND 25(OH)D LEVELS WITH PHYSICAL PERFORMANCE FOR MALES AND FEMALES

	Handgrip strength			Stork standing time			Normal walking speed		
	β	SE	p	β	SE	p	β	SE	p
Men									
Albumin	0.096	0.852	0.001	0.002	3.644	0.947	0.025	0.053	0.576
25(OH)D	0.067	0.037	0.020	0.075	0.152	0.030	0.111	0.002	0.012
Women									
Albumin	0.109	0.459	<0.001	0.037	2.502	0.106	0.045	0.030	0.051
25(OH)D	0.062	0.020	0.003	0.109	0.105	<0.001	0.143	0.001	<0.001

Values are adjusted for age. p values are derived from multiple regression analysis.
β, standardized regression coefficient.

carried out to confirm the correlation among the three physical performance tests. The results showed high and significant intercorrelation for these three variables; correlation coefficients were from 0.23 (handgrip strength and stork standing time) to 0.35 (stork standing time and normal walking speed) in men and from 0.31 (handgrip strength and stork standing time) to 0.47 (stork standing time and normal walking speed) in women, and all were significant at $p < 0.001$. Therefore, we adopted only "normal walking speed" to represent the physical performance tests as well as the independent variable for the final multiple logistic regression model.

Table 4 shows the associations of fall experience over the previous year with normal walking speed, serum albumin, and 25(OH)D levels by multiple logistic regression models with age adjustment. Normal walking speed (unit = 0.1 m/s) showed a significant protective effect against falls in

TABLE 4. MULTIPLE LOGISTIC REGRESSION MODEL OF FACTORS ASSOCIATED WITH FALL EXPERIENCE OVER THE PREVIOUS YEAR

Risk factor	Male: OR	Male: 95% CI	Male: p	Female: OR	Female: 95% CI	Female: p
Age (yr)	1.02	0.95–1.10	NS	1.02	0.99–1.06	NS
Normal walking speed (0.1 m/s)	0.87	0.77–0.97	0.015	0.92	0.88–0.97	0.001
Albumin (g/dl)	1.69	0.45–6.33	NS	1.60	0.88–2.90	NS
25(OH)D (ng/ml)	1.00	0.95–1.06	NS	0.97	0.94–0.99	0.010

Dependent variable was "fall experience over the previous year" (yes = 1, no = 0).
The unit of normal walking speed was transferred from meters per second to 0.1 m/s in this final multiple logistic regression model.
NS, not significant.

both men (OR = 0.87, 95% CI = 0.77–0.97) and women (OR = 0.92, 95%CI = 0.88–0.97). Serum 25(OH)D level (unit = 1 ng/ml) also had a significant and independent protective effect for falls found only in women (OR = 0.97, 95% CI = 0.94–0.99, $p = 0.01$).

DISCUSSION

Maintenance of physical performance in old age is an important factor not only for a healthy and independent life in the community but also a way to prevent falls that can lead to a marked decline in activities of daily living (ADLs). A national survey in Japan has shown that the annual frequency of falls is >20% in those >65 yr of age and that ~10% of these falls result in fractures.[27]

This study showed that the proportion of people who reported falls in the previous year increased with age and that falls were more common in women than in men.[20] These findings are consistent with the results of other studies of falls among community-dwelling elderly.[28–32] Aoyagi et al.[33] reported that the proportion of falls in the previous year after age standardization for Japanese was about one half of that of whites. Furthermore, the incidence of hip fracture among Japanese elderly was found to be much lower than that reported for whites in North America and Europe.[34] This difference is probably partly the result of the lower fall rate among Japanese, suggesting that both ethnicity (genetics) and lifestyle (environmental) factors may be involved.[14] Recently, some studies have shown that lower serum vitamin D level is a risk factor for falls and fall-associated physical performance among the elderly.[9,10,35] At present, however, there are few studies on the association between serum 25(OH)D level and falls in Japanese community elderly, whose frequency of falls is less than that observed in Europe and the United States.[6–8,13]

In this study, we found that there were significant sex differences of 25(OH)D level on average and in a pattern of decline along with aging; namely, women had significant lower serum 25(OH)D levels at any age group and showed remarkable declines with aging. One of the reasons for this sex difference may be general inactivity and lower intake of vitamin D from daily food among Japanese elderly women compared with men. One Japanese national survey showed that, compared with 39.1% of men, 32.6% of women engage in physical activity for at least 30 min two or more times a week.[36] Our previous study also reported that women had significantly lower rates of regular sports activity than men (13.8% versus 21.5%).[37] Furthermore, we recently reported that one of the significant predictors for cessation of regular activity was "female sex" as well as "smoking" and "slow walking speed" from a population-based, 2-yr follow-up study.[38] The national survey also showed that women took smaller amounts of vitamin D than men (8.6 ± 9.0 versus 8.9 ± 10.0 μg/d on average). In particular, for elderly respondents ≥70 yr of age, the average intake of vitamin D in women (8.6 ± 9.0 μg/d) was much less than that in men (10.3 ± 10.1 μg/d).[36] These factors of physical inactivity and lower intake of daily vitamin D in elderly women may have caused their observed higher frequency of 25(OH)D insufficiency compared with men. It is known that the main source of vitamin D in humans is considered to be through the skin, where vitamin D is produced during exposure to UVB sunlight.[39,40] In our study, to avoid any seasonal variation of serum 25(OH)D, data collection was carried out only during autumn (October/November), which meant that serum 25(OH)D levels would be almost stable and at an average throughout the year among a normal Japanese population.[41]

The range of serum 25(OH)D levels was 8–42 ng/ml in men and 9–38 ng/ml in women. Although it is still uncertain what an optimal 25(OH)D level is, it has been suggested that the range of 25(OH)D levels should be 32–100 ng/ml, with a lower limit somewhere between 15 and 36 ng/ml.[41–43] In this study, we defined a 25(OH)D level of <20 ng/ml as insufficiency. From this, we judged that the prevalence of 25(OH)D insufficiency was significantly predominant in women (17.7%) compared with men (4.8%; $p < 0.001$). Studies concerning the prevalence of 25(OH)D insufficiency in various populations have been challenged because of the lack of standardization of assays and different cut-off points.[44] A comparison of serum 25(OH)D level between hip fracture patients and nonhip fracture controls in Japan showed that average serum 25(OH)D concentrations were significantly different: 17.8 ng/ml in hip fracture patients and 25.8 ng/ml in nonhip fracture controls.[45] Furthermore, 62% of the hip fracture patients ($N = 50$) had 25(OH)D insufficiency, defined as having a serum 25(OH)D concentration <20 ng/ml. In this context, the elderly whose 25(OH)D levels were <20 ng/ml can be considered to be in insufficiency and at high risk of a hip fracture, which indeed has increased sharply during last two decades in Japan.[46]

In comparisons of serum 25(OH)D levels and fall-associated variables between the group of participants in the lowest quartile and the groups of the three other higher quartiles of serum 25(OH)D level, all variables but normal walking speed in men were significantly lower in the lower 25(OH)D group than in the higher group. Our findings are consistent with the results from a Swedish population-based study of 986 community-living elderly women[47] that showed that the lower 25(OH)D group was significantly correlated with inferior gait speed, inferior balance test, and lower knee extension/flexion strength results, all of which are fall-associated variables.

The rate of fall experience over the previous year by serum 25(OH)D level was significantly different only in women [i.e., 22.4% in the lower 25(OH)D group and 17.0% in the higher group ($p = 0.02$) and also 25.8% in the insufficiency group and 17.0% in the normal group ($p = 0.001$), respectively]. The average numbers of falls were also significantly different between the lower and higher groups ($p = 0.021$) and between the insufficient and normal groups ($p = 0.006$), respectively. This finding that lower serum 25(OH)D level or 25(OH)D insufficiency status is associated with falls among elderly women is consistent with many previous studies.[3,4,11] However, there is a controversy about which type of vitamin D [i.e., 25(OH)D or $1,25(OH)_2D_3$] is associated with fall risk. Faulkner et al.,[48] who examined the relationship of vitamin D supplementation and the serum concentration of vitamin D metabolites

with falls in older white, community-dwelling women (n = 389) in the Unites States, reported that only the higher serum $1,25(OH)_2D_3$ concentration was associated with a lower fall risk but that 25(OH)D concentration was not associated with falls. In our study, as one of the study limitations, serum $1,25(OH)_2D_3$ was not assessed in the participants undergoing the mass health examination.

Further analysis on the association of serum albumin and 25(OH)D levels with the fall-associated variables in this study showed that only serum 25(OH)D level had a significant association with all three fall-associated variables in both sexes. On the other hand, serum albumin had a significant association only with handgrip strength in both sexes. The mechanism connecting serum albumin and muscle mass or power is not clear.[49,50] However, serum albumin concentration may be a marker of the protein status of an individual, with lower values indicating a diminished protein reserve and stimulated catabolic processes leading to muscle break down and also muscle strength decline.[50] Thus, low serum albumin, even within a normal range, is independently associated with weaker muscle strength and future decline in older men and women.[51,52]

Serum 25(OH)D concentration is an important determinant of muscle mass and sarcopenia. In an observational study of community-dwelling elderly in the Netherlands, incident sarcopenia, defined as a minimum of 40% decline in muscle strength and 3% decline in muscle mass, was found to be twice as likely among 25(OH)D-deficient elderly [25(OH)D level < 10 ng/ml] than among elderly with a 25(OH)D level of >20 ng/ml.[7] With respect to the role of vitamin D in muscle strength, the majority of the actions of vitamin D are mediated through $1,25(OH)_2D_3$ binding to nuclear vitamin D receptor (VDR) that can directly modulate the transcription of the gene possessing a functional binding site for VDR in its regulatory region.[8,53] Therefore, muscle strength seems to be influenced by the VDR genotype in the muscle cell. With the use of specific restriction endonucleases, several VDR polymorphisms have been determined. In nonobese, older women, a 23% difference in quadriceps strength and a 7% difference in grip strength between two homozygote types of a restriction site have been found.[54] The action of vitamin D is affected by allelic variance of the VDR. A genomic study on VDR polymorphism has shown that Japanese women had much lower frequency of homozygote BB (1.4%) than white women (16.7%).[55] In this context, if the VDR polymorphism affects not only the BMD but also muscle strength of elderly women, Japanese women in general may have an advantage with respect to their lower frequency of falls and associated hip fractures.

As for the association of serum 25(OH)D level and fall experience over the previous year by multiple logistic regression models, even after the adjustment of other fall-associated variables, serum 25(OH)D level was independently associated with falls in women as well as normal walking speed in this study. A considerable number of population-based studies have also been conducted on walking ability in relation to the occurrence of falls in the elderly.[56–60] Increased body sway, uneven distances, and uneven timing during walking were identified as risk factors for falls.[61,62] The authors have previously reported that both fall experience over the previous year and a decline in walking speed were very strong predicators of the occurrence of frequent falls in a 5-yr follow-up cohort study among Japanese community-living elderly.[18] Muscle function or strength as the single most important component for walking ability has been consistently identified as a risk factor for hip fractures as a consequence of falls in the elderly. Subclinical 25(OH)D insufficiency is also considered to be an important risk factor for hip fractures in elderly people in both white[63,64] and Japanese[45] populations. We have suggested that elderly women with lower 25(OH)D levels and with a significant decline in their fall-associated variables tend to decline in walking capability and be more vulnerable to falls even in elderly populations of Japanese women, whose fall rate has been reported to be low.

A relevant issue regarding the role of 25(OH)D in physical performance is that vitamin D supplementation has been reported to be significantly effective in maintaining or improving physical performance and preventing falls among the elderly. In a recent randomized and multiple-dose study, Broe et al.[65] reported that a high dose of vitamin D (800 IU/d) reduced the risk of falls dramatically by 72% lower (adjusted-incidence rate ratio) than participants taking a placebo over the same 5-mo period in a nursing home. However, the question of which type of vitamin D supplementation (i.e., either cholecalciferol or calciferol) is more effective at reducing falls among community-living elderly is still controversial. The association of vitamin D supplementation with better physical performance related to the risk of falls and/or reduced falls is unclear at present. For example, a meta-analysis of five randomized controlled trials provided some evidence that vitamin D supplementation might reduce falls,[10] whereas the results of a second meta-analysis of four randomized controlled trials of vitamin D found no such evidence.[66]

Our findings suggesting that there are significant relationships between serum 25(OH)D and fall-associated physical performance and with falls themselves could provide guidance about how to prevent falls and fractures, particularly hip fractures resulting from falls among community-living elderly. Two such countermeasures are to improve muscle strength, especially in the lower extremities, and to enhance balance ability.[67,68] For example, from a randomized controlled exercise intervention trial for Japanese community-dwelling elderly, we have proven that a moderate exercise intervention program in addition to a home-based program significantly improved fall-associated variables and, consequently, decreased the incidence of falls for 1.5 yr after the intervention.[67]

Another countermeasure would be to maintain a high level of serum 25(OH)D by adequate intake of foods containing vitamin D, supplementation, and exposure to sunlight. Incidentally, fish consumption seems to play an important role in maintaining adequate vitamin D nutrition among elderly Japanese.[69] In general, these countermeasures seem to be consistent with the traditional Japanese lifestyle. Our earlier study using risk factor analysis of hip fractures in elderly Japanese showed that such a traditional

Japanese lifestyle, including living on Japanese tatami mats and eating fish daily, was strongly associated with a decrease in the risk of hip fractures.[14] Living on Japanese tatami mats, including futon-style bedding, seems have great benefits for preventing falls and hip fractures by continuously strengthening the muscles of the hip girdle and lower extremities by sitting, squatting, and frequent standing over the course of many years. Furthermore, consumption of dark-meat fish, which is rich in vitamin D, also seems to be beneficial for maintaining adequate 25(OH)D levels in the elderly, especially in the winter season.[69]

Before detailing our final conclusions, some limitations of our study must be considered. (1) The subjects analyzed were not selected randomly from the study population; as well, they were relatively healthy elderly persons who were able to travel from their homes to the health checkup venue. As a result, elderly persons with lower physical functional capacity were excluded. (2) Plasma $1,25(OH)_2D_3$, albumin-corrected calcium, and PTH, which would provide information on the extent of any primary vitamin D deficiency,[8,48,70] and creatine clearance that may affect the metabolism of vitamin D through the kidney,[71] were not assessed in this study. It is well known that increased secretion of PTH is associated with decreased serum 25(OH)D levels, which may commonly occur in the elderly. However, according to a survey on the nutritional status of vitamin D among Japanese community-dwelling elderly, Nakamura et al.[72] reported that only 1.8% of the subjects had elevated intact PTH levels. (3) We did not analyze the genotype of the VDR that could influence muscle strength and, likely, the fall rate as well. (4) This study was cross-sectional and therefore did not provide cause/effect relationships, although we showed a significant correlation between physical performance and serum 25(OH)D levels in Japanese community-dwelling elderly. Therefore, a longitudinal follow-up study and controlled clinical trials would seem necessary to confirm the role of serum 25(OH)D in falls and its association with the physical performance of the elderly.

In conclusion, our findings showed that a lower serum 25(OH)D level was significantly associated with fall experience over the previous year and with fall-associated variables in Japanese women whose fall rate has been reported to be about one half that of white women. This indicates that serum 25(OH)D level has a common and positive relationship with the occurrence of falls in elderly women, and probably beyond any genetic background represented by VDR phenotype differences and anthropometric and nutritional differences.

Muscle weakness or sarcopenia, frailty, and falls, all of which can be frequent among the elderly and therefore are often categorized as geriatric syndrome, have a major impact on the elderly in terms of both morbidity and mortality. The connections between these items related to geriatric syndrome and 25(OH)D has been well established by many population-based epidemiological studies including this one. Such geriatric syndromes could be prevented by both exercise interventions and adequate levels of serum 25(OH)D; these would help maintain good physical performance and functional capacity for a high quality of life among community-dwelling elderly.

ACKNOWLEDGMENTS

This work was supported in part by a Grant-in-Aid for Scientific Research from the Ministry of Education and Culture of Japan (16390187) and a Research Grant from the Research Society for Metabolic Bone Diseases in Japan.

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Received in original form August 15, 2007; revised form March 14, 2008; accepted March 21, 2008.

生活習慣病ガイドブック

編集　兵庫県医師会生活習慣病対策プロジェクト会議

Ⅷ 脳卒中

－脳血管障害の診断と危険因子について－

櫻井　孝

❶ 脳卒中の概説

1．致死的な脳血管障害は減少しているが、後遺症を残す患者が増加している。機能予後の改善のため、超急性期治療の可能性を考える。
2．超急性期に診断に必要なすべての所見をとることは不可能である。治療方針を決定するための必要最小限の診断を行い、一刻も早く必要な画像検査を行う。
3．急性発症する神経精神症候には脳卒中以外の疾患の可能性も考える。
4．脳卒中の局在診断のみならず、閉塞血管、発症機序を明らかにし、病型分類に応じた治療、再発予防を行う。

❷ 脳卒中超急性期の診断と全身管理

1．問診のポイント：「今回、何が起ったか」を明確にする。家族の立ち会いを得て、発症前の ADL と比較して今回の発症後にできなくなったことを明らかにする。「急性発症か、緩徐進行性か、階段状悪化、何をしていたときか？」、発症時刻の特定、随伴症状（頭痛、頚部痛、発熱）など。高血圧、糖尿病、高脂血症、心疾患、心房細動、内服薬などの既往。
2．診察のポイント：一般身体所見、意識・精神状態（Japan Coma Scale）、注意・見当識、精神状態、認知機能。神経学的診察では、脳神経系、運動系（Barre 徴候、Mingazzini 徴候）、感覚系（顔面・体幹・四肢の最低各一点で確認）、反射（深部腱反射、病的反射）、協調運動（指鼻・膝踵試験、つぎ足歩行）。
3．脳梗塞全般としては、発症直後には絶対安静が必要（15度程度の頭部挙上は可能）。
4．脳卒中発症直後の高血圧治療は、高血圧性脳症、クモ膜下出血が強く疑われる場合以外は病型診断が確定してから行う。
5．脳梗塞超急性期の組織プラスミノーゲンアクチベーター（t-PA）の静注療法：治療開始時刻は発症後 3 時間以内。アテローム血栓性脳梗塞、ラクナ梗塞、心原性脳塞栓症はいずれも対象となる。

Japan Coma Scale（JCS）

Ⅲ．刺激しても覚醒しない状態（3桁の点数で表現）
（deep coma、coma、semicoma）

300．痛み刺激に全く反応しない
200．痛み刺激で少し手足を動かしたり顔をしかめる
100．痛み刺激に対し、払いのけるような動作をする

Ⅱ．刺激すると覚醒する状態（2桁の点数で表現）
（stupor、lethargy、hypersomnia、somnolence、drowsiness）

30．痛み刺激を加えつつ呼びかけを繰り返すと辛うじて開眼する
20．大きな声または体を揺さぶることにより開眼する
10．普通の呼びかけで容易に開眼する

Ⅰ．刺激しないでも覚醒している状態（1桁の点数で表現）
（delirium、confusion、senselessness）

3．自分の名前、生年月日が言えない
2．見当識障害がある
1．意識清明とは言えない

注　R：Restlessness（不穏）、I：Incontinence（失禁）、A：Apallic state または Akinetic mutism
たとえば30Rまたは30不穏とか、20Iまたは20失禁として表す。

❸ 脳血管障害（脳卒中）の分類

National Institute of Neurological Disorders and Stroke の分類による（注1）

A．無症候性脳血管障害
B．局所障害型の脳血管障害
　1．一過性脳虚血発作（注2）
　2．脳卒中
　　a．くも膜下出血
　　b．脳出血
　　c．脳梗塞
　　(1)　アテローム血栓性
　　(2)　心原性塞栓性
　　(3)　ラクナ梗塞
　　(4)　その他
C．脳血管性痴呆
D．高血圧性脳症

注1：脳の血管の破綻により生じる疾患を脳血管障害という。脳血管障害の中で突然発症をするものだけを脳卒中として区別する。
注2：脳虚血によると考えられる局所脳神経症状が一過性に出現し、24時間以内に完全に消失するもの。

④ 脳卒中慢性期：危険因子の管理と予防

1．脳梗塞

1）高血圧は脳梗塞の最大の危険因子であり、降圧療法が推奨される（グレードA）。脳卒中の予防には血圧は低ければ低いほどよい（The lower, the better）。降圧目標は140/90mmHg未満（高齢者）、130/85mmHg未満（若年・中年）。

2）糖尿病は脳梗塞発症のリスク（2～3倍）。血糖の管理だけでは脳卒中を予防しにくく、合併した危険因子すべてに対処する（血圧は130/80mmHg未満）。

3）脳卒中予防効果が証明された脂質異常治療薬はスタチンのみ。

4）喫煙は脳梗塞発症のリスク（2～4倍）。禁煙により脳卒中発症リスクは禁煙後2年以内に急速に減少し、5年以内に非喫煙者と同じレベルになる。

5）適量を超える飲酒は脳梗塞のリスク。日本酒1日3合（エタノール60～70g）以上の飲酒で、全脳卒中の発症増加（1.9倍）。少量の飲酒は脳梗塞のリスクを下げると言う。

6）弁膜症を伴わない心房細動（NVAF）を伴う脳梗塞の予防にワルファリンが有効（international normalized ratio（INR）2.0～3.0でコントロール）。しかし日本人、特に70歳以上では、やや低用量のワルファリン（INR 1.6～2.6）が勧められる。INR >2.6にて出血性合併症は急増する。

7）無症候性脳梗塞は、脳梗塞の危険因子。無症候性脳梗塞から発症する脳卒中の約2割が脳出血であり、抗血小板薬の投与は高血圧の管理を厳重に行った上で行う。

8）非心原性脳梗塞（アテローム血栓性脳梗塞、ラクナ梗塞）の再発予防上、最も有効な抗血小板療法はアスピリン（75～150mg／日）。ラクナ梗塞の再発予防に対してエビデンスを有する抗血小板薬は現時点ではシロスタゾールのみ。抗血小板薬（アスピリン、チクロピジン、クロピドグレル）による頭蓋内出血の危険性は0.2～0.3％／年、ワルファリンでは0.3～1.1％／年。

9）脳循環代謝改善薬：イブジラスト、酒石酸イフェンプロジルは脳梗塞後のめまいに、ニセルゴリンは脳梗塞後の認知障害に有効。

10）脳卒中の18～62％にうつ状態を合併する。うつ状態は、認知機能低下、ADL回復の遅延、死亡（3倍）のリスクとなる。選択的セロトニン再取り込み阻害薬（SSRI）を含む抗うつ薬の投与が推奨される。

11）中等度以上の症候性頸動脈狭窄病変（狭窄率50％以上、特に70％以上）では、内科的治療（抗血小板療法を含む）＋頸動脈内膜剥離術（CEA）が有効。

2．脳出血

1）脳出血の発症の危険因子：年齢、性別、高血圧、過量飲酒、血清総コレステロール低値。拡張期血圧＞95mmHgでは、40～59歳で9.0倍、60歳以上で3.4倍増加。多量飲酒は脳出血のリスク（1日60g以上で2.18倍）。

2）定期的な運動は、脳出血の予防に有効である可能性がある。

3） 1日3種類の果物や野菜を取るごとに脳出血の危険性が51%減少すると言う。
4）脳出血後の脳卒中再発では、約半数が脳出血、残り半数が脳梗塞である。
5）高血圧性脳出血では血圧のコントロール不良例で再発が多い。脳出血の再発予知因子としては、脳葉出血が重要であり、ApoEの遺伝子多型が関連する。
6）維持透析患者では、脳出血を発症する危険性が高い（5～10倍）。

3．クモ膜下出血

1）女性に多い（男女比1：2）。
2）予後不良例が約40%存在する。発症時の意識障害の程度が予後と相関する。
3）クモ膜下出血の危険因子：脳動脈瘤や脳動静脈奇形の存在の他、喫煙習慣、高血圧保有、一週間に150g以上の飲酒。
4）一般医療機関から脳神経外科専門施設への搬送は、速やかに行われるべきである。移送中の再出血の予防のため、血圧管理、鎮痛鎮静、医師の同乗が望ましい。

参考資料

1）日本脳卒中学会：脳卒中治療ガイドライン2004（http://www.jsts.gr.jp/jss08.html）
2）日本高血圧学会：高血圧治療ガイドライン2004

生活習慣病ガイドブック

編集　兵庫県医師会生活習慣病対策プロジェクト会議

Ⅸ 認知症

－認知症の診断と予防－

櫻井　孝

❶ 認知症の概説

1．認知症とは、いったん獲得した知的機能が持続的に低下し、複数の認知障害があるために社会生活に支障をきたすようになった状態である。
2．認知症の頻度は65歳以上の高齢者で約６～７％であり、加齢とともに増加する。
3．近年、認知症に対する社会の見方も一変しており、全診療科の積極的な関わりが求められる。

❷ 認知症を来す疾患

1．アルツハイマー病と血管性認知症が最多（両疾患を合わせると80％程度）。
2．脳腫瘍・慢性硬膜下血腫・正常圧水頭症などの脳外科的治療の対象となる疾患、甲状腺機能低下症などの内分泌疾患、重症の肝臓病や腎臓病、ビタミン欠乏症などの「治療により脳機能が改善する認知症」を見逃さない（表１）。

表１　日常診療でよく見られる認知症の原因疾患

1．脳血管性の疾患
　脳血管障害（脳出血、脳梗塞など）による認知症
2．退行変性疾患
　アルツハイマー病、パーキンソン病、びまん性レビー小体病など
3．内分泌・代謝性中毒性疾患
　甲状腺機能低下症、下垂体機能低下症、ビタミン B_{12} 欠乏症、ビタミン B_1 欠乏症、ペラグラ、ミトコンドリア脳筋症、肝性脳症、透析脳症、低酸素症、低血糖症、アルコール脳症、薬物中毒など
4．感染性疾患
　脳炎・髄膜炎、脳膿瘍、進行麻痺、クロイツフェルト・ヤコブ病など
5．腫瘍性疾患
　脳腫瘍、髄膜浸潤など
6．外傷性疾患
　慢性硬膜下血腫、頭部外傷後遺症など
7．その他
　正常圧水頭症、神経ベーチェット、サルコイドーシス、シェーグレン症候群など

3．脳血管障害、脳症や薬剤の副作用（表2）によるせん妄状態など治療可能な状態も少なくない。
4．うつ病や他の統合失調症は認知症と混乱されることがある（仮性認知症）。

表2　高齢者のせん妄の原因

1．薬剤性：抗パーキンソン病薬、抗コリン薬、抗潰瘍薬（H_2ブロッカー）、抗ヒスタミン薬、解熱鎮痛消炎剤、抗精神薬、抗不安・鎮静・睡眠薬、抗うつ薬、抗ウイルス薬（アシクロビル）、抗腫瘍薬（植物アルカロイド、L-asparaginase）、循環器用薬：（抗不整脈薬、β遮断薬、ジギタリス、硝酸薬）、気管支拡張剤（キサンチン）、咳止め（リン酸コデイン）、副腎皮質ステロイド、インターフェロン、甲状腺末、抗結核薬（エタンブトール、イソニアジド、サイクロセリン）、アルコールなど
2．感染症：肺炎、尿路感染症、敗血症など
3．代謝異常：脱水、電解質異常、低血糖、尿毒症、肝性脳症、甲状腺機能亢進症、クッシング症候群、ビタミン欠乏症
4．循環器疾患：心不全、心筋梗塞、不整脈
5．中枢神経疾患：脳血管障害、認知症、慢性硬膜下血腫、脳髄膜炎、脳腫瘍
6．呼吸不全、CO_2ナルコーシス
7．SLEなどの自己免疫疾患
8．悪性腫瘍
9．手術・全身麻酔

3 認知症の診断

日常診療上のヒント

認知症の診断において、詳細な問診を行うことが診断に到達する早道である。またすべての一般内科、神経内科的診察を行うことは困難であり、主要症候をまずスクリーニングする。

1．問診のポイント：1）もともとの認知能（職歴、学歴、生活歴を参考）、2）発症時期、3）発症後の経過（進行の速さ、階段状悪化）、4）生活上の支障（ADLの低下）、5）記憶、見当識、注意、言語、遂行機能障害、失認、失行を示すエピソード、6）神経脱落症状、7）他の身体症候、8）体重変化など。他の身体・神経疾患、頭部外傷、生活習慣病などの既往、内服薬、飲酒、喫煙などの情報を得る。
2．診察のポイント：脳神経（眼球運動、眼振、対光反射、構音・嚥下障害）、パーキンソン症候（安静時振戦、筋トーヌス）、筋力（Barre test）、深部腱反射、病的反射、歩行、協調運動、構成機能（狐、リング、鳩の手まね）など。
3．高次脳機能のスクリーニングには、改訂長谷川式簡易知能評価スケール（HDS-R）（表3）、ミニメンタルテスト（MMSE）が有用である。
4．採血検査で治療可能な認知症をチェックする（WBC、RBC、Hb、Hct、Plt、

APTT、PT、Fib、総蛋白、アルブミン、AST、ALT、LDH、γ-GTP、ALP、BUN、Cr、CK、Na、K、Ca、P、T-Chol、TG、HDL-C、血糖、葉酸、ビタミンB_1、ビタミンB_{12}、fT_4、TSH、アンモニア、RPR、尿検査一般）。

5．脳画像検査（頭部CT／MRI）で、慢性硬膜下血腫、脳腫瘍などの疾患を除外する。血管病変の程度を評価する。

6．高齢者のアルツハイマー病では、遅延再生（短期記憶）、時間見当識の障害が早期から現れ、認知障害は緩除に進行する。

7．脳血管性認知症の診断には、①認知症の確認、②血管病変に伴う神経所見と脳画像で示される脳血管障害の存在、③脳血管障害との時間的関係（3ヵ月以内の認知症発症、または認知機能の急速な低下、動揺性・階段的な悪化）を示すことが要件となる。

日常診療上のヒント

皮質下白質病変（ラクナー梗塞を含む）は認知障害の原因となる。しかし脳画像検査でみられる白質病変の程度のみから、血管性認知症の診断はできない。

表3　改訂長谷川式簡易知能評価スケール

氏名	年令　（男・女）　年　月　日生	
	質問内容	配点
1	お年はいくつですか？（2年までの誤差は正解）	0，1
2	今日は何年の何日ですか？何曜日ですか？ （年、月、日、曜日が正解でそれぞれ1点ずつ）	0，1 0，1 0，1 0，1
3	私たちがいまいる所はどこですか？ （自発的にできれば2点、5秒おいて家ですか？病院ですか？施設ですか？のなかから正しい選択をすれば1点）	0，1，2
4	これから言う3つの言葉を言ってみて下さい。あとでまた聞きますのでよく覚えておいて下さい。 （以下の系列のいずれか1つで、採用した系列に○印をつけておく） 1：a）桜　b）猫　c）電車 2：a）梅　b）犬　c）自動車	0，1 0，1 0，1
5	100から7を順番に引いて下さい。 （100－7は？、それからまた7をひくと？と質問する。最初の答えが不正解の場合、打ち切る。それぞれ1点。）	0，1 0，1
6	私がこれから言う数字を逆からいって下さい。 （6－8－2，3－5－2－9を逆に言ってもらう。3桁逆唱に失敗したら、打ち切る）	0，1 0，1
7	先ほど覚えてもらった言葉をもう一度言ってみて下さい。（自発的に回答があれば各2点、もし回答が無い場合以下のヒントを与え正解であれば1点） a）植物　b）動物　c）乗り物	a：0，1，2 b：0，1，2 c：0，1，2
8	これから5つの品物を見せます。それを隠しますのでなにがあったか言って下さい。（時計、鍵、タバコ、硬貨など必ず相互に無関係なもの）	0，1，2 3，4，5
9	知っている野菜の名前をできるだけ多く言って下さい。（答えた野菜の名前を右欄に記入する。途中で詰まったり、約10秒間待っても答えない場合はそこで打ち切る） 0～5＝0点、6＝1点、7＝2点、8＝3点、9＝4点、10＝5点	0，1，2 3，4，5
満点30点　20点以下　認知症の疑い		合計点数

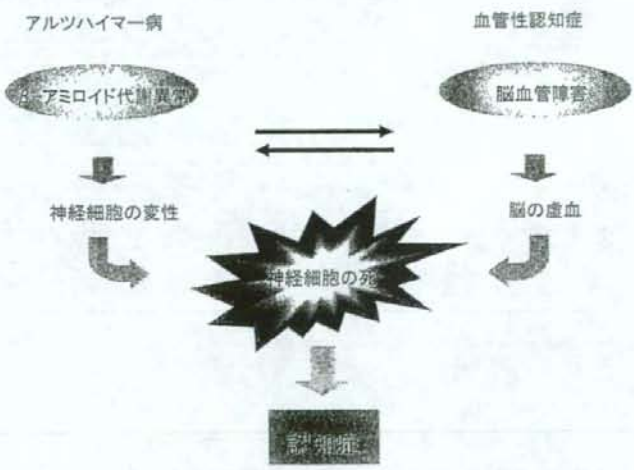
4 認知症の治療

1．高齢者および認知症への処方は若年者よりも少量から始める。また服薬法をできるだけ簡単にする。
2．アルツハイマー病では、ドネペジルが第1選択薬。著効は数10%であるが、多くの症例で会話力や協調性、社会的活動の改善が期待できる。
3．焦燥、妄想、攻撃性に対しては抗精神病薬（ハロペリドール、オランザピン、リスペリドンなど）が用いられるが、生命予後を低下させるとの報告があり、慎重な投与が必要。
4．非薬物療法（回想法、音楽・絵画など）は、患者のストレス減少、残在能力の活用などに有用とされる。またデイ・ケアなどでのグループ活動への参加はADL低下の抑制に効果がある。介護保険を積極的に利用し、精神的・身体的な機能維持を計る。
5．成年後見制度は、医療や財政に関する意志決定の代行制度など、本人の権利を守る意義がある。本人や家族へ助言することが必要。

5 認知症の予防

1．脳血管障害は血管性認知症のリスクである。
2．アルツハイマー病の危険因子として、介入できない危険因子（年齢、遺伝子異常：アポEε4保持）の他に、環境因子が重要である。即ち、動脈硬化、脳卒中、糖尿病、高血圧・低血圧、喫煙、飲酒、高コレステロール、心臓病、高脂肪食、血栓症、高ホモシスティン、高フィブリノーゲン、頭部外傷、抑うつ、閉経、低教育レベルなどで、これらは脳血管障害のリスクとほぼ共通する。アルツハイマー病による神経変性と血管障害は、相加的・相乗的に脳の障害を増悪させる（図1）。

図1　アルツハイマー病と血管性認知症の境界



3．壮年期よりの生活習慣病をきめ細かく管理することで、高齢者になっての認知症の発症を抑制し得る可能性がある。