Prevalence and Risks of Dementia in the Japanese Population: RERF's Adult Health Study Hiroshima Subjects

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OBJECTIVES: To study the prevalence rate of dementia and its subtypes in Japan and to investigate the relationship of risk factors, such as demographic features and disease history, to the prevalence of Alzheimer's disease or vascular dementia.

DESIGN: A prevalence study within a longitudinal cohort study.

SETTING: The original Adult Health Study (AHS) cohort consisted of atomic-bomb survivors and their controls selected from residents in Hiroshima and Nagasaki using the 1950 national census supplementary schedules and the Atomic Bomb Survivors Survey. Since 1958, the AHS subjects have been followed through biennial medical examinations.

PARTICIPANTS: Subjects were 637 men and 1585 women aged 60 years or older in the AHS cohort. Forty-eight subjects resided in hospitals and institutions.

MEASUREMENTS: In addition to the biennial medical examinations ongoing since 1958, a screening test for cognitive impairment (CASI) was conducted by trained nurses between September 1992 and September 1996. The prevalence of dementia and its subtypes was assessed in 343 subjects suspected to have dementia and in 272 subjects with high CASI scores who were selected randomly.

RESULTS: The prevalence of dementia based on *DSM III/R* criteria, using neurological examination, the IQCODE, and CDR $\geq$ 1, was 7.2%. The prevalence of Alzheimer's disease was 2.0% in men and 3.8% in women, and the prevalence of vascular dementia was 2.0% in men and 1.8% in women. The relationship of risk factors to Alzheimer's disease or vascular dementia was investigated by the multivariate logistic linear regression analysis. Odds ratios of Alzheimer's disease for age (in 10-year increments), attained education (in 3-year increments), history of head trauma, and history of cancer are 6.3, 0.6, 7.4, and 0.3, respectively. Odds ratios of vascular dementia for age, history of stroke, and history of hypertension are 2.0, 35.7, and 4.0, respectively. Neither type of dementia showed any significant effect of sex or radiation exposure.

CONCLUSION: This study is the first study of Japanese dementia rates carried out with a protocol similar enough to that of a US study to allow meaningful comparisons. The prevalence rates demonstrated are more similar to US rates than were found in many previous reports in Japan. J Am Geriatr Soc 47:189–195, 1999.

Key words: dementia; prevalence; risk factors; Alzheimer's disease; vascular dementia

Reports up till the 1980s indicated that the prevalence of dementia in the Japanese population was about the same as in the Caucasian population, but the ratios of Alzheimer's disease and vascular dementia differed between the two populations.[1–3] During the 1980s, many prevalence studies in Japan reported a predominance of vascular dementia.[2,3] However, an increased prevalence of Alzheimer's disease has recently been reported.[4] In the present study, participants in the Adult Health Study (AHS) of the Radiation Effects Research Foundation (RERF) were investigated to determine the prevalence of dementia and its subtypes in the Japanese population. Although age is the most important factor for the prevalence of dementia, various other dementia-associated factors have been reported along with Alzheimer's disease, including sex, level of attained education, family history, history of head trauma, and smoking history.[5–7] High incidence of stroke has been regarded as a factor influencing the predominance of vascular dementia in the Japanese.[3,8,9] Because effects of radiation exposure on the central nervous system, such as small head size and mental retardation, were observed in the RERF population of prenatally exposed atomic-bombs survivors,[10] the relationship of radiation dose to prevalence of dementia was also examined.

METHODS

In 1958, the Atomic Bomb Casualty Commission, later succeeded by the Radiation Effects Research Foundation, began the Adult Health Study (AHS) to survey the occurrence of illnesses and changes in physiological and biochemical function resulting from exposure to atomic-bomb radiation. The original AHS cohort consisted of atomic-bomb survivors

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and their controls, selected from residents in Hiroshima and Nagasaki, using the 1950 national census supplementary schedules and the Atomic Bomb Survivors Survey. Members of the AHS are invited to participate in biennial health examinations that include clinical evaluations and routine laboratory assessments.[11] Between September 1992 and September 1996, 2934 men and women aged 60 and older who resided in Hiroshima were examined in the AHS. The biennial health examinations included recording of disease history, physical examination, chest X-ray, ECG, blood tests, and inquiries concerning medicines being taken and activities of daily living (ADL). A screening test for cognitive impairment was also conducted by trained nurses during the period of the present study. After excluding those who refused the dementia screening test at the time of the biennial health examination, 2222 members of the AHS (637 men, 1585 women), which constituted 75.7% of the eligible AHS population, were screened for dementia (baseline examination). To assess cognitive impairment, the Cognitive Ability Screening Instrument (CASI),[12] developed by Japanese and American researchers, was used in the baseline examination. The CASI consists of items either identical to or similar to those used in Hasegawa's Dementia Scale, widely used in epidemiologic studies in Japan,[13] or the Mini-Mental State Examination (MMSE). The CASI also includes an item on judgment because impaired judgment may contribute to a diagnosis of dementia according to *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised (DSM III/R)*[14] criteria. The score range of the CASI is 0 to 100. CASI was conducted completely for 2052 members. For 170, it was either discontinued without completion or administered in its shorter form, CASI-short.[12] A total of 2053 participants underwent the baseline examination in the outpatient clinic. Seven of those participants lived in institutions. Participants unable to come to RERF because of chronic illness or advanced age were visited for screening, and 128, 16, and 25 members, respectively, underwent the baseline examination at home or in the hospital or in the institution where they were residing.

In the AHS, those who scored less than 75 out of 100 were assessed as "dementia-suspected." A preliminary study conducted between January 1990 and July 1992 showed that a cutoff point of 75, where the sensitivity curve crossed the specificity curve, was optimal. A second examination was conducted with 339 of these "dementia-suspected" individuals and 272 study participants selected randomly from among those with high, i.e., 75 and over, CASI scores. Among those not selected for a second examination, four study members had high CASI scores but were suspected of cognitive impairment based on disease history, physical examination, and reported ADL. These four members were also investigated in the second examination in addition to the above-mentioned two groups. The second examination included completion by caregivers of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE),[15,16] a neurological examination by a neurologist, a cognitive test other than CASI, such as Hasegawa's Dementia Scale[13] or MMSE, Hachinski's Ischemic Score,[17] and assessment using the Clinical Dementia Rating (CDR).[18] The participation rate in the second examination was 90.1%. For 44 subjects, MRI was requested based on the judgment of a neurologist, and CT scans for 24 subjects and MRI for 17 subjects taken within the past 2 or 3 years at outside hospitals in the city were reviewed.

A consensus panel of three neurologists and two internists determined the presence of dementia based on *DSM III/R* diagnostic criteria[14]; this required impairment in both long- and short-term memory and one other domain, with the additional requirement that the impairment be severe enough to interfere with social or occupational functioning based on information at first and second examinations. Significant interference with work or usual social activities was determined using IQCODE, reported ADL, and CDR. Cases with CDR of 1 or greater were classified as dementia in order to minimize the number of false positives diagnosed. This meant that very mild dementia cases might not be diagnosed and, thus, would become false negatives. In the subtype diagnosis, *DSM III/R* diagnostic criteria for primary degenerative dementia of the Alzheimer type and for multi-infarct dementia were used, although participants were also classified using several additional criteria, such as those of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA)[19] and the criteria for the diagnosis of ischemic vascular dementia proposed by the State of California Alzheimer's Disease Diagnostic and Treatment Centers.[20] Standardization of clinical diagnosis of dementia and its subtypes using *DSM III/R* was developed as a part of a cross-national dementia study in which investigators from Seattle, Honolulu and Hiroshima participated. Patients with evidence of cerebrovascular disease on brain imaging without clinical history or focal signs were not diagnosed with vascular dementia. A patient whose deteriorating course was not confirmed by Hachinski's Ischemic Score, an informant's assessment of the functional impairment, or nurse's assessment of ADL at biennial health examinations was classified as an unknown type.

History of disease that might adversely affect the cognitive function was ascertained by the three-digit International Classification of Diseases (ICD) nomenclature recorded during biennial clinical examinations. Diseases and incidence reported were: heart disease (including angina pectoris), 265; hypertension, 834; stroke, 150; epilepsy, 5; thyroid disease (one of the radiation-related diseases), 197; alcohol dependence, 4; Parkinson's disease (excludes Parkinsonism related to cerebrovascular disease or medication), 11; mental disorder (includes depression), 44; and all cancer, 230. In addition, review of medical records of 30 head trauma patients indicated loss of consciousness in 23. Educational history was obtained from a past epidemiological questionnaire. Radiation dose was computed total kerma, i.e., the simple sum of γ-ray and neutron kermas, taking into account the detailed shielding histories of atomic-bomb survivors to adjust for the effects of shielding from structures, such as wooden houses, or terrain.

Crude prevalence rates of dementia in the 2222 participants screened between 1992 and 1996 were estimated assuming that the number of dementia cases was a binomial variate. Ninety-five percent confidence intervals (CI) of crude prevalence were calculated based on a normal approximation of the binomial variate. The dependency of prevalence of Alzheimer's disease or vascular dementia on variables, such as sex, age, level of attained education, radiation dose, and presence or absence of the above-cited diseases or injury was examined using a multiple logistic linear regression model.[21]

The maximum likelihood method was used to estimate the parameters. The significance of the parameter estimates was based on the likelihood ratio test. A P value of less than .05 was considered to be significant. After nonsignificant terms were removed from the model step by step, the odds ratios (ORs) of the prevalence and the likelihood-based 95% CIs were obtained based on the final model.

RESULTS

The sex and age distribution of the screened subjects at the baseline examination are shown in Table 1. Women comprised 71.3% of subjects. This female majority reflects the longer average life span of Japanese women compared with Japanese men,[22] and the ratio for women was approximately two times that for men at the inception of the AHS because many men who were in military service outside Japan at the time of the atomic bombings were not selected as members of the AHS cohort. Demographic features of the subjects are shown in Table 2. Mean educational levels of men aged 60 to 74 and men 75 years of age and older were 10.2 and 9.2 years, respectively. Those for women were 9.5 and 8.4 years, respectively. Five men and 43 women lived in institutions. About one-third of subjects aged 85 and older were unable to come to RERF. The proportion who underwent examination at home or other institutions was 4.7% in men and 8.8% in women.

Based on *DSM III/R*, 156 subjects among those with low CASI scores (40 men and 116 women) and no subjects selected randomly from among those with high scores were diagnosed with dementia. Four subjects added in the second examination, who had high CASI scores but were suspected of cognitive impairment, were diagnosed with mild dementia. The observed sex-age-specific prevalence rates by subtypes are shown in Table 3, although sample sizes of some strata are small. The numbers of cases of Alzheimer's disease and vascular dementia was equal for men. For women, the number of cases of Alzheimer's disease was larger than that of vascular dementia. One typical mixed dementia case was a 75-year-old woman included in other dementia. When the deteriorating course was not confirmed or did not meet the course for primary degenerative dementia of the Alzheimer type and multi-infarct dementia according to *DSM III/R* diagnostic criteria, cases were diagnosed as of unknown type. The proportion of unknown-type dementia was 16.3%. The overall crude prevalence of dementia was 7.2% (95% CI (6.1, 8.3)) in total, 6.6% (95% CI (4.7, 8.5)) in men, and 7.4% (95% CI (6.1, 8.7)) in women. Logistic linear analysis regressed on sex and age showed that dementia prevalence was related significantly to age ($P < .01$), and suggested a relationship to sex ($P = .065$) and sex-age interaction ($P = .065$), according to the model;

$$\log[p/(1-p)] = -12.47 - 4.10 \times \text{sex} + 0.128 \times \text{age} + 0.051 \times \text{sex} \times \text{age},$$

where p = the probability of dementia, and sex = 1 for women and sex = 0 for men. The estimated and observed sex-age-specific prevalence rates are given in Figure 1. The logistic model indicated that the slope of prevalence with age was steeper in women than in men; thus, the probability of dementia for women was higher than for men after eighty years of age. In the type of dementia, the crude prevalence of Alzheimer's disease was 2.0% (95% CI (1.0, 3.1)) in men and 3.9% (95% CI (2.9, 4.7)) in women, and the prevalence of vascular dementia, 2.0% (95% CI (1.0, 3.1)) in men and 1.8% (95% CI (1.2, 2.5)) in women. The estimated sex-age-specific prevalence curves of Alzheimer's disease and vascular dementia using logistic linear regression model are shown in Figure 2. The estimated prevalence of Alzheimer's disease depends on age ($P < .01$) and increases remarkably after age 80. The prevalence of Alzheimer's disease looks higher in women than in men, but sex difference is not statistically significant ($P = .34$).

The prevalence was 4.0% for those who underwent the first screening by coming to the foundation, and the rates were 35%, 63%, and 88%, respectively, for those who underwent the first screening at home, hospital, or institution. Five men and 43 women, 2.2% of the participants, lived in hospitals or in institutions such as nursing homes. The prevalence for community-dwelling populations was 5.8%, and that for institutional residence was 68.8%. There were 20.6% of dementia cases living in hospitals or in institutions such as nursing homes (Table 4).

Mean age and mean level of attained education for all subjects, overall dementia participants, those with Alzheimer's disease, and those with vascular dementia are shown in Table 4. The relationship of sex, age, educational history, radiation dose, and history of 10 diseases to the prevalence of Alzheimer's disease or vascular dementia was sought by multivariate logistic linear regression analysis (Table 5). Alzheimer's disease increased remarkably with age (OR = 6.3 with a 10-year increase in age) compared with vascular dementia (OR = 2.0). The prevalence of Alzheimer's disease increased with a reported history of head trauma and decreased with a history of cancer. Vascular dementia increased with history of stroke and hypertension. Reported history of other diseases were not related to Alzheimer's disease or vascular dementia. Neither type of dementia showed any significant effect of sex or radiation exposure. Educational history showed a significant effect in the prevalence of Alzheimer's disease, which decreased among those with higher attained education (OR = .6 with 3-year increments of attained education). On the other hand, there was no relationship between vascular dementia and educational history.

Table 1. Age and Sex Distribution of 2222 Persons Screened in the Baseline Examination

Age (Years)	Men		Women	
	Screened Population		Screened Population	
	No.	%	No.	%
60–64	161	71	219	62
65–69	221	77	426	75
70–74	65	72	363	80
75–79	79	77	234	80
80–84	62	77	185	82
85–89	38	86	109	83
90–	11	85	49	80
Total	637	75	1585	76

%: Percentage of eligible population who participated in the AHS biennial health examination.

Table 2. Demographic Characteristics of 2222 Persons Screened in the Baseline Examination

Age (years)	Men							Women						
	Education (Years)			Place of the Baseline Exam				Education (Years)			Place of the Baseline Exam			
	≤8	≥9	Missing	RERF	Home	Other*	Total	≤8	≥9	Missing	RERF	Home	Other*	Total
60–64	45	114	2	159	2	0	161	42	177	0	217	2	0	219
65–69	80	138	3	212	9	0	221	132	289	5	417	7	2	426
70–75	35	30	0	64	0	1	65	166	192	5	343 (2)**	14	6	363
75–79	46	32	1	76	2	1	79	126	107	1	216 (1)	15	3	234
80–84	32	30	0	58	3	1	62	115	69	1	158 (3)	21	6	185
85–89	20	17	1	31	6	1	38	69	38	2	75 (1)	24	10	109
90–	10	1	0	7	3	1	11	34	11	4	20	20	9	49
Total	268	362	7	607	25	5	637	684	883	18	1446	103	36	1585

*Other includes hospitals and institutions such as nursing homes.
**( ) shows those who underwent the baseline examination in the outpatient clinic and lived in institutions.

Table 3. Prevalence (Percentage) of Dementia by Subtype, Sex, and Age

Sex	Dementia Type	Age (years)							
		60–64	65–69	70–74	75–79	80–84	85–89	≧90	Total
Male	Number of subjects	161	221	65	79	62	38	11	637
	Alzheimer's disease	0	0.5 (1)	0	2.5 (2)	4.8 (3)	10.5 (4)	27.3 (3)	2.0 (13)
	Vascular dementia	0.6 (1)*	1.8 (4)	3.1 (2)	2.5 (2)	3.2 (2)	5.3 (2)	0	2.0 (13)
	Other	0.6 (1)	1.8 (4)	1.5 (1)	3.8 (3)	0	0	0	1.4 (9)
	Type unknown	0	0	1.5 (1)	1.3 (1)	3.2 (2)	7.9 (3)	0	1.1 (7)
Female	Number of subjects	219	426	363	234	185	109	49	1585
	Alzheimer's disease	0	0.2 (1)	1.4 (5)	2.6 (6)	4.9 (9)	26.6 (29)	22.5 (11)	3.9 (61)
	Vascular dementia	0.5 (1)	0.5 (2)	0.8 (3)	3.0 (7)	3.2 (6)	6.4 (7)	6.1 (3)	1.8 (29)
	Other	0.5 (1)	0.5 (2)	0.6 (2)	0.9 (2)	0.5 (1)	0.9 (1)	0	0.6 (9)
	Type unknown	0	0	0.8 (3)	0.9 (2)	1.1 (2)	3.7 (4)	16.3 (8)	1.2 (19)

*( ) shows number of observed cases.

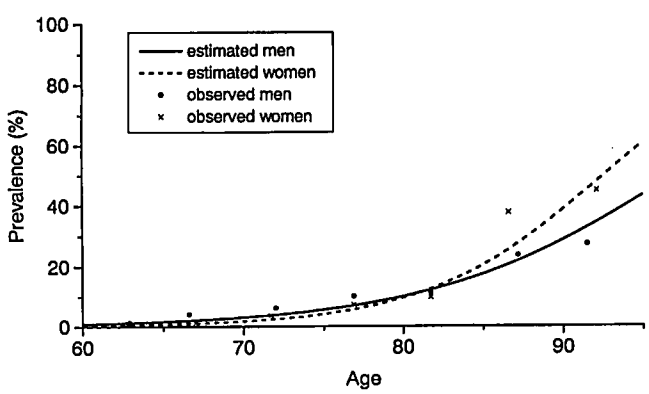

Figure 1. The estimated and observed prevalence of dementia by sex and age.

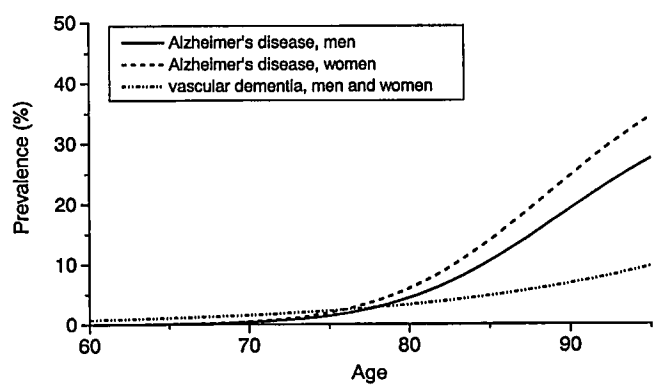

Figure 2. The estimated sex-age-specific prevalence of Alzheimer's disease and vascular dementia.

DISCUSSION

Teng et al.[12] conducted a pilot study of CASI with dementia patients who met the *DSM III/R* criteria for dementia and control subjects. This study without population-based sampling showed that CASI was comparable to the Mini-Mental State Examination (MMSE) and Hasegawa's Dementia Scale in sensitivity and specificity for dementia.[12] In the population-based dementia study in Machida City, a suburb of Tokyo, using CASI as a screening instrument, Imai et al. showed the sensitivity of CASI for dementia was 100% when 77 was the CASI cutoff score.[23] Thus, it was felt that if CASI scores under 75 at the baseline examination were used to

Table 4. Demographic Characteristics by Dementia Subtype, Sex, and Age

	Sex	Age	Mean age	Mean education	Residence	
					Community	Institutions
All subjects	Men	60–74	66.0	10.2	446	1
		≥75	81.4	9.2	186	4
	Women	60–74	67.8	9.5	998	10
		≥75	81.6	8.4	544	33
All dementia	Men	60–74	67.9	10.6	14	1
		≥75	83.3	7.9	24	3
	Women	60–74	70.0	7.3	14	6
		≥75	85.4	7.5	75	23
Alzheimer's disease	Men	60–74	68.0	11.0	1	0
		≥75	85.5	7.6	11	1
	Women	60–74	71.3	8.8	5	1
		≥75	86.0	7.6	45	10
Vascular dementia	Men	60–74	68.4	11.0	7	0
		≥75	81.8	8.0	5	1
	Women	60–74	68.7	7.8	6	0
		≥75	83.1	7.8	16	7

Table 5. Odds Ratios (OR)+ of Alzheimer's Disease and Vascular Dementia

Risk Factor		Alzheimer's Disease		Vascular Dementia	
		OR	95% CI	OR	95% CI
Sex	(Female/Male)	1.4	(0.7–3.1)	1.2	(0.5–2.7)
Age	10-year increments	6.3*	(4.3–9.6)	2.0*	(1.2–3.2)
Education	3-year increments	0.6*	(0.4–0.9)	0.9	(0.5–1.6)
Radiation dose	1 gray	1.1	(0.7–1.6)	1.0	(0.5–1.6)
Cancer	(+/−)	0.3*	(0.05–0.98)		
Head trauma	(+/−)	7.4*	(1.4–30.3)		
Stroke	(+/−)			35.7*	(16.6–82.5)
Hypertension	(+/−)			4.0*	(1.8–9.8)

+The null hypothesis of OR = 1 was tested using multivariate logistic regression analysis.
95% CI: 95% confidence interval.
*P < .05.

define "dementia-suspected" cases who would undergo a second examination, almost all dementia cases would be detected in the second examination. Since health examinations are conducted biennially in the AHS, longitudinal follow-up of cognitive impairment is possible based on physical examination, history recording, and several other kinds of inquiry. Compared with cross-sectional prevalence studies, this study is believed to be more sensitive to mild deterioration of cognitive function. Four of the subjects in the present study who showed deterioration on comparison with the previous examination were diagnosed with mild dementia.

As reported in Japan and other countries, the prevalence of dementia was found to increase exponentially with age.[1,2,6] The results of the present study show the highest age-specific prevalence among the rates reported in Japan.[1,24,25] This is because many of the prevalence studies in Japan were conducted only among older people living in the community.[2,24] On the other hand, 2.2% of the participants of our study were inpatients of hospitals and institutions, and 20.6% of dementia cases lived in these institutions. The results of our study approximate the age-specific prevalence detected among subjects of Okinawa Prefecture and Hisayama Town in western Japan. Those studies included hospitalized and institutionalized persons.[4,26] The prevalence of dementia as a whole was predominant in women after their mid-eighties. The results are similar to those reported for Japan[4,25] and for Rochester, Minnesota,[27] but in Seattle, Washington,[28] dementia was predominant in women at all ages.

While vascular dementia and Alzheimer's disease account for most dementia cases, it has been reported that vascular dementia is more frequent than Alzheimer's disease in Japan,[1,3] and Alzheimer's disease is more frequent in European and North American countries.[1,6] Among Asian countries, vascular dementia was reported to be as common or more common than Alzheimer's disease in China,[29] but Alzheimer's disease was more prevalent in rural Korea.[30] Recent reports of epidemiological studies in Japan have reported greater rates of Alzheimer's disease or lower rates of vascular dementia.[4,26] In this study cohort, the increase in rates of Alzheimer's disease was marked in participants aged

80 years and older. Multivariate logistic analysis confirmed a notable increase in the prevalence of Alzheimer's disease with advance of age. These results imply that the prevalence of Alzheimer's disease will increase greatly in populations in which the number of people aged 80 years and older increases as is currently the case in Japan and the US.

Similarly designed prevalence studies conducted in the Japanese-American populations in Seattle and Honolulu followed the methodology developed by the Ni-Hon-Sea Dementia Project.[28,31] The prevalence of Alzheimer's disease was slightly higher and the prevalence of vascular dementia slightly lower at every age in the Seattle study than seen in our study. The Honolulu study on Japanese-American men reported a prevalence of Alzheimer's disease higher than our report.

In this study, overall prevalence rates for Alzheimer's disease and vascular dementia were equal in men, but Alzheimer's disease was predominant in women. The result that Alzheimer's disease was predominant in women is consistent with the results of numerous studies carried out in urban and rural areas of Japan.[24] This may be attributable to a longer average life span for Japanese women compared with Japanese men.

Multivariate logistic analysis suggests strong association between the prevalence of vascular dementia and history of stroke. The Stroke Data Bank cohort study by Tatemichi et al. reported that the probability of new-onset dementia at 1 year was 5.4% for stroke patients aged 60 years and 10.4% for stroke patients aged 90 years.[32] In an incidence study on several diseases conducted in 1992 in RERF's cohort, the sex ratio of the incidence of stroke is reported about three times higher in men.[11] In this study, multivariate logistic analysis showed no difference between the sexes for vascular dementia. This result was contradictory to the sex difference in the incidence of stroke.

The predominance of vascular dementia in Japan has heretofore been attributed to the high incidence of stroke.[3] To avoid the bias resulting from difference in methodology, interpretation of the *DSM III/R* passage "evidence of significant vascular dementia disease" was discussed in a standardization meeting of the Ni-Hon-Sea Dementia Project. In a comparison of the Honolulu study on Japanese-American men and our study, the prevalence of vascular dementia in those under 80 years of age was higher in our study, and its prevalence at ages 80 and older was higher in the Honolulu study.[30] In the cardiovascular disease study that has been conducted since 1965 as a part of the Ni-Hon-San Study,[8,9] the incidence of stroke in Japan has been reported to be remarkably higher than that in the Japanese-Americans in Hawaii. The difference of prevalence of vascular dementia between the Honolulu study and the present study cannot be explained by the difference of stroke incidence alone. The difference of survival rate from stroke or severity of stroke at two sites should be investigated in the future.

Effects of education were observed only in Alzheimer's disease. The Seattle study report states, "Persons with lower education had higher overall rates of dementia than those with higher education, but this tendency became weak and inconsistent when rates were age-stratified."[28] In the present study, the effect of education remained when adjustment was made for age.

A positive association between a prior history of head trauma and Alzheimer's disease was seen here. Mortimer et al.[33] reported similar results. However, other studies reported no association.[1] One reason for these inconsistencies might be recall bias. The history of disease based on biennial health examination over many years in the AHS may offer more accurate information regarding head trauma.

The effect of radiation on the central nervous system in adulthood has been observed to be unrelated to prevalence of dementia. The argument that the negative relationship of cancer to Alzheimer's disease is due to protective effect or differential survival bias will need to be discussed. The investigation of mortality for dementia cases and nondementia cases, or dementia incidence study and cancer history, will give an opportunity for resolution.

There are several limitations to the present study. The AHS cohort does not represent the overall Japanese population of the same generation because it comprises persons who survived the atomic bombings and their controls and excludes a generation of men in military duty at the time of the bombings. Regarding the characteristics of this population, RERF surveys show a clear correlation between radiation dose and the development of malignant tumors.[34] Although subjects unable to come to RERF were examined at home or in the hospital or institution, we can not rule out a bias by nonparticipation in the AHS examination. The use of a CDR greater than or equal to 1 for the study may have caused false-negative results for dementia. However, given these limitations, the ongoing biennial medical examinations in the AHS are effective detectors of mild cases of dementia, and this study provides a unique opportunity to address frequently noted differences in rates of Alzheimer's disease and vascular dementia in Japan and the US and to look at risk factors of dementia.

This is the first study of Japanese dementia rates carried out with a protocol similar enough to that of a US study to allow meaningful comparisons. The rates among Japanese appear more similar to US rates than in many previous reports. This study reveals associations between age, attained education, history of head trauma, and history of cancer and Alzheimer's disease. Age, history of stroke, and history of hypertension are risks of vascular dementia.

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