Original Research Article

Prevalence of Dementia and Mild Cognitive Impairment in the Rural Island Town of Ama-cho, Japan

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Key Words

Alzheimer's disease · Vascular dementia · Dementia with Lewy bodies · Mild cognitive impairment · Epidemiology

Abstract

Aims: In order to determine the prevalence of dementia and mild cognitive impairment (MCI), we conducted a population-based study in Japan. ***Methods:*** Participants included 924 subjects aged 65 years or older who resided in the town of Ama-cho. In phase 1 of the study, the Mini-Mental State Examination and Clinical Dementia Rating were administered for screening purposes. In phase 2 of the study, the subjects who screened positive were further examined by neurologists. Dementia and MCI were diagnosed by means of DSM-IV and International Working Group on MCI criteria, respectively. ***Results:*** By the prevalence date of June 1, 2010, 24 subjects had deceased or lived outside the town. In total, 723 of the remaining 900 subjects received a phase 1 test. In phase 2, 98 subjects were diagnosed with amnestic MCI, 113 subjects with non-amnestic MCI, and 82 subjects with dementia. Of the subjects who did not receive the phase 1 test, 66 subjects were diagnosed as having dementia according to data from their town medical card or the Long-term Care Insurance System. The crude prevalence of amnestic MCI, non-amnestic MCI, and dementia were 10.9, 12.6, and 16.4%, respectively. ***Conclusion:*** Consistent with the striking increase in the number of elderly individuals, we report higher prevalence of MCI and dementia in Japan than previously described.

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Introduction

With the substantial aging of the global population, the number of people with dementia will likely increase. Alzheimer's Disease International estimated the prevalence of dementia worldwide after conducting an evidence-based Delphi consensus study [1]. The Delphi study indicated that there were 24.3 million people with dementia in the world in 2001. The number of people with dementia is expected to increase to 42.3 million by 2020 and to 81.1 million by 2040. Life expectancy has been rising, and Japanese women have attained the longest life expectancy worldwide. Moreover, the speed of aging in the Japanese population is projected to be one of the fastest in the world. The identification of subjects at risk for dementia is important for the implementation of potential treatments that may delay or prevent cognitive decline. Mild cognitive impairment (MCI) is one of several terms describing a stage between normal cognitive changes in aging and dementia and is proposed to be prodromal to dementia in some elderly people [2]. Whereas several epidemiological studies on dementia have been conducted in Japan, scarce epidemiological data exist regarding MCI, especially in terms of the prevalence of MCI examined directly alongside the prevalence of dementia. In order to examine the prevalence of both MCI and dementia, we conducted a population-based study in Ama-cho, a rural island town in western Japan.

Methods

Subjects

This study was conducted in the municipality of Ama-cho, a rural island town located 70 km from Yonago City, in the northwestern part of Japan. For about 30 years, board-certificated neurologists have visited this town to examine dementia patients along with public health nurses. To be included in the study, subjects were required to be living and to be legally residing in the town on October 1, 2009. The total population of Ama-cho was 2,434 (1,197 men and 1,237 women). The number of elderly people aged 65 years or older was 924 (374 men, mean age ± SD 77.3 ± 7.8 years), which represented 38.0% of the total population.

The study was approved by the Committee for Medical Research Ethics at Tottori University following the principles outlined in the Declaration of Helsinki. Public health nurses supported us in the identification of participants, and all participants provided written informed consent to participate in the study.

Phase 1 Study

In phase 1 of the study, a screening of subjects aged 65 years or older was performed by 5 clinical psychologists in the town. The screening included an interview with both subjects and their families that surveyed cognitive changes, as well as the application of the Mini-Mental State Examination (MMSE) [3] and Clinical Dementia Rating (CDR) [4]. Subjects with an MMSE score under 27 points and/or CDR judged to be 0.5 or more were deemed positive.

Phase 2 Study

In phase 2 of the study, the subjects who screened positive in phase 1 were examined to confirm or exclude the presence of dementia or MCI and to classify the type of dementia or MCI. All subjects in phase 2 were examined by board-certificated neurologists. To confirm the diagnosis, neurologists met with the candidates and their family members at home or in official day care centers. Assessment of these subjects involved a careful study of the medical history, a physical examination, a drug inventory, a neurological examination, and a com-

prehensive cognitive evaluation using the Psychogeriatric Assessment Scale (PAS) [5] and the Logical Memory Test of the Wechsler Memory Scale-Revised (WMS-R) [6].

Using magnetic resonance imaging (MRI; Philips Gyroscan Intera 1.5 Tesla), we evaluated hippocampal atrophy and cerebrovascular lesions since both are important criteria for a diagnosis of dementia.

Dementia was diagnosed according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, 4th edition revised (DSM-IV) [7]. For patients with dementia, we analyzed dementia-related disorders using the following criteria: (1) Alzheimer's disease (AD) was defined according to the criteria of the National Institute of Neurological and Communication Disorders Association [8]; (2) vascular dementia (VaD) was defined according to the criteria of the National Institute of Neurological Disorders and Stroke and the Association Internationale pour la Recherche et l'Enseignement en Neurosciences [9]; (3) dementia with Lewy bodies (DLB) was defined according to the consensus guidelines for the clinical diagnosis of DLB [10]; (4) Parkinson's disease dementia (PDD) was defined according to the clinical diagnostic criteria for dementia-associated Parkinson's disease [11]; (5) progressive supranuclear palsy (PSP) was defined according to the National Institute of Neurological Disorders and the Society for PSP [12]; (6) frontotemporal lobar degeneration (FTLD) was defined according to international criteria [13], and (7) possible idiopathic normal pressure hydrocephalus (iNPH) was defined according to the clinical guidelines of the Japanese Society of Normal Pressure Hydrocephalus [14]. We excluded cases of cognitive decline secondary to major depression and other mental disorders such as schizophrenia only if these were proven to be the main cause for the cognitive decline through a psychiatric interview and the patients' medical history. The severity of dementia was assessed according to a functional assessment staging test (FAST) of AD and classified as follows: FAST4 = mild, FAST5 = moderate, and FAST6/7 = severe [15].

The diagnosis of MCI was given according to the International Working Group on MCI criteria [16]. The following criteria were obligatory for the diagnosis: (1) the subject or the informant had to express some concern about the subject's cognitive function (cognitive complaints); (2) there had to be evidence of a decline in cognitive function on administered objective cognitive tasks that were abnormal for the subject's age and education level; (3) the participant had to show no impairment of functional activities of daily living, and (4) the subject did not fulfill the DSM-IV dementia criteria. Among the subjects who met the criteria for MCI, subjects having a score 1.5 SD below average on the WMS-R were diagnosed as having amnestic MCI [17]. The other subjects who did not meet the amnestic MCI criteria were diagnosed as having non-amnestic MCI. We examined all the subjects directly in phase 2 of the study.

Data Analysis

The prevalence and 95% confidence intervals (CIs) were calculated for all types of dementia as well as for MCI. In order to identify subjects with dementia out of the non-responder pool, we used data from town medical records where the diagnosis of dementia was performed by board-certified neurologists (K.W.-I., Y.U., K.N.) in our follow-up survey or using data from the Long-term Care Insurance System of Japan.

Results

Figure 1 shows the general design of the door-to-door two-phase prevalence survey. By the prevalence date of June 1, 2010, 24 subjects (2.7%) had deceased or migrated from the town. Of the remaining 900 subjects, 723 (80.3%) received a phase 1 test. Compared to phase
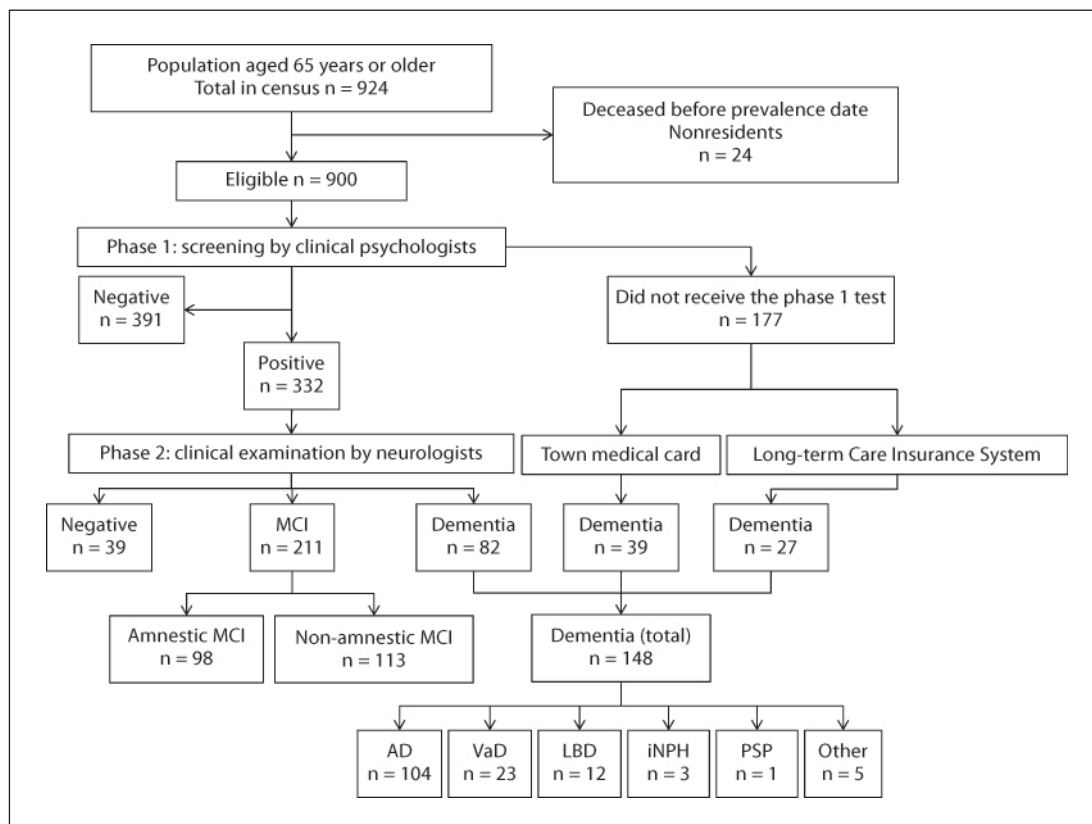
Fig. 1. General design of the door-to-door two-phase prevalence survey in Ama-cho. The number of subjects involved at each step is shown.
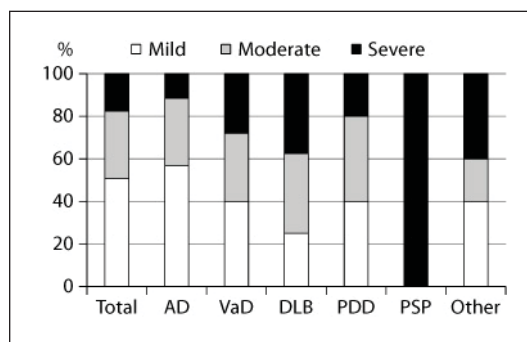

Fig. 2. Severity of dementia subtypes.

1 non-responders, responders were younger (mean 81.7 vs. 76.8 years, respectively) and were similar in gender (40.9% male vs. 37.4% male, respectively).

In total, 332 subjects were classified as having cognitive impairment in phase 1 of the study. In phase 2 of the study, 98 subjects were diagnosed with amnestic MCI, 113 subjects with non-amnestic MCI, and 82 subjects with dementia. Of the subjects who did not receive the phase 1 test, 39 subjects were diagnosed as having dementia according to data from their town medical records in our follow-up study, and 27 subjects were diagnosed as having dementia according to the Long-term Care Insurance System. The severity of dementia accord-

Table 1. Age- and sex-specific prevalence of dementia

	Population at risk	All types of dementia		AD		VaD		DLB		PDD		iNPH		PSP		Others	
		n	prevalence	n	prevalence	n	prevalence	n	prevalence	n	prevalence	n	prevalence	n	prevalence	n	prevalence
Both genders																	
65–69 years	156	1	0.6	–	–	1	0.6	–	–	–	–	–	–	–	–	–	–
70–74 years	182	3	1.6	–	–	2	1.1	–	–	1	0.5	–	–	–	–	–	–
75–79 years	210	23	11.0	15	7.1	6	2.9	–	–	–	–	–	–	–	–	2	1.0
80–84 years	170	32	18.8	22	12.9	4	2.4	3	1.8	–	–	1	0.6	–	–	2	1.2
85–89 years	105	45	42.9	32	30.5	5	4.8	2	1.9	2	1.9	2	1.9	1	1.0	1	1.0
≥90 years	77	44	57.1	35	45.5	5	6.5	3	3.9	1	1.3	–	–	–	–	–	–
Total	900	148	16.4	104	11.6	23	2.6	8	0.9	4	0.4	3	0.3	1	0.1	5	0.6
Men																	
65–69 years	72	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
70–74 years	83	2	2.4	–	–	1	1.2	–	–	1	1.2	–	–	–	–	–	–
75–79 years	86	14	16.3	6	7.0	6	7.0	–	–	–	–	–	–	–	–	2	2.3
80–84 years	68	12	17.6	6	8.8	3	4.4	1	1.5	–	–	–	–	–	–	2	2.9
85–89 years	28	15	53.6	9	32.1	4	14.3	–	–	–	–	1	3.6	1	3.6	–	–
≥90 years	25	9	36.0	4	16.0	3	12.0	2	8.0	–	–	–	–	–	–	–	–
Total	362	52	14.4	25	6.9	17	4.7	3	0.8	1	0.3	1	0.3	1	0.3	4	1.1
Women																	
65–69 years	84	1	1.2	–	–	1	1.2	–	–	–	–	–	–	–	–	–	–
70–74 years	99	1	1.0	–	–	1	1.0	–	–	–	–	–	–	–	–	–	–
75–79 years	124	9	7.3	9	7.3	–	–	–	–	–	–	–	–	–	–	–	–
80–84 years	102	20	19.6	16	15.7	1	1.0	2	2.0	–	–	1	1.0	–	–	–	–
85–89 years	77	30	39.0	23	29.9	1	1.3	2	2.6	2	2.6	1	1.3	–	–	1	1.3
≥90 years	52	35	67.3	31	59.6	2	3.8	1	1.9	1	1.9	–	–	–	–	–	–
Total	538	96	17.8	79	14.7	6	1.1	5	0.9	3	0.6	2	0.4	–	–	1	0.2

Prevalence = Cases/100.

ing to FAST is shown in figure 2. Seventy-five individuals (50.7%) were at a mild stage, 47 (31.7%) at a moderate stage, and 26 (17.6%) at a severe stage of dementia. More than half of the subjects with AD were at a mild stage; however, more than half of the subjects with VaD were at a moderate or severe stage. Forty-five subjects with dementia were instituted in nursing homes in the town, while 16 subjects with dementia were instituted in nursing homes or hospitalized outside the town.

Prevalence of Dementia and MCI

Table 1 shows the number and prevalence of each dementia subtype. Overall, 148 subjects (52 men and 96 women) fulfilled the diagnostic criteria for dementia, yielding a crude prevalence for all dementia types of 16.4% (95% CI 14.0–18.9) in elderly individuals aged 65 years or older. The mean age was 83.1 ± 5.9 years (range 72–95) for men and 87.6 ± 6.8 years (range 68–102) for women. The age-specific prevalence of dementia displayed an exponential increase with advancing age for women. However, for men, the prevalence was highest between 85 and 89 years. The prevalence was higher in men than in women aged less than 90 years. The age-adjusted prevalence for dementia by the direct method in those aged 65 years and older compared with the population structure of Japan in 2008 was estimated to be 11.6% according to data from this study.

Of the 148 demented subjects, 104 (70.3%) were diagnosed with AD (25 men, 79 women), 23 (15.5%) with VaD (17 men, 6 women), 8 (5.4%) with DLB (3 men, 5 women), 4 (3.4%)

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Table 2. Age- and sex-specific prevalence of MCI

	Population at risk	All types of MCI		Amnestic MCI		Non-amnestic MCI	
		n	prevalence	n	prevalence	n	prevalence
Both genders							
65–69 years	156	26	16.7	8	5.1	18	11.5
70–74 years	182	38	20.9	18	9.9	20	11.0
75–79 years	210	56	26.7	23	11.0	33	15.7
80–84 years	170	59	34.7	33	19.4	26	15.3
85–89 years	105	25	23.8	13	12.4	12	11.4
≥90 years	77	7	9.1	3	3.9	4	5.2
Total	900	211	23.4	98	10.9	113	12.6
Men							
65–69 years	72	17	23.6	4	5.6	13	18.1
70–74 years	83	20	24.1	9	10.8	11	13.3
75–79 years	86	19	22.1	10	11.6	9	10.5
80–84 years	68	20	29.4	13	19.1	7	10.3
85–89 years	28	7	25.0	4	14.3	3	10.7
≥90 years	25	5	20.0	3	12.0	2	8.0
Total	362	88	24.3	43	11.9	45	12.4
Women							
65–69 years	84	9	10.7	4	4.8	5	6.0
70–74 years	99	18	18.2	9	9.1	9	9.1
75–79 years	124	37	29.8	13	10.5	24	19.4
80–84 years	102	39	38.2	20	19.6	19	18.6
85–89 years	77	18	23.4	9	11.7	9	11.7
≥90 years	52	2	3.8	–	–	2	3.8
Total	538	123	22.9	55	10.2	68	12.6

Prevalence = Cases/100.

with PDD (1 man, 3 women), 3 (2.0%) with iNPH (1 man, 2 women), and 1 (0.7%) with PSP (1 man). Five (3.4%) were diagnosed with mixed or other dementias not classifiable (4 men, 1 woman). The overall crude prevalence was 11.6% (95% CI 9.5–13.6) for AD and 2.6% (95% CI 1.5–3.6) for VaD. The prevalence of AD was three times higher in women than in men, while that of VaD was almost three times higher in men than in women. The AD/VaD ratio was 13.2 in women and 1.5 in men. Crude prevalences were 0.89% (95% CI 0.28–1.5) for DLB and 0.56% (95% CI 0.07–0.10) for PDD. The AD/DLB ratio in both sexes was 13.0.

Table 2 shows the number and prevalence of MCI cases. In total, 211 subjects (88 men and 123 women) fulfilled the diagnostic criteria for MCI, yielding a prevalence of 23.4% (95% CI 20.7–26.2) in elderly individuals aged 65 years or older. Crude prevalences were 10.9% (95% CI 8.9–12.9) for amnestic MCI and 12.6% (95% CI 10.4–14.7) for non-amnestic MCI. The mean age of the subjects with amnestic MCI was 78.7 ± 7.7 years for men and 78.7 ± 5.5 years for women. The mean age of the subjects with non-amnestic MCI was 74.4 ± 6.9 years for men and 78.1 ± 5.7 years for women. Whereas there was no significant difference in the mean age of the subjects with amnestic MCI between men and women, the mean age of the subjects with non-amnestic MCI was lower for men than women.

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Discussion

We conducted a population-based study on dementia and MCI in Ama-cho, a rural island town in western Japan. Ama-cho has evidently a stable population in terms of elderly population due to very low levels of migration. Three public health nurses working as permanent care providers had kept detailed information about the physical and mental health of the entire town for about 30 years. Almost all of the subjects with dementia lived in their own home or were instituted in a nursing home within the town. Thus, these features proved suitable for investigations into the prevalence of dementia.

We previously reported the crude prevalence of dementia to be 11.0% in elderly individuals aged 65 years or older [18]. In that study, screening for dementia depended upon information collected by public health nurses in the town. The screening included an interview with both subjects and their families and surveyed cognitive changes, psychiatric symptoms, personality changes, problem behaviors, activities of daily living, and psychological and medical symptoms. Recorded subjects with dementia were limited to people who were actually living in the town, meaning that people with dementia who were institutionalized in nursing homes outside the town or lived with their families outside the town were excluded. In comparison, in the present study, the screening of subjects displaying cognitive impairment based on MMSE and CDR by clinical psychologists in a phase 1 study allowed us to detect individuals with mild dementia who had not been recognized by public nurses or doctors in the town. This might account for the greater prevalence of dementia reported in this study compared to the values presented in our previous study. Further, we examined the state of cognitive function in survey non-responders according to data from their town medical card or the Long-term Care Insurance System of Japan. We could also extensively examine subjects suffering from various stages of cognitive impairment ranging from mild to severe.

This study suggests that AD is the most common and VaD is the second most common subtype of dementia in elderly individuals. We also examined the prevalence of dementia subtypes other than AD and VaD. The proportion of patients with DLB (among patients with any type of dementia) was 5.4%, while the proportion of patients with PDD was 2.7%. These values are consistent with previous estimates reported in systematic reviews [19, 20]. We did not discover any patients with FTLD in this study, although a larger number of subjects may be needed to examine the exact prevalence of FTLD in the elderly via community-based studies.

Previous reports have demonstrated the prevalence of MCI to be 4.9 and 5.3% in Japanese communities [21, 23]. Our estimate of the crude prevalence of MCI (23.4%) was higher compared to these previous reports. The non-amnestic type of MCI was included in the construct of MCI in the current study but not in previous studies, and this might account for the greater estimated prevalence of MCI. However, the crude prevalence of amnestic MCI (10.6%) in the current study is also higher compared to previous reports. Recently, Sasaki et al. [23] reported a prevalence of all types of MCI of 18.9% when using a –1.5 SD cut-off level. Taken together with our results, around 20% of elderly people aged 65 years or older might suffer from MCI in Japan. In comparison, the prevalence of MCI has also been reported in areas outside of Japan. A previous review showed that the prevalence of MCI in the general elderly population (older than 65 years) was between 3.1 and 19% in the United States and Europe [24]. The prevalence of MCI among Koreans aged 65 years or older was estimated to be 24.1% (95% CI 21.0–27.2) in a nationwide survey [25]. A systematic analysis of 22 studies in China described a pooled prevalence of MCI in elderly populations of 12.7% (95% CI 9.7–16.5) [26]. One of the challenges of studying the prevalence of MCI in population-based studies is that the reported prevalence of MCI varies between reports due to different diagnostic criteria as well as disparate assessment procedures. Another confound is that up to 44% of subjects with

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MCI at their first visit were estimated to return to normal after a year [24, 27]. Apart from neurodegeneration, numerous factors including vascular risk factors, education, psychiatric status, genetic background, use of anticholinergic drugs, and hormonal changes can affect cognitive function in elderly populations [28]. Recently, the National Institute on Aging-Alzheimer's Association workgroup (NIA-AA) and the American Heart Association/American Stroke Association have published a diagnostic recommendation of MCI due to AD [29] and a statement on vascular cognitive impairment [30], respectively. It will be important to incorporate these new criteria for MCI in future population-based studies.

There are some limitations regarding our measurements of MCI prevalence. First, we did not conduct cognitive tests in subjects who did not answer the survey. A recent community-based study describing a 2.3-fold increase in the prevalence of MCI in delayed responders compared to quick responders forces us to consider the possibility of undetected MCI in our non-responder subjects [31]. Therefore, the prevalence of MCI reported in this study likely represents a minimum value. Second, we did not perform more extensive tests measuring other cognitive domains aside from memory due to the time limitations for assessing community residents, and we classified MCI into only amnestic and non-amnestic types.

We conducted a door-to-door epidemiological study on the prevalence of mild to severe cognitive impairment in a rural island town in western Japan. With the striking increase in the elderly population, the number of individuals with dementia or preclinical stages of dementia would appear to be increasing in Japan.

Acknowledgments

Disclosure Statement

The authors declare no conflicts of interest

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