

MMSE 得点 8 といった背景因子、前医の診療科、前医における認知症症状に対する処方 (ChEIs、他の認知機能障害に対する薬剤、抗精神病薬、抗うつ薬、抗不安薬、気分調整薬、漢方薬など) の有無とその内容、介護保険取得状況、専門医の最終診断などを調査した。

(倫理面への配慮)

患者の匿名性に関しては十分な配慮がなされており、各施設の倫理委員会の承認を各々得ている。

C. 研究結果

今回対象となったのは、87 例であり、男女比はほぼ同等で、平均年齢が 66.9 歳、平均の初診時 MMSE 得点は 18.4 であった。紹介医の診断は FTD および疑い、前頭側頭葉変性症 (: FTLT) および疑い、側頭葉優位型圏内、ピック病および疑い、運動ニューロン疾患 (FTD-MND) 圏内などであり、FTD の診断が 6 割以上を占めた。紹介医の属性は精神科、神経内科、内科、脳神経外科、その他であり、精神科が 6 割以上を占めた。

87 例のうち、何らかの認知症に対する薬剤の使用を用いていた例は 49.4% であった。認知機能に対する薬剤を用いていたのは 23% であり、ChEIs は 20.7% に用いられていた。一方で精神症状に対する薬剤 (以下向精神薬: 抗精神病薬、抗うつ薬、抗不安薬、気分調整薬、漢方薬を含む) は 35.6% に用いられていた。抗うつ薬が 16.1% に、漢方薬が 11.5% に、抗精神病薬が 10.3% に、抗不安薬が 9.2% に、気分調整薬が 1.1% に用いられていた。

診療科によって処方の傾向が異なるかの検討では、ChEIs は、精神科では 24.5%、神経内科では 11.8%、内科では 22.2%、その他は 12.5% であった。 χ^2 検定で有意差は認められなかった。一方で向精神薬は精神科では 49.1% に処方されていたのに対し、神経内科では 5.9%、内科では 22.2%、その他は 25.0% と χ^2 検定で有意に精神科で多く処方されていた。抗精神病薬が処方されていた 9 例のうち 8 例は精神科での処方であり、抗うつ薬は

14 例全例が精神科での処方であった。漢方薬は 10 例中 8 例が精神科での処方であった。

紹介医の診断による処方割合の検討では、ChEIs が処方されていた 18 例の内訳は、診断は FTD および疑いが 61.1%、側頭葉優位型圏内が 22.2%、ピック病および疑いが 16.7% であった。FTLT および疑い、FTD-MND 圏内には ChEIs は処方されていたなかった。向精神薬が処方されていた 31 例の診断内訳は、FTD および疑いが 67.7%、側頭葉優位型圏内が 9.7%、ピック病および疑いが 22.6% であった。FTLT および疑い、FTD-MND 圏内には向精神薬は処方されていたなかった。

ChEIs の使用に影響を与えるような背景因子があるかどうか、ChEIs の使用の有無によって 2 群に分け、比較を行った。しかしながら、性別、年齢、教育年数、罹病期間、MMSE 得点、介護保険の取得状況などいずれも 2 群間の有意差はなかった。

D. 考察

ChEIs の処方率の 2 割という割合をどのように判断するかは、意見の分かれるところである。FTD に対する ChEIs の投与の報告では、有効性は認められなかったとの結果が多い。認知症という診断で他に選択肢がなく ChEIs を使用していると推測されるが、これはなるべく避けるべきである。

一方で 35% という向精神薬の処方割合は、他の疾患より行動症状が目立ち、それに伴う介護負担も大きいはずの FTD において、それほど高くはないと考えられる。これは、まず FTD と診断された場合、不用意に向精神薬を処方せず、専門医への紹介を優先させている可能性がある。また、本研究は入院例を含まない外来例であることも関与している可能性がある。安易な向精神薬の処方を行っていないという点では、好ましいことと思われる。

向精神薬のなかで、抗うつ薬の使用が最も頻度が高かった。選択的セロトニン再取り込み阻害薬 (SSRI) が FTD の常同行動や食行動異常に対して

有用であると報告されており、その抗うつ薬が抗精神病薬や抗不安薬よりも用いられているということは、これらの知識が普及しているということである。

E. 結論

本研究は、本邦ではじめてなされた FTD に対する薬物療法の実態調査である。約半数の例に何らかの認知症症状に対する薬剤が用いられており、ChEIs は 2 割の例に処方されていることが明らかになった。向精神薬は 1/3 以上に処方されており、中では抗うつ薬の処方が多かった。今後は薬剤使用に対する啓発や、非薬物療法を含めた FTD への治療ガイドラインの整備が望まれる。

F. 健康危険情報

なし

G. 研究発表

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H. 知的財産権の出願・登録状況

1. 特許取得

なし

2. 実用新案登録

なし

3. その他

なし

Ⅲ．研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

書籍

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繁信和恵	認知症患者の退院へ向けた連携 (後半)	精神科看護	41(2)	72-79	2014
品川俊一郎, ほか	アセチルコリンと神経疾患研究の現在地を知る アルツハイマー病治療	Brain and Nerve	66	507-516	2014

IV . 研 究 成 果 の 刊 行 物 ・ 別 刷

Regular Article

Multicenter population-based study on the prevalence of early onset dementia in Japan: Vascular dementia as its prominent cause

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Aim: In Japan, the government and media have become aware of the issues of early onset dementia (EOD), but policies for EOD have not yet been established and support systems are inadequate. To provide practical data about EOD, a two-step postal survey was performed.

Methods: A questionnaire requesting information on EOD cases was sent to target institutions in five catchment areas in Japan. According to the answers from the institutions, we estimated the prevalence of EOD using census data and determined the illnesses causing EOD. As a quality control study, the authors reviewed every diagnosis in a quarter of the reported cases using the medical and psychiatric records and neuroimaging data. This study was conducted from 2006 to 2007.

Results: Information from 2469 patients was collected from 12 747 institutions, and 2059 subjects with EOD were identified. The estimated prevalence of EOD was 47.6 per 100 000 (95% confidence interval, 47.1–48.1) for all of Japan. Of the illnesses causing EOD, vascular dementia (VaD) was the most frequent (39.8%), followed by Alzheimer's disease.

Conclusions: The prevalence of EOD in Japan appeared to be similar to that in Western countries. However, unlike previously reported international experience, VaD was the most frequent cause of EOD in all catchment areas in Japan.

Key words: Alzheimer's disease, early onset dementia, prevalence, vascular dementia.

IN DEVELOPED COUNTRIES, dementia with onset before the age of 65 years, defined as early onset dementia (EOD), has presented a unique challenge to society and those who care for such individuals.¹

In Japan, although several reports have described the prevalence of EOD and the frequency of illnesses causing EOD, their results differ depending on the study settings. Two university-hospital-based studies reported that the most common dementia diagnosis

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was Alzheimer's disease (AD).^{2,3} On the other hand, one community-based study and one nationwide study, including five catchment areas, reported that the most frequent illness causing EOD was VaD.^{4,5} Recently, we reported on a population-based study in a single catchment area with a population of 3 million.⁶ Our study revealed also that vascular dementia (VaD) was the most common cause of EOD. Using the same methodology in a much larger population of over 9 million, we estimated the prevalence of EOD and examined the prominence of VaD among illnesses causing EOD.

METHODS

This study was conducted in five catchment areas in Japan: Ibaraki (population, 3 million), Gunma (2 million), Toyama (1 million), Ehime (1.5 million) and Kumamoto (1.8 million). These areas are representative of Japan's geographic, economic and educational composition. The productive-age population ratio of all Japan was 65.5 in 2006 and 65.0 in 2007, and in those five areas the average was 63.1 (range 61.3–66.0). Therefore, in order to reduce the influence of biased sample populations, prevalence in each area was adjusted using the standardized population. EOD subjects were defined as those whose age at onset and age on the census day was less than 65 years. The observation period in each area was 6 months: from 1 April to 31 October 2006 for Ibaraki and Gunma, from 1 April to 31 October 2007 for Toyama, and from 1 July to 31 December 2007 for Ehime and Kumamoto (Fig. 1). The reason why this period was employed was to allow direct comparison with a previous Japanese EOD study, which used 6 months.⁵

The survey was approved by the local ethics committees, including those of the University of Tsukuba, Kumamoto University, Ehime University, Gunma University, and Toyama Medical Association.

Step 1

A questionnaire was mailed to all of the following: medical institutions (including psychiatric and neurological hospitals and clinics), home-visit nursing services, long-term care insurance (LTCL)-related facilities, local branches of prefectural health, and local welfare commissioners. In Japan, all care services for community-dwelling individuals with EOD are provided by a publicly funded LTCL, which is separate from medical care insurance.

Each institution was asked, 'How many EOD patients did you care for in the last 6 months?' The criteria for the diagnosis of dementia were based on the DSM-III-R.⁷

Step 2

For the second step, respondent institutions with one or more cases were asked to provide additional patient data, including: initials, demographics, coexisting illnesses, duration and type of dementia, illnesses causing dementia (in the case of VaD, specifying the subtype of cerebrovascular disease [CVD]), severity of dementia, and functional status. Patients were then classified into subgroups according to the cause of dementia. AD, vascular dementia and alcohol-related dementia were defined according to the DSM-IV.⁸ It is noteworthy that, in contrast to other VaD criteria, including National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherche et l'Enseignement en Neurosciences,⁹ the DSM-IV criteria for VaD requires neither temporal relation between dementia and recognized stroke nor progressive cognitive decline. Dementia with Lewy bodies (DLB) and Parkinson's disease with dementia (PDD) were diagnosed according to the revised criteria for the clinical diagnosis of dementia with Lewy bodies,¹⁰ and frontotemporal lobar degeneration (FTLD) was diagnosed according to the Lund and Manchester Criteria.¹¹ Finally, patients fulfilling the DSM-III-R criteria for dementia but not fulfilling criteria for any of the above diagnostic categories were designated 'Other'. Individuals with two or more comorbid diseases causing dementia, such as AD with VaD, were classified as 'overlap' and included in the 'Other' category.

The age at onset of disease was defined as the age of the patient at which the earliest conclusive dementia symptom was noticed by caregivers or other close informants.

Determination of dementia severity was based on the original manuals used by a previous Japanese EOD study⁵ for comparison. Three stages of severity were defined as follows. Mild: the person can mostly live independently, with adequate personal hygiene and relatively intact judgment, but social activities and employment are both significantly impaired. Moderate: independent living is fraught with hazard to the extent that supervision is required. Severe: there is severe impairment of daily activities and continual supervision is needed.

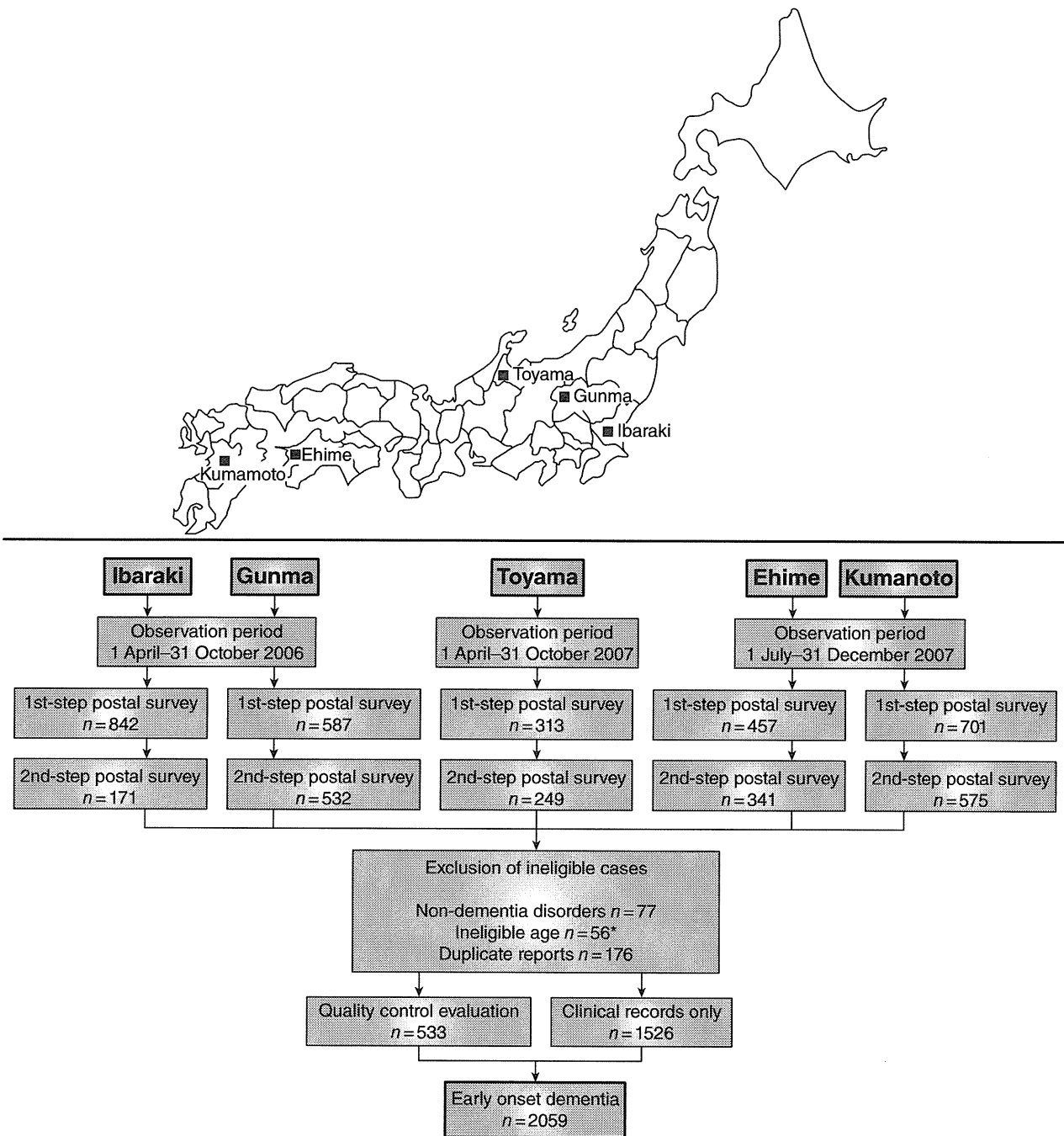


Figure 1. Map of Japan and schedule of each catchment area's survey.

Answers to the additional information for reported cases from non-medical institutions were based on comments by the consulting physicians.

It should be noted that in Japan acute illnesses, including stroke, are diagnosed and managed ini-

tially in hospitals then intensive rehabilitation units, prior to discharge home or to longer-term care in LTCI institutions. Degenerative illnesses are usually managed in specialist hospital outpatient clinics, prior to LTCI institutions for advanced stages. Hence,

almost all patients in this study would have received specialist evaluation at some stage of their illness, and hence their assigned diagnoses should be clinically accurate.

Quality control

In order to validate the accuracy of reported diagnoses, we conducted a quality control (QC) study using data from a quarter of the reported cases. We selected the institutions for this sub-study in descending order of reported case numbers. The authors of this paper visited such institutions and reviewed the patients' medical and psychiatric records and neuroimaging data, including magnetic resonance imaging (MRI), computed tomography (CT) and single photon emission computed tomography (SPECT). A separate diagnosis was made independently for each subject. In this way, the accuracy of the diagnosis of the attending physician from each institution could be evaluated.

Statistical analysis

The data to estimate the prevalence are based on the last governmental reports before the start of the observation period. The reports were published on 1 April 2006 for Ibaraki, on 1 October 2006 for Gunma and on 1 October 2007 for Toyama, Ehime, Kumamoto and the whole of Japan. The population denominators used were derived from census data of the target areas.

In each area, in order to reduce sampling bias due to case reporting failures, we adjusted using the response rates. The reciprocal of the product of the response rate for steps 1 and 2 (sample weight) was calculated, and the number of EOD patients was estimated using the sample weight multiplied by the reported number of cases as follows.

n_{ij} = reported number of dementia cases by area i and age strata j

w_i = sampling weight of area i

P_{ij} = population of area i and age strata j .

We defined the estimated number of dementia cases of area i , age strata j

as $m_{ij} = w_i n_{ij}$.

and the estimated prevalence per X as $\hat{\lambda}_{ij} = \frac{m_{ij}}{P_{ij}} X$.

Then, the estimated prevalence was adjusted by the standardized population, and the weighted average

prevalence was calculated for the purpose of reducing the influence of different population distributions as follows.

T_j = all Japan population of age strata j at study period $S_j = \frac{T_j}{\sum_j T_j}$.

The estimated prevalence adjusted by the standardized population in area i was obtained by

$$\hat{T}_i = \sum_j S_j \hat{\lambda}_{ij}$$

We defined the population of area i as $P_i = \sum_j P_{ij}$.

The weighted average prevalence was obtained by

$$\hat{T} = \sum_i \Phi_i \hat{T}_i$$

and $\Phi_i = \frac{\sum_j P_{ij}}{\sum_{ij} P_{ij}}$.

The EOD prevalence for the total Japanese population was estimated by integration of the adjusted prevalence in the five catchment areas. We regarded this prevalence as the Japanese standardized prevalence.

We calculated 95% confidence intervals (CI) based upon a standard normal distribution. The significance of differences between rates was estimated by χ^2 -test or Fisher's exact tests. All analyses were carried out using SAS version 9.1 (SAS Institute, Cary, NC, USA) and R version 2.8.1 (The R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

As shown in Table 1, information from 2469 patients was collected from 12 747 institutions. Approximately 50% of the diagnoses were made in hospitals or clinics, and only 10% by general practitioners. For the remaining cases mainly cared for in LTCI institutions, diagnoses were made by either specialists or general practitioners to consider the appropriateness of their admission before the patients moved into their LTCI institutions.

After careful review of the answer sheets, patients with the following diagnoses were excluded: schizophrenia ($n = 8$), developmental disorder ($n = 38$), depression ($n = 6$), and other non-dementia disorders ($n = 25$). None of these patients were considered to have had concomitant EOD. Fifty-six patients were excluded because their age on the census day was over 65, although their age at onset of dementia was less than 65.

We received reports from two or more institutions for the same 157 cases. Consequently, 176 reports for

Table 1. Response rates of the postal surveys

Institutions	Step 1			Step 2			Reported cases
	Target population	<i>n</i> [†]	Response rate (%)	Target population	<i>n</i> [†]	Response rate (%)	
Hospitals	1 489	1 231	(82.7)	254	210	(82.7)	1429
Clinics	5 573	4 622	(82.9)	151	119	(78.8)	276
Health service facilities	385	326	(84.7)	95	81	(85.3)	185
Special nursing homes	919	847	(92.2)	137	112	(81.8)	214
Group homes	812	733	(90.3)	97	78	(80.4)	123
Welfare service center for disabled people	464	427	(92.0)	12	11	(91.7)	115
Day center	362	332	(91.7)	45	37	(82.2)	66
Home-visit nursing facilities	488	266	(54.5)	38	35	(92.1)	62
Welfare living centers	356	316	(88.8)	47	42	(89.4)	80
Government services	156	139	(89.1)	13	12	(92.3)	90
Local welfare commissioners	201	186	(92.5)	14	9	(64.3)	28
Care managers	1 542	1 156	(75.0)	174	147	84.5	233
Total	12 747	10 582	(83.0)	1077	893	(82.9)	2901

[†]Number of respondent institutions.

the 157 cases were excluded. Among these cases, nine received different diagnoses according to the informants: AD and DLB for four cases, AD and brain infection for one, AD and Behçet's disease for one, AD and FTLD for one, AD and alcohol-related dementia for one, and VaD and alcohol-related dementia for one. Overall percent agreement of diagnosis for the 157 doubly or triply reported cases was 95.1%, and the percent for 40 of the 157 patients with diagnosis of VaD was as high as 97.5%.

For the cases lacking diagnostic agreement, we prioritized the diagnoses according to the following order: diagnosed by neurologists or psychiatrists at general hospitals, including university hospitals; diagnosed by psychiatrists or neurologists; diagnosed by physicians at general hospitals; diagnosed by physicians at clinics; and diagnosed by physicians from other health-care facilities. The final sample population comprised 2059 subjects (61.0% male). The mean age and age at dementia onset on the census day were 56.4 years (SD, 8.0; range, 18–64 years) and 51.3 years (9.8; 18–64 years), respectively.

As shown in Figure 2, of the illnesses causing EOD, VaD was the most frequent (40.1%), followed by AD (24.3%), head trauma (8.4%), FTLD (3.6%), alcohol-related dementia (3.2%), DLB/PDD (2.8%)

and others (14.2%). The 'Other' category included seven subcategories: dementia secondary to neurodegenerative disorders (4.4%), for example, spinocerebellar degeneration, multiple system atrophy and progressive supranuclear palsy; infection (3.1%); surgery for brain tumor (1.9%); hypoxia (1.4%); other organic brain syndrome (2.9%), for example, normal pressure hydrocephalus and epilepsy; unknown dementia (3.4%); and overlap (0.5%). Six patients with both AD and VaD were included in the overlap category. The main subtypes of VaD were single large infarction (37.3%), intra-cerebral hemorrhage (35.7%), and subarachnoid hemorrhage (18.6%) (Fig. 2). Table 2 shows the prevalence rate of AD and VaD by sex for each catchment area. The most frequent illness causing EOD was VaD for men in all catchment areas, and AD for women in four areas. There was no significant difference in the distribution of VaD and AD for both sexes among the catchment areas. The prevalence of dementia in terms of dementia severity and the ratio for living places are shown in Table 2.

The QC evaluations were performed for 545 EOD individuals (26.5%). The percentage of agreement between the authors and doctors at the selected institutions for diagnosis of overall dementia was 98.9% and for VaD, it was 100%. The frequency of illnesses

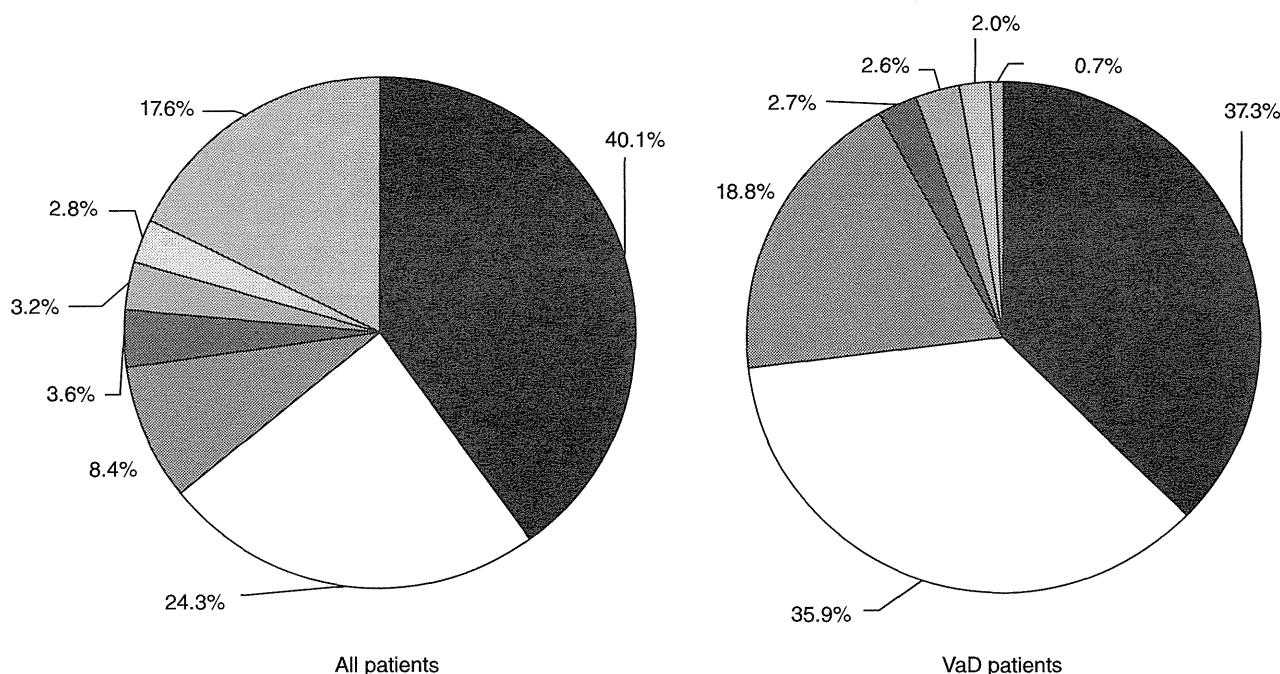


Figure 2. Distribution of diagnoses. All patients: (■) vascular dementia (VaD); (□) Alzheimer's disease; (▨) Head trauma; (▩) frontotemporal lobar degeneration; (▧) alcohol-related dementia; (▦) dementia with Lewy bodies/Parkinson's disease with dementia; and (▥) Others. VaD patients: (■) Large cortical infarct; (□) Cerebral hemorrhage; (▨) Subarachnoid hemorrhage; (▩) Unspecified; (▧) Mixed cerebrovascular disease; (▦) Multiple infarction; and (▥) Others.

causing EOD was calculated for two subgroups among the target individuals: university hospitals ($n = 252$) and others ($n = 293$). There were significant differences between the two groups ($P < 0.0001$): higher frequencies of AD (46.0%) and DLB (11.9%) and lower frequencies of VaD (6.3%) for the university hospital group. We reviewed CT or MRI images for 26.5% of patients during the 6-month study period and 18.6% after 6 months retrospectively because we offered quality control after we received the reports from institutions.

The total estimated number of patients adjusted by the standardized population of Japan was calculated to be 37 800. The prevalence rate in those aged 18–64 years was 47.6 per 100 000 (95%CI, 45.5–49.7). From the age of 30 onwards, the prevalence rate of dementia approximately doubled with each 5-year increase in age (Table 3).

DISCUSSION

To our knowledge, this is the largest population-based epidemiological study targeting EOD. There was no

significant difference between our study and those from Western countries (Table 4) in the prevalence of all types of EOD combined.^{4,5,12–17}

The proportion of illnesses causing EOD was quite different from the UK. Harvey *et al.*¹⁶ reported causes there as AD 34%, VaD 18%, FTL 12%, DLB 7%, alcoholic dementia 10%, and others 19%. Ratnavalli *et al.*¹⁵ reported that primary degenerative dementias accounted for 71%, of which 35% were AD and 22% were FTL. Namely, our study showed prominence of VaD, especially in men.

A nationwide study of Japanese EOD prevalence in 1997 also reported a higher prevalence of VaD (43.9%) than AD (16.8%).⁵ The Strategies against Stroke Study for Young Adults in Japan (SASSY-Japan) used data from 7245 stroke patients from 18 centers and compared the salient features of stroke in younger (<50 years old) and older groups (<51 years old).¹⁸ The SASSY-Japan study reported that male sex was a risk factor for the younger group. Even in Western countries, men have higher stroke prevalence than women, especially at young ages.¹⁹

Table 2. Comparison of five catchment areas

	Total	Ibaraki	Gunma	Toyama	Ehime	Kumamoto	P-value
Total population (all ages)	9 370 651	2 965 931	2 019 120	1 105 312	1 452 000	1 828 288	–
Target population aged 18–64 years, male (%)	5 664 741 (50.2)	1 862 942 (51.2)	1 238 395 (50.9)	654 646 (50.3)	848 641 (49.1)	1 060 137 (48.6)	–
Estimated number of patients	2 965	761	748	258	504	694	–
Prevalence [†] for age range 18–64	52.4	40.8	60.4	39.4	59.4	65.5	–
Prevalence [†] for age range 45–64	103.2	83.3	121.0	81.6	114.7	120.8	–
Prevalence [†] of AD and VaD by sex							
Male							
VaD	26.0	23.5	40.2	14.6	29.5	29.8	0.012
AD	9.7	9.0	11.8	12.1	14.3	8.0	0.448
Female							
VaD	11.9	12.0	14.1	7.4	12.6	16.7	0.675
AD	13.4	12.9	16.7	13.4	11.9	17.7	0.779
Both sexes							
VaD	19.1	18.1	27.4	11.0	21.3	23.1	0.113
AD	11.6	10.9	14.2	12.8	13.1	13.0	0.978
Severity of dementia							
Mild	24.3%	25.3%	24.3%	19.0%	22.8%	25.0%	–
Moderate	33.2%	29.0%	36.3%	29.9%	32.6%	37.9%	–
Severe	35.5%	36.0%	34.5%	46.0%	39.2%	29.4%	–
Living places							
Hospitalized and institutionalized	29.4%	36.8%	21.2%	30.8%	47.2%	35.8%	–
Living at home	38.3%	47.5%	62.1%	42.2%	40.5%	59.1%	–
Missing	32.3%	15.7%	16.7%	27.0%	12.3%	5.1%	–

[†]Prevalence per 100 000 population.
AD, Alzheimer's disease; VaD, vascular dementia.

Although several explanations, including the role of estrogen, have been proposed, the true reason why Japanese men are more vulnerable to stroke than women remains an open question. At any rate, the high frequency of VaD in men accounts for the main result. On the other hand, it should be noted that AD prominence in women was observed in four of the five areas. Another important issue is the difference between presenile and senile populations in Japan in the pathogenesis of VaD. The SASSY-Japan reported that cerebral and subarachnoid hemorrhage were the major cause of presenile stroke, whereas lacunar infarction was the major cause in senile stroke victims. Our study also revealed that cerebral and subarachnoid hemorrhage were the major cause of EOD. Additionally, a population-based study of persons aged 65 years and older in a Japanese community found that the most frequent illness caus-

ing VaD was multiple lacunar infarction.²⁰ Taken together, the causes of stroke in the younger population appear to be quite different from those affecting the older population.

Our QC study and the examination of doubly or triply reported cases showed a high concordance between the diagnosis of illnesses causing EOD in general and VaD in particular. The QC also revealed that the most common EOD-causing illness was AD for all of the five university hospitals, which replicated the results of previous university-hospital-based EOD studies in Japan.^{2,3} On the other hand, VaD was the leading cause for patients in the non-university hospitals. Considering the above-described Japanese medical system for acute and degenerative illnesses, this difference may be understandable. A possible reason for the discrepancy between the university-hospital-based diagnoses and those in other institu-

Table 3. Prevalence of early onset dementia in Japan

Age range, years	Japanese population (thousands)			All causes of dementia			Male			Female		
	Total	Male	Female	n [†]	Prevalence	95%CI [†]	n	Prevalence	95%CI	n	Prevalence	95%CI
18–19	2 618	1 341	1 277	21.6	0.8	(0.5–1.3)	21.9	1.6	(1.1–2.5)	0.0	0.0	0.0–0.3
20–24	7 238	3 716	3 521	367.3	5.1	4.6–5.6	289.5	7.8	6.9–8.7	78.6	2.2	1.8–2.8
25–30	7 795	3 967	3 828	451.6	5.8	5.3–6.4	330.5	8.3	7.5–9.3	120.3	3.1	2.6–3.8
30–34	9 363	4 748	4 615	552.6	5.9	5.4–6.4	434.9	9.2	8.3–10.1	117.0	2.5	2.1–3.0
35–39	9 426	4 763	4 663	839.8	8.9	8.3–9.5	539.2	11.3	10.4–12.3	301.8	6.5	5.8–7.2
40–44	8 220	4 141	4 079	1 218.4	14.8	14.0–15.7	766.3	18.5	17.2–19.9	455.6	11.2	10.2–12.2
45–49	7 733	3 879	3 854	2 094.9	27.1	26.0–28.3	1 303.7	33.6	31.8–35.5	795.5	20.6	19.3–22.1
50–54	8 051	4 018	4 033	4 163.6	51.7	50.2–53.3	2 737.3	68.1	65.6–70.7	1 407.9	34.9	33.1–36.8
55–59	10 433	5 162	5 271	12 006.8	115.1	113.0–117.2	7 460.2	144.5	141.3–147.8	4 492.8	85.2	82.8–87.8
60–64	8 473	4 130	4 343	16 036.9	189.3	186.2–192.1	9 173.5	222.1	217.6–226.7	6 740.3	155.2	151.5–158.9
18–64	79 350	39 865	39 484	37 753.5	47.6	47.1–48.1	23 056.9	57.8	57.1–58.6	14 509.8	36.7	36.2–37.4
45–64	34 690	17 189	17 501	34 302.2	98.9	97.8–99.9	20 674.7	120.3	118.7–121.9	13 436.5	76.8	75.5–78.1

[†]Estimated number of patients. [†]95%CI: based on standard normal distribution. CI, confidence interval.

tions might be that cerebrovascular disease as an underlying illness of VaD is a common disease in middle age, so patients usually get medical treatment in general hospitals in Japan. On the other hand, early onset AD and DLB are still difficult to diagnose, so patients are referred from general hospitals or clinics to university hospitals for detailed examination.

The prevalence of FTLD in this study was lower than that in the UK (15.4%)^{15,16} and the Nether-

lands (15.1%).¹⁷ One possible reason is the rarity of familial FTLD cases in Japan, but otherwise the cause of this finding remains unknown.²¹

A limitation of the current study is that we could not confirm the accuracy of the diagnosis by neuropathological examination. Thus it remains possible that pathological diagnoses might alter the distribution due to mixed pathologies,²² and vascular lesions might co-exist with other pathologies reducing the

Table 4. Comparison of prevalence of dementia per 100 000 in the 30–64-year-old age group among studies

Authors	Year	Country	Place	Population		Prevalence	Target	
				Age range	at risk			
Mölsä <i>et al.</i> ¹²	1982	Finland	Turku	45–54	–	10	All dementia	
				55–64	–	24	144.0	
Kokmen <i>et al.</i> ¹³	1989	USA	Rochester	45–49	–	2	All dementia	
				50–54	–	1	40.0	
				55–59	–	2	86.0	
				60–64	–	5	249.0	
Newens <i>et al.</i> ¹⁴	1993	UK	Northern Health Region	45–64	655 800	227	34.6	AD
Ohshiro <i>et al.</i> ⁴	1994	Japan	Tottori	40–64	209 621	100	81.4	All dementia
Ichinowatari <i>et al.</i> ⁵	1997	Japan	5 catchment areas	18–64	3 729 706	1203	48.1	All dementia
Ratnavalli <i>et al.</i> ¹⁵	2002	UK	London	45–64	326 019	59	81.0	All dementia
Harvey <i>et al.</i> ¹⁶	2003	UK	–	30–64	240 766	130	54.0	All dementia
Rosso <i>et al.</i> ¹⁷	2003	Netherlands	Zuid-Holland	30–59	1 435 769	21	1.5	FTLD
Present study	2009	Japan	5 catchment areas	18–64	9 370 651	2059	47.6	All dementia

AD, Alzheimer’s disease; FTLD, frontotemporal lobar degeneration; VaD, vascular dementia.