Intracerebral Hemorrhage in a Japanese Community, Hisayama: Incidence, Changing Pattern During Long-term Follow-up, and Related Factors

Kazuo Ueda, MD, Yutaka Hasuo, MD, Yutaka Kiyohara, MD, Junichi Wada, MD, Hideo Kawano, MD, Isao Kato, MD, Ichiro Fujii, MD, Toshiro Yanai, MD, Teruo Omae, MD, and Masatoshi Fujishima, MD

The incidence of intracerebral hemorrhage over 13 years is compared between two Hisayama cohorts. Among men aged 40 years or older, the annual incidence declined significantly from 3.1/1,000 in the early cohort (1961–1970) to 1.2/1,000 in the recent cohort (1974–1983). Massive ganglionic hemorrhage decreased, while small or medium-sized intracerebral hemorrhage increased in the recent cohort on pathologic or computed tomographic examination. These trends could be due to the reduced prevalence of hypertension in the Hisayama population. The association of serum total cholesterol with intracerebral hemorrhage is discussed based on the results during a 22-year follow-up period. (*Stroke* 1988;19:48–52)

Downloaded from http://ahajournals.org by on March 12, 2022

It was generally conceded in the 1950s that the rate of intracerebral hemorrhage (ICH) was extraordinarily high in Japan, with high mortality deriving from the high prevalence of hypertension. Some investigators[1] contended that the alleged prevalence of ICH in the Japanese was the result of bias in diagnostic style and a low autopsy rate. During the last 20 years, mortality from ICH in the Japanese has declined conspicuously in the vital statistics[2] as well as in actual community studies.[3] This decline is partly ascribable to a reduction in the prevalence of hypertension[4] as well as to nutritional changes in the Japanese diet. The latter was concluded from the evidence reported in a community study[5] in Japan that showed that low serum cholesterol is a strong contributory factor for ICH in the Japanese. However, controversy still remains as to whether ICH was truly the main type of cerebral stroke in the past and, if the incidence of ICH has really decreased, what the main factor in its decline has been. An answer can be obtained only from the results of a long-term population survey based on accurate diagnostic determination. The autopsy-based Hisayama study was originally designed to establish the specific type and incidence of cerebral stroke in the Japanese.[6] This article describes the incidence of and risk factors for ICH during a 22-year follow-up period and the change in the incidence of ICH observed in two Hisayama populations over a 13-year period. We were particularly concerned with the relation between blood pressure and serum total cholesterol as risk factors for ICH.

From the Second Department of Internal Medicine, Faculty of Medicine, Kyushu University, Fukuoka City, and the National Cardiovascular Disease Center, Osaka (T.O.), Japan.

Supported in part by Research Grants for Cardiovascular Disease A-60-4 and I-60-4 from the Ministry of Health and Welfare, Japan; facilitated by the Japan-U.S. Cooperative Agreement in the Cardiovascular Area by the Japanese National Cardiovascular Center and the National Heart, Lung, and Blood Institute.

Received November 28, 1986; accepted July 1, 1987.

Subjects and Methods

The Hisayama prospective population study was initiated in 1961 to explore the epidemiology of cerebrovascular disease in a general population sample of 1,621 men and women aged 40 years or older at entry. The subjects comprised about 90% of all the residents in this age group in the town of Hisayama (first cohort). The study subjects have been followed continuously since November 1961, and causes of death among the cohort population were examined by autopsy in 82.4% of the 722 deceased for a period of 22 years. Follow-up for subjects who moved out of town has been reasonably complete, with only 0.1% of the study subjects lost.

In 1973, two thirds of the study population had entered the geriatric age group and 20% had died. A new group of 1,156 persons aged 40 years or older was added to the original cohort, resulting in a second cohort of 2,135 subjects. This cohort comprised 80% of all residents aged 40 years or older in the town in 1973.[7] Excluding the 82 subjects who died during the period of examination or who had already had a cerebral stroke, a total of 2,053 subjects (second cohort) has been followed from November 1974 to October 1983 without loss of any subject to follow-up.[8]

Average age at entry was 55.5 years for men and 56.9 years for women in the first cohort and 56.5 years for men and 58.3 years for women in the second. More elderly persons were included in the second cohort. The autopsy rate during the study period was 81.4% of 290 deceased for the first cohort and 85.9% of 263 for the second.

Table 1. Type-Specific Frequency of Cerebral Stroke, First Cohort, Hisayama, 1961–1983

	Men		Women		Total	
	No.	%	No.	%	No.	%
Cerebral infarction*	109	71.7	100	71.4	209	71.6
Intracerebral hemorrhage	34	22.4	15	10.7	49	16.8
Subarachnoid hemorrhage	6	3.9	20	14.3	26	8.9
Ill-defined	3	2.0	5	3.6	8	2.7
Total	152	100.0	140	100.0	292	100.0

*Embolic and nonembolic stroke.

Details of methods of examination and follow-up have been described elsewhere.[3]

We compared the incidence of cerebral stroke for 9 years between the two cohorts from November 1961 to October 1970 for the first cohort and from November 1974 to October 1983 for the second. In 22 years of follow-up, the type-specific fatal rate of cerebral stroke was 91.8% for ICH, 69.2% for subarachnoid hemorrhage, and 43.5% for cerebral infarction (CI). Of those, 75.6, 85.7, and 84.6%, respectively, were autopsied. Mortality from ICH in the second cohort during 9 years of follow-up was 72.7%, with an autopsy rate of 100%.

As the multivariate analysis for possible risk factors of ICH, we used the multiple logistic regression of Walker and Duncan,[9] in which appropriately determined scores were assigned ordinal values, and continuous variables were entered directly into the equation. We applied two types of analysis to the estimation of serum total cholesterol, evaluating cholesterol values as both continuous and ordinal variables.

Results

Table 1 indicates the type-specific frequency of cerebral stroke for the first cohort during 22 years of follow-up. Of 292 newly occurred cerebral strokes, CI was the most frequent (71.6%); ICH accounted for 16.8%, subarachnoid hemorrhage for 8.9%, and poorly defined types for 2.7%. Table 2 depicts the average annual incidence of CI and ICH for the first cohort by sex and age during the 22-year follow-up. The rate for CI increased with advancing age in both sexes, while that for ICH did not. ICH was notably more frequent in men than in women, with the ratio of CI to ICH 3.2 in men and 6.7 in women.

Because of the high mortality rate from ICH (92%) during the 22-year follow-up, an analysis of risk factors was restricted to fatal ICH. The incidence of fatal ICH in the first cohort was calculated by serum total cholesterol levels at entry (Table 3). The study subjects were grouped by cholesterol level; those in the 10th percentile (76–106 mg/dl) were the low group, while those in the 90th percentile (193–284 mg/dl) were the high group. The remainder were the middle group (107–192 mg/dl). Among men, the rate of fatal ICH was highest in the high cholesterol group, followed by the low and middle groups; for women, fatal ICH more frequently occurred in the low cholesterol group than in the high or middle groups.

Seven possible risk factors for fatal ICH for men were analyzed using a multiple logistic regression model. The standardized regression coefficients of these variables are given in Table 4. In Analysis I, actual cholesterol values were entered into the equation as continuous variables, whereas cholesterol levels were coded in Analysis II as follows: low group as 1, moderate group as 2, and high group as 3. The only significant risk factor for fatal ICH was mean blood pressure in Analysis I; low and high cholesterol groups, as well as mean blood pressure, were independent risk factors for fatal ICH in Analysis II. This evidence suggests that both high and low cholesterol values may contribute to fatal ICH.

Table 5 compares the incidence of ICH for 9 years between the two Hisayama populations each over a 13-year period. The annual incidence of ICH for men in the second cohort decreased to 1.2/1,000 from 3.1/1,000 for that in the first cohort. For women there was no difference between the cohorts in the incidence of ICH, although for both sexes combined the inci-

Table 2. Average Annual Incidence Rates of Cerebral Infarction and Intracerebral Hemorrhage by Sex and Age at Entry, First Cohort, Hisayama, 1961–1983

	Men					Women				
Age at entry	No. of subjects	CI		ICH		No. of subjects	CI		ICH	
		Rate	Cases	Rate	Cases		Rate	Cases	Rate	Cases
40–49	246	2.8	15	1.1	6	305	1.0	7	0.9	6
50–59	216	6.3	30	3.2	15	263	4.1	24	0.9	5
60–69	168	10.8	40	2.4	9	194	8.0	34	0.2	1
70+	77	14.2	24	2.4	4	152	10.5	35	0.9	3
Total	707	7.0	109	2.2	34	914	5.6	100	0.7	15

CI, cerebral infarction; ICH, intracerebral hemorrhage; rate, cases/1,000/yr. CI:ICH for men 3.2, for women 6.7.

Downloaded from http://ahajournals.org by on March 12, 2022

Table 3. Rate of Fatal Intracerebral Hemorrhage and Cholesterol Levels, First Cohort, Hisayama, 1961–1983

Cholesterol group	Men			Women		
	No. of subjects	ICH	Rate	No. of subjects	ICH	Rate
Low	74	6	3.7	98	4	1.9*
Middle	538	16	1.4	692	7	0.5
High	77	9	5.3†	90	2	1.0

For definition of cholesterol levels, see text. Rate, cases/1,000/yr. 52 cases without cholesterol data were excluded.
*$p<0.05$ (Mantel-Haenszel $\chi^2=4.69$ vs. Middle).
†$p<0.01$ (Mantel-Haenszel $\chi^2=11.21$ vs. Middle).

dence of ICH in the second cohort was still significantly decreased. Of particular interest was a trend in the second cohort for increased incidence of ICH in men aged ≥70 years.

Possible risk factors for ICH were compared for men with ICH in both cohorts (Table 6). More elderly patients were included in the second cohort, and diastolic blood pressure was significantly lower in this group. In addition, systolic blood pressure tended to be lower and serum total cholesterol higher in the second cohort, although the difference was not significant.

Pathologic characteristics of ICH were studied in men from the two cohorts (Table 7). Only cases in which hematomas were confirmed either by autopsy or by computed tomography were included in the study. The incidence of massive cerebral hemorrhage was significantly reduced in the second cohort, whereas the incidence of small or medium-sized cerebral hemorrhage (<2 cm²) increased ($p<0.05$, χ^2 with Yates' modification); ganglionic hemorrhage was responsible for most of this increase.

Discussion

Data on proportional frequency of ICH among all types of cerebral stroke can be obtained from surveys of stroke registries, which have recently been conducted in the United States and Europe. ICH caused 4–11% of all strokes in the Harvard Cooperative Stroke Registry,[10] National Stroke Survey,[11] Stroke Data Bank,[12] and community hospital-based stroke programs.[13] Frequency of ICH in the community-based stroke registries in Sweden,[14] the Netherlands,[15] and Finland[16] was approximately 10%. Tanaka et al[17] reported a higher frequency of ICH in the stroke registry of Shibata, Japan.

Some of these studies are based on hospital records as the source of data and may be selectively biased by emphasizing strokes that are severe and require hospitalization; general population survey data can be more representative. According to the results from the Framingham Study[18] for a 26-year follow-up, the frequency of ICH among total strokes was 5% for men and 3% for women. The Framingham data[19] show that nine ICHs developed over 24 years in an original population of 2,282 men and seven in a group of 2,845 women, thus permitting an estimated crude incidence of ICH of 0.16/1,000/yr for men and 0.10/1,000/yr for women. Compared with these figures, ICH was observed more frequently in our study (22% of total strokes for men and 10% for women), with the crude incidence 2.2/1,000/yr and 0.7/1,000/yr, respectively. This evidence suggests that the notably higher mortality from ICH indicated by the vital statistics of Japan in 1950 reflects both the bias originating from the death-certificate practice of Japanese physicians and from the higher incidence of ICH.

The age-adjusted death rate from cerebrovascular disease has decreased in Japan since 1965 and, in particular, since 1971.[20] This downward trend has been more marked in mortality resulting from ICH and may be due to decreasing incidence, rather than to just an improvement in death-certificate practice. In our study, ICH significantly decreased among men in the second cohort. The prevalence of hypertension, which is well known to be the most powerful contributor to the development of ICH especially in those subjects with elevated diastolic blood pressure, was decreased prominently in the recent Hisayama population.[4,8] There is no doubt, therefore, that the decreasing incidence of ICH may be related to this reduction in hypertensive subjects. On the other hand, the prevalence of obesity or hypercholesterolemia has recently increased in Hisayama men.[4] A question arises as to whether these metabolic changes are also related to the decreasing incidence of ICH. Ueshima et al[5] reported that low serum total cholesterol was strongly associated with ICH incidence in a community in northern Japan. In our study, both high and low cholesterol levels seemed to be risk factors.

Several possible explanations can be drawn from our study. First, serum total cholesterol has no effect on the development of ICH, and an association of serum cholesterol with ICH mortality may be temporal and not causative. Second, hypercholesterolemia may be a risk factor for ICH, and moderate levels of serum cholesterol might prevent ICH. It is quite conceivable that some additional factor(s) may account for the ob-

Table 4. Risk Factors for Fatal Intracerebral Hemorrhage and Standardized Logistic Regression Coefficients, First Cohort, Hisayama Men, 1961–1983

	Analysis I	Analysis II
Cholesterol	0.135	
Low cholesterol group		0.374*
High cholesterol group		0.484†
Age	−0.059	−0.012
Mean blood pressure	1.022†	1.013†
Abnormal electrocardiogram‡	0.012	−0.019
Quetelet index	−0.108	−0.114
Alcohol§	0.169	0.114
Cigarettes‖	0.101	0.019

Analysis I, cholesterol level as continuous variables; Analysis II, cholesterol group as ordinal variables.
*$p<0.05$; †$p<0.01$.
‡Minnesota code III_1 and/or IV_{1-3}.
§33 g ethanol or more daily.
‖10 cigarettes or more daily.

Downloaded from http://ahajournals.org by on March 12, 2022

Table 5. Average Annual Incidence Rate for Intracerebral Hemorrhage by Age at Entry, Two Hisayama Cohorts, 1961–1970 and 1974–1983

	Men						Women						Total					
	First cohort			Second cohort			First cohort			Second cohort			First cohort			Second cohort		
Age at entry	No.	Rate	Cases	No.	Rate	Cases	No.	Rate	Cases	No.	Rate	Cases	No.	Rate	Cases	No.	Rate	Cases
40–49	246	1.4	3	295	0.4	1	305	0.4	1	341	—	—	551	0.8	4	636	0.2	1
50–59	216	4.6	9	239	0.5	1	263	0.8	2	346	1.0	3	479	2.6	11	585	0.8	4
60–69	168	3.3	5	198	1.1	2	194	—	—	270	1.2	3	362	1.5	5	468	1.2	5
70+	77	4.3	3	130	6.0	7	152	1.5	2	234	0.9	2	229	2.4	5	364	2.7	9
Total	707	3.1	20	862	1.4	11	914	0.6	5	1191	0.7	8	1621	1.7	25	2053	1.0	19
Age-adjusted		3.1*			1.2			0.6			0.7			1.7*			0.9	

Rate, cases/1,000/yr; age-adjusted, adjusted to first cohort population by direct method.
*$p<0.05$ vs. second cohort, Mantel-Haenszel χ^2.

served association of serum cholesterol with ICH mortality. Meanwhile, our study may suggest another interesting point concerning the relation between ICH and serum cholesterol. ICH was more frequently observed in elderly Hisayama men in the second cohort despite a reduction in the total incidence of ICH. Moreover, mean systolic or diastolic blood pressure was lower in the patients with ICH from the second cohort compared with those from the first cohort, whereas mean serum total cholesterol was higher in those from the second cohort. Comparing pathologic characteristics of ICH between cohorts, massive ICH, especially ganglionic hemorrhage, was reduced while small or medium-sized hemorrhages increased. Any conclusion still remains controversial because the number of cases analyzed was small and because five cases with equivocal location of hematoma were excluded.

Since the introduction of computed tomography, a number of small encapsulated hematomas, which in the past would have been diagnosed clinically as infarcts, have been identified. It has been reported that small hemorrhages on the basal ganglia clinically reveal lacunar syndrome[21–23] as delineated by Fisher and associates,[24–27] and the underlying cause is considered to be hypertensive changes in penetrating arteries. Sustained hypertension initiates an acceleration of vascular permeability, resulting in deposition of fibrin and forming lipohyalinosis. Arterioles are liable to become occluded with thrombosis resulting in microinfarction, or there may be weakening of the vascular wall, microaneurysms, and diapedesis. Brain arteriosclerosis may be accelerated by hypertension, aging, and high serum cholesterol. If these factors promote arteriosclerosis rather than microaneurysmal formation, a massive cerebral hemorrhage due to consecutive occurrence of microaneurysmal ruptures could be prevented.

Since the cause of ICH varies, another etiology less related to hypertension should be considered. Two cases with lobar ICH were observed in the second cohort. Compared with hematomas reported by others,[28,29] there is a low incidence of hypertension in this group. Of those etiologies not resulting from hypertension, arteriovenous malformation, tumor, blood dyscrasia, or cerebral amyloid angiopathy (CAA) are well recognized. CAA should be important as an underly-

Table 6. Possible Risk Factors in Men With Intracerebral Hemorrhage in Two Hisayama Cohorts

	First cohort ($n=20$)	Second cohort ($n=11$)
Age at onset	62.5 yrs	73.3 yrs*
Blood pressure		
Systolic	171.0 mm Hg	155.3 mm Hg
Diastolic	98.9 mm Hg	81.3 mm Hg*
Cholesterol	159.1 mg/dl	173.5 mg/dl
Quetelet index	22.0	20.8
Electrocardiogram		
High R	65%	18%
ST depression	0%	18%
Alcohol	35%	46%
Cigarettes	65%	73%
Diabetes mellitus	20%	36%

Data obtained in 1961 for first cohort and in 1973–1974 for second cohort. *n*, cases with intracerebral hemorrhage.
*$p<0.05$ vs. first cohort.

Table 7. Pathologic Characteristics of Cerebral Hemorrhage for Men in Two Hisayama Cohorts

	First cohort ($n=16$)	Second cohort ($n=10$)
Massive hemorrhage	14*	4
Putaminal	7	2
Thalamic	2	1
Pontine	2	0
Lobar	3	1
Small or medium-sized hemorrhage	2	6
Ganglionic	2	4
Lobar	0	1
Cerebellar	0	1

Hematomas were confirmed by autopsy or computed tomography. Small or medium-sized hematomas were localized and not ruptured into ventricular and subarachnoid space. *n*, cases with intracerebral hemorrhage.
*$p<0.05$ vs. second, χ^2 test modified by Yates.

Downloaded from http://ahajournals.org by on March 12, 2022

ing cause of ICH in the elderly. However, on histologic examination of the cerebral arteries of Hisayama residents autopsied consecutively using Congo red stain and polarized light microscopy,[30] only one of 26 cerebellar hemorrhages examined was attributed to CAA. Therefore, ICH due to CAA is considered to be less frequent in the general population. In our study, an etiologic consideration of ICH was limited to men because of the few cases of ICH in women. Since ICH is reported to be less frequent among women, a further study may be necessary to determine risk factors for ICH in women.

References

1. Goldberg ID, Kurland LT: Mortality in 33 countries from diseases of the nervous system. *World Neurol* 1962;3:444–465
2. Omae T: Prevention of stroke (in Japanese). *Jpn J Stroke* 1981;3:97–99
3. Ueda K, Omae T, Hirota Y, Takeshita M, Katsuki S, Tanaka K, Enjoji M: Decreasing trend in incidence and mortality from stroke in Hisayama residents, Japan. *Stroke* 1981;12:154–160
4. Ueda K, Omae T: Control of hypertension in a Japanese community, in Bulpitt CJ (ed): *Handbook of Hypertension*, vol 6. *Epidemiology of Hypertension*. Amsterdam, Elsevier Science Publishers, 1985, pp 412–423
5. Ueshima H, Iida M, Simamoto T, Komishi M, Komachi Y: Multivariate analysis of risk factors for stroke. Eight-year follow-up study of farming villages in Akita, Japan. *Prev Med* 1980;9:722–740
6. Katsuki S: Epidemiological and clinicopathological study on cerebrovascular disease in Japan. *Prog Brain Res* 1966; 21B:64–89
7. Omae T, Ueda K, Kikumura T, Shikata T, Fujii I, Yamai T, Hasuo Y: Cardiovascular deaths among hypertensive subjects of middle to old age: A long-term follow-up study in a Japanese community, in Onesti G, Kim KE (eds): *Hypertension in the Young and Old*. New York, Grune & Stratton Inc, 1981, pp 285–297
8. Omae T, Ueda K: Risk factors of cerebral stroke in Japan: Prospective epidemiological study in Hisayama community, in Katsuki S, Tsubaki T, Toyokura Y (eds): *Proceedings of the 12th World Congress of Neurology*. Amsterdam, Excerpta Medica, 1982, pp 119–135
9. Walker SH, Duncan DB: Estimation of the probability of an event as a function of several independent variables. *Biometrika* 1967;54:167–179
10. Mohr JP, Caplan LR, Melski JW, Goldstein RJ, Duncan GW, Kistler JP, Pessin MS, Bleich HL: The Harvard Cooperative Stroke Registry: A prospective registry. *Neurology* 1978; 28:754–762
11. Walker AE, Robins M, Weinfeld FD: Clinical findings. The National Survey of Stroke. *Stroke* 1981;12(suppl 1):I-13–I-31
12. Kunitz SC, Gross CR, Heyman CS, Kase CS, Mohr JP, Price TR, Wolf PA: The Pilot Stroke Data Bank: Definition, design, and data. *Stroke* 1984;15:740–746
13. Yatsu FM, Becker C, McLeroy KR, Coull B, Feibel J, Howard G, Toole JF, Walker MD: Community hospital-based stroke programs: North Carolina, Oregon, and New York. I: Goals, objectives, and data collection procedures. *Stroke* 1986;17: 276–284
14. Mettinger KL, Söderström CE, Allander E: Epidemiology of acute cerebrovascular disease before the age of 55 in the Stockholm county 1975–1977: I. Incidence and mortality rates. *Stroke* 1984;15:795–801
15. Herman B, Schulte BPM, Luijk JH, Leyten ACM, Frenken CWGM: Epidemiology of stroke in Tilbung, the Netherlands. The population-based stroke incidence register: I. Introduction and preliminary results. *Stroke* 1980;11:162–165
16. Sivenius J, Heinonen OP, Pyörälä J, Salonen J, Reikkinen P: The incidence of stroke in the Kupio area of east Finland. *Stroke* 1985;16:188–192
17. Tanaka H, Ueda Y, Date C, Baba T, Yamashita H, Hayashi M, Shoji H, Owada K, Baba K-I, Shibuya M, Kon T, Detels R: Incidence of stroke in Shibata, Japan: 1976–1978. *Stroke* 1981;12:460–466
18. Kannel WB, Wolf PA: Epidemiology of cerebrovascular disease, in Ross Russell RW (ed): *Vascular Disease of the Central Nervous System*. London, Churchill Livingstone, 1983, pp 1–24
19. Dawber TR: *The Framingham Study: The Epidemiology of Atherosclerotic Disease*. Cambridge, Mass, Harvard University Press, 1980
20. Tanaka H, Tanaka Y, Hayashi M, Ueda Y, Date C, Baba T, Shoji H, Horimoto T, Owada K: Secular trends in mortality for cerebrovascular disease in Japan, 1960 to 1979. *Stroke* 1982;13:574–581
21. Mori E, Tabuchi M, Yamadori A: Lacunar syndrome due to intracerebral hemorrhage. *Stroke* 1985;16:454–459
22. Rascol A, Clanet M, Manelfe C, Guiraud B, Bonafe A: Pure motor hemiplegia: CT study of 30 cases. *Stroke* 1982;13:11–17
23. Tapia JF, Kase CS, Sawyer RH, Mohr JP: Hypertensive putaminal hemorrhage presenting as pure motor hemiparesis. *Stroke* 1983;14:505–506
24. Fisher CM: Pure sensory stroke involving face, arm and leg. *Neurology* 1965;15:76–80
25. Fisher CM: A lacunar stroke. The dysarthria clumsy hand syndrome. *Neurology* 1967;17:614–617
26. Fisher CM, Cole H: Homolateral ataxia and crural paresis: A vascular syndrome. *J Neurol Neurosurg Psychiatry* 1965; 28:48–65
27. Fisher CM, Curry HB: Pure motor hemiplegia of vascular origin. *Arch Neurol* 1965;13:30–44
28. Ropper AH, Davis KR: Lobar cerebral hemorrhages: Acute clinical syndromes in 26 cases. *Ann Neurol* 1980;8:141–147
29. Weisberg LA: Subcortical lobar intracerebral hemorrhage: Clinical–computed tomographic correlations. *J Neurol Neurosurg Psychiatry* 1986;49:346–352
30. Masuda J: Incidence and distribution of cerebral amyloid angiopathy in autopsied brain of Hisayama residents in Japan (in Japanese with English abstract). *Nippon Ronen Igakkai Zasshi* 1985;22:138–143

KEY WORDS • epidemiology • intracerebral hemorrhage • Japan

Downloaded from http://ahajournals.org by on March 12, 2022