

Population-Based Incidence Rates of Subarachnoid Hemorrhage in Japan: The Shiga Stroke and Heart Attack Registry

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Dear Sir:

Stroke is the second leading cause of global deaths and disability-adjusted life years lost worldwide; although Japan had the highest stroke mortality in 1965, it has decreased rapidly, decreasing by approximately 80% in the past four decades, while the age-adjusted stroke mortality rate has also decreased worldwide in the past two decades.¹⁻³ Of all strokes, subarachnoid hemorrhage (SAH) is unique in that it develops in younger age groups, and the functional prognosis tends to be worse compared with ischemic stroke and intracerebral hemorrhage.^{4,5} Despite advances in diagnostic and treatment strategies, and the gradual improvement of the fatality rate, SAH still exacts high economic and social costs.^{4,5} It is well known that Finland and Japan have high incidence rates of SAH compared to the rest of the world.⁵ This study aimed to evaluate the incidence rate of SAH in Japan using data from a large-scale, population-based stroke registry in Shiga Prefecture, Japan, between 2011 and 2015.

The design and information regarding the Shiga Stroke and Heart Attack Registry (SSHR) has previously been described.⁶ In summary, it is an ongoing population-based registry that covers approximately 1.4 million residents of Shiga Prefecture in Japan and all cases of acute stroke that occur within that pop-

ulation. SSHR uses central-local coordination and monitoring, combined with remote data collection and quality control systems to create an integrated surveillance system that involves the registration of cases among a network of all acute-care hospitals with neurology and neurosurgery facilities in Shiga Prefecture. All stroke cases from January 1, 2011, to December 31, 2015, were included, and a total of 1,056 first-ever patients with SAH who were residents of Shiga Prefecture were included in the final analyses. The determination of stroke, patients' variables, and statistical analyses are shown in the Supplementary Methods.^{7,8} The age- and sex-standardized incidence rates were also calculated using the direct method with the population of the 2015 Japanese vital statistics as a reference.⁸

The SSHR has been approved by the Institutional Review Board of Shiga University of Medical Science (Reference number: 23-186-1) and is in accordance with the Declaration of Helsinki and the ethical standards of the responsible committee on human experimentation. Written informed consent of participants was waived due to the nature of this study.

Table 1 shows the annual distribution of patients with SAH. A total of 1,056 patients had first-ever SAH. Women were affected approximately twice as often as men for the 5-year period. The baseline characteristics of 1,056 patients are presented in Table

Table 1. The number of patients with subarachnoid hemorrhage (n=1,056): The Shiga Stroke and Heart Attack Registry, Shiga, Japan, 2011–2015

	2011	2012	2013	2014	2015	Total
Men	64	53	69	68	80	334
Women	160	142	148	139	133	722
Total	224	195	217	207	213	1,056

Table 2. Baseline characteristics of patients with subarachnoid hemorrhage stratified by sex (n=1,056): The Shiga Stroke and Heart Attack Registry, Shiga, Japan, 2011–2015

Variable	Overall (n=1,056)	Men (n=334)	Women (n=722)	P for trend
Age (yr)	66±15	60±15	68±15	<0.001
WFNS grade				
I	294 (28.1)	107 (32.3)	187 (26.1)	0.243
II	160 (15.3)	46 (13.9)	114 (15.9)	
III	60 (5.7)	20 (6.0)	40 (5.6)	
IV	149 (14.2)	48 (14.5)	101 (14.1)	
V	385 (36.7)	110 (33.2)	275 (38.4)	
Presentation				
Ambulance	873 (82.8)	265 (79.3)	608 (84.3)	0.150
Walk-in	147 (13.9)	58 (17.4)	89 (12.3)	
Hospitalized	16 (1.5)	6 (1.8)	10 (1.4)	
Hypertension	588 (55.7)	170 (50.9)	418 (57.9)	0.033
Systolic blood pressure (mm Hg)	161±38 (42–296)	163±37 (46–281)	160±38 (42–296)	0.133
Diastolic blood pressure (mm Hg)	90±23 (12–198)	95±24 (12–198)	87±23 (24–190)	<0.001
Diabetes mellitus	239 (22.6)	85 (25.5)	154 (21.3)	0.137
History of coronary heart disease	39 (3.7)	16 (4.8)	23 (3.2)	0.199
Smoking habit				
Never	572 (62.5)	77 (26.6)	495 (79.1)	<0.001
Past	96 (10.5)	71 (24.5)	25 (4.0)	
Current	248 (27.1)	142 (49.0)	106 (16.9)	
Drinking habit				
Never	560 (64.2)	94 (33.3)	466 (79.0)	<0.001
Past	9 (1.0)	5 (1.8)	4 (0.7)	
Occasional	75 (8.6)	30 (10.6)	45 (7.6)	
Current	228 (26.2)	153 (54.3)	75 (12.7)	
mRS score at discharge				
0	105 (19.9)	28 (8.4)	77 (10.7)	0.092
1	190 (18.0)	76 (22.8)	114 (15.8)	
2	95 (9.0)	34 (10.2)	61 (8.5)	
3	78 (7.4)	23 (6.9)	55 (7.6)	
4	136 (12.9)	43 (12.9)	93 (12.9)	
5	122 (11.6)	35 (10.5)	87 (12.1)	
6	325 (30.8)	92 (27.5)	233 (32.3)	

Values are presented as mean±standard deviation, number (%), or mean±standard deviation (range). The *P*-values for the trend between variables were computed using linear regression for continuous variables or the Mantel–Haenszel test for categorical variables.

WFNS, World Federation of Neurosurgical Societies; mRS, modified Rankin Scale.

2. The mean age (±standard deviation) at the time of hemorrhage was 66±15 years. Regardless of sex, the worst grade

(World Federation of Neurosurgical Societies [WFNS] grade=V) was observed most frequently (36.7%), followed by the mildest

Table 3. Age- and sex-specific incidence rates of subarachnoid hemorrhage per 100,000 person-years in the Shiga Stroke and Heart Attack Registry, Shiga, Japan, 2011–2015

Sex/Age (yr)	No. of events	Person-years	Incidence rate	95% CI
Men				
0–19	2	722,814	0.3	0.02–0.8
20–29	3	401,287	0.7	0.1–1.9
30–39	24	477,953	5.0	3.2–7.3
40–49	62	492,028	12.6	9.6–16.0
50–59	68	412,448	16.5	12.7–20.7
60–69	81	469,163	17.3	13.6–21.3
70–79	63	312,726	20.1	15.4–25.5
≥80	31	162,383	19.1	12.8–26.6
Total	334	3,450,802	9.7	8.6–10.8
Adjusted (JP2015)			10.4	10.2–10.7
Women				
0–19	2	682,130	0.3	0.03–0.9
20–29	3	363,384	0.8	0.1–2.1
30–39	17	467,883	3.6	2.1–5.6
40–49	68	484,487	14.0	10.8–17.6
50–59	112	420,950	26.6	21.8–31.9
60–69	158	484,012	32.6	27.7–38.0
70–79	177	353,762	50.0	42.8–57.8
≥80	185	301,421	61.4	52.7–70.7
Total	722	3,558,029	20.3	18.8–21.8
Adjusted (JP2015)			22.4	22.0–22.8
Overall				
0–19	4	1,404,944	0.3	0.07–0.6
20–29	6	764,671	0.8	0.3–1.6
30–39	41	945,836	4.3	3.1–5.8
40–49	130	976,515	13.3	11.1–15.8
50–59	180	833,398	21.6	18.5–24.9
60–69	239	953,175	25.1	21.9–28.4
70–79	240	666,488	36.0	31.5–40.8
≥80	216	463,804	46.6	40.4–53.1
Total	1,056	7,008,831	15.1	14.2–16.0
Adjusted (JP2015)			16.6	16.4–16.8

CI, confidence interval; JP2015, the 2015 Japanese Population.

grade (WFNS grade=I) (28.1%). More than 80% of the patients were transported to the hospital by ambulance and hypertension was found in 55.7% of all patients. Current smokers accounted for 49.0% of men and 16.9% of women; current drinkers accounted for 54.6% of men and 12.8% of women, and 30.8% of all patients died in the acute stage. Table 3 shows the distribution of the patients according to sex and 10-year age band and the age- and sex-standardized incidence rates according to Japan Vital Statistics 2015. Patients with SAH were most often identified in the 70s age group (22.7%), followed by the 60s age group (22.6%). The age- and sex-standardized SAH incidence rate, with the population of the 2015 Japanese vital statistics as

a reference, was 10.4 per 100,000 person-years (95% confidence interval [CI], 10.2 to 10.7) in men and 22.4 per 100,000 person-years (95% CI, 22.0 to 22.8) in women.

To the best of our knowledge, these data provide an initial estimate of the overall impact of SAH and the incidence data derived from the Japanese prefectural complete enumeration registry in the 2010s for several years, where the burden of stroke has been generally higher than that of coronary heart disease.¹ The strength of this study is that a comprehensive case ascertainment protocol was used to identify non-fatal or non-hospitalized stroke cases. Determining this in a relatively large multicenter database sheds light on important aspects of

patient care and can guide future research and funding. Recently, a meta-analysis showed that while worldwide SAH incidence has decreased by 40% between 1980 and 2010, SAH incidence has conversely increased by 59.1% over the last three decades in Japan.⁹ In this study, the age- and sex-adjusted SAH incidence was 16.6 per 100,000 person-years (95% CI, 16.4 to 16.8), and these figures remained high compared with other countries, but were lower compared with previous Japanese registry studies; however, there are large differences in population distribution, climate, and the prevalence of risk factors between regions in Japan.^{8,9} As mentioned in the meta-analysis, compared with men aged 45 to 54 years from the same region, Japanese women aged >75 years had a higher risk ratio than European women aged >75 years, and there were 362 patients (50.1%) among women aged >70 years in this study.⁹ Hypothetically, this could be a consequence of the distinctly higher share of people aged ≥65 years within the total population in Japan compared with other countries; addressing the threat posed by the declining birthrate and aging population is an urgent priority for Japan, and is a challenge that has never been faced before in the world.¹⁰ It must also be noted that most of the figures compared in the meta-analysis were obtained from hospital-based studies. Taken together, these factors suggest that further cooperation between regions and countries is desirable to encourage the establishment of nationwide registry systems, such as the nationwide Hospital Discharge Register and Causes of Death Register in Finland.¹¹

There are some limitations to this study. First, the present findings cannot be generalized to other Japanese regions, given the geographic and climatic disparities throughout the country. Second, there was no information on patients with stroke admitted to hospitals outside of Shiga Prefecture, which may have led to underestimating the SAH incidence rate.

In conclusion, the findings of this study underline that Japan has one of the highest SAH incidence rates in the world. The SAH incidence rate in Japan appears to be decreasing but remains high compared with that in other countries.

Supplementary materials

Supplementary materials related to this article can be found online at <https://doi.org/10.5853/jos.2022.00087>.

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Supplementary Methods

Study design

The Shiga Stroke Registry is an ongoing multicenter population-based registry study designed to build a complete information system for the management of acute ischemic and nontraumatic hemorrhagic stroke in Shiga Prefecture, Japan. Shiga Prefecture is located in the central part of Honshu Island, and more than half of its residents live in an urban area (Keihanshin Metropolitan Area as specified by the Ministry of Internal Affairs and Communications). The population of Shiga Prefecture was 1,399,047 (688,787 men and 710,260 women) in the 2015 census.

Determination of stroke

A diagnosis of stroke was defined according to the World Health Organization Multinational Monitoring of Trends and Determinants in Cardiovascular Disease Project (MONICA) criteria as "rapidly developing signs of focal (or global) disturbance of cerebral function lasting more than 24 hours (unless interrupted by surgery or death), without apparent nonvascular cause."⁷ Stroke was further categorized as ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage, or undetermined type. All cases were confirmed clinically and radiologically, and the final diagnosis was made by more than two independent investigators. The records of all suspected cases and the final stroke adjudication were based on meetings between study investigators to resolve potential disagreements.

Variables

Information on the level of consciousness of patients as defined by the World Federation of Neurological Surgeons grade, sex, age, evidence of prior stroke or coronary heart disease, consultation method, smoking and drinking status, findings of imaging investigations, treatment methods, and modified Rankin Scale scores at discharge were obtained from their medical records. Laboratory results were also obtained from medical records and hypertension was defined as systolic/diastolic blood pressure $\geq 140/90$ mm Hg or the use of antihypertensive medications; diabetes mellitus was defined as fasting glucose ≥ 126 mg/dL, glycated hemoglobin (HbA1c; Japan Diabetic Society) $\geq 6.1\%$ (equivalent to HbA1c [National Glycohemoglobin Standardization Program] $\geq 6.5\%$), or the use of anti-diabetic medications. Smoking habits were categorized into three groups (current, past, and never) and drinking habits into four groups (current, occasional, past, and never).

Statistical analysis

Age- and sex-standardized incidence rates were estimated using the person-year approach (per 100,000 person-years), with person-years estimated as the sum of the total Shiga prefectural mid-year population for each year from 2011 to 2015 for eight age groups (<20 years, and 10-year age bands starting from 20–29, 30–39, 40–49, 50–59, 60–69, 70–79, and ≥ 80 years). Age- and sex-standardized incidence rates were also calculated using the direct method with the population of the 2015 Japanese vital statistics as reference.⁸