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Epidemiology of Subarachnoid Hemorrhage in Isolated Islands in Japan: A Population-based Study in the Miyako Islands

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Abstract

The Miyako Islands (with a population of approximately 50,000) are located in southwestern Japan, with a subtropical oceanic climate. This isolated location permitted a retrospective population-based epidemiological study of subarachnoid hemorrhage. We retrospectively enrolled 110 consecutive patients from 2010 to 2019 using the subarachnoid hemorrhage database at Okinawa Miyako Hospital, which is the only local facility with neurosurgeons. We calculated the incidence of subarachnoid hemorrhage standardized to the entire Japanese population. The seasonal distribution of subarachnoid hemorrhage onset and patients' epidemiological characteristics were also investigated. The standardized annual incidence of subarachnoid hemorrhage was 21.4 per 100,000 population, as reported previously in Japan. The patients' mean age was 62.1 ± 15.4 years, and women constituted 60.9%. Anterior communicating artery aneurysms were most common. The endovascular treatment for ruptured aneurysms was increasing as standard levels in Japan. The rates of symptomatic vasospasm and secondary hydrocephalus requiring additional neurosurgical treatment were 2.7% and 19.1%, respectively. The mortality rate was 23.6%. The percentage of patients with a modified Rankin scale score of 0-2 at discharge was 55.5%. There were no differences in the frequency of subarachnoid hemorrhage associated with seasonal distribution or climatic factors. The incidence, baseline characteristics, and clinical outcomes of subarachnoid hemorrhage in the Miyako Islands were similar to those in other regions of Japan. There are preferable epidemiological backgrounds for further practical clinical research.

Keywords: subarachnoid hemorrhage, subtropical climate, epidemiology, isolated island, endovascular surgery

Introduction

The incidence of subarachnoid hemorrhage (SAH) varies between countries, with previous studies reporting a higher incidence of SAH in Japan and Finland, for example.[1-8] Thus, further epidemiological studies examining SAH in Japan are important. Okinawa Miyako Hospital is a public hospital and a core medical center located in the isolated Miyako Islands in Japan. Because there is no other hospital or clinic with adequate neurosurgical facilities to treat SAH on the Miyako Islands, all patients with suspected or diagnosed SAH are transferred to Okinawa Miyako Hospital. This geographic isolation and limited medical facilities provided the opportunity for an epidemiological study of SAH in the island population. Herein, we performed a retrospective population-based incidence study using the SAH database of Okinawa Miyako Hospital. We also assessed the seasonal variation of SAH onset, patients' characteristics, and current SAH treatments and outcomes in this population.

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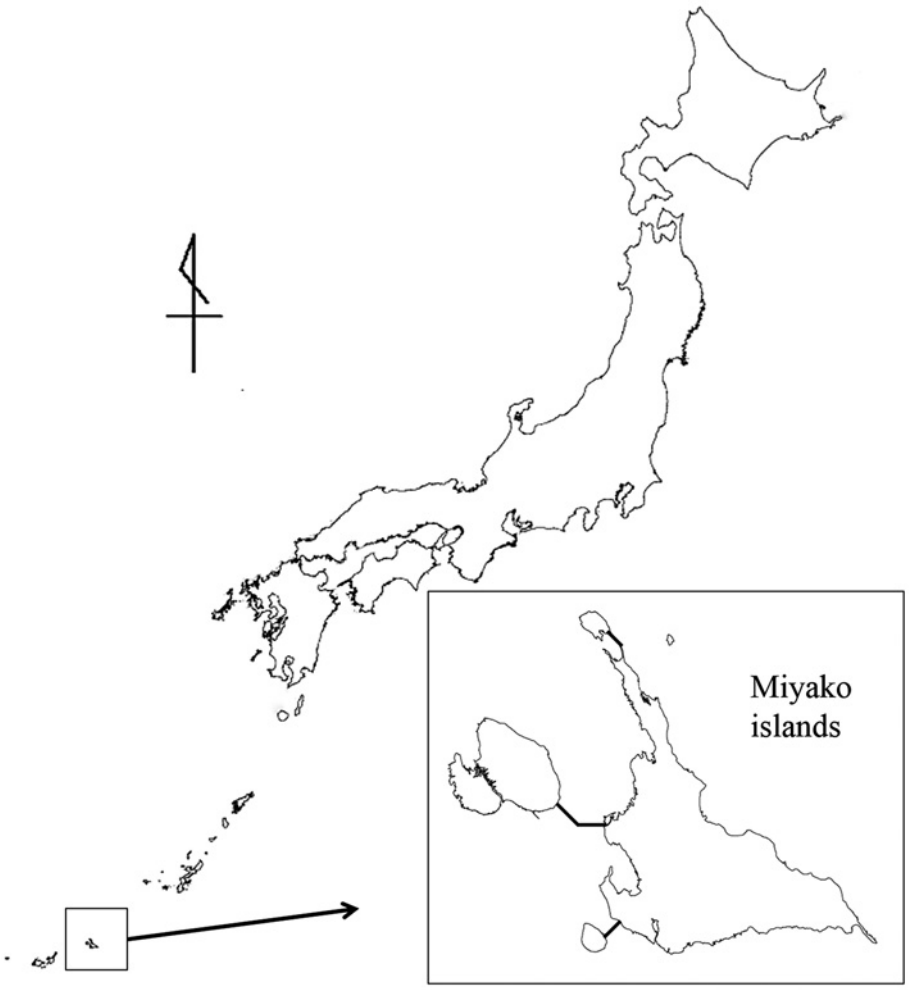

Fig. 1 Geographical location of the Miyako Islands.

Materials and Methods

Study design

The Miyako Islands are located at a latitude of 24° North and a longitude of 125° East (Fig. 1) and comprise the main island of Miyako Island and three small neighboring islands connected with bridges. These are remote isolated islands in Okinawa Prefecture in Japan, which is approximately 1300 miles southwest of Tokyo and 200 miles from the prefecture's main island of Okinawa. The surface area of the Miyako Islands is 78.4 square miles. The islands have a subtropical oceanic climate characterized by many approaching typhoons, which differs from that of most other islands in Japan. The population of the Miyako Islands was 51,186 (25,131 men and 26,055 women) in the 2015 census. All residents of the Miyako Islands are covered by the nationwide healthcare system under the control of the Ministry of Health, Labor and Welfare of Japan, which records the history of disease in Japan. Each suspected SAH patient with clinical symptoms and patients diagnosed with SAH at other hospitals or clinics on the islands are transferred to Okinawa Miyako Hospital. Thus, all SAH patients on the islands are treated at a single hospital. All patients in this study were diagnosed using computed tomography (CT) or lumbar puncture, and cerebral aneurysms were assessed by CT angiography or cerebral angiography.

Data collection

We recruited all consecutive patients between January 2010 and December 2019 using the SAH database for patients treated at the Department of Neurosurgery in Okinawa Miyako Hospital. The exclusion criteria were patients with traumatic SAH, travelers or international visitors, patients with recurrent SAH, and patients introduced from other regions outside of the islands (Fig. 2). The institutional review board approved this study and waived the requirement for informed consent.

We collected the following clinical information, including the reported risk factors for cerebral aneurysms or aneurysmal rupture,[4,9,10] from the database using hospital records and telephone interviews: date of onset, patients'

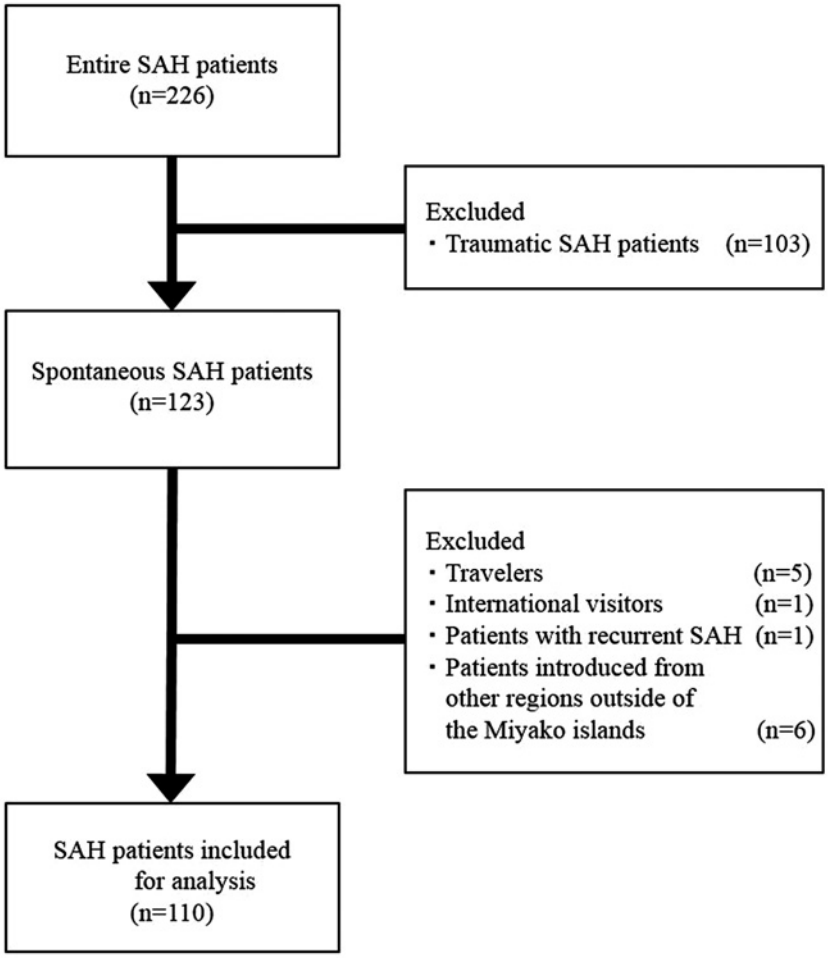

Fig. 2 Flow diagram of study enrollment for patients with subarachnoid hemorrhage (SAH).

characteristics (age, sex, comorbidities, medications, family history of SAH, and smoking and drinking habits), clinical data on admission (neurological findings based on the Hunt and Hess grade[11] and radiological imaging data [i.e., characteristics of the ruptured aneurysm, including the lesion site and size as the largest aneurysm dimension]), the CT Fisher grade, surgical treatment, the presence of symptomatic vasospasm, hydrocephalus requiring operation, and the modified Rankin scale score at discharge (Table 1). We defined a family history of SAH as any patient with second-degree relatives with previous SAH.[12]

Meteorological data for the Miyako Islands and the approach of typhoons in Japan from 2010 to 2019 were obtained from the Japan Meteorological Agency Data Network (https://www.data.jma.go.jp/),[13] which provides the authoritative climate data for Japan. As previously reported, seasons were divided into spring (March to May), summer (June to August), autumn (September to November), and winter (December to February).[14,15] A typhoon was defined meteorologically as a tropical area of low atmospheric pressure with a maximum wind speed of ≥34 knots in Japan and ≥64 knots internationally, which is characterized by strong wind and heavy rain. We defined the closest approach of a typhoon (CAT) as the location of its center within a circular area of <186 miles from the observation point, as previously reported.[16] Using the climate data, the number of patients who developed SAH during 3 days before and after a CAT to the Miyako Islands was calculated.

The primary end-point was the incidence of SAH by person-years in the islands' population. The secondary end-point was the association between patients' epidemiological characteristics and outcomes of SAH treatment, which we compared with findings from previous studies. Additionally, we assessed the influence of seasonal distribution or climatic factors (i.e., seasonal temperature variation, atmospheric pressure, and approaching typhoons) on SAH onset.

Statistical analysis

Statistical analyses were performed using statistical software (SPSS software v24; IBM Corp., Armonk, NY, USA). Continuous variables were expressed as means and standard deviations, and categorical variables were expressed

Table 1 Characteristics of patients with subarachnoid hemorrhage (SAH; n = 110)

Variable	Value	Variable	Value
Sex, n (%)		5-6 mm	18 (18.8)
Men	43 (39.1)	7-9 mm	18 (18.8)
Women	67 (60.9)	>10 mm	9 (9.4)
Age, years (mean ± SD)	62.1 ± 15.4	Not available	6 (6.1)
Hunt and Hess grade on admission, n (%)		Comorbidity, n (%)	
I	16 (14.5)	Hypertension	63 (57.3)
II	30 (27.3)	Diabetes mellitus	8 (7.3)
III	19 (17.3)	Dyslipidemia	19 (17.3)
IV	11 (10.0)	Ischemic heart disease	6 (5.5)
V	34 (30.9)	Drinking habit, n (%)	34 (30.9)
CT Fisher group on admission, n (%)		Smoking, n (%)	29 (26.1)
1	0 (0.0)	Family history of SAH, n (%)	5 (4.5)
2	8 (7.3)	Surgical treatment for aneurysm, n (%)	
3	78 (70.9)	Clipping	63 (57.2)
4	24 (21.8)	Coil embolization	18 (16.4)
Aneurysm, n (%)		Conservative treatment	29 (26.3)
Location		Symptomatic vasospasm, n (%)	3 (2.7)
MCA	25 (22.7)	Hydrocephalus requiring operation, n (%)	21 (19.1)
AComA	27 (24.6)	Modified Rankin scale at discharge, n (%)	
ICA	10 (9.1)	0	44 (40.0)
PComA	15 (13.6)	1	11 (10.0)
VA-BA	10 (9.1)	2	6 (5.5)
Other	9 (8.2)	3	5 (4.5)
Unknown	14 (12.7)	4	9 (8.2)
Size		5	9 (8.2)
<3 mm	10 (10.4)	6	26 (23.6)
3-4 mm	35 (36.5)		

AComA, anterior communicating artery; CT, computed tomography; ICA, internal carotid artery; MCA, middle cerebral artery; PComA, posterior communicating artery; SD, standard deviation; VA-BA, vertebral artery and basilar artery

as numbers and percentages. The incidence of SAH by person-years with 95% confidence intervals was estimated using Poisson's distribution according to sex, and the 10-year age-group strata of the population in the Miyako Islands in 2015—data were standardized using a direct method with the entire Japanese population in 2015.[17] The relationship between SAH frequency and seasonal distribution was evaluated with the Kruskal-Wallis test. The relationship between climate conditions (CAT, mean atmospheric pressure, and temperature) and SAH frequency was evaluated with the Pearson's rank correlation test.

Results

For epidemiological evaluation, we retrospectively enrolled 226 consecutive patients with SAH between 2010 and 2019. After applying the exclusion criteria, 110 patients were included in the final study (Fig. 2). The crude annual incidences of SAH in men, women, and both sexes were 17.3, 25.5, and 21.5 per 100,000 people, respectively, and the annual incidences adjusted to the entire Japanese population were 17.3, 25.3, and 21.4 per 100,000 people, respectively (Table 2). The patients' mean age was 62.1 ± 15.4 years (range, 27-92 years), and women constituted 60.9% of the patients. The Hunt and Hess grade involving the largest number of patients on admission was grade V, and the CT Fisher grade was 3. Aneurysms in the anterior communicating artery and aneurysms measuring from 3 to <5 mm were most common.

As a reported risk for SAH,[18] hypertension was the most common factor, present in 57.3% of patients, followed by dyslipidemia at 17.3% and diabetes mellitus at 7.3%. The distribution of aneurysmal profiles and background comorbidities was similar to that in the unruptured cerebral aneurysm study (UCAS) in Japan[10] and the 2015 Japan stroke data bank.[18] There were no diseases as comorbidi-

Table 2 Annual incidence of subarachnoid hemorrhage per 100,000 population in the Miyako Islands from 2010 to 2019

	Total		Men		Women	
Age, y	n/person-years	Rate (95% CI)	n/person-years	Rate (95% CI)	n/person-years	Rate (95% CI)
0-9	0/56,550	0.0	0/29,240	0.0	0/27,310	0.0
10-19	0/50,490	0.0	0/25,800	0.0	0/24,690	0.0
20-29	1/31,670	3.2 (0.0-9.3)	1/15,680	6.4 (0.0-18.9)	0/15,990	0.0
30-39	8/62,600	12.8 (3.9-21.6)	5/30,410	16.4 (2.0-30.9)	3/32,190	9.3 (0.0-19.9)
40-49	14/59,830	23.4 (11.1-35.7)	7/30,430	23.0 (6.0-40.0)	7/29,400	23.8 (6.2-41.4)
50-59	27/77,530	34.8 (21.7-48.0)	11/39,730	27.7 (11.3-44.0)	16/37,800	42.3 (21.6-63.1)
60-69	26/73,900	35.2 (21.7-48.7)	10/37,410	26.7 (10.2-43.3)	16/36,490	43.8 (22.4-65.3)
70-79	14/46,000	30.4 (14.5-46.4)	5/22,260	22.5 (2.8-42.2)	9/23,740	37.9 (13.1-62.7)
80-89	16/39,460	40.5 (20.7-60.4)	4/15,960	25.1 (0.5-49.6)	12/23,500	51.1 (22.2-80.0)
>90	3/9,660	31.1 (0-66.2)	0/2,340	0.0	3/7,320	41.0 (0.0-87.4)
Crude		21.5 (17.4-25.5)		17.3 (12.1-22.4)		25.5 (19.4-31.7)
Adjusted*		21.4 (17.3-25.5)		17.3 (12.0-22.5)		25.3 (19.1-31.5)

CI, confidence interval
*Adjusted to the entire Japanese population.

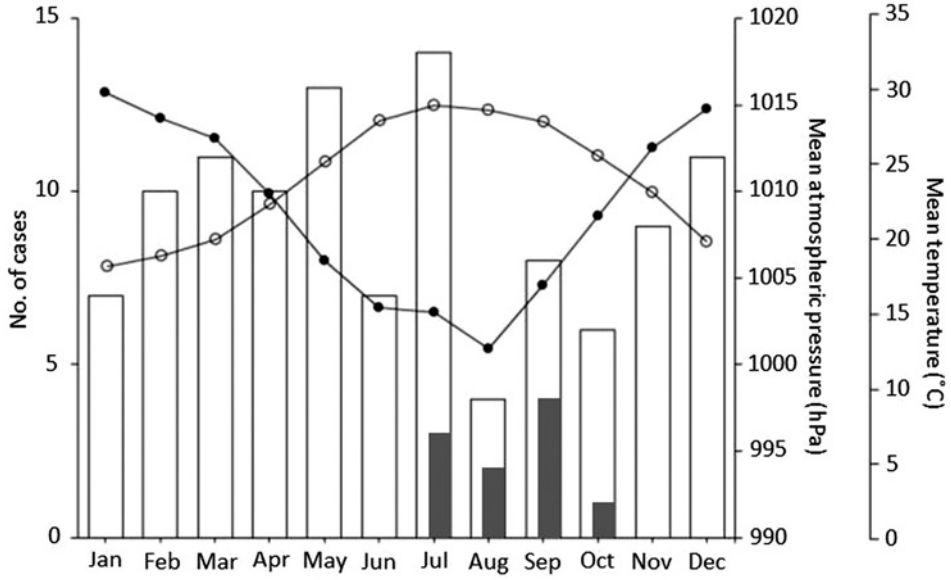

Fig. 3 Monthly distribution of mean temperature, atmospheric pressure, and subarachnoid hemorrhage (SAH) patients from 2010 to 2019. White bar graph: monthly number of SAH cases. Gray bar graph: monthly number of SAH cases at closest approach of a typhoon. ○: mean temperature. ●: mean atmospheric pressure.

ties reported to be associated with cerebral aneurysms.[9] A family history of SAH was present in 4.5% (five cases) of included patients. More clipping than coil embolization was performed in the included patients (Table 1). However, endovascular treatment increased from 2016 when neurointerventionalists joined the Okinawa Miyako Hospital (coil embolization: 11.9% for 2010-2014 vs 30.8% for 2015-2019; odds ratio, 3.42; 95% confidence interval, 1.074-10.943; p = 0.030). The rates of symptomatic vasospasm and secondary hydrocephalus following SAH requiring additional neurosurgical treatment were 2.7% and 19.1%, respectively. The modified Rankin scale score at discharge indicated 23.6% mortality. By contrast, the percentage of patients with a modified Rankin scale score of 0-2 as a good outcome at discharge was 55.5%. The mortality and good outcome rates were similar to the distribution in the Japan stroke data bank.[18]

The monthly results of the relationship between SAH frequency and mean temperature/mean atmospheric pressure are shown in Fig. 3. From 2010 to 2019, the annual

mean temperature was 24.0°C (range, 18.2°C-29.0°C) and atmospheric pressure was 1008.9 hPa (range, 1000.9-1015.7 hPa). SAH occurred constantly from December to May (but excluding January), with a relatively high frequency of >10 cases per month. Additionally, July had the highest SAH frequency, with 14 cases. However, there were no differences in the SAH frequency associated with the four seasons (p = 0.358) or with climatic factors, including seasonal temperature variation (p = 0.602) and atmospheric pressure (p = 0.600). Within our 10-year study window, only 7 months showed a CAT to the Miyako Islands (from May to November), with 69 occurrences. By assessing the timing of SAH onset relative to before and after 3 days of CAT,[16] the highest incidence was in both August and September (50% for both), followed by July (21%) and October (17%) (Fig. 3). Nevertheless, there was no significant relationship between CAT and SAH onset (p = 0.802).

Discussion

Epidemiological studies of SAH in Japan are important given the higher SAH incidence compared with most Western countries.[18] Indeed, several epidemiological studies of SAH have targeted local areas in Japan.[4-8,19] Ideal epidemiological studies can be difficult to perform because of requirements for restricted geographical backgrounds and minimal population movement, and there is a risk of inaccurate case ascertainment because of the participation of multiple hospitals.[20] Importantly, the Miyako Islands are geographically isolated and have a single core hospital used for SAH treatment, thus reducing the error and chance of underestimating cases in epidemiological studies. To our knowledge, this is the first study with a primary focus of evaluating SAH incidence from a population-based perspective performed using consecutive data from a single core clinical hospital treating all SAH patients in a geographically isolated area in Japan.

The annual SAH incidence was similar to that of previous epidemiological SAH studies of other Japanese local areas or the stroke data bank in Japan.[4-8,18,19] For example, in a study examining the relationship between seasonal variation and SAH incidence in Tokyo, Abe et al.[15] reported a significantly higher monthly variation of SAH onset from December to May (defined as winter to spring). Furthermore, the authors found a significant association between the low mean temperature and the high mean atmospheric pressure with SAH incidence. However, because of their subtropical oceanic climate, the Miyako Islands are generally warmer and more humid throughout the year, with relatively smaller temperature fluctuations, than most other regions in Japan. To our knowledge, there are only three epidemiological studies of SAH in a comparable subtropical oceanic climate.[14,16,21] For example, Oyoshi et al. reported the first epidemiological study of SAH in a subtropical region, with evidence of trends toward a higher incidence of SAH during winter and spring.[21] Note that significant correlations between SAH occurrence and seasonal changes in climatic conditions such as temperature or atmospheric pressure were not observed.

The present study also showed a trend toward a seasonal increase in SAH during winter and spring but with no significant relationships with mean atmospheric pressure or temperature. The milder variations in temperature and atmospheric pressure from winter to spring in the subtropical areas in Japan may have affected our findings. Another climatic characteristic of subtropical climate regions in Japan involves approaching typhoons in the summer season, which trigger short-term fluctuations in atmospheric pressure. These are unique meteorological events that may influence the chance of aneurysmal rupture. For example, Izumihara et al. reported an increased SAH frequency during the period before and after approaching typhoons in summer, with a significant association between increased risk of aneurysmal rupture and abrupt short-term changes in atmospheric pressure.[14] Atmospheric pressure was also reported to influence systemic blood pressure and/or intracranial pressure and to increase transmural pressure in the aneurysmal wall.[22,23] In the present study, the peak incidence of SAH occurred in July, although there was no association between SAH onset and the 3 days around the CAT. Further studies using a larger sample size are required to clarify these associations.

In the present study, there were several important findings related to the utility of SAH research in the Miyako Islands. First, the incidence of SAH was similar to that in previous epidemiological studies of other regions in Japan (Table 3).[4-8,19] Furthermore, the characteristics associated with SAH, including mean age, higher probability in women, radiological findings of SAH on admission, profiles of the ruptured aneurysms, comorbidities, treated hydrocephalus, and outcomes, were similar to those in a recent Japan stroke database.[18] The second finding relates to therapeutic interventions for SAH, especially for aneurysm rupture. The Japan stroke database identified a transition in treatment modality selection for ruptured aneurysms,[18] with an increasing rate of endovascular surgery. The current proportional use of clipping and coil embolization for SAH in the Miyako Islands is the same as that used nationwide in Japan (clipping vs coil embolization: 69.5% vs 30.5%, respectively).[24] The guidelines for the management of aneurysmal SAH are also updated every few years, with increasing indication for endovascular treatment of ruptured aneurysms with technological advances.[25] The Miyako Islands may be particularly advantageous for epidemiological studies, as well as for future practical clinical studies, including prospective cohort studies of SAH treatment.

Table 3 Age-adjusted annual incidence of subarachnoid hemorrhage per 100,000 population in published studies

Study	Study years	Population	Age, y	Sex, % (men/women)	Number of SAH, n	Annual incidence*
Inagawa, Izumo[4]	1980-1984	79,026	All ages	39.8/60.2	83	18.3
Yamashita, Yamaguchi[19]	1985-1995	1,500,000	All ages	—	598	13.9
Ohkuma, Shimokita[5]	1989-1998	89,991	All ages	36.4/63.6	198	21.0
Hamada, Kumamoto[6]	1996-2000	1,860,000	0-99	33.2/66.8	2115	21.6
Omama, Iwate[7]	2004-2008	235,280	All ages	29.6/70.4	328	17.5
Takashima, Shiga[8]	2011	1,400,745	All ages	30.3/69.7	201	15.2
present study	2010-2019	51,186	All ages	39.1/60.9	110	21.4

*Adjusted to the entire Japanese population.

Study limitations

There are several limitations of this study. The relatively small number of patients and lack of prehospital fatality provide potential source of bias and variation. Additionally, patients' information was collected retrospectively based on the clinical records or partial telephone interviews. Further prospective studies of larger populations in similar conditions are required to confirm our findings.

Conclusion

This epidemiological study in the Miyako Islands involving geographic isolation and a limited medical environment revealed similar characteristics and incidence of SAH compared with Japan's major cities and with Japan overall. SAH onset was unaffected by seasonal variation and approaching typhoons. Our findings provide a useful current-state report of SAH incidence and treatment in the Miyako Islands and suggest that the Miyako Islands may be useful for future practical clinical studies.

Conflicts of Interest Disclosure

All authors have no conflict of interest for this work.

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