Trends in the Incidence of Stroke and its Subtypes from 1963 to 2018 in Japanese Urban and Rural Communities: The Circulatory Risk in Communities Study (CIRCS)

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ABSTRACT

Background: Few studies have provided observational data on long-term trends in the incidence of stroke and its subtypes, and shown the urban-rural disparities of stroke incidence in Japan.

Methods: A multiple-source, community-based stroke surveillance was performed since 1963/1964 to determine all first-ever stroke cases among Japanese residents aged ≥ 40 years living in the Minami-Takayasu district in Yao city, an urban community, and Ikawa town, a rural community. Sex-specific, age-standardized incidence per 1000/year with 95% confidence intervals were calculated during seven periods of 1963/1964–1971 [urban population (% men): 3242 (47.3%); rural population (% men): 2311 (46.0%)], 1972–1979, 1980–1987, 1988–1995, 1996–2003, 2004–2011, and 2012–2018 [13,307 (46.7%); 3586 (44.8%)].

Results: The age-standardized incidence of all strokes in the Japanese urban community, decreased from 6.60 to 1.15 per 1,000/year for men and 3.28 to 0.59 for women. In the rural community, the corresponding incidence decreased from 11.51 to 1.98 for men and 6.46 to 1.31 for women. Similar reductions were observed in the incidence of intracerebral hemorrhage, subarachnoid hemorrhage, ischemic stroke, and lacunar stroke. In the period of 2012–2018, the incidence ratios (95% confidence intervals) of all strokes for the rural compared to the urban community were 1.72 (1.08–2.75) for men and 2.23 (1.23–4.03) for women.

Conclusion: The stroke incidence continued to decline in both urban and rural Japanese communities with the regional disparities over the past half century, whereas it remained higher than that in many western countries. (Word counts: 246)

Key words: Stroke; Incidence; Urban-rural disparities; Trend; Asia; Epidemiology

Introduction

Stroke remains a major cardiovascular concern worldwide because of its high mortality and contribution to healthy life lost in stroke survivors with physical and mental disabilities [1]. Asian countries such as Japan have had a higher stroke burden than ischemic heart disease [2]. Stroke was once the primary cause of death among the Japanese population from 1951 to 1980 and dropped to the fourth rank in 2018 [3]. Sustained improvements in the stroke epidemic started in the mid-1960s, mainly attributable to community-based prevention programs for hypertension, increased coverage of antihypertensive medication use in patients with hypertension, dietary education such as salt reduction campaigns and balanced dietary guidelines, and strategies for discouraging cigarette smoking [2].

Special attention has been given to the urban-rural disparities in stroke epidemiology because rural residents had a higher prevalence of hypertension and other stroke risk factors than urban residents [4]. The urban-rural disparities are reported previously [5, 6]. However, these studies about the urban-rural disparities of stroke were performed with a cross-sectional design, and few data have been published comparing long-term trends in the stroke incidence between urban and rural communities.

The Circulatory Risk in Communities Study (CIRCS) is one of the frontier community-based epidemiological studies in Japan [7], designed to investigate cardiovascular risk factors and lead the community cardiovascular prevention programs in both urban and rural communities since 1963. This study design permitted comparing stroke incidence based on unified public health interventions and surveillance systems. A previous CIRCS reported declining trends in the incidence of all strokes in urban and rural communities between 1963 and 2003 [7]. Accordingly, the aim of the present study was to provide updated data including the incidence of stroke subtypes and focus on the urban-rural disparities in Japan.

Methods

Study Population

This study comprised two Japanese communities in which the CIRCS research team participated and led their cardiovascular prevention programs since 1963/1964. The Minami-Takayasu district of Yao City is an urban community in Osaka Prefecture, mid-western Japan, with a census population of 22,286 (of 268,983 in Yao city) in 2015. Ikawa town is a rural farming community located in Akita Prefecture, northwestern Japan, with a census population of 4,986 in 2015. The present study targeted residents aged 40 years or older, which was different from the 40 to 69 years in the previous report of CIRCS [7]. The population of residents aged 40 years or older changed from 3242 (population density: 3242 residents / 5.45 km^2 = 595 residents/km^2) in 1965 to 13,307 (2442 residents/km^2) in 2015 for the urban community, and 2311 (population density: 2311 residents / 47.95 km^2 = 48 residents/km^2) to 3586 (75 residents/km^2) for the rural community. The Ethics Committees of Osaka Center for Cancer and Cardiovascular Disease Prevention and Osaka University approved this study, and informed consents were obtained collectively from community representatives since this study involved the secondary use of data obtained for public health practice on cardiovascular disease prevention in the local communities according to the guidelines of the Council for International Organizations of Medical Science.

Registration Process and Ascertainment of Stroke Cases

Stroke registrations were conducted from the community and local hospitals/clinics to avoid omissions of incident cases. The surveillance sources of candidate cases included annual household questionnaires, cardiovascular risk surveys, death certificates (i.e., national death records), ambulance records, national insurance claims, and reports from local physicians, public health nurses, and health volunteers. To validate the diagnoses, those with suspected stroke were telephoned, visited, or invited to take part in a survey to further confirm the diagnosis. For cases of death, medical histories and records were obtained from the bereaved families or attending physicians. The final diagnosis was based on comprehensive medical records with standardized case report forms reviewed by a team comprising experienced physician epidemiologists. Stroke was defined as a focal neurological disorder with a rapid onset that persisted for at least 24 hours or until death. Transient ischemic attacks were ruled out accordingly.

Stroke subtypes were categorized as intracerebral hemorrhage, subarachnoid hemorrhage, ischemic stroke, or undetermined types according to clinical criteria, or computed tomography (CT) and magnetic resonance imaging (MRI) [8]. According to our previous study, the diagnostic accuracy of stroke versus non-stroke according to clinical criteria was confirmed comparing with autopsy findings; sensitivity = 97.8% and specificity = 96.9% [9]. A Japanese collaborative study on stroke registry examined the diagnostic accuracy of stroke subtypes according to clinical criteria comparing with CT/MRI findings among the stroke cases; sensitivity = 85.9% and specificity = 94.7% for intracerebral hemorrhage, sensitivity = 87.8% and specificity = 99.6% for subarachnoid hemorrhage, and sensitivity = 92.9% and specificity = 90.3% for ischemic stroke [10]. Ischemic stroke subtypes were classified as lacunar, large-artery occlusive, embolic, or unclassified infarctions according to CT/MRI imaging data. Brain imaging data were available after the 1980s, and the proportions of CT/MRI utilization among all stroke cases between 1980 and 1987, 1988 and 1995, 1996 and 2003, 2004 and 2011, and 2012 and 2018 were 40.6%, 94.1%, 94.1%, 76.4%, and 94.0% in the urban community, and 64.0%, 94.1%, 96.6%, 92.8%, and 97.1% in the rural community, respectively. We did not calculate the incidence of ischemic stroke subtypes between 1980 and 1987 because of the lower proportion of CT/MRI utilization.

Statistical Analyses

The study periods were established from 1964 to 2018 for the urban community and from 1963 to 2018 for the rural community. The sex-specific, age-standardized incidence of all strokes and stroke subtypes were calculated during the seven study periods with 8-year time intervals: 1964–1971 (1963–1971 in the rural community), 1972–1979, 1980–1987, 1988–1995, 1996–2003, 2004–2011, and 2012–2018. The community population of each survey period was calculated using the single or average number of the regional census population in 1965 and 1970, 1975, 1980 and 1985, 1990 and 1995, 2000, 2005 and 2010, and 2015, respectively. The incidence was calculated using the direct standardization method and adjusted by age, referring to the 1985 Japanese national model population. The Cochran-Armitage test, a modified Pearson chi-squared test for trend analysis, was used to depict time trends across the seven study periods. Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

The number of residents and sex-specific, age-standardized incidence of all strokes and stroke subtypes in the urban and rural communities are presented in Table 1, and the age-specific incidence for all strokes in rural and urban communities are illustrated in Supplemental Figure 1. The incidence of all strokes in the urban community decreased from 6.60 per 1,000/year in 1964–

1971 to 1.15 in 2012–2018 for men; P for trend < 0.001, and from 3.28 to 0.59 for women; P for trend < 0.001. Similar decreasing trends were observed in the incidence of intracerebral hemorrhage and ischemic stroke for both sexes; all P for trend < 0.001, and subarachnoid hemorrhage for women; P for trend = 0.08. The incidence of all strokes in the rural community decreased distinctly from 11.51 in 1963–1971 to 1.98 in 2012–2018 for men; P for trend < 0.001, and from 6.46 to 1.31 for women; P for trend < 0.001. Similar findings were observed in the incidence of intracerebral hemorrhage and ischemic stroke for both sexes; all P for trend < 0.001, and subarachnoid hemorrhage for men; P for trend = 0.10, and women; P for trend = 0.01. For ischemic stroke subtypes, the incidence of lacunar stroke decreased consistently in both urban and rural communities from 1988–1995 to 2012–2018, but no decreasing trend was observed for large-artery occlusive or embolic infarctions (Supplemental Table 1).

Figure 1 shows the trends in the incidence ratios of all strokes for rural versus urban residents during the seven survey periods. For both men and women, rural residents had higher stroke incidence than urban residents, and no substantial increasing or decreasing trends in incidence ratios were observed during the period from 1963/1964–1971 to 2012–2018; the incidence ratios (95% CIs) for men were 1.74 (1.25–2.43) in 1963/1964–1971, 1.45 (1.04–2.04) in 1972–1979, 0.98 (0.70–1.36) in 1980–1987, 1.26 (0.90–1.75) in 1988–1995, 1.88 (1.39–2.55) in 1996–2003, 2.10 (1.48–2.98) in 2004–2011, and 1.72 (1.08–2.75) in 2012–2018, and the corresponding incidence ratios (95% CIs) for women were 1.96 (1.28–3.01), 1.31 (0.91–1.89), 1.24 (0.89–1.74), 1.58 (1.09–2.28), 1.12 (0.74–1.71), 1.70 (1.11–2.59), and 2.23 (1.23–4.03).

Discussion

In both urban and rural communities, the incidence of all strokes decreased continually from the period of 1963/1964–1971 to 2012–2018. The findings were consistent with our previous report between 1963 and 2003 [7], and continually decreased incidence trends were observed in this updated study. Similar decreasing trends were observed in the incidence of stroke subtypes. However, there remained higher risk of incidence from all strokes for the rural compared to the urban communities.

The declining trend in stroke incidence among the Japanese population has been reported previously. The Hisayama study showed decreasing trends in the incidence of all strokes, intracerebral hemorrhage, and ischemic stroke from 1961–1968 to 2002–2009 [11], and of lacunar stroke, but not of other ischemic stroke subtypes, from 1961–1973 to 1988–2002 [12], among the suburban population. Similar to our findings, the incidence of all strokes in the Hisayama study decreased substantially from 1961–1968 to 1974–1981, then decreased with a slowdown from 1974–1981 to 2002–2009 [11]. Slow decreasing trends from the 1980s was also reported in a stroke registry study [13].

To the best of our knowledge, the CIRCS, including the previous reports [2, 7] and this update, is the only Japanese study that could compare the long-term stroke trends based on unified surveillance systems between the urban and rural communities. At the beginning of the CIRCS survey, the rural community (Ikawa town, Akita Prefecture) had the highest stroke mortality in both Japan and the world, and the urban community (Yao City, Osaka Prefecture) had lower stroke mortality in Japan [2], so that obvious urban-rural disparities of stroke incidence were observed in the 1960s. As a result of positive and targeted cardiovascular preventive measures in the urban and rural communities, a decreased trend was observed over the past half century. The incidence of all strokes in the period of 2012-2018 in our data were 1.15 (0.86–1.44) per 1000/year for men and 0.59 (0.39–0.79) for women in the urban community, and 1.98 (1.20–2.77) and 1.31 (0.67-1.94) in the rural community, respectively, which were close to the 2019 global incidence of 1.51 (1.37–1.68) and 1.50 (1.36–1.67) for women except for urban women, whereas the incidence in Japan remained higher than that in many western countries including the United States, the United Kingdom, and France [1, 14]. Furthermore, this decreased trend slowed down since the 1980s, and the urban-rural disparities remain apparent more recently.

The strengths of our study lie in comparing stroke incidence in two communities under continued cardiovascular prevention programs. These prevention programs were formulated according to community circumstances and improved with time. For example, a prior CIRCS report showed that our rural hypertension control program, containing intensive, accessible, community-based interventions and health education, was associated with effectively prevented incident stroke in rural men [15]. Accordingly, the stroke burden switched from severe/moderate to mild hypertension between 1963 and 1997 [16]. We used consistently the clinical criteria for the diagnosis of all strokes, which was barely changed over time, throughout the whole study period for the primary analysis of trends in all strokes. The limitations of this study are noteworthy. First, trends for the incidence of ischemic stroke subtypes were not well explored because of the small number of cases, the improvements in CT/MRI techniques over time, and difficulty in distinguishing subtypes between large-artery occlusive and embolic infarctions. Second, the number of enrolled communities was small, and hence it restricted the generalization power to other Japanese communities.

In conclusion, Japan had a very high stroke incidence among the world in the 1960s, followed by substantial decreasing trends in both urban and rural Japanese communities, albeit a higher incidence in the rural than in the urban communities. The stroke incidence in Japanese communities remained higher than that in many western countries. These findings suggest the necessity of continued public health efforts to reduce stroke incidence in Japan.

Competing Interest

None declared.

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Table 1. Sex-specific, age-standardized incidence (95% confidence intervals) for stroke and its subtypes per 1,000/years in urban and rural residents aged ≥ 40 years from 1963/64 to 2018.

	Urban residents								Rural residents							
	1964-1971	1972-1979	1980-1987	1988-1995	1996-2003	2004-2011	2012-2018	P for trend	1963-1971	1972-1979	1980-1987	1988-1995	1996-2003	2004-2011	2012-2018	P for trend
Men																
No. of residents	1533	2326	3495	4969	5493	5807	6217		1063	1234	1335	1594	1703	1661	1607	
All strokes, n	65	79	110	111	107	88	70		97	67	54	53	75	59	35	
Age-standardized incidence	6.60	5.20	5.47	3.06	2.40	1.58	1.15	<0.001	11.51	7.56	5.34	3.84	4.51	3.32	1.98	<0.001
95% confidence interval	4.91-8.28	4.00-6.40	4.40-6.53	2.48-3.64	1.94-2.86	1.24-1.92	0.86-1.44		9.11-13.91	5.69-9.43	3.89-6.78	2.80-4.89	3.46-5.57	2.40-4.25	1.20-2.77	
Intracerebral hemorrhage, n	14	17	27	29	27	25	17		25	11	16	9	23	16	4	
Age-standardized incidence	1.37	1.05	1.27	0.73	0.61	0.47	0.31	<0.001	3.06	1.20	1.53	0.65	1.53	0.96	0.21	<0.001
95% confidence interval	0.61-2.14	0.53-1.56	0.77-1.78	0.46-1.00	0.37-0.84	0.28-0.66	0.15-0.47		1.79-4.33	0.49-1.91	0.77-2.30	0.22-1.07	0.88-2.17	0.45-1.47	0.00-0.41	
Subarachnoid hemorrhage, n	1	2	7	8	6	9	4		5	4	4	6	3	4	1	
Age-standardized incidence	0.08	0.12	0.29	0.19	0.13	0.22	0.11	0.77	0.51	0.42	0.36	0.51	0.22	0.41	0.03	0.10
95% confidence interval	0.00-0.23	0.00-0.29	0.07-0.51	0.06-0.32	0.02-0.24	0.07-0.37	0.00-0.22		0.06-0.96	0.01-0.83	0.01-0.71	0.10-0.91	0.00-0.46	0.00-0.85	0.00–0.08	
Ischemic stroke, n	42	54	70	72	69	51	49		54	46	32	38	49	37	30	
Age-standardized incidence	4.23	3.67	3.62	2.08	1.53	0.84	0.73	<0.001	6.25	5.19	3.17	2.69	2.77	1.84	1.75	<0.001
95% confidence interval	2.89-5.57	2.64-4.69	2.74-4.49	1.59-2.57	1.17-1.90	0.61-1.08	0.52-0.95		4.52-7.97	3.64-6.74	2.05-4.29	1.83-3.55	1.97-3.56	1.23-2.45	0.99-2.51	
Women																
No. of residents	1709	2638	3764	5570	6193	6756	7090		1248	1457	1606	1867	1969	2062	1979	
All strokes, n	36	70	87	75	95	73	47		61	53	57	49	44	52	35	
Age-standardized incidence	3.28	3.76	3.35	1.65	1.59	0.92	0.59	<0.001	6.46	4.92	4.16	2.60	1.79	1.56	1.31	<0.001
95% confidence interval	2.18-4.38	2.86-4.67	2.64-4.06	1.27-2.03	1.26-1.93	0.69-1.15	0.39-0.79		4.76-8.15	3.56-6.28	3.08-5.25	1.85-3.35	1.13-2.44	1.02-2.09	0.67-1.94	
Intracerebral hemorrhage, n	12	19	21	11	23	20	15		21	10	12	11	14	11	9	
Age-standardized incidence	1.03	0.96	0.81	0.24	0.37	0.25	0.20	<0.001	2.25	0.84	0.87	0.58	0.58	0.33	0.60	<0.001
95% confidence interval	0.43-1.63	0.52-1.40	0.46-1.15	0.10-0.39	0.22-0.53	0.13-0.38	0.08-0.33		1.22-3.27	0.32-1.36	0.38-1.37	0.22-0.93	0.24-0.92	0.08-0.58	0.09-1.12	
Subarachnoid hemorrhage, n	1	7	14	17	12	17	7		7	5	6	10	1	4	4	
Age-standardized incidence	0.07	0.33	0.52	0.39	0.24	0.27	0.13	0.08	0.61	0.42	0.45	0.62	0.02	0.18	0.22	0.01
95% confidence interval	0.00-0.21	0.09-0.58	0.25-0.80	0.20-0.58	0.10-0.38	0.14-0.41	0.02-0.25		0.16-1.06	0.05-0.79	0.09-0.81	0.23-1.01	0.00-0.06	0.00-0.35	0.00-0.48	
Ischemic stroke, n	17	35	40	45	55	33	24		29	34	35	25	29	36	22	
Age-standardized incidence	1.66	1.93	1.53	0.97	0.90	0.36	0.24	<0.001	3.10	3.26	2.55	1.23	1.19	1.04	0.49	<0.001
95% confidence interval	0.85-2.47	1.27-2.59	1.05-2.01	0.68-1.26	0.65-1.15	0.23-0.50	0.13-0.34		1.93-4.26	2.13-4.40	1.70-3.39	0.74-1.72	0.63-1.75	0.60-1.47	0.23-0.75	

Numbers at risk in seven periods are based on the regional census population in 1965 and 1970, 1975, 1980 and 1985, 1990 and 1995, 2000, 2005 and 2010, and 2015, respectively.

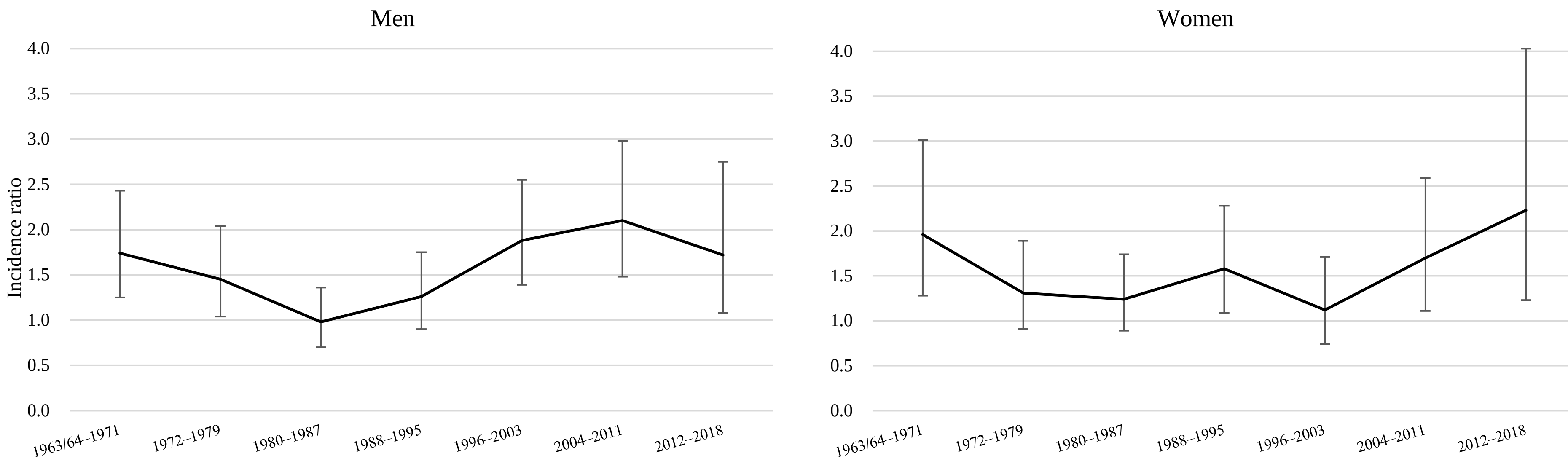

Figure 1. Sex-specific, age-standardized incidence ratios (95% confidence intervals) of all strokes in rural versus urban residents aged ≥ 40 years during the seven survey periods.