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Original Article

Long-Term Survival after Stroke in 1.4 Million Japanese Population: Shiga Stroke and Heart Attack Registry

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Background and Purpose Although numerous measures for stroke exist, stroke remains one of the leading causes of death in Japan. In this study, we aimed to determine the long-term survival rate after first-ever stroke using data from a large-scale population-based stroke registry study in Japan.

Methods Part of the Shiga Stroke and Heart Attack Registry, the Shiga Stroke Registry is an ongoing population-based registry study of stroke, which covers approximately 1.4 million residents of Shiga Prefecture in Japan. A total 1,880 patients with non-fatal first-ever stroke (among 29-day survivors after stroke onset) registered in 2011 were followed up until December 2016. Five-year cumulative survival rates were estimated using the Kaplan-Meier method, according to subtype of the index stroke. Cox proportional hazards models were used to assess predictors of subsequent all-cause death.

Results During an average 4.3-year follow-up period, 677 patients died. The 5-year cumulative survival rate after non-fatal first-ever stroke was 65.9%. Heterogeneity was present in 5-year cumulative survival according to stroke subtype: lacunar infarction, 75.1%; large-artery infarction, 61.5%; cardioembolic infarction, 44.9%; intracerebral hemorrhage, 69.1%; and subarachnoid hemorrhage, 77.9%. Age, male sex, Japan Coma Scale score on admission, and modified Rankin Scale score before stroke onset were associated with increased mortality during the chronic phase of ischemic and hemorrhagic stroke.

Conclusions In this study conducted in a real-world setting of Japan, the 5-year survival rate after non-fatal first-ever stroke remained low, particularly among patients with cardioembolic infarction and large-artery infarction in the present population-based stroke registry.

Keywords Stroke; Epidemiology; Population surveillance; Survival rate

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Introduction

During the past five decades, age-standardized stroke mortality has decreased in Japan.[1] However, in Japan, stroke is still one of the leading causes of death[2] and disability.[3] In all regions of the world, the age-adjusted stroke mortality rate has rapidly decreased whereas the incidence rate has less steep decreased in high-income Asian pacific or Southeast Asian countries or increased in China.[4] The rapid decrease in age-adjusted mortality rates and less steep decrease or increase in age-adjusted incidence rates have led to an increased number of stroke survivors.[4] Using data from the Shiga Stroke registry study, we previously reported that case fatality rates were lower than those of previous studies from Japan and other countries,[5] which might also suggest increase in number of stroke survivors during the past few decades. The excess risk of death has been reported to be highest during the acute phase but persists during the several years following stroke.[6-8] However, there is limited evidence of long-term mortality among patients who experience non-fatal stroke in Japan, which is the most aged society and the first nation to face a super-aging society in the world.[9]

As a part of the Shiga Stroke and Heart Attack Registry, the Shiga Stroke Registry is one of the largest ongoing population-based registry study of stroke in Japan. We previously reported the incidence rate[5] and both acute and 2-year survival rates[10] of stroke, using data from this study. We aimed to investigate the current cumulative and relative 5-year survival rates after non-fatal first-ever stroke, using a large-scale comprehensive population-based stroke registry in Shiga Prefecture, Japan.

Methods

Study design

The design of the Shiga Stroke Registry has been described elsewhere in detail.[5,10] The Shiga Stroke Registry is a population-based registry study designed to build a complete information system regarding acute ischemic and non-traumatic hemorrhagic stroke management in Shiga Prefecture, Japan. Shiga Prefecture is located in the central part of Honshu Island. According to the 2011 census, the population of Shiga Prefecture was 1,400,745 residents (689,859 men and 710,866 women).

Diagnosis of stroke was defined as a sudden onset of focal neurological deficits persisting for more than 24 hours, according to the Monitoring Trends and Determinants in Cardiovascular Disease (WHO-MONICA) Project.[11] A total 2,176 cases of first-ever stroke, with onset dates ranging from 1 January to 31 December in 2011, were followed up until December 2016. A patient with non-fatal stroke was defined as a person who experienced stroke and was alive at 29 days after onset of the index stroke. We excluded 296 patients with fatal stroke who died within 28 days. A total 1,880 patients with non-fatal first-ever stroke were included in the present analysis. A sensitivity analysis using 2,176 fatal/non-fatal first-ever stroke patients was also conducted. The present study was approved by the Institutional Review Board of Shiga University of Medical Science. Written informed consent by the patients was waived due to a retrospective nature of our study.

Definition of index stroke and its subtypes

Stroke was classified as ischemic or hemorrhagic stroke. Ischemic stroke was further divided into four clinical categories: lacunar infarction, large-artery infarction, cardioembolic infarction, or undetermined type, based on the criteria for the type of stroke of the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) study.[12] Hemorrhagic stroke was further divided into two clinical categories: intracerebral hemorrhage and subarachnoid hemorrhage.

Clinical features and medical histories

Information on clinical features, including transient ischemic attack (TIA), atrial fibrillation, myocardial infarction, hypertension medication, diabetes, dyslipidemia, modified Rankin Scale (mRS) score[13] before onset, and smoking and drinking status at baseline, was obtained from the medical records of all patients with stroke. Atrial fibrillation was defined as a history of atrial fibrillation and/or a clinical diagnosis based on electrocardiogram (ECG) and/or ECG monitoring during hospitalization. The Japan Coma Scale (JCS)[14] score is a 10-grade scale that is widely used in Japan to assess consciousness (JCS 0, alert; JCS 1–3, possible eye-opening, not lucid; JCS 10–30, possible eye-opening upon stimulation; JCS 100–300, no eye-opening, coma) (Supplementary Table 1). Hypertension medication was defined as the use of antihypertensive medication before onset of the index stroke. Diabetes was defined as casual blood glucose ≥11.1 mmol/L, use of antidiabetic medication, and/or a history of diabetes. Dyslipidemia was defined as total cholesterol ≥5.69 mmol/L, low density lipoprotein cholesterol ≥4.14 mmol/L, taking medication for dyslipidemia, and/or a history of dyslipidemia. Smoking and drinking habits were categorized as none, past, and current.

Follow-up survey and outcome

All patients with first-ever stroke were followed up until December 2016, using death certificate information. Information from the death certificates of all deceased individuals was collected, with the permission of the Japanese Ministry of Health,

Table 1. Characteristics of non-fatal first-ever stroke patients survived acute phase by type of index stroke in the Shiga Stroke Registry

Characteristic	Ischemic stroke	Hemorrhagic stroke	Total stroke
Total no.	1,296	583	1,880
Men	743 (57.3)	260 (44.6)	1,003 (53.4)
Age (yr)	74.1±13.2	68.2±15.1	72.3±14.1
Past history			
Transient ischemic attacks			
Yes	71 (5.5)	8 (1.4)	79 (4.2)
No	1,222 (94.3)	572 (98.1)	1,795 (95.5)
Unknown	3 (0.2)	3 (0.5)	6 (0.3)
Atrial fibrillation			
Yes	286 (22.1)	38 (6.5)	324 (17.2)
No	1,004 (77.5)	540 (92.6)	1,545 (82.2)
Unknown	6 (0.5)	5 (0.9)	11 (0.6)
Myocardial infarction			
Yes	79 (6.1)	27 (4.6)	107 (5.7)
No	1,215 (93.8)	554 (95)	1,769 (94.1)
Unknown	2 (0.2)	2 (0.3)	4 (0.2)
Hypertension medication			
Yes	656 (50.6)	224 (38.4)	880 (46.8)
No	635 (49)	355 (60.9)	991 (52.7)
Unknown	5 (0.4)	4 (0.7)	9 (0.5)
Diabetes			
Yes	360 (27.8)	114 (19.6)	474 (25.2)
No	930 (71.8)	466 (79.9)	1,397 (74.3)
Unknown	6 (0.5)	3 (0.5)	9 (0.5)
Dyslipidemia			
Yes	510 (39.4)	158 (27.1)	668 (35.5)
No	748 (57.7)	377 (64.7)	1,126 (59.9)
Unknown	38 (2.9)	48 (8.2)	86 (4.6)
Modified Rankin Scale before on set			
0	907 (70.0)	450 (77.2)	1,358 (72.2)
1	133 (10.3)	48 (8.2)	181 (9.6)
2	57 (4.4)	35 (6.0)	92 (4.9)
3	86 (6.6)	17 (2.9)	103 (5.5)
4	81 (6.3)	17 (2.9)	98 (5.2)
5	26 (2.0)	3 (0.5)	29 (1.5)
Unknown	6 (0.5)	13 (2.2)	19 (1.0)
Japan Coma Scale on admission			
0	810 (62.5)	206 (35.3)	1,017 (54.1)
1	114 (8.8)	70 (12)	184 (9.8)
2	77 (5.9)	32 (5.5)	109 (5.8)
3	122 (9.4)	55 (9.4)	177 (9.4)
10	64 (4.9)	102 (17.5)	166 (8.8)
20	22 (1.7)	18 (3.1)	40 (2.1)
30	20 (1.5)	14 (2.4)	34 (1.8)
100	18 (1.4)	22 (3.8)	40 (2.1)
200	35 (2.7)	45 (7.7)	80 (4.3)
300	11 (0.8)	17 (2.9)	28 (1.5)
Unknown	3 (0.2)	2 (0.3)	5 (0.3)
Smoking			
Nonsmoker	734 (56.6)	352 (60.4)	1,087 (57.8)
Past smoker	152 (11.7)	57 (9.8)	209 (11.1)
Current smoker	309 (23.8)	129 (22.1)	438 (23.3)
Unknown	101 (7.8)	45 (7.7)	146 (7.8)
Drinking			
Nondrinker	642 (49.5)	296 (50.8)	938 (49.9)
Past drinker	21 (1.6)	7 (1.2)	28 (1.5)
Current drinker	468 (36.1)	213 (36.5)	682 (36.3)
Unknown	165 (12.7)	67 (11.5)	232 (12.3)
Index stroke subtype			
Ischemic stroke	1,296 (100.0)		1,296 (68.9)
Lacunar infarction	346 (26.7)		346 (18.4)
Large artery infarction	413 (31.9)		413 (22.0)
Cardioembolic infarction	305 (23.5)		305 (16.2)
Ischemic stroke with other determined etiology	38 (2.9)		38 (2.0)
Ischemic stroke with undetermined etiology	194 (15.0)		194 (10.3)
Intracerebral hemorrhage		447 (76.7)	447 (23.8)
Subarachnoid hemorrhage		136 (23.3)	136 (7.2)
Stroke, not specified as hemorrhage or infarction			1 (0.1)

Values are presented as number (%) or mean±standard deviation.

Labor and Welfare, and matched with all stroke cases. The main outcome of this study was all-cause death.

Statistical analysis

Cumulative survival rates of first-ever stroke cases at 5 years were estimated using Kaplan-Meier methods. Log-rank tests were used to compare survival rates across subtypes of stroke and ischemic stroke. Relative survival rate was defined as the ratio of observation survival rate during the follow-up period to the expected survival rate in the population matched by age, sex, and calendar year of the observational group. The expected survival rate was calculated using the Ederer I method[15] and Japanese cohort survival tables.[16] In addition, excess mortality risk was calculated, to compare the cumulative mortality rate with the expected mo-

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Table 2. Cumulative 5-year survival rate after non-fatal first-ever stroke by types of stroke and gender in the Shiga Stroke Registry

Variable	Men			Women			Men and Women		
	Death/total no.	Survival rate (%)	95% CI	Death/total no.	Survival rate (%)	95% CI	Death/total no.	Survival rate (%)	95% CI
Total stroke	319/1,003	68.2	66.7–69.7	322/877	63.3	61.7–64.9	641/1,880	65.9	64.8–67.0
Ischemic stroke	247/743	66.8	65.0–68.5	226/553	59.1	57.0–61.2	473/1,296	63.5	62.2–64.8
Lacunar infarction	50/208	76.0	73.0–78.9	36/138	73.9	70.2–77.7	86/346	75.1	72.8–77.5
Large artery infarction	91/252	63.9	60.9–66.9	68/161	57.8	53.9–61.7	159/413	61.5	59.1–63.9
Cardioembolic infarction	79/152	48.0	44.0–52.1	89/153	41.8	37.8–45.8	168/305	44.9	42.1–47.8
Other/undetermined*	27/131	79.4	75.9–82.9	33/101	67.3	62.7–72.0	60/232	74.1	71.3–77.0
Hemorrhagic stroke	72/260	72.3	69.5–75.1	96/323	70.3	67.7–72.8	168/583	71.2	69.3–73.1
Intracerebral hemorrhage	64/221	71.0	68.0–74.1	74/226	67.3	64.1–70.4	138/447	69.1	66.9–71.3
Subarachnoid hemorrhage	8/39	79.5	73.0–86.0	22/97	77.3	73.1–81.6	30/136	77.9	74.4–81.5

CI, confidence interval.
*Ischemic stroke with other determined etiology or ischemic stroke with undetermined etiology.

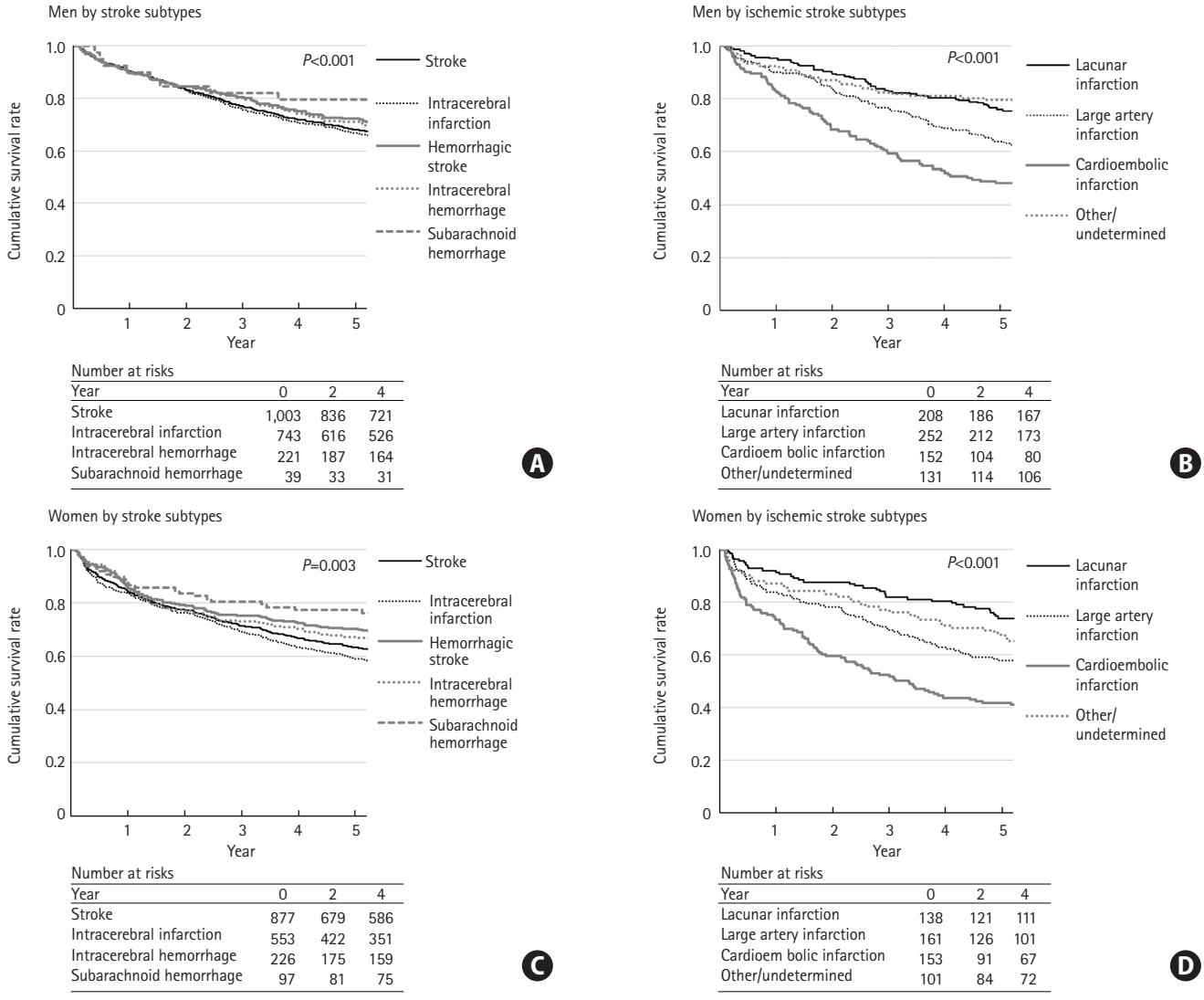

Figure 1. Five-year survival rate curve after non-fatal first-ever stroke for men by stroke subtypes (A), for men by ischemic stroke subtypes (B), for women by stroke types (C), and for women by ischemic stroke subtypes (D). *P*-values were calculated by log-rank test across subtypes of stroke (ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage) and ischemic stroke (lacunar infarction, large artery infarction, cardioembolic infarction, and other/undetermined).

rality rate in the general population using Japanese cohort survival tables.[16] A Cox proportional hazards model was used to evaluate possible predictors for subsequent death. Cases with missing data on TIA or atrial fibrillation (n=17), or a stroke case, not specified as hemorrhage or infarction (n=1) were excluded from the Cox proportional hazards analysis. A *P*-value less than 0.05 was considered statistically significant. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

The baseline characteristics of patients after non-fatal first-ever stroke are shown according to type of index stroke (Table 1). A total of 1,880 cases of first-ever non-fatal stroke were ascertained in 2011. The mean patient age was 74.1 years for ischemic stroke and 68.2 years for hemorrhagic stroke. The frequencies of male sex, atrial fibrillation, moderate to severe disability before stroke onset (mRS 3 to 5), and coma (JCS score 100 to 300) on admission were 53.4%, 17.2%, 12.2%, and 7.9%, respectively.

During an average 4.3-year follow-up period, 677 patients died (641 patients died within the 5 years). Table 2 shows the cumulative survival rates after non-fatal first-ever stroke and its subtypes. Among survivors of first-ever stroke, the 5-year cumulative survival rate was 65.9%. The 5-year cumulative survival rates were 63.5% for ischemic stroke, 69.1% for intracerebral hemorrhage, and 77.9% for subarachnoid hemorrhage. Cumulative survival curves of non-fatal first-ever stroke and ischemic stroke subtypes were plotted separately for men and women (Figure 1).

Table 3. Relative survival rate after non-fatal first-ever stroke by types of stroke and gender in the Shiga Stroke Registry

Variable	Men		Women		Men and women	
	Survival rate (%)	95% CI	Survival rate (%)	95% CI	Survival rate (%)	95% CI
Total stroke	83.2	79.7–86.7	80.6	76.5–84.6	82.0	79.4–84.7
Ischemic stroke	83.3	79.0–87.5	79.1	73.7–84.6	81.6	78.2–84.9
Lacunar infarction	92.1	85.1–99.2	93.3	84.0–100.0	92.6	87.0–98.2
Large artery infarction	79.8	72.4–87.2	77.9	67.7–88.1	79.1	73.1–85.1
Cardioembolic infarction	65.5	54.7–76.4	62.3	50.7–73.8	64.0	56.1–71.9
Other/undetermined*	93.7	85.5–100.0	83.2	71.9–94.6	89.3	82.5–96.0
Hemorrhagic stroke	83.1	76.9–89.3	82.7	76.8–88.6	82.9	78.6–87.1
Intracerebral hemorrhage	82.7	75.8–89.6	81.9	74.5–89.4	82.3	77.2–87.4
Subarachnoid hemorrhage	85.2	71.6–98.8	84.2	75.1–93.3	84.5	76.9–92.1

Relative survival rates were calculated the ratio of observational survival rates to the expected survival rates in the age, sex, and calendar year matched general Japanese population. The expected survival rate were calculated by Ederer I methods.[15]
CI, confidence interval.
*Ischemic stroke with other determined etiology or ischemic stroke with undetermined etiology.

Table 4. Cumulative 5-year survival rate after both nonfatal and fatal first-ever stroke by types of stroke and gender in the Shiga Stroke Registry

Variable	Men			Women			Men and women		
	Death/total no.	Survival rate (%)	95% CI	Death/total no.	Survival rate (%)	95% CI	Death/total no.	Survival rate (%)	95% CI
Total stroke	454/1,138	60.1	58.7–61.6	483/1,038	53.5	51.9–55.0	937/2,176	56.9	55.9–58.0
Ischemic stroke	287/783	63.4	61.6–65.1	288/615	53.2	51.2–55.2	575/1,398	58.9	57.6–60.2
Lacunar infarction	50/208	76.0	73.0–78.9	42/144	70.8	67.0–74.6	92/352	73.9	71.5–76.2
Large artery infarction	101/262	61.5	58.4–64.5	84/177	52.5	48.8–56.3	185/439	57.9	55.5–60.2
Cardioembolic infarction	97/170	42.9	39.1–46.7	120/184	34.8	31.3–38.3	217/354	38.7	36.1–41.3
Other/undetermined*	39/143	72.7	69.0–76.5	42/110	61.8	57.2–66.5	81/253	68.0	65.1–70.9
Hemorrhagic stroke	153/341	55.1	52.4–57.8	184/411	55.2	52.8–57.7	337/752	55.2	53.4–57.0
Intracerebral hemorrhage	123/280	56.1	53.1–59.0	119/271	56.1	53.1–59.1	242/551	56.1	54.0–58.2
Subarachnoid hemorrhage	30/61	50.8	44.4–57.2	65/140	53.6	49.4–57.8	95/201	52.7	49.2–56.3

CI, confidence interval.
*Ischemic stroke with other determined etiology or ischemic stroke with undetermined etiology.

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Table 5. Multivariable analysis of prognostic predictors for fatality after non-fatal first-ever stroke

Variable	Hemorrhagic stroke			Ischemic stroke		
	HR	95% CI	*P*	HR	95% CI	*P*
Age (yr)						
<45	Reference			Reference		
45–64	6.08	0.75–49.45	0.092	3.86	0.60–24.69	0.153
65–74	12.13	1.49–98.98	0.020	7.54	1.21–46.79	0.030
75–84	29.18	3.69–230.51	0.001	15.67	2.53–96.86	0.003
≥85	57.69	7.04–472.40	<0.001	37.03	5.96–230.24	<0.001
Women (vs. men)	0.48	0.32–0.72	<0.001	0.59	0.47–0.74	<0.001
JCS						
0	Reference			Reference		
1	1.77	0.97–3.23	0.063	1.90	1.43–2.52	<0.001
2	2.65	1.37–5.12	0.004	1.65	1.17–2.33	0.005
3	2.15	1.23–3.75	0.007	1.72	1.26–2.35	0.001
10	1.88	1.12–3.16	0.017	2.54	1.74–3.70	<0.001
20	4.04	1.56–10.44	0.004	2.90	1.74–4.85	<0.001
30	2.99	1.26–7.12	0.013	3.35	1.63–6.89	0.001
100	2.16	0.87–5.36	0.097	3.95	2.26–6.91	<0.001
200	5.26	2.86–9.67	<0.001	5.74	3.51–9.40	<0.001
300	10.50	5.17–21.33	<0.001	3.36	1.60–7.06	0.001
Unknown	11.94	0.89–159.70	0.061	6.30	3.34–11.90	<0.001
History of TIA (vs. no)						
Yes	0.97	0.33–2.86	0.952	0.88	0.59–1.32	0.534
Hypertension medication (vs. no)						
Yes	0.91	0.65–1.26	0.570	0.94	0.78–1.14	0.539
Unknown	0.65	0.10–4.27	0.652	5.78	1.22–27.43	0.027
Diabetes (vs. no)						
Yes	1.33	0.90–1.98	0.151	1.22	0.98–1.50	0.070
Unknown	1.18	0.42–3.34	0.751	0.56	0.13–2.41	0.436
Dyslipidemia (vs. no)						
Yes	0.85	0.58–1.24	0.388	0.79	0.65–0.97	0.022
Unknown	1.11	0.61–2.00	0.739	1.10	0.73–1.67	0.643
Atrial fibrillation (vs. no)						
Yes	1.58	0.95–2.61	0.078	1.40	1.14–1.73	0.002
Myocardial infarction (vs. no)						
Yes	1.43	0.71–2.89	0.315	0.93	0.66–1.31	0.664
Unknown	-	-	-	-	-	-
Smoking (vs. nonsmoker)						
Past smoker	0.59	0.31–1.12	0.107	1.23	0.90–1.67	0.196
Current smoker	1.27	0.81–2.01	0.302	1.07	0.81–1.42	0.619
Unknown	0.87	0.38–1.97	0.730	0.66	0.43–1.03	0.066
Drinker (vs. nondrinker)						
Past drinker	3.09	1.23–7.76	0.016	0.74	0.26–2.09	0.569
Current drinker	0.68	0.46–1.02	0.064	0.80	0.63–1.02	0.072
Unknown	1.37	0.65–2.86	0.411	1.25	0.90–1.72	0.179

Table 5. Continued

Variable	Hemorrhagic stroke			Ischemic stroke		
	HR	95% CI	*P*	HR	95% CI	*P*
mRS before onset						
0	Reference			Reference		
1	1.42	0.89–2.27	0.143	1.19	0.89–1.60	0.243
2	1.62	0.90–2.91	0.108	1.91	1.32–2.76	<0.001
3	1.45	0.71–2.98	0.311	1.53	1.09–2.15	0.014
4	1.07	0.51–2.23	0.863	2.37	1.71–3.29	<0.001
5	9.52	3.35–27.07	<0.001	2.88	1.67–4.97	<0.001
Unknown	3.81	2.01–7.23	<0.001	2.24	0.78–6.44	0.136

HR, hazard ration; CI, confidence interval; JCS, Japan Coma Scale (JCS 0, alert; JCS 1–3, possible eye-opening, not lucid; JCS 10–30, possible eye-opening upon stimulation; JCS 100–300, no eye-opening and coma); TIA, transient ischemic attack; mRS, modified Rankin Scale.

Table 3 shows the relative survival rates of non-fatal first-ever stroke and its subtypes. The 5-year relative survival rate after non-fatal first-ever stroke was 82.0%. The 5-year relative survival rates were 81.6% for ischemic stroke (lacunar infarction, 92.6%; large-artery infarction, 79.1%; and cardioembolic infarction, 64.0%), 82.3% for intracerebral hemorrhage, and 84.5% for subarachnoid hemorrhage. The 5-year excess mortality risk after non-fatal stroke was 1.75-fold higher than that among the general Japanese population. Excess mortality risks were 1.66 for ischemic stroke (lacunar infarction, 1.32; large-artery infarction, 1.75; and cardioembolic infarction, 1.88), 1.93 for intracerebral hemorrhage, and 2.84 for subarachnoid hemorrhage.

As for sensitivity analysis, the 5-year cumulative survival rates after both fatal and non-fatal first-ever stroke are shown in Table 4. Approximately 30% (296 out of 937) of fatal cases were observed during the first 28 days after stroke onset. The 5-year cumulative survival rate after first-ever stroke was 56.9%. Five-year cumulative survival rates were 58.9% for ischemic stroke, 56.1% for intracerebral hemorrhage, and 52.7% for subarachnoid hemorrhage. The 5-year relative survival rates after both fatal and non-fatal first-ever stroke were 76.6% for ischemic stroke, 68.6% for intracerebral hemorrhage, and 58.7% for subarachnoid hemorrhage.

Results of multivariable analysis for predictors of death after non-fatal first-ever stroke are shown in Table 5. Age, male sex, higher JCS score, atrial fibrillation, and disability before stroke onset were associated with a higher risk of subsequent death after non-fatal first-ever ischemic stroke; dyslipidemia was associated with a lower risk of future death. In non-fatal first-ever hemorrhagic stroke, age, male sex, JCS score, past drinker, and disability before onset were associated with subsequent death.

Discussion

In the present study using data of a large-scale, recent comprehensive population-based stroke registry, we demonstrated the current status of 5-year prognosis after first-ever stroke in a real-world setting of Japan. The 5-year cumulative survival rate after non-fatal first-ever stroke was 65.9%. Lower 5-year cumulative survival rates were observed for cardioembolic infarction (44.9%) and large-artery infarction (61.5%). The relative 5-year survival rate after non-fatal first-ever stroke was 82.0%, and lower relative survival rates were observed for cardioembolic infarction (64.0%) and large-artery infarction (79.1%). Older age, male sex, higher JCS score on admission, and higher mRS score before stroke onset were associated with higher risk of subsequent death in both non-fatal first-ever ischemic and hemorrhagic stroke.

Five-year cumulative survival rates have been reported to be 50% to 70% after total stroke[6-8,17,18] and 30% to 40% after intracerebral hemorrhage[19-21] in studies conducted during the 1980s, 1990s, and early 2000s. In the present study conducted during the 2010s in Japan, whose participants were slightly older than those of many previous studies, we demonstrated similar 5-year survival rates in a sensitivity analysis using 2,176 fatal/no-fatal first-ever stroke patients. These findings suggest possible improvement in age-standardized 5-year survival rates during the past few decades, which might be derived from improvement in stroke care, advances in medical technology, and/or reduction of stroke severity owing to improved management of cardiovascular risk factors, such as hypertension.

Cumulative survival rates might not be a useful indicator for older patients whose risk of death is very high. In our study, therefore, we also used the relative survival rate, which is an established method in population-based cancer epidemiology[22] for examining long-term survival. Relative survival rate is a

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method to evaluate a corrected survival rate without cause of death information. To our knowledge, this is the first report to calculate recent relative survival rates after non-fatal stroke over the 5-year study period. We also estimated the excess mortality risk after non-fatal stroke over the 5-year study period to be approximately 1.8-fold. These findings are consistent with prior studies reporting the excess mortality risk after non-fatal stroke for more than 5 years as 1.9- to 2.9-fold greater.[6-8]

In this study, older age, male sex, severity of index stroke, and disability (mRS) before onset of the index stroke increased the risk of future death after non-fatal first-ever stroke. These findings are consistent with prior review articles of intracerebral hemorrhage, which reported old age and severity of the index stroke as predictors for long term fatality,[20,23] as well as epidemiological studies reporting that the pre-stroke Barthel Index was associated with subsequent death after non-fatal first-ever stroke.[6] Cumulative and relative survival rates in men were better than these in women. The discrepancy might be due to that mean age of stroke onset in women was 6 years older than that in men (75 years vs. 69 years). We previously reported that high JCS scores on admission predicted fatality at more than 2 years after stroke[10] as well as short-term death.[24,25] In this study, we confirmed these prior findings and demonstrated that the association between high JCS scores on admission and high case fatality persists for more than 5 years after first-ever non-fatal ischemic and hemorrhagic stroke.

To our knowledge, this is the first study to report the current status of 5-year prognosis for type-specific stroke based on a large-scale, comprehensive, population-based registry in Asia. This study also has several limitations. First, owing to a lack of information about the causes of death, we could not examine cause-specific survival rates. Second, we only used information obtained from death certificates for residents of Shiga Prefecture. Patients with stroke who relocated after stroke onset were lost to follow-up. Therefore, the survival rates after stroke onset might have been overestimated. However, according to reports on internal migration derived from the Basic Resident Registers, 5.1% of residents moved out of Shiga Prefecture during the 5-year study period.

Conclusions

In the present study using data of a large-scale comprehensive population-based stroke registry in a real-world setting of Japan, resent 5-year survival after non-fatal first-ever stroke remained low, particularly after cardioembolic infarction and large-artery infarction. These findings reemphasize the importance of secondary stroke prevention in Japan.

Supplementary materials

Supplementary materials related to this article can be found online at https://doi.org/10.5853/jos.2020.00325.

Disclosure

The authors have no financial conflicts of interest.

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Supplementary Table 1. Description of Japan Coma Scale[14]

JCS levels	Description
0	Alert
1	Almost alert
2	Disoriented
3	Does not recall name and birthday
10	Opens eyes in response to normal voice
20	Opens eyes in response to loud voice or shaking body
30	Opens eyes in response to painful stimuli with repeated call
100	Does not open eyes but respond with movements to avoid painful stimuli
200	Does not open eyes but respond with slight movements to avoid painful stimuli (including decerebrate and decorticate response)
300	Does not open eyes and make any movements in response to painful stimuli

JCS, Japan Coma Scale.