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Multivariate Analysis of Risk Factors for Cerebral Infarction Based on Specific Health Checkups in Japan

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Abstract: Stroke is a progressive disease with remissions and exacerbations; it significantly reduces the quality of life of patients and their family and caregivers. Primary prevention is necessary to reduce the growing incidence of stroke globally. In this study, we determined the risk factors for cerebral infarction in elderly Japanese residents and proposed a primary care strategy to prevent cerebral infarction. We investigated the relationship between the incidence of cerebral infarction and the results of checkups 10 years ago. Multivariate logistic regression analysis was performed to determine the variables related to the occurrence of cerebral infarction in biochemical tests and questionnaires administered ten years ago. Hypertension and abnormal creatinine levels were related to increased risk of cerebral infarction based on our findings of the health checkups conducted 10 years previously. Furthermore, weight gain or loss of >3 kg over the last year and habit of eating an evening meal within 2 h before going to bed were associated with an increased risk of cerebral infarction based on the questionnaire results from the specific health checkups. Long-term, large-scale prospective studies are required to determine the specific health items related to increased risk of cerebral infarction.

Keywords: cerebral infarction; stroke; primary care; risk factor; checkups; weight change

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1. Introduction

In the 2019 Global Burden of Disease study, stroke was found to be the second-leading cause of death and the third-leading cause of death and disability combined globally [1]. Between 1990 and 2019, the number of affected individuals, prevalence, deaths, and disability-adjusted life-years of stroke increased by 70.0%, 85.0%, 43.0% and 32.0%, respectively [1]. Ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage accounted for 62.4%, 27.9% and 9.7% of all strokes in 2019, respectively. Stroke is a progressive disease with remissions and exacerbations; it significantly reduces the quality of life of patients and their family and caregivers. Primary prevention is necessary to reduce the growing incidence of stroke globally.

In Japan, the leading cause of death is malignant neoplasm (cancer), followed by heart disease and cerebrovascular disease [2]. Circulatory system diseases, including stroke, cause slightly fewer deaths than cancer in all age groups [2]. However, among individuals aged $\geq$ 75 years, stroke is the leading cause of death and causes almost 40,000 more deaths annually than cancer [2]. Considering that the number of elderly people is expected to increase in the future, primary prevention of stroke is essential to extend the average life expectancy. In addition, the major diseases requiring nursing care in Japan are stroke (16.1%) and heart disease (4.5%), which together account for one-fifth of the total diseases [3]. The next most common disease is dementia (17.6%); almost 30% of patients with dementia aged $\geq$ 65 years have vascular dementia due to cerebrovascular diseases [4]. In 2017, 1.11 million patients in Japan received continuous medical care for cerebrovascular diseases, and the annual medical cost for cerebrovascular disease was JPY 1.8 trillion (almost USD 22 billion). Furthermore, the rate of cognitive impairment and the nursing care burden increase after stroke. In particular, the risk factors of ischemic stroke, which accounts for 60% of all strokes, in elderly individuals should be identified and primary prevention strategies should be implemented to reduce the long-term medical and nursing care costs.

The Framingham Stroke Risk Profile (FSRP) is most commonly used for stroke risk assessment [5]. The FSRP study used Cox proportional hazards regression modeling to determine the 10-year risk factors of stroke based on the Framingham study. This study identified age, systolic blood pressure, use of antihypertensives, diabetes mellitus, current smoking, history of cardiovascular disease (coronary heart disease, heart failure, or intermittent claudication), history of atrial fibrillation, and left ventricular hypertrophy as risk factors of stroke [6–8]. However, the prevalence and predictors of stroke vary by race, country, temperature, and economic level, which requires the identification of stroke risks factors in Japanese people [1,5]. In addition, although many cohort studies have evaluated the risk factors for all strokes, few cohort studies have explored the risk factors for cerebral infarction only.

In 2008, the Japanese Ministry of Health, Labor and Welfare introduced the Japanese health checkup/guidance program to detect individuals with risk factors for metabolic syndrome. This program was designed to reduce the prevalence of metabolic syndrome and associated medical costs using medium- to long-term lifestyle changes [9]. The Specified Health Checkups in Japan contains 29 items based on an annual physical examination for the assessment of risk factors for metabolic syndrome, as well as a 23-item questionnaire. Since 1961, Japan has provided a universal health insurance system. Anonymized data from The Specified Health Checkups and information issued by medical institutions to the National Health Insurance are stored in the respective databases [6]. Analysis of these databases are permitted for academic research on medical cost optimization and improvement of the quality of medical services [10]. In this study, we conducted a new study to analyze the risk factor by combining the results of past Specific Health Checkup and the receipt data 10 years later.

We explored the association of incidence of cerebral infarction with findings of the Specific Health Checkups in Japan. We determined the risk factors for cerebral infarction in elderly Japanese residents and proposed a primary care strategy to prevent cerebral infarct.

2. Materials and Methods

2.1. Study Participants

We enrolled 33,824 individuals with insurance from a total of 106,978 residents of Mishima City, Japan. These 33,824 residents were treated at clinics and hospitals in this city in 2019 using the National Health Insurance. In 2009, 7438 residents aged > 40 years underwent a specific health checkup based on 29 physical examinations, laboratory tests, and a 23-item questionnaire. Of them, we selected 5909 individuals (2140 men and 3769 women; mean age: 75.0 ± 6.69 years, 49–84 years) who had received both medical treatment at a medical institution using the National Health Insurance in 2019 as well as a standard health examination in 2009. Individuals with history of stroke in 2009 were excluded. We investigated the relationship between the incidence of cerebral infarction in 2019 and the results of checkups 10 years ago.

2.2. Statistical Analysis

Logistic regression analysis (LRA) was performed to identify factors related to cerebral infarction. To exclude confounding factors among explanatory variables, multiple LRA was performed and calculate adjusted odds ratios (OR). All items on the questionnaire or biochemical tests were entered simultaneously as explanatory variables. Participants were categorized according to the presence or absence of cerebral infarction using the receipt data from the 2019 National Health Insurance. Cerebral infarction was defined as ICD10 classification of I630-639.

For the multivariate LRA, the dependent and independent variables were selected as incidence of cerebral infarction (existence/nonexistence) and results of the Specific Health Checkup plus questionnaire, respectively. Multivariate LRAs were conducted individually for biochemical tests and questionnaires. Potential common confounders (age, sex, drug intake, outpatient medical expenditures in 2009, and medical history) were included as explanatory variables in both multivariate LRAs. Data were analyzed using SPSS v. 27 and Modeler v. 18.3 (IBM Corp., Armonk, NY, USA). The National Institute of Public Health (NIPH-IBRA #12386) and the ethics committee municipal assembly of Mishima provided permission for this study. The study was performed in accordance with the International Ethical Guidelines for Epidemiology [11], Guidelines for the utilization of the Database for National Health Insurance Claim, Specific Medical Checkup/Health Guidance [12], and Guidelines of Security for Health Information Systems [13]. Participant data were anonymized by the local administration.

3. Results

We cross-tabulated the biochemical tests in 2009 and incidence of cerebral infarction in 2019 (Table 1); *p*-value was calculated by chi-square test and four items were identified as significantly different: "creatinine", "urinary acid", "leucocyte", and "HbA1C".

Table 1. Cross-tabulation results of the biochemical tests in 2009 and incidence of cerebral infarction in 2019.

		Incidence of Cerebral Infarction			
Item	**Category**	**Nonexistence**	**Existence**	**Total**	***p*-Value**
Uric protein	Normal	4736	825	5561	0.592
		85%	15%	100%	
	Follow-up	9	3	12	
		75%	25%	100%	
	Requires further testing	223	35	258	
		86%	14%	100%	
	Requires treatment	64	14	78	
		82%	18%	100%	
Urinary sugar	Normal	4935	854	5789	0.083
		85%	15%	100%	
	Follow-up	6	0	6	
		100%	0%	100%	
	Requires further testing	44	7	51	
		86%	14%	100%	
	Requires treatment	47	16	63	
		75%	25%	100%	
Uric blood	Normal	4162	734	4896	0.589
		85%	15%	100%	
	Follow-up	51	11	62	
		82%	18%	100%	

Table 1. *Cont.*

		Incidence of Cerebral Infarction			
Item	Category	Nonexistence	Existence	Total	*p*-Value
	Requires further testing	706	110	816	
		87%	13%	100%	
	Requires treatment	113	22	135	
		84%	16%	100%	
Creatinine	Normal	4733	791	5524	<0.001
		86%	14%	100%	
	Follow-up	299	86	385	
		78%	22%	100%	
	Requires further testing	0	0	0	
		0%	0%	0%	
	Requires treatment	0	0	0	
		0%	0%	0%	
Urea nitrogen	Normal	4863	845	5708	0.662
		85%	15%	100%	
	Follow-up	169	32	201	
		84%	16%	100%	
	Requires further testing	0	0	0	
		0%	0%	0%	
	Requires treatment	0	0	0	
		0%	0%	0%	
Urinary acid	Normal	4661	793	5454	0.024
		85%	15%	100%	
	Follow-up	371	84	455	
		82%	18%	100%	
	Requires further testing	0	0	0	
		0%	0%	0%	
	Requires treatment	0	0	0	
		0%	0%	0%	
Leucocyte	Normal	4739	844	5583	0.014
		85%	15%	100%	
	Follow-up	293	33	326	
		90%	10%	100%	
	Requires further testing	0	0	0	
		0%	0%	0%	
	Requires treatment	0	0	0	
		0%	0%	0%	

Table 1. *Cont.*

		Incidence of Cerebral Infarction			
Item	**Category**	**Nonexistence**	**Existence**	**Total**	***p*-Value**
Erythrocyte	Normal	3409	607	4016	0.690
		85%	15%	100%	
	Follow-up	1451	241	1692	
		86%	14%	100%	
	Requires further testing	0	0	0	
		0%	0%	0%	
	Requires treatment	172	29	201	
		86%	14%	100%	
Hemoglobin	Normal	4477	776	5253	0.906
		85%	15%	100%	
	Follow-up	459	83	542	
		85%	15%	100%	
	Requires further testing	0	0	0	
		0%	0%	0%	
	Requires treatment	96	18	114	
		84%	16%	100%	
Hematocrit	Normal	4734	824	5558	0.950
		85%	15%	100%	
	Follow-up	266	48	314	
		85%	15%	100%	
	Requires further testing	0	0	0	
		0%	0%	0%	
	Requires treatment	32	5	37	
		86%	14%	100%	
Platelet	Normal	4887	857	5744	0.319
		85%	15%	100%	
	Follow-up	145	20	165	
		88%	12%	100%	
	Requires further testing	0	0	0	
		0%	0%	0%	
	Requires treatment	0	0	0	
		0%	0%	0%	
AST(GOT)	Normal	4443	766	5209	0.689
		85%	15%	100%	
	Follow-up	536	102	638	
		84%	16%	100%	
	Requires further testing	0	0	0	
		0%	0%	0%	
	Requires treatment	53	9	62	
		85%	15%	100%	

Table 1. *Cont.*

		Incidence of Cerebral Infarction			
Item	**Category**	**Nonexistence**	**Existence**	**Total**	***p*-Value**
ALT(GPT)	Normal	4365	754	5119	0.826
		85%	15%	100%	
	Follow-up	547	101	648	
		84%	16%	100%	
	Requires further testing	0	0	0	
		0%	0%	0%	
	Requires treatment	120	22	142	
		85%	15%	100%	
γGTP	Normal	4357	751	5108	0.563
		85%	15%	100%	
	Follow-up	493	88	581	
		85%	15%	100%	
	Requires further testing	0	0	0	
		0%	0%	0%	
	Requires treatment	182	38	220	
		83%	17%	100%	
Amylase	Normal	4753	830	5583	0.824
		85%	15%	100%	
	Follow-up	279	47	326	
		86%	14%	100%	
	Requires further testing	0	0	0	
		0%	0%	0%	
	Requires treatment	0	0	0	
		0%	0%	0%	
ALP	Normal	4775	830	5605	0.755
		85%	15%	100%	
	Follow-up	257	47	304	
		85%	15%	100%	
	Requires further testing	0	0	0	
		0%	0%	0%	
	Requires treatment	0	0	0	
		0%	0%	0%	
LDL-cholesterol	Normal	1817	312	2129	0.762
		85%	15%	100%	
	Follow-up	3215	565	3780	
		85%	15%	100%	
	Requires further testing	0	0	0	
		0%	0%	0%	
	Requires treatment	0	0	0	
		0%	0%	0%	

Table 1. *Cont.*

Item	Category	Incidence of Cerebral Infarction			*p*-Value
		Nonexistence	Existence	Total	
Total protein	Normal	4876	853	5729	0.563
		85%	15%	100%	
	Follow-up	156	24	180	
		87%	13%	100%	
	Requires further testing	0	0	0	
		0%	0%	0%	
	Requires treatment	0	0	0	
		0%	0%	0%	
Total-cholesterol	Normal	2335	414	2749	0.335
		85%	15%	100%	
	Follow-up	2093	373	2466	
		85%	15%	100%	
	Requires further testing	0	0	0	
		0%	0%	0%	
	Requires treatment	604	90	694	
		87%	13%	100%	
HDL-cholesterol	Normal	4859	845	5704	0.107
		85%	15%	100%	
	Follow-up	137	20	157	
		87%	13%	100%	
	Requires further testing	0	0	0	
		0%	0%	0%	
	Requires treatment	36	12	48	
		75%	25%	100%	
Neutral fat	Normal	4034	680	4714	0.110
		86%	14%	100%	
	Follow-up	864	176	1040	
		83%	17%	100%	
	Requires further testing	0	0	0	
		0%	0%	0%	
	Requires treatment	134	21	155	
		86%	14%	100%	
Blood glucose level	Normal	3481	574	4055	0.086
		86%	14%	100%	
	Follow-up	1194	231	1425	
		84%	16%	100%	
	Requires further testing	0	0	0	
		0%	0%	0%	
	Requires treatment	357	72	429	
		83%	17%	100%	

Table 1. *Cont.*

		Incidence of Cerebral Infarction			
Item	**Category**	**Nonexistence**	**Existence**	**Total**	***p*-Value**
HbA1C	Normal	2634	400	3034	0.001
		87%	13%	100%	
	Follow-up	1974	384	2358	
		84%	16%	100%	
	Requires further testing	0	0	0	
		0%	0%	0%	
	Requires treatment	424	93	517	
		82%	18%	100%	
Total		5032	877	5909	
		85%	15%	100%	

p-Value: Chi-square test.

Table 2 presents the findings from the cross-tabulation of questionnaires administered in 2009 and incidence of cerebral infarction in 2019, which showed significant differences in seven items: “a medicine to lower blood pressure”, “insulin injections or a medicine to lower blood glucose”, “a medicine to lower cholesterol”, “heart disease history”, “current regular smoker”, “weight gain or loss of >3 kg over the last year”, “skip breakfast 3 days or more per week”.

Table 2. Cross-tabulation results of questionnaires conducted in 2009 and incidence of cerebral infarction in 2019.

		Incidence of cerebral infarction			
		Nonexistence	**Existence**	**Total**	***p*-Value**
A medicine to lower blood pressure	Yes	1776	410	2186	<0.001
		81.2%	18.8%	100.0%	
	No	3256	467	3723	
		87.5%	12.5%	100.0%	
Insulin injections or a medicine to lower blood glucose	Yes	383	103	486	<0.001
		78.8%	21.2%	100.0%	
	No	4649	774	5423	
		85.7%	14.3%	100.0%	
A medicine to lower cholesterol	Yes	1151	248	1399	0.001
		82.3%	17.7%	100.0%	
	No	3881	629	4510	
		86.1%	13.9%	100.0%	
Heart disease history	Yes	258	77	335	<0.001
		77.0%	23.0%	100.0%	
	No	4774	800	5574	
		85.6%	14.4%	100.0%	

Table 2. *Cont.*

		Incidence of cerebral infarction			
		Nonexistence	**Existence**	**Total**	***p*-Value**
Chronic renal failure history	Yes	8	2	10	0.646
		80.0%	20.0%	100.0%	
	No	5024	875	5899	
		85.2%	14.8%	100.0%	
Anemia history	Yes	555	95	650	0.863
		85.4%	14.6%	100.0%	
	No	4477	782	5259	
		85.1%	14.9%	100.0%	
Current regular smoker	Yes	621	72	693	<0.001
		89.6%	10.4%	100.0%	
	No	4411	805	5216	
		84.6%	15.4%	100.0%	
Weight gained more than10kg since 20 years old	Yes	1545	289	1834	0.184
		84.2%	15.8%	100.0%	
	No	3487	588	4075	
		85.6%	14.4%	100.0%	
Exercising for 30 minutes or more, 2 days or more every week	Yes	2256	404	2660	0.498
		84.8%	15.2%	100.0%	
	No	2776	473	3249	
		85.4%	14.6%	100.0%	
Walking more than 1hour everyday	Yes	2620	469	3089	0.443
		84.8%	15.2%	100.0%	
	No	2412	408	2820	
		85.5%	14.5%	100.0%	
Walk faster than people of your age and sex	Yes	2803	471	3274	0.272
		85.6%	14.4%	100.0%	
	No	2229	406	2635	
		84.6%	15.4%	100.0%	
Weight gain or loss of more than 3kg over the last year	Yes	911	185	1096	0.035
		83.1%	16.9%	100.0%	
	No	4121	692	4813	
		85.6%	14.4%	100.0%	
Eating pace	Faster	383	64	447	0.551
		85.7%	14.3%	100.0%	
	Normal	3505	599	4104	
		85.4%	14.6%	100.0%	
	Slower	1144	214	1358	
		84.2%	15.8%	100.0%	

Table 2. *Cont.*

		Incidence of cerebral infarction			
		Nonexistence	**Existence**	**Total**	***p*-Value**
Evening meal within 2 hours before going to bed	Yes	506	106	612	0.069
		82.7%	17.3%	100.0%	
	No	4526	771	5297	
		85.4%	14.6%	100.0%	
Have snack after the evening meal	Yes	498	75	573	0.214
		86.9%	13.1%	100.0%	
	No	4534	802	5336	
		85.0%	15.0%	100.0%	
Skip breakfast 3 days or more per week	Yes	295	32	327	0.008
		90.2%	9.8%	100.0%	
	No	4737	845	5582	
		84.9%	15.1%	100.0%	
Drink alcohol	Rarely(can't drink)	972	155	1127	0.383
		86.2%	13.8%	100.0%	
	Sometimes	1096	205	1301	
		84.2%	15.8%	100.0%	
	Everyday	2964	517	3481	
		85.1%	14.9%	100.0%	
Feel refreshed after a night's sleep	Yes	3929	675	4604	0.463
		85.3%	14.7%	100.0%	
	No	1103	202	1305	
		84.5%	15.5%	100.0%	
Start lifestyle modifications	no plan to improve	1059	199	1258	0.83
		84.2%	15.8%	100.0%	
	going to start in the future (within 6 months)	413	73	486	
		85.0%	15.0%	100.0%	
	going to start soon (in a month)	566	93	659	
		85.9%	14.1%	100.0%	
	already started (<6 months ago)	1453	252	1705	
		85.2%	14.8%	100.0%	
	already started (≥6 months ago)	1541	260	1801	
		85.6%	14.4%	100.0%	
Willing to have Health Guidance	Yes	2565	471	3036	0.135
		84.5%	15.5%	100.0%	
	No	2467	406	2873	
		85.9%	14.1%	100.0%	
	Total	5032	877	5909	
		85.2%	14.8%	100.0%	

p-Value: Chi-square test.

LRA was performed to determine the variables related to the occurrence of cerebral infarction in biochemical tests (Table 3).

Table 3. Multivariate logistic regression analysis of biochemical tests in 2009.

Item	Multivariate Adjusted Odds Ratio	95% CI		p-Value
		Lower Limit	Upper Limit	
Age	1.081	1.064	1.098	<0.001
Sex(Women/Men)	1.070	0.824	1.389	0.613
Height (cm)	0.996	0.979	1.012	0.590
Weight (kg)	0.999	0.982	1.016	0.881
Abdominal circumference(cm)	1.007	0.992	1.021	0.382
A medicine to lower blood pressure(+/−)	1.166	0.988	1.376	0.070
Insulin injections or a medicine to lower blood glucose(+/−)	1.294	0.995	1.682	0.055
A medicine to lower cholesterol (Yes/No)	1.044	0.876	1.245	0.628
Systolic blood pressure(mmHg)	1.009	1.003	1.016	0.005
Diastolic blood pressure(mmHg)	0.999	0.989	1.009	0.865
Uric protein(+±/−)	0.853	0.619	1.176	0.331
Urinary sugar(+±/−)	1.164	0.710	1.909	0.548
Uric blood(+±/−)	0.937	0.764	1.148	0.529
Creatinine(+±/−)	1.494	1.136	1.964	0.004
Urea nitrogen(+±/−)	0.966	0.643	1.451	0.866
Urinary acid(+±/−)	1.186	0.896	1.569	0.232
Leucocyte(+±/−)	0.784	0.537	1.143	0.206
Erythrocyte(+±/−)	0.919	0.773	1.092	0.338
Hemoglobin(+±/−)	0.967	0.753	1.243	0.796
Hematocrit(+±/−)	1.005	0.713	1.416	0.977
Platelet(+±/−)	0.755	0.463	1.231	0.260
AST(GOT)(+±/−)	0.985	0.737	1.316	0.918
ALT(GPT)(+±/−)	1.022	0.768	1.360	0.882
γGPT(+±/−)	1.092	0.858	1.390	0.473
Amylase(+±/−)	0.856	0.613	1.196	0.362
ALP(+±/−)	0.969	0.696	1.348	0.851
LDL-cholesterol(+±/−)	1.033	0.851	1.255	0.742
Total protein(+±/−)	0.779	0.494	1.231	0.285
Total-cholesterol(+±/−)	1.027	0.853	1.237	0.780
HDL-cholesterol(+±/−)	0.836	0.554	1.262	0.394
Neutral fat (+±/−)	1.049	0.867	1.270	0.622
Blood glucose level (+±/−)	0.929	0.774	1.115	0.428
HbA1C (+±/−)	1.104	0.935	1.303	0.243
Outpatient Medical Expenditures in 2009	1.000	1.000	1.000	<0.001
_cons	0.000			0.000

A Total of 34 items were entered simultaneously as the independent variables.

The crude ORs showed statistically significant associations for 13 items. However, to eliminate potential confounding factors, all explanatory variables possibly related to cerebral infarction were entered into the multivariate LRA, irrespective of the results of univariate LRA. Significant OR was identified for the incidence of cerebral infarction in four items, namely "age", "systolic blood pressure", "creatinine" and "outpatient medical expenditures in 2009" (Table 3).

LRA was performed to investigate the variables related to the incidence of cerebral infarction in questionnaires administered in 2009 (Table 4).

Table 4. Multivariate logistic regression analysis of questionnaires administered in 2009.

Item		Multivariate Adjusted Odds Ratio	95% CI		*p*-Value
			Lower Limit	Upper Limit	
Age	years	1.066	0.886	1.281	0.499
Sex	(Female/Male)	1.086	1.070	1.103	0.000
A medicine to lower blood pressure	(−/+)	1.272	1.086	1.489	0.003
Insulin injections or a medicine to lower blood glucose	(−/+)	1.291	1.011	1.648	0.041
A medicine to lower cholesterol	(−/+)	1.052	0.886	1.248	0.566
Heart disease history	(−/+)	1.300	0.984	1.719	0.065
Chronic renal failure history	(−/+)	1.101	0.227	5.336	0.905
Anemia history	(−/+)	1.038	0.815	1.322	0.764
Current regular smoker	(−/+)	0.799	0.607	1.051	0.108
Weight gained more than10kg since 20 years old	(−/+)	0.971	0.821	1.149	0.734
Exercising for 30 minutes or more, 2 days or more every week	(−/+)	0.947	0.802	1.119	0.524
Walking more than 1hour everyday	(−/+)	0.977	0.829	1.152	0.784
Walk faster than people of your age and sex	(−/+)	0.923	0.790	1.079	0.314
Weight gain or loss of more than 3kg over the last year		1.232	1.019	1.489	0.031
Eating pace Normal	Reference Group				0.239
Faster		1.160	0.970	1.388	0.103
Slower		0.971	0.729	1.293	0.840
Evening meal within 2 hours before going to bed	(−/+)	1.322	1.042	1.677	0.022
Have snack after the evening meal	(−/+)	0.962	0.736	1.256	0.774
Skip breakfast 3 days or more per week	(−/+)	0.788	0.532	1.166	0.233
Drink alcohol Rarely (can't drink)	Reference Group				0.171
Sometimes		1.184	0.982	1.429	0.078
Everyday		1.000	0.794	1.261	0.997
Feel refreshed after a night's sleep	(−/+)	0.897	0.751	1.073	0.234
Start lifestyle modifications					0.941
no plan to improve	Reference Group				
going to start in the future (within 6 months)		0.949	0.704	1.280	0.733

Table 4. *Cont.*

Item		Multivariate Adjusted Odds Ratio	95% CI		*p*-Value
			Lower Limit	Upper Limit	
going to start soon (in a month)		1.001	0.747	1.341	0.995
already started (<6 months ago)		0.919	0.653	1.294	0.630
already started (≥6 months ago)		1.013	0.748	1.372	0.932
Willing to have Health Guidance	(−/+)	1.138	0.972	1.332	0.109
Outpatient Medical Expenditures (2009)		1.000	1.000	1.000	0.001
_cons		0.001			0.000

A Total of 32 items were entered simultaneously as the independent variables.

The crude ORs showed statistically significant associations for seven items (Table 4). All items, irrespective of the results of the univariate analysis, were entered into the multivariate LRA to identify those associated with the incidence of cerebral infarction. Significant ORs were observed for the incidence of cerebral infarction and six items, namely, "sex", "a medicine to lower blood pressure", "insulin injections or a medicine to lower blood glucose", "weight gain or loss of >3 kg over the last year", "evening meal within 2 h before going to bed" and "outpatient medical expenditures in 2009".

4. Discussion

A recent research study reported that each USD 1 spent on cerebrovascular and cardiovascular disease prevention yields a return on investment of USD 10.9 [14]. Global and regional risk factors for cerebral infarction need to be considered for evidence-based healthcare planning, priority setting, primary prevention, and research [1]. Increased prevalence of several major stroke risk factors between 1990 and 2019 suggests that the existing primary stroke prevention strategies and countermeasures are inadequate and need to be strengthened worldwide [15,16]. The World Health Organization (WHO) recommends that efforts should be made to prevent stroke by appropriately managing hypertension, elevated lipids, diabetes, smoking, reduced physical activity, unhealthy diet, and abdominal obesity [17].

In this research, multivariate LRA demonstrated that hypertension (high systolic blood pressure) was related to a higher risk of incidence of cerebral infarction. The results are consistent with the WHO prevention strategies and FSRP risk factors of stroke. A point-based prediction model for stroke risk was developed and validated in a Japanese cohort study of healthy individuals in 2013. In this model, the group with blood pressure of ≥140 mmHg was associated with a hazard ratio of ≥3 compared to the normotensive group [18]. Antihypertensive drug use was also a predictor of stroke in the FSRP study [5]. In this study, there was a significant multivariate-adjusted OR for use of antihypertensives medicine to lower the blood pressure in the questionnaire, but a multivariate LRA that included blood pressure as an explanatory variable in biochemical tests did not show a significant OR ($p = 0.07$).

Our results of multivariate LRA showed that abnormal creatinine levels were related to an increased occurrence of cerebral infarction. Since creatinine is filtered by the kidneys and excreted in the urine, elevated blood creatinine levels indicate impaired kidney function. A previous study reported that chronic kidney disease was related to increased risks of stroke, asymptomatic cerebrovascular abnormalities, and cognitive impairment [19–22]. In Japan, patients with cerebral infarction patients and CKD have anemia, hypercoagulability, and inflammation. Furthermore, cardiogenic cerebral embolism is the most common clinical type [23]. In addition, renal failure was independently associated with cardiogenic cerebral embolism and subsequent poor outcomes [24]. In this study, most participants with abnormal creatinine levels had no history of renal disease (data not shown). Therefore, the onset of cerebral infarction may be prevented by early treatment.

Diabetes is associated with increased risk of stroke. Our results showed significant multivariate-adjusted ORs, insulin injections or use of antidiabetic drugs in the questionnaire, and significant crude ORs were obtained for biochemical blood glucose levels and HbA1C. However, the multivariate LRA did not show significant ORs of biochemical tests [5,17].

The relationship between weight change and cerebrovascular disease is not well-known [25,26]. Our findings from the multivariate LRA showed that "weight gain or loss of >3 kg over the last year" in the questionnaire was related to increased occurrence of cerebral infarction. In Japan, Kisanuki et al. reported that weight gain during middle age was related to high risk of stroke in women and high risk of coronary heart disease in men, and weight loss was related to high risks of stroke in men as well as women [27]. Although the previous study enrolled middle-aged participants, a similar risk was observed in the elderly participants in the present study. Furthermore, although the above study focused on alterations in body weight over a period of 5 years, our results of changes in body weight over a period of 1 year also increased the risk of cerebral infarction.

Our findings from the multivariate LRA showed that "evening meal within 2 h before going to bed" in the questionnaire was related to an increased risk of incidence of cerebral infarction. Regarding dietary risk, although a diet high in sodium, red meat, and alcohol, and low in fruits, vegetables, and whole grains is associated with stroke risk [5], there are few reports on the rhythm of meals. The item "evening meal within 2 h before going to bed" could be associated with high caloric intake. According to a WHO report, elevated lipids, diabetes, and abdominal obesity are reported to be risk factors [5] and eating before going to bed may be a background factor for these. The questionnaire used in this study did not include questions on caloric intake. More detailed research is needed in the future about the relationship with meals.

Future studies should investigate the risk of lifestyle and biochemical tests on the incidence of cerebral infarction to establish a more accurate screening method. It has been reported that specific medical health checkups in Japan are useful for screening for dementia [28,29]. It would be very efficient if specific health checkups, which screen for metabolic syndrome, could also be used for screening for cerebral infarction or dementia. Because this research was performed retrospectively, a large-scale prospective study is required to identify specific health checkup items associated with stroke risk.

5. Conclusions

Hypertension and abnormal creatinine levels were related to increased risk of cerebral infarction based on our findings of health checkups conducted 10 years previously. Furthermore, weight gain or loss of >3 kg over the last year and habit of eating evening meal within 2 h before going to bed were associated with an increased risk of cerebral infarction based on the questionnaire results from the specific health checkups. Long-term, large-scale prospective studies are required to determine the specific health items related to increased risk of cerebral infarction.

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Informed Consent Statement: The data used in this study was anonymous data with personal information removed by the municipality. In Japan, the national data of medical receipts and specific medical examinations can be used for academic research with high public interest for purposes other than the original purpose without the consent of the residents. (December 24, 2010 Minister of Health, Labor and Welfare Notification No. 424).

Data Availability Statement: To protect the participants' anonymity, data will not be shared unless requested through an administrative procedure.

Conflicts of Interest: All authors report no conflict of interest related to this work.

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