

Relationships between Alcohol Intake and Ischemic Stroke Severity in Sex Stratified Analysis for Japanese Acute Stroke Patients

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Background: The aim of this study is to evaluate in the relationships between alcohol intake and ischemic stroke severity in Japanese stroke patients. **Methods:** Of a total of 101,165 registered cases of stroke in Japan, patient data of total strokes (n = 60,836), cardiogenic strokes (n = 11,894), and noncardiogenic strokes (n = 29,129) were extracted. The National Institutes of Health Stroke Scale (NIHSS) score at admission and the modified Rankin Scale (mRS) score at discharge were used. Significant alcohol consumption in regard to stroke severity at admission and discharge was identified by multivariate adjusted logistic regression analysis. **Results:** Among all subject and males, nondrinkers had significantly poorer NIHSS scores of cardiogenic strokes as did those consuming greater than or equal to 60 g/day, whereas there was a significant difference in past heavy drinkers with noncardiogenic strokes. Among females, nondrinkers had a significance of cardiogenic stroke and non-cardiogenic strokes. Among all subjects and males, 20-39 g/day and 40-59 g/day were significantly associated with protective effects on mRS severity of cardiogenic strokes, whereas 40-59 g/day also had significant protective effects for noncardiogenic strokes. Among females, greater than or equal to 60 g/day had a significant protective effect for cardiogenic strokes. **Conclusions:** For males, alcohol intake of less than 60 g/day played a protective role in functional prognosis at discharge and showed a J-shape relationship. For females, although there was a limitation that the number of female drinkers was small, negative effects were shown at admission with less consumption than males.

Key Words: Ischemic stroke—Sex stratified analysis—Alcohol intake—J-curve—Social environment—Severity—Female drinker
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Introduction

Stroke is a serious debilitating disease that can lead to death. Despite the recent advancements in medical care, most patients who survive a stroke experience after-effects.¹⁻³ In 2016, approximately 16% of stroke patients in Japan developed after-effects requiring long-term care.⁴

Previous studies conducted in various countries have reported a linear increase in the risk of hemorrhagic stroke onset with excessive alcohol intake,⁵⁻¹² whereas moderate alcohol intake has been associated with a reduced risk of ischemic stroke onset. Moreover, a J-curve relationship has been reported between alcohol intake and ischemic stroke onset.⁷⁻¹⁴

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Most past studies reporting a relationship between stroke and excessive alcohol intake were adjusted for the effects of sex. Therefore, to reveal the effects of alcohol intake on the risk of stroke in both males and females, large-scale prospective studies with large numbers of cases are needed.¹¹ However, few retrospective studies have investigated the correlation between the amount of alcohol intake and functional prognosis of stroke patients at discharge.

The Japan Standard Stroke Registry (JSSR) is a database developed by Kobayashi et al. with the aim of establishing a standard for verification of the data for acute stroke treatment in Japan.^{15,16} The study of the JSSR reported that a moderate level of alcohol consumption prior to stroke onset had a J-curve relationship with the functional prognosis of ischemic stroke patients (20-59 g/day),¹⁷ and with the stroke severity at admission in intracerebral hemorrhage patients (<46 g/day).¹⁸

However, the number of cases was insufficient to identify differences between the sexes.

Therefore, the aim of the present study is to investigate the relationship between alcohol intake and the severity of ischemic stroke for each of the men and women in Japanese stroke patients.

Materials and Methods

Ethical Approval

The study protocol was approved by the Institutional Ethical Board for Epidemiological Studies of Asahikawa Medical University (authorization number 17174: November 24, 2017).

Scope of Data and Subtype Classification

As of March 2013, a total of 101,165 stroke patients (59,496 males and 41,669 females) were registered in the JSSR.^{15,16} On this occasion, the records of 60,836 acute phase stroke patients (32,872 males and 27,964 females) with data compliant to the cerebrovascular disease classification of the National Institute of Neurological Disorders and Stroke¹⁹ in respect to a definitive diagnosis of the clinical stroke subtypes, sex, age, drinking history, smoking history, history of hypertension, and diabetic history were extracted as total strokes from the JSSR. Of these, 19,813 cases with cerebral infarction of no known cause, hemorrhagic stroke, and transient ischemic attack were excluded. Furthermore, cases of ischemic strokes were categorized into one of two subtypes based on differences in the mechanism of thrombus formation: 11,894 cardiogenic cases (5,810 males and 6,084 females) and 29,129 noncardiogenic cases (17,036 males and 12,093 females) (Fig 1).

Statistical Analysis

Data were analyzed for 3 separate groups: all subjects, and males and females separately.

The amount of alcohol intake prior to stroke onset was made into a set of ordinal data as 0 = nondrinker; 1 = occasional drinker; 2 = current drinker (20-39 g/day); 3 = current drinker (40-59 g/day); 4 = current drinker (≥ 60 g/day); and 5 = past heavy drinker. A "past heavy drinker" was defined as a habitual drinker who was advised by a doctor to stop drinking at least 1 year before stroke onset.

The statistical significance of factors related to the amount of alcohol intake before stroke onset was determined using

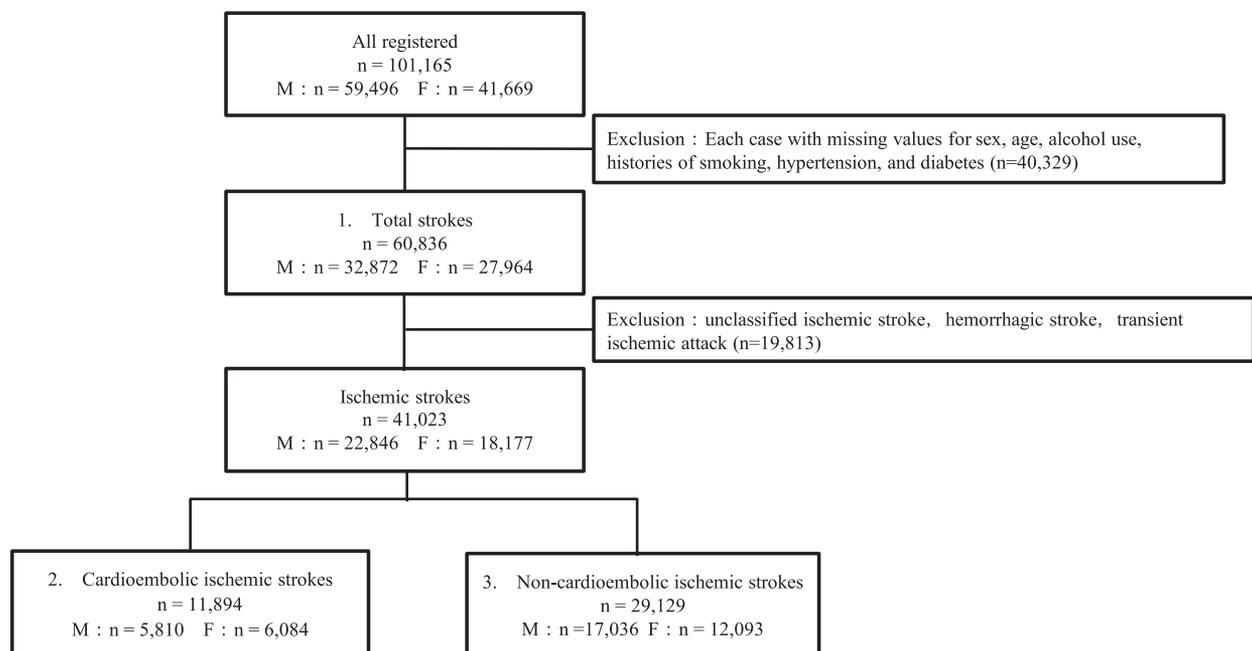


Figure 1. Study flowchart. Abbreviations: F, female; M, male.

the nonparametric Kruskal-Wallis and Mann-Whitney's U tests. As described in our previous report,¹⁷ stroke severity and the clinical index of functional prognosis at hospital admission and discharge were estimated according to the National Institutes of Health Stroke Scale (NIHSS)²⁰ and the modified Rankin Scale (mRS),²¹ respectively. The clinical index was interpreted as mild when the NIHSS score at admission was less than or equal to 4 and the mRS score at discharge was 0-2, and severe when the NIHSS score was greater than or equal to 5 at admission and the mRS score at discharge was 3-6.

With "severe" at admission and discharge for each stroke subtype as the outcome, univariate logistic regression analysis was used to calculate crude odds ratios (ORs) with "occasional drinker" as the reference. Furthermore, multivariate logistic regression analysis was adjusted for age, sex (not using for sex-stratified analysis) the use of an ambulance at admission, smoking habit, diabetes, and hypertension at admission. All these variables and the NIHSS score were included in "severe" at discharge analyses.

We also tested for curvilinear associations between the amount of alcohol intake and outcome by using quadratic trend analyses.

A probability (*P*) value of <.05 was considered statistically significant. All calculations were conducted using SPSS 11.5J for Windows software (SPSS Inc., Chicago, IL).

Results

For each subtype, the amount of alcohol intake prior to stroke onset and stroke-related factors (sex, age, use of an ambulance at admission, smoking habit, hypertension, and diabetes) are shown in Table 1. The clinical index at admission and discharge were shown as the proportion of those being admitted with a NIHSS score of less than or equal to 4 and those with a mRS score of 0-2 at discharge.

Total Strokes

Among nondrinkers, females were significantly older, while among current drinkers, males were significantly older. The proportion of nondrinkers with a NIHSS score of less than or equal to 4 at admission was significantly greater among males. The proportion of nondrinkers, occasional drinkers, and current drinkers (20-39 and 40-59 g/day, respectively) with a mRS score of 0-2 at discharge was significantly greater among males.

Cardiogenic Ischemic Stroke

Among nondrinkers, occasional drinkers and past heavy drinkers, females were significantly older. The proportion of nondrinkers, occasional drinkers, and current drinkers (20-39 g/day) with a NIHSS score less

than or equal to 4 was significantly greater among males. Meanwhile, the proportion of nondrinkers, occasional drinkers, and current drinkers (40-59 g/day) with a mRS score of 0-2 at discharge was significantly greater among males.

Noncardiogenic Ischemic Stroke

Among nondrinkers and occasional drinkers, females were significantly older, while among current drinkers (20-39 g/day), males were significantly older. The proportion of nondrinkers with a NIHSS score at admission less than or equal to 4 was significantly greater among males. The proportion of nondrinkers and current drinkers (40-59 g/day) with a mRS score of 0-2 at discharge was significantly greater among males. The crude and adjusted ORs for the NIHSS score at admission and the mRS score at discharge are shown in Tables 2 and 3, respectively.

Total Stroke Cases

NIHSS Scores at Admission (Fig 2)

The crude ORs of nondrinkers, current drinkers (≥ 60 g/day), and past heavy drinkers were significantly higher in all subjects analysis (a). Among males, in sex stratified analysis showed similar results (b). These significant differences showed a J-shape relationship that remained after multivariate adjustments.

Among females, the crude OR of nondrinkers was significantly higher and this significant difference remained after multivariate adjustments, with additional links with current drinkers (20-39 g/day) (c).

In all subjects analysis, quadratic trend of alcohol consumption was significant after multivariate adjustment. In sex stratified analysis, this trend was also similar for males and females respectively (Table 2).

mRS Score at Discharge (Fig 3)

In all subjects analysis, the crude ORs of nondrinkers and past heavy drinkers were significantly increased, but those of current drinkers (20-39 and 40-59 g/day) were significantly decreased. After adjustments, the significance of these remained similarly (a).

Among males, the crude ORs of nondrinkers, current drinkers (≥ 60 g/day), and past heavy drinkers were significantly increased, but those of current drinkers (20-39 and 40-59 g/day) were significantly decreased. After adjustments, these effects of nondrinkers and past heavy drinkers remained significantly high, and the effect of current drinkers (20-39 and 40-59 g/day) remained significantly low. These correlations showed a J-shaped relationship (b). Among females, the crude ORs of nondrinkers was significantly greater. After adjustments, the significance of nondrinkers remained (c).

Table 1. Characteristics of related factors for alcohol intake before onset

			Non-drinker		Occasional drinker		Current drinker				Past heavy drinker		p			
			N	p	N	p	20-39 g/day	p	40-59 g/day	p	≥60 g/day	p		N	p	
Total strokes, N			60,836		36,715		8,543		9,827		3,370		1,982		399	
Sex, N (%)	M	32,872(100.0)		12,973(39.5)		5,919(18.0)		8,619(26.2)		3,142(9.6)		1,852(5.6)		367(1.1)		<0.001
	F	27,964(100.0)		23,742(84.9)		2,624(9.4)		1,208(4.3)		228(0.8)		130(0.5)		32(0.1)		
Age, median (25%,75%)	M	68.0(60.0,76.0)	<0.001	73.0(64.0,80.0)	<0.001	67.0(57.0,75.0)	0.092	67.0(59.0,75.0)	<0.001	63.0(56.0,70.0)	0.001	61.0(55.0,68.0)	<0.001	68.0(60.0,76.0)	0.205	<0.001
	F	76.0(66.0,83.0)		77.0(68.0,84.0)		67.0(57.0,77.0)		63.0(55.0,73.0)		61.0(53.0,67.5)		57.0(49.0,65.0)		72.0(61.5,79.0)		<0.001
Used an ambulance, N (%)	M	16,870(51.3)	<0.001	6,785(52.3)	<0.001	3,027(51.1)	<0.001	4,319(50.1)	<0.001	1,517(48.3)	0.127	1,035(55.9)	0.005	187(51.0)	0.211	<0.001
	F	16,253(58.1)		13,851(58.3)		1,491(56.8)		680(56.3)		122(53.5)		89(68.5)		20(62.5)		0.036
History of smoking, N (%)	M	15,480(47.1)	<0.001	3,954(30.5)	<0.001	2,704(45.7)	<0.001	4,936(57.3)	<0.001	2,252(71.7)	0.006	1,396(75.4)	0.019	238(64.9)	0.007	<0.001
	F	2,507(9.0)		1,277(5.4)		503(19.2)		484(40.1)		144(63.2)		86(66.2)		13(40.6)		<0.001
History of hypertension, N (%)	M	22,738(69.2)	0.017	8,677(66.9)	<0.001	4,012(67.8)	0.043	6,163(71.5)	0.029	2,267(72.2)	0.135	1,355(73.2)	0.718	264(71.9)	0.129	<0.001
	F	19,592(70.1)		16,767(70.6)		1,720(65.5)		827(68.5)		154(67.5)		97(74.6)		27(84.4)		<0.001
History of diabetes, N (%)	M	9,391(28.6)	<0.001	3,723(28.7)	<0.001	1,641(27.7)	<0.001	2,386(27.7)	<0.001	951(30.3)	<0.001	551(29.8)	0.011	139(37.9)	0.759	<0.001
	F	5,967(21.3)		5,225(22.0)		489(18.6)		178(14.7)		37(16.2)		25(19.2)		13(40.6)		<0.001
Hospitalization, median (25%, 75%)	M	18.0(11.0,32.0)	<0.001	18.0(11.0,33.0)	<0.001	18.0(11.0,32.0)	<0.001	17.0(11.0,31.0)	0.001	17.0(11.0,30.0)	<0.001	19.0(11.0,35.0)	0.257	22.0(14.0,37.0)	0.896	<0.001
	F	21.0(12.0,37.0)		21.0(12.0,38.0)		20.0(13.0,35.0)		19.0(12.0,32.0)		22.0(14.0,40.5)		21.5(14.0,36.0)		26.0(12.5,49.0)		<0.001
NIHSS score at hospital admission (≤4), N (%)	M	18,647(56.7)	<0.001	6,953(53.6)	<0.001	3,496(59.1)	0.491	5,127(59.5)	0.051	1,896(60.3)	0.390	993(53.6)	0.772	182(49.6)	0.768	<0.001
	F	13,421(48.0)		10,995(46.3)		1,529(58.3)		683(56.5)		131(57.5)		68(52.3)		15(46.9)		<0.001
mRS score at hospital discharge (≤2), N (%)	M	20,755(63.1)	<0.001	7,243(55.8)	<0.001	3,960(66.9)	0.002	5,907(68.5)	0.038	2,263(72.0)	0.007	1,185(64.0)	0.394	197(53.7)	0.460	<0.001
	F	13,764(49.2)		11,060(46.6)		1,664(63.4)		792(65.6)		145(63.6)		88(67.7)		15(46.9)		<0.001
Cardioembolic ischemic strokes, N			11,894		7,904		1,466		1,720		473		282		49	
Sex, N (%)	M	5,810(100.0)		2,467(42.5)		1,026(17.7)		1,558(26.8)		447(7.7)		268(4.6)		44(0.8)		<0.001
	F	6,084(100.0)		5,437(89.4)		440(7.2)		162(2.7)		26(0.4)		14(0.2)		5(0.1)		
Age, median (25%,75%)	M	73.0(65.0,80.0)	<0.001	76.0(69.0,82.0)	<0.001	71.0(63.0,78.0)	<0.001	71.0(64.0,78.0)	0.582	68.0(62.0,75.0)	0.228	66.0(60.0,74.0)	0.976	71.5(65.0,78.0)	0.024	<0.001
	F	81.0(74.0,87.0)		82.0(75.0,87.0)		74.0(66.0,82.0)		70.0(62.0,82.0)		68.0(65.0,79.0)		68.0(65.0,69.0)		79.0(78.0,89.0)		<0.001
Used an ambulance, N (%)	M	3,885(66.9)	<0.001	1,669(67.7)	<0.001	689(67.2)	0.064	1,034(66.4)	0.235	278(62.2)	0.264	185(69.0)	0.450	30(68.2)	0.587	0.315
	F	4,568(75.1)		4,102(75.4)		317(72.0)		115(71.0)		19(73.1)		11(78.6)		4(80.0)		0.519
History of smoking, N (%)	M	2,139(36.8)	<0.001	512(20.8)	<0.001	362(35.3)	<0.001	769(49.4)	<0.001	286(64.0)	0.517	183(68.3)	0.754	27(61.4)	0.357	<0.001
	F	285(4.7)		149(2.7)		54(12.3)		56(34.6)		15(57.7)		9(64.3)		2(40.0)		<0.001
History of hypertension, N (%)	M	3,589(61.8)	<0.001	1,462(59.3)	<0.001	602(58.7)	0.882	1,025(65.8)	0.097	312(69.8)	0.440	158(59.0)	0.144	30(68.2)	0.587	<0.001
	F	4,056(66.7)		3,665(67.4)		260(59.1)		96(59.3)		20(76.9)		11(78.6)		4(80.0)		0.002
History of diabetes, N (%)	M	1,307(22.5)	<0.001	521(21.1)	0.001	227(22.1)	0.005	350(22.5)	<0.001	119(26.6)	0.973	70(26.1)	0.839	20(45.5)	0.816	<0.001
	F	1,067(17.5)		969(17.8)		69(15.7)		16(9.9)		7(26.9)		4(28.6)		2(40.0)		0.029
Hospitalization, median (25%, 75%)	M	21.0(14.0,37.0)	<0.001	22.0(14.0,38.0)	0.005	21.0(13.0,38.0)	0.220	20.0(13.0,35.0)	0.657	20.0(14.0,36.0)	0.020	23.0(15.0,40.0)	0.074	26.5(16.3,44.5)	0.766	0.004
	F	24.0(14.0,42.0)		24.0(14.5,42.0)		23.0(14.0,36.8)		20.0(14.0,34.3)		28.0(19.0,44.3)		16.5(13.5,27.3)		28.0(15.5,109.0)		0.093
NIHSS at hospital admission (≤4), N (%)	M	2,353(40.5)	<0.001	893(36.2)	<0.001	447(43.6)	0.013	681(43.7)	0.007	202(45.2)	0.502	113(42.2)	0.563	17(38.6)	0.413	<0.001
	F	1,512(24.9)		1,280(23.5)		161(36.6)		53(32.7)		10(38.5)		7(50.0)		1(20.0)		<0.001
mRS at hospital discharge (≤2), N (%)	M	2,996(51.6)	<0.001	1,083(43.9)	<0.001	567(55.3)	<0.001	908(58.3)	0.084	275(61.5)	0.006	146(54.5)	0.077	17(38.6)	0.413	<0.001
	F	1,819(29.9)		1,516(27.9)		199(45.2)		83(51.2)		9(34.6)		11(78.6)		1(20.0)		<0.001

(Continued)

Non-cardioembolic ischemic strokes, N		29,129	17,356	4,043	4,913	1,711	864	242
Sex, N (%)		M 17,036(100.0) F 12,093(100.0)	6,901(40.5) 10,455(86.5)	3,019(17.7) 1,024(8.5)	4,428(26.0) 485(4.0)	1,629(9.6) 82(0.7)	828(4.9) 36(0.3)	231(1.4) 11(0.1)
Age, median (25%,75%)		M 69.0(61.0,76.0) F 76.0(67.0,83.0)	72.0(64.0,79.0) 77.0(69.0,83.0)	68.0(59.0,75.0) 70.0(61.0,78.0)	68.0(60.5,75.0) 65.0(58.0,74.0)	64.0(57.0,70.0) 64.0(57.0,72.0)	62.0(57.0,68.0) 63.0(51.5,72.0)	68.0(61.0,75.5) 72.0(65.0,77.5)
Used an ambulance, N (%)		M 6,338(37.2) F 4,748(39.3)	2,735(39.6) 4,177(40.0)	1,126(37.3) 3,69(36.0)	1,574(34.9) 171(35.3)	549(33.7) 18(22.0)	293(35.4) 10(27.8)	88(38.1) 3(27.3)
History of smoking, N (%)		M 8,599(50.5) F 1,095(9.1)	2,392(34.7) 628(6.0)	1,503(49.8) 201(19.6)	2,701(61.0) 188(38.8)	1,218(74.8) 52(63.4)	641(77.4) 23(63.9)	144(62.3) 3(27.3)
History of hypertension, N (%)		M 12,198(71.6) F 9,046(74.8)	4,796(69.5) 7,825(74.8)	2,141(70.9) 766(74.8)	3,301(74.5) 360(74.2)	1,171(71.9) 59(72.0)	623(75.2) 26(72.2)	166(71.9) 10(90.9)
History of diabetes, N (%)		M 6,097(35.8) F 3,498(28.9)	2,442(35.4) 3,067(29.3)	1,048(34.7) 290(28.3)	1,561(35.3) 106(21.9)	627(38.5) 19(23.2)	329(39.7) 12(33.3)	90(39.0) 4(36.4)
Hospitalization, median (25%, 75%)		M 16.0(11.0,28.0) F 18.0(12.0,31.0)	17.0(11.0,31.0) 19.0(12.0,32.0)	16.0(11.0,27.0) 16.0(11.0,26.0)	16.0(11.0,26.0) 16.0(11.0,25.0)	16.0(11.0,24.0) 17.0(11.0,34.0)	16.0(10.0,29.0) 13.0(10.0,19.5)	22.0(14.5,34.0) 18.0(15.0,37.0)
NIHSS at hospital admission (≤4), N (%)		M 11,136(65.4) F 7,224(59.7)	4,284(62.1) 6,088(58.2)	2,033(67.3) 701(68.5)	3,005(67.9) 347(71.5)	1,135(69.7) 57(69.5)	550(66.4) 24(66.7)	129(55.8) 7(63.6)
mRS at hospital discharge (≤2), N (%)		M 11,897(69.8) F 6,974(57.7)	4,272(61.9) 5,790(55.4)	2,230(73.9) 725(70.8)	3,319(75.0) 371(76.5)	1,305(80.1) 56(68.3)	628(75.8) 25(69.4)	143(61.9) 7(63.6)

p: Kruskal Wallis test, p: Mann-Whitney U test.

Abbreviations: F, female; M, male; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale.

In all subjects and males analyses, quadratic trend of alcohol consumption was significant after multivariate adjustment (Table 3).

Cardiogenic Ischemic Stroke

NIHSS Score at Admission (Fig 4)

Crude ORs were significantly high for nondrinkers in all subjects analysis (a). Among both males and females analyses also showed similar results (b, c).

After adjustments, the significance of these remained.

In all subjects analysis, quadratic trend of alcohol consumption was significant after multivariate adjustment. In sex stratified analysis, after adjustment, this trend was remained only males (Table 2).

mRS Score at Discharge (Fig 5)

In all subjects analysis, crude ORs of nondrinkers and past heavy drinkers were significantly high, and that of current drinkers (20-39 and 40-59 g/day) were significantly low. After adjustments, the significance of nondrinkers and current drinkers (20-39 g/day) remained (a).

Among males crude ORs of nondrinkers and past heavy drinkers were significantly high, and that of current drinkers (40-59 g/day) was significantly low. After adjustments, the significance of nondrinkers and current drinkers (40-59 g/day) remained. In additional, the OR of current drinkers (20-39 g/day) was significantly low (b).

Among females, the crude OR of nondrinkers was significantly high and that of current drinkers (≥60 g/day) was significantly low. After adjustments, the significance of current drinkers (≥60 g/day) remained (c).

In all subjects analysis, quadratic trend of alcohol consumption was significant after multivariate adjustment. In sex stratified analysis, this trend was shown among males (Table 3).

Noncardiogenic Ischemic Stroke

NIHSS Score at Admission (Fig 6)

Crude ORs of nondrinkers and past heavy drinkers were significantly high in analysis including both males and females (a). Among males also showed similar results (b). After adjustments, the significance of these remained. Among females, the crude OR of nondrinkers was significantly high. After multivariate adjustments, the significance remained (c).

In all subjects analysis, quadratic trend of alcohol consumption was significant after multivariate adjustment. In sex stratified analyses, this trend was also similar respectively (Table 2).

mRS Score at Discharge (Fig 7)

In all subjects analysis, the crude ORs of nondrinkers and past heavy drinkers were significantly high, and that

Table 2. Logistic regression analysis for NIHSS at hospital admission

		Nondrinker		Occasional drinker (Reference)		Current drinker				Past heavy drinker		P							
						20-39 g/day		40-59 g/day		≥60 g/day		for quadratic trend							
		P				P		P		P									
Total strokes																			
N	M	32,872	12,973	5919	8619	3142	1852	367											
	F	27,964	23,742	2624	1208	228	130	32											
All subjects analysis																			
ORs (95%CI)																			
Crude ORs		1.494	(1.424-1.567)	<.001	1.000	.988	(.931-1.048)	.677	.946	(.872-1.027)	.184	1.240	(1.124-1.368)	<.001	1.465	(1.198-1.791)	<.001	<.001	
Age adjusted ORs		1.219	(1.160-1.281)	<.001	1.000	.979	(.923-1.039)	.487	.996	(.918-1.081)	.926	1.345	(1.217-1.486)	<.001	1.421	(1.161-1.738)	.001	<.001	
Adjusted ORs		1.176	(1.113-1.243)	<.001	1.000	1.016	(.950-1.086)	.646	1.075	(.977-1.182)	.137	1.306	(1.165-1.465)	<.001	1.516	(1.214-1.893)	<.001	<.001	
Sex stratified analysis																			
ORs (95%CI)																			
Crude ORs		M	1.249	(1.174-1.329)	<.001	1.000	.983	(.919-1.051)	.612	.948	(.868-1.036)	.238	1.248	(1.124-1.386)	<.001	1.467	(1.188-1.811)	<.001	<.001
	F	1.619	(1.492-1.757)	<.001	1.000	1.073	(.935-1.232)	.314	1.034	(.786-1.360)	.811	1.273	(.895-1.812)	.180	1.583	(.787-3.182)	.198	<.001	
Age adjusted ORs		M	1.144	(1.074-1.219)	<.001	1.000	.967	(.904-1.035)	.334	.982	(.899-1.074)	.694	1.319	(1.186-1.468)	<.001	1.433	(1.160-1.771)	<.001	<.001
	F	1.225	(1.125-1.334)	<.001	1.000	1.138	(.989-1.309)	.070	1.204	(.911-1.592)	.192	1.627	(1.134-2.333)	.008	1.445	(.713-2.930)	.307	<.001	
Adjusted ORs		M	1.135	(1.059-1.216)	<.001	1.000	.987	(.916-1.063)	.723	1.050	(.950-1.160)	.337	1.294	(1.147-1.459)	<.001	1.539	(1.220-1.940)	<.001	<.001
	F	1.271	(1.159-1.394)	<.001	1.000	1.173	(1.004-1.371)	.045	1.330	(.972-1.820)	.075	1.373	(.926-2.035)	.155	1.367	(.633-2.954)	.426	<.001	
Cardioembolic ischemic stroke																			
N	M	5810	2467	1026	1558	447	268	44											
	F	6084	5437	440	162	26	14	5											
All subjects analysis																			
ORs (95%CI)																			
Crude ORs		1.869	(1.666-2.097)	<.001	1.000	.952	(.827-1.096)	.494	.872	(.708-1.075)	.200	.957	(.739-1.238)	.736	1.220	(.676-2.202)	.508	<.001	
Age adjusted ORs		1.458	(1.293-1.644)	<.001	1.000	.967	(.838-1.116)	.646	.959	(.775-1.187)	.700	1.146	(.879-1.495)	.314	1.177	(.645-2.148)	.595	<.001	
Adjusted ORs		1.348	(1.176-1.545)	<.001	1.000	1.055	(.893-1.247)	.531	1.131	(.876-1.459)	.346	1.144	(.839-1.560)	.395	1.280	(.644-2.542)	.481	.002	
Sex stratified analysis																			
ORs (95%CI)																			
Crude ORs		M	1.361	(1.173-1.578)	<.001	1.000	.994	(.848-1.165)	.943	.936	(.749-1.171)	.546	1.059	(.807-1.390)	.680	1.226	(.660-2.278)	.519	.001
	F	1.874	(1.528-2.298)	<.001	1.000	1.187	(.811-1.738)	.379	.923	(.409-2.083)	.848	.577	(.199-1.675)	.312	2.308	(.256-2.829)	.456	.019	
Age adjusted ORs		M	1.218	(1.046-1.417)	.011	1.000	.982	(.836-1.154)	.827	.986	(.786-1.236)	.899	1.177	(.892-1.554)	.249	1.193	(.638-2.231)	.579	.004
	F	1.464	(1.185-1.808)	<.001	1.000	1.362	(.915-2.027)	.128	1.053	(.452-2.454)	.905	.945	(.311-2.873)	.920	1.376	(.147-12.854)	.780	.223	
Adjusted ORs		M	1.267	(1.073-1.496)	.005	1.000	1.010	(.842-1.210)	.916	1.135	(.871-1.479)	.348	1.164	(.846-1.603)	.352	1.289	(.629-2.641)	.488	.012
	F	1.527	(1.209-1.928)	<.001	1.000	1.447	(.920-2.277)	.110	1.113	(.422-2.935)	.829	.635	(.181-2.236)	.480	1.583	(.128-19.581)	.720	.398	
Noncardioembolic ischemic stroke																			
N	M	17,036	6901	3019	4428	1629	828	231											
	F	12,093	10,455	1024	485	82	36	11											
All subjects analysis																			
ORs (95%CI)																			
Crude ORs		1.406	(1.308-1.512)	<.001	1.000	.973	(.890-1.063)	.542	.909	(.805-1.028)	.128	1.055	(.903-1.233)	.499	1.628	(1.252-2.116)	<.001	<.001	
Age adjusted ORs		1.181	(1.095-1.272)	<.001	1.000	.973	(.890-1.065)	.554	.980	(.865-1.109)	.744	1.156	(.986-1.355)	.073	1.620	(1.245-2.108)	<.001	<.001	
Adjusted ORs		1.161	(1.071-1.258)	<.001	1.000	.976	(.886-1.075)	.622	.978	(.853-1.122)	.753	1.148	(.966-1.364)	.116	1.632	(1.236-2.155)	.001	<.001	
Sex stratified analysis																			
ORs (95%CI)																			
Crude ORs		M	1.260	(1.151-1.379)	<.001	1.000	.976	(.885-1.078)	.635	.897	(.788-1.022)	.103	1.042	(.885-1.227)	.619	1.630	(1.244-2.137)	<.001	<.001

(Continued)

Table 2 (Continued)

	Nondrinker	Occasional drinker (Reference)		Current drinker		Past heavy drinker		P for quadratic trend
		P		20-39 g/day	40-59 g/day	≥60 g/day	P	
F	1.557 (1.357-1.786)	<.001	1.000	.863 (.681-1.094)	.224 .952 (.584-1.551)	.843 1.085 (.536-2.197)	.820 1.240 (.360-4.266)	.733 <.001
M	1.155 (1.054-1.267)	.002	1.000	.963 (.872-1.063)	.455 .956 (.838-1.091)	.502 1.123 (.951-1.326)	.170 1.613 (1.229-2.116)	.001 <.001
F	1.251 (1.086-1.441)	.002	1.000	.926 (.728-1.178)	.531 1.061 (.647-1.739)	.815 1.301 (.634-2.668)	.473 1.180 (.341-4.079)	.794 .004
M	1.130 (1.026-1.244)	.013	1.000	.987 (.889-1.097)	.814 .971 (.843-1.118)	.971 1.146 (.960-1.369)	.132 1.659 (1.248-2.206)	<.001 .001
F	1.263 (1.089-1.464)	.002	1.000	.902 (.698-1.165)	.428 1.146 (.674-1.949)	.614 1.288 (.612-2.713)	.505 1.327 (.365-4.819)	.668 .001

Abbreviations: adjusted ORs, multivariate adjusted odds ratios; CI, confidence interval; crude ORs, crude odds ratios; F, female; M, male; NIHSS, National Institute of Health Stroke Scale; ORs, odds ratios.

NIHSS score was converted to binary data as follows: 0 = NIHSS ≤ 4, 1 = NIHSS ≥ 5.

of current drinkers (20-39 and 40-59 g/day) were significantly low. After adjustments, the significance of current drinkers (20-39 g/day) had disappeared (a).

Among males, the crude ORs of nondrinkers and past heavy drinkers were significantly high, and that of current drinkers (40-59 g/day) was significantly low. After adjustments, the significance of these remained (b).

Among females, the crude OR of nondrinkers was significantly high and that of current drinkers (20-39 g/day) was significantly low, but the significance of current drinkers (20-39 g/day) had disappeared after adjustment (c).

Among all subjects, quadratic trend of alcohol consumption was significant after multivariate adjustment. In sex-stratified analyses, this trend was also similar respectively (Table 3).

Discussion

Possibility of Sexual Differences in Alcohol Tolerance

A limiting factor of our previous report¹⁷ was that the nondrinker category may have included “those who do not (cannot) drink due to pathological reasons,” which was difficult to differentiate from “those who do not like to drink.”

A report of genetic characteristics found that that 44% of the Japanese population cannot tolerate drinking alcohol due to the lack of the *ALDH2* gene, which codes for an enzyme that breaks down acetaldehyde, and hence, this condition has the potential to be harmful.²² Thus, acetaldehyde tends to accumulate in about one half of the Japanese population. Based on genetic characteristics and difference in alcohol tolerance,²³⁻²⁶ females may be negatively impacted by less alcohol consumption than males. However, unfortunately, the number of female heavy drinkers was small in our present study to elucidate the influence of heavy drinking on women.

Impact of Alcohol Consumption Prior to Stroke Onset on Disease Severity at Admission and Discharge

For total strokes, in all subjects and males analyses, the severity at admission was greater in nondrinkers and current drinkers (≥60 g/day) than occasional drinkers. But, among nondrinkers for whatever reason, the risk of severity at stroke onset should be considered among those who consume large quantities of alcohol (≥60 g/day) (Table 2, Fig 2). The severity of stroke at admission was greater for female nondrinkers than occasional drinkers, thus the risk of severity should be considered. Moreover, there is a possibility of stroke being more severe among females who consume 20-39 g/day of alcohol as compared to males (Table 2, Fig 2). In all subjects and males analyses, a negative impact on functional prognosis remained at discharge for nondrinkers and those who consume large quantities of alcohol, suggesting that functional prognosis may be better

Table 3. Logistic regression analysis for mRS at hospital discharge

		Nondrinker		Occasional drinker (Reference)		Current drinker			Past heavy drinker			<i>P</i>	
						20-39 g/day	<i>P</i>	40-59 g/day	<i>P</i>	≥60 g/day	<i>P</i>	for quadratic trend	
Total strokes													
N	M	32,872	12,973	5919	8619	3142		1852		367			
	F	27,964	23,742	2624	1208	228		130		32			
All subjects analysis													
ORs (95%CI)													
Crude ORs		1.938 (1.845-2.036)	<.001	1.000	.900 (.846-.957)	.001	.770 (.706-.840)	<.001	1.073 (.969-1.188)	.176	1.699 (1.389-2.079)	<.001	<.001
Age adjusted ORs		1.373 (1.303-1.447)	<.001	1.000	.887 (.833-.945)	<.001	.865 (.791-.945)	.001	1.300 (1.169-1.445)	<.001	1.629 (1.326-2.000)	<.001	<.001
Adjusted ORs		1.290 (1.208-1.377)	<.001	1.000	.890 (.821-.964)	.004	.859 (.765-.965)	.010	1.126 (.982-1.292)	.090	1.657 (1.280-2.144)	<.001	<.001
Sex stratified analysis													
ORs (95%CI)													
Crude ORs	M	1.599 (1.500-1.705)	<.001	1.000	.928 (.865-.996)	.039	.785 (.714-.863)	<.001	1.138 (1.020-1.269)	.021	1.744 (1.411-2.157)	<.001	<.001
	F	1.988 (1.828-2.160)	<.001	1.000	.910 (.789-1.050)	.198	.992 (.749-1.314)	.956	.827 (.568-1.205)	.323	1.964 (.977-3.951)	.058	<.001
Age adjusted ORs	M	1.333 (1.247-1.426)	<.001	1.000	.901 (.838-.968)	.005	.864 (.784-.952)	.003	1.334 (1.192-1.494)	<.001	1.677 (1.352-2.080)	<.001	<.001
	F	1.272 (1.163-1.392)	<.001	1.000	1.015 (.875-1.178)	.842	1.295 (.967-1.736)	.083	1.247 (.844-1.844)	.267	1.747 (.851-3.587)	.129	<.001
Adjusted ORs	M	1.351 (1.244-1.467)	<.001	1.000	.885 (.809-.967)	.007	.819 (.724-.926)	.001	1.147 (.993-1.325)	.062	1.669 (1.276-2.184)	<.001	<.001
	F	1.212 (1.086-1.352)	.001	1.000	.929 (.772-1.118)	.434	1.325 (.914-1.922)	.137	.860 (.536-1.382)	.534	1.617 (.640-4.087)	.309	.006
Cardioembolic ischemic strokes													
N	M	5810	2467	1026	1558	447		268		44			
	F	6084	5437	440	162	26		14		5			
All subjects analysis													
ORs (95%CI)													
Crude ORs		2.234 (1.996-2.500)	<.001	1.000	.805 (.700-.926)	.002	.728 (.590-.899)	.003	.871 (.674-1.126)	.292	1.885 (1.045-3.399)	.035	<.001
Age adjusted ORs		1.514 (1.341-1.709)	<.001	1.000	.822 (.710-.952)	.009	.848 (.681-1.055)	.139	1.163 (.887-1.524)	.274	1.880 (1.016-3.477)	.044	<.001
Adjusted ORs		1.274 (1.092-1.486)	.002	1.000	.770 (.635-.933)	.008	.771 (.573-1.037)	.086	.999 (.698-1.428)	.994	2.010 (.881-4.585)	.097	<.001
Sex stratified analysis													
ORs (95%CI)													
Crude ORs	M	1.579 (1.363-1.828)	<.001	1.000	.884 (.754-1.037)	.130	.773 (.616-.969)	.026	1.032 (.788-1.352)	.818	1.962 (1.056-3.644)	.033	<.001
	F	2.136 (1.754-2.600)	<.001	1.000	.786 (.548-1.127)	.191	1.560 (.680-3.575)	.294	.225 (.062-.818)	.024	3.303 (.366-29.789)	.287	.001
Age adjusted ORs	M	1.299 (1.114-1.514)	.001	1.000	.864 (.733-1.019)	.083	.854 (.676-1.079)	.185	1.283 (.967-1.703)	.085	1.959 (1.032-3.717)	.040	<.001
	F	1.445 (1.168-1.788)	.001	1.000	.903 (.613-1.331)	.607	1.935 (.810-4.623)	.137	.367 (.098-1.370)	.136	2.005 (.214-18.753)	.542	.138
Adjusted ORs	M	1.314 (1.084-1.592)	.005	1.000	.774 (.627-.954)	.017	.688 (.504-.940)	.019	1.076 (.745-1.556)	.695	1.947 (.821-4.614)	.130	<.001
	F	1.245 (.958-1.618)	.101	1.000	.797 (.487-1.305)	.368	2.784 (.924-8.387)	.069	.189 (.037-.973)	.046	2.685 (.121-59.454)	.532	.589
Noncardioembolic ischemic strokes													
N	M	17,036	6901	3019	4428	1629		828		231			
	F	12,093	10,455	1024	485	82		36		11			
All subjects analysis													
ORs (95%CI)													
Crude ORs		1.969 (1.825-2.124)	<.001	1.000	.900 (.819-.990)	.030	.698 (.609-.801)	<.001	.878 (.740-1.040)	.132	1.666 (1.273-2.179)	<.001	<.001
Age adjusted ORs		1.435 (1.325-1.554)	<.001	1.000	.905 (.821-.998)	.045	.832 (.723-.958)	.011	1.132 (.948-1.352)	.170	1.686 (1.280-2.220)	<.001	<.001
Adjusted ORs		1.392 (1.266-1.531)	<.001	1.000	.916 (.815-1.028)	.136	.824 (.694-.977)	.026	1.087 (.878-1.344)	.445	1.525 (1.104-2.107)	.010	<.001

(Continued)

Table 3 (Continued)

		Nondrinker		Occasional drinker (Reference)	Current drinker			Past heavy drinker			<i>P</i>		
			<i>P</i>		20-39 g/day	<i>P</i>	40-59 g/day	<i>P</i>	≥60 g/day	<i>P</i>	<i>P</i> for quadratic trend		
Sex stratified analysis													
ORs (95%CI)													
Crude ORs	M	1.739 (1.582-1.912)	<.001	1.000	.944 (.850-1.050)	.290	.702 (.606-.812)	<.001	.900 (.753-1.076)	.248	1.739 (1.318-2.296)	<.001	<.001
	F	1.954 (1.698-2.247)	<.001	1.000	.745 (.581-.956)	.021	1.126 (.694-1.827)	.632	1.067 (.518-2.196)	.860	1.386 (.403-4.768)	.605	<.001
Age adjusted ORs	M	1.462 (1.325-1.612)	<.001	1.000	.924 (.829-1.029)	.150	.810 (.697-.941)	.006	1.115 (.926-1.342)	.251	1.730 (1.303-2.297)	<.001	<.001
	F	1.352 (1.165-1.568)	<.001	1.000	.890 (.684-1.159)	.388	1.503 (.905-2.496)	.115	1.641 (.760-3.542)	.207	1.275 (.360-4.513)	.707	<.001
Adjusted ORs※	M	1.461 (1.303-1.637)	<.001	1.000	.935 (.825-1.060)	.297	.783 (.656-.935)	.007	1.071 (.860-1.335)	.539	1.564 (1.123-2.179)	.008	<.001
	F	1.282 (1.080-1.522)	.005	1.000	.854 (.627-1.163)	.316	1.715 (.925-3.179)	.087	1.403 (.559-3.521)	.470	1.296 (.304-5.533)	.726	.001

Abbreviations: adjusted ORs, multivariate adjusted odds ratios; CI, confidence interval; crude ORs, crude odds ratios; F, female; M, male; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; ORs, odds ratios.

※Adjusted for sex (not using for sex-stratified analysis), age, use of an ambulance at admission, smoking status, diabetes, hypertension, and severity at admission. mRs score was converted to binary data as follows: 0 = mRS0-2, 1 = mRS3-6.

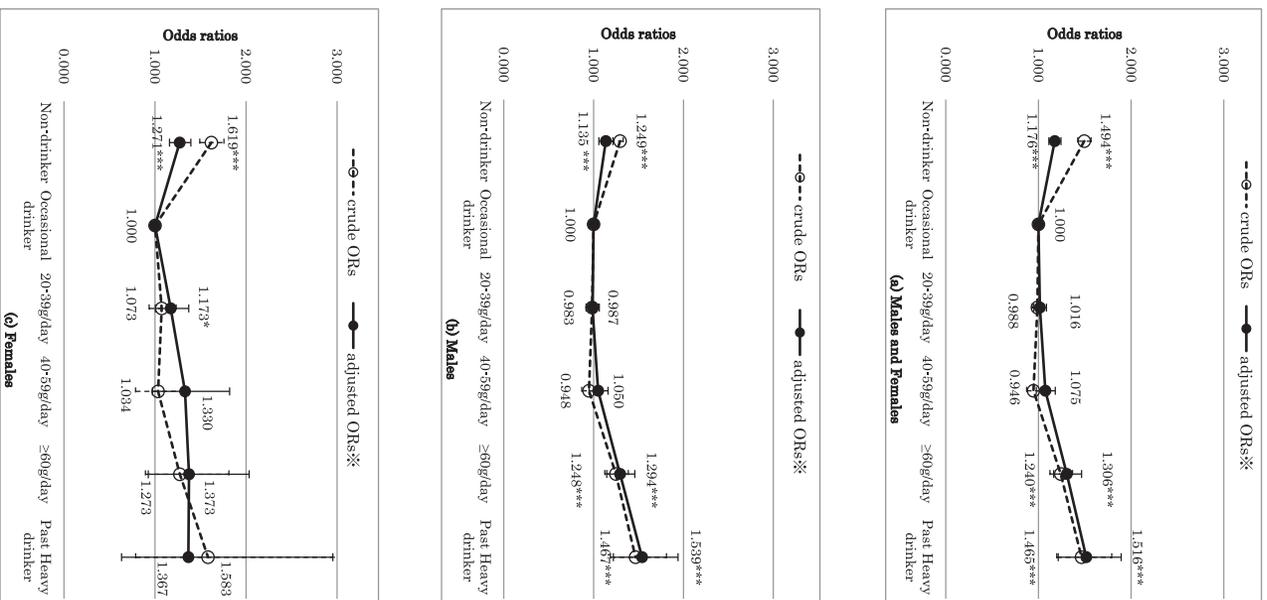


Figure 2. Relationship between level of alcohol consumption prior to onset and NIHSS score at admission (total strokes). There was a significant negative impact among nondrinkers. In all subjects analysis (a) and among males in sex stratified analysis (b), even after multivariate adjustments ※, the negative impact remained for current drinkers (≥60 g/day) and past heavy drinkers with a J-shape correlation. ※ Adjusted for sex (not using for sex-stratified analysis), age, use of an ambulance at admission, smoking status, diabetes, and hypertension. Abbreviations: mRS, modified Rankin Scale; NIHSS, The National Institutes of Health Stroke Scale. ****P* < .001, ***P* < .05.

for those who had been consuming up to 59 g/day of alcohol. In particular, the results of the current study showed that there is the possibility that the protective role was higher for those consuming 40-59 g/day (Table 3, Fig 3). However, the study of alcohol risk for total strokes, including hemorrhagic, showed a linear increase in impact against alcohol consumption.¹³

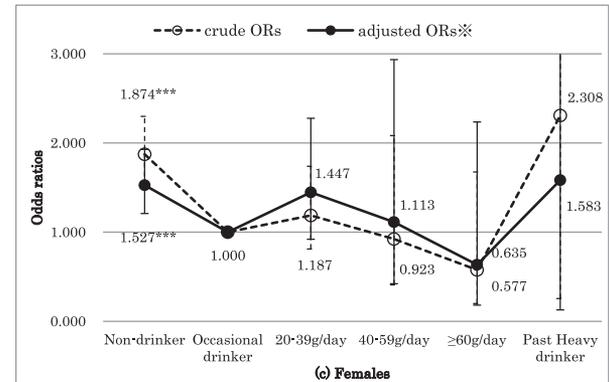
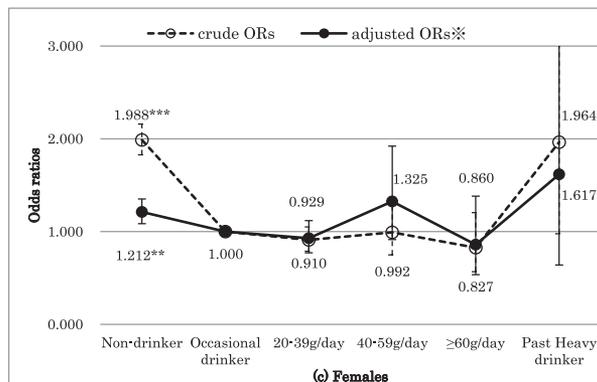
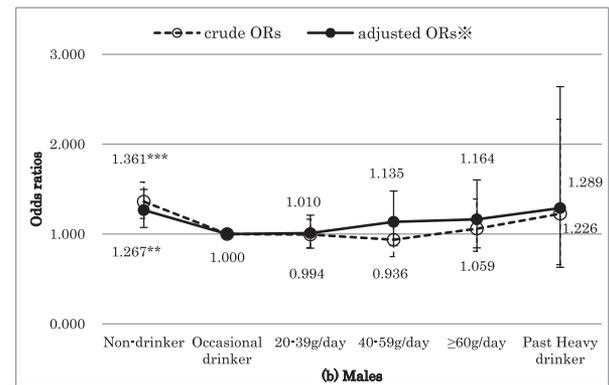
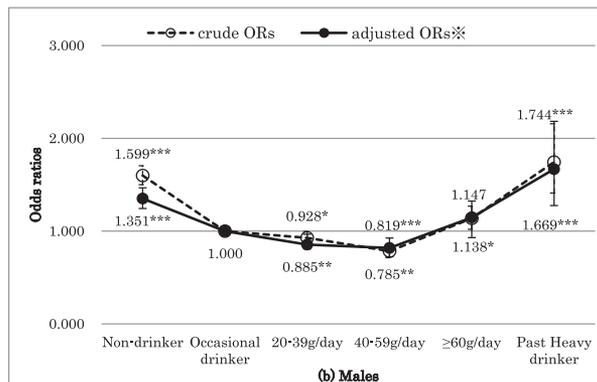
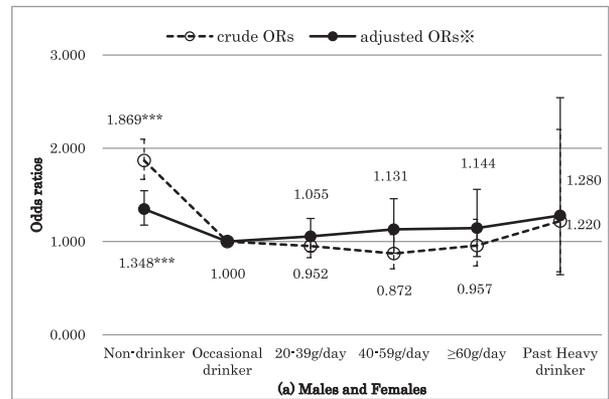
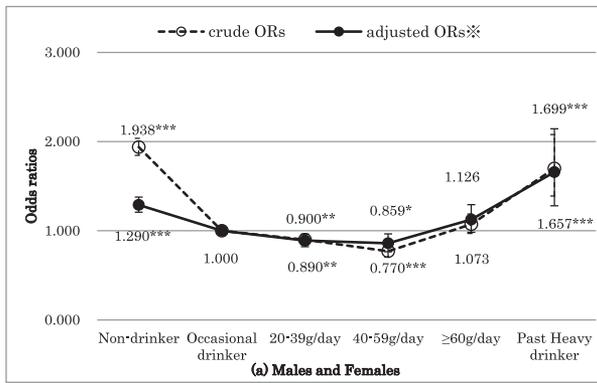


Figure 3. Relationship between alcohol consumption before onset and mRS score at discharge (total strokes). In all subjects analysis (a), and among males in sex stratified analysis (b), positive impact remained even after multivariate adjustments ✂ and a J-shape was shown for current drinkers (20-39 and 40-59 g/day). Negative impact remained for nondrinkers following multivariate adjustments. ✂ Adjusted for sex (not using for sex-stratified analysis), age, use of an ambulance at admission, smoking status, diabetes, hypertension, and severity at admission. Abbreviation: mRS, modified Rankin Scale ***P < .001, **P < .01, *P < .05.

Figure 4. Relationship between alcohol consumption prior to onset and NIHSS score at admission (cardioembolic ischemic stroke). Negative impact was shown for nondrinkers. The impact remained significantly after adjustment. ✂ Adjusted for sex (not using for sex-stratified analysis), age, use of an ambulance at admission, smoking status, diabetes, and hypertension. Abbreviation: NIHSS, The National Institutes of Health Stroke Scale. ***P < .001, **P < .01.

Among past heavy drinkers in all subjects and males analyses, the multivariate adjusted odds ratios were about 1.6. However, the results of females were not significant. This discrepancy may also be due to smaller number of female heavy drinkers.

In respect to the severity of ischemic stroke at admission, in all subjects and males analysis, for cardioembolic case, a negative impact was seen only among the nondrinkers and

although there was no clear correlation at each level of alcohol intake, in the noncardiogenic group, there was negative impact of severity on those consuming large amounts of alcohol (≥60 g/day). These differences are thought to be due to the mechanism of onset between two types of ischemic strokes.^{27,28} That is, the main mechanism of onset of the cardioembolic group is fibrin thrombus formation due to atrial fibrillation, which might be associated with a lower

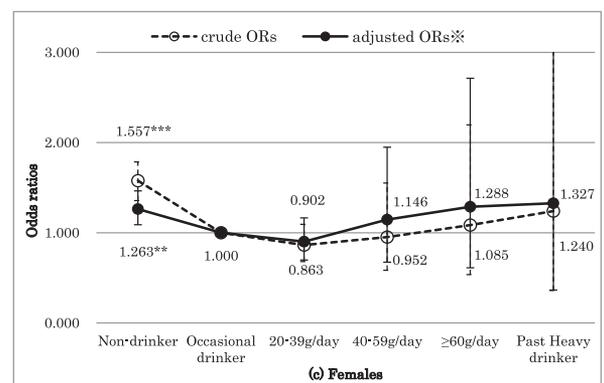
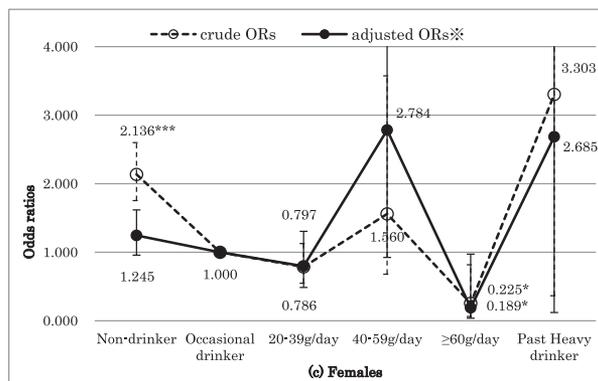
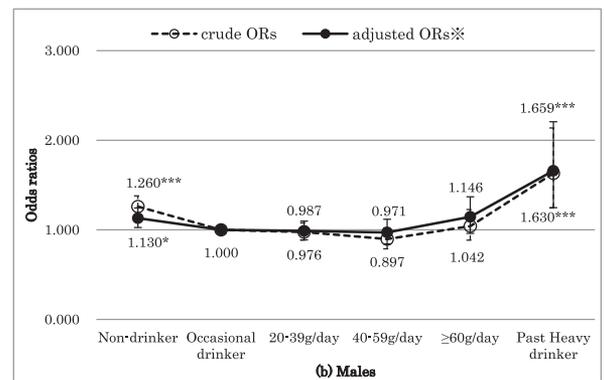
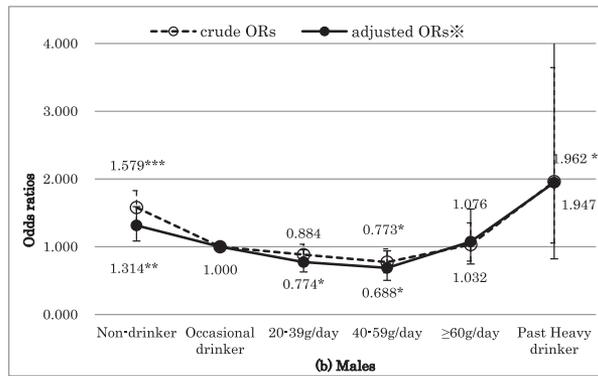
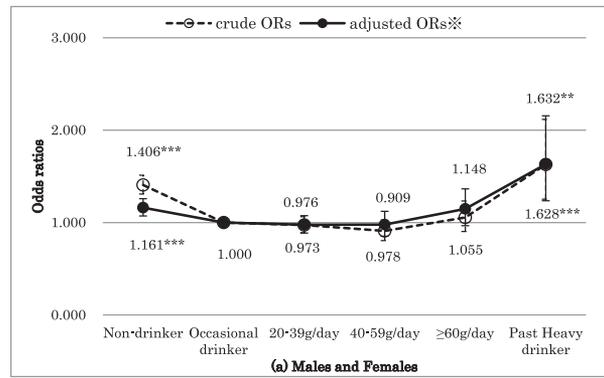
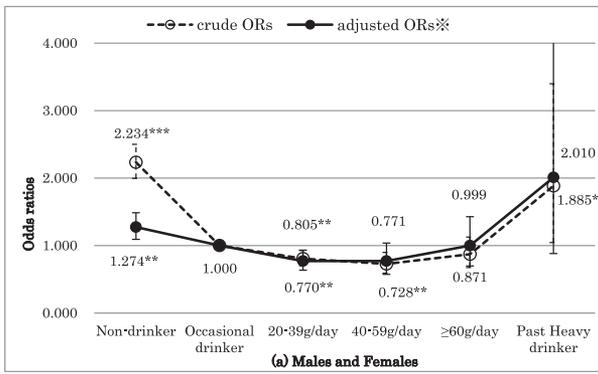


Figure 5. Relationship between alcohol consumption before onset and mRS score at discharge (cardioembolic ischemic stroke). In all subjects analysis (a), and among males in sex stratified analysis (b), after multivariate adjustments ✕, a J-shape with positive impact were shown. Positive impact was shown for female current drinker (≥ 60 g/day) (c), but the number of cases was small. ✕ Adjusted for sex (not using for sex-stratified analysis), age, use of an ambulance at admission, smoking status, diabetes, hypertension, and severity at admission. Abbreviation: mRS, modified Rankin Scale. ***P < .001, **P < .01, *P < .05.

Figure 6. Relationship between alcohol consumption prior to onset and NIHSS score at admission (noncardioembolic ischemic stroke). In all subjects analysis (a), and among males in sex-stratified analysis (b), negative impact was shown with those consuming large quantities after multivariate adjustment ✕ and a J-shape was shown. For females, negative impact on nondrinkers remained even after multivariate adjustments ✕ (c). ✕ Adjusted for sex (not using for sex-stratified analysis), age, use of an ambulance at admission, smoking status, diabetes, and hypertension. Abbreviation: NIHSS, The National Institutes of Health Stroke Scale. ***P < .001, **P < .01, *P < .05.

anticoagulation status among nondrinkers, as a past study reported that moderate alcohol intake had an anticoagulant effect.²⁸ In contrast, the main mechanism of onset in the noncardiogenic group is arterial thrombus due to damage to the vessel wall, which might be responsible for the negative impact of severity due to inflammation of the vessels associated with heavy drinking.²⁸

In females, the negative impact of severity at admission was only seen in the nondrinkers in both the cardiogenic and noncardiogenic groups, and although no clear correlation was seen at each level of alcohol consumption, there may be a need to consider the proportion of nondrinkers as a measure of severity specific to women, such as the drinking environment.

Not only for all subjects analysis, but also for males analysis, the functional prognosis at discharge in both the cardiogenic and noncardiogenic ischemic stroke groups showed a link between the amount of alcohol consumed and clinical index showed a J-shaped curve (P for quadratic trend $<.001$), suggesting that those consuming up to 59 g/day of alcohol have good functional prognosis at discharge (Table 3). In particular, the risk was significantly low for those consuming 40-59 g/day (Table 3, Figs 5 and 7). Previous studies have reported that the relationship between ischemic stroke and the level of alcohol consumption showed a J-shaped relationship.⁷⁻¹⁴ Furthermore, a meta-analysis conducted by Reynolds et al.¹³ found that the onset rate was lower for those consuming alcohol at <60 g/day as compared with nondrinkers.¹³ According to the results of the present study, alcohol intake of up to 59 g/day may have a positive influence on ischemic stroke. However, for further clarification, other factors must be considered.

The OR of current drinkers (≥ 60 g/day) for the mRS score at discharge among females with cardiogenic ischemic stroke was significantly low even after being adjusted for age, smoking history, hypertension, diabetes, and the use of an ambulance at admission (Table 3, Fig 5).

Some studies have reported that younger females consume more alcohol than older females²⁹ and that the poor prognosis of cardiogenic ischemic stroke is related to ageing.³⁰ Moreover, other studies have reported a relationship between alcohol consuming environments with social support.³¹ Thus, there is a possibility that the drinking environment of the mid to older females may be related to improved quality of life.³² In the present study, the number of female cardioembolic ischemic strokes current drinkers consuming greater than or equal to 60 g/day was low, but this group had the adverse effect of alcohol at discharge. Nonetheless, the accumulation of data from future female drinkers through change over time of female drinking patterns, further detailed conclusions will become apparent.

Limitations

Number of Female Drinkers

Since the number of female drinkers, especially heavy drinkers, was small, female analyses did not have adequate statistical power compared to males.

Therefore, further study with a larger female sample size will be necessary.

Environment of Alcohol Consumption

Although the level of alcohol consumption was categorized, there was insufficient information for nondrinkers. Some studies have reported that the environment of alcohol consumption differs among cultures and changes with time.^{33,34} For example, some studies found a decrease in alcohol consumption among young Japanese

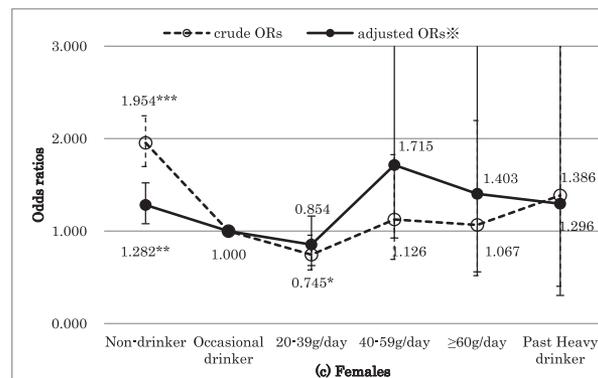
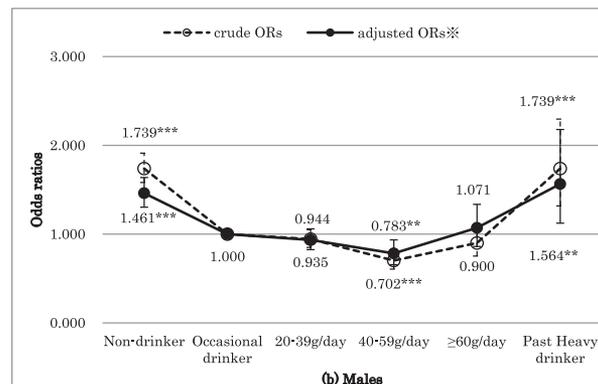
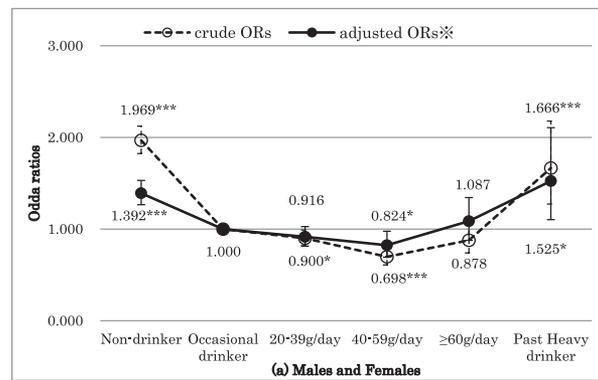


Figure 7. Relationship between alcohol consumption before onset and mRS score at discharge (noncardioembolic ischemic stroke). In all subjects analysis (a), and among males in sex stratified analysis (b), after multivariate adjustments ※, a J-shape with positive impact was shown for current drinkers (of 40-59 g/day). There was no clear impact for females (c). ※ Adjusted for sex (not using for sex-stratified analysis), age, use of an ambulance at admission, smoking status, diabetes, hypertension, and severity at admission. Abbreviation: mRS, modified Rankin Scale. *** $P < .001$, ** $P < .05$.

drinkers due to income restraints³³ or heightened health awareness,³⁴ while others reported a 20% increase in the number of female Japanese drinkers over the past 30 years due to increased social status.³⁴

Though personal information in medical records is limited, future research with more details requires an approach like this from a sociomedical point of view.

Genetic Characteristics

Since there was no information of genetic characteristics available, alcohol-related effects due to genetic characteristics could not be verified.

Cerebral Infarction of Unknown Cause

Since the mechanisms of onset of cerebral infarction of unknown cause (cryptogenic ischemic stroke) and embolic stroke of undetermined sources (ESUS) are unclear, these patients were excluded from analysis. Moreover, the JSSR is mainly composed of acute phase stroke patients and does not include data on primary diseases linked with cerebral apoplexy, which may be discovered during long-term hospitalization for recovery and rehabilitation. In recent years, the need to consider the link of cryptogenic ischemic strokes or ESUS with cancers has been shown,³⁵ but should be further studied to arrive at detailed conclusions.

Conclusions

In conclusion, the results of this study suggest that there is a possibility that alcohol intake of <60 g/day plays a protective role in the functional prognosis of males with ischemic stroke at hospital discharge. In addition, there is a possibility that the level of alcohol consumption prior to onset may be one of the measures for not only the onset risk of stroke, but also the impact from onset to discharge.

Changes over time due to the increase in female drinking may lead to more detailed conclusions and the effect for each stroke subtype from alcohol consumption will be clarified. Moreover, paying attention to socio-medical points of view may lead to clinical conclusions, starting with the social environment and the background characteristics of individuals, to arrive at even more detailed conclusions.

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