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Cross-Sectional Survey of Workload and Burnout Among Japanese Physicians Working in Stroke Care: The Nationwide Survey of Acute Stroke Care Capacity for Proper Designation of Comprehensive Stroke Center in Japan (J-ASPECT) Study

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Consciousness Level and Off-Hour Admission Affect Discharge Outcome of Acute Stroke Patients: A J-ASPECT Study

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Background—Poor outcomes have been reported for stroke patients admitted outside of regular working hours. However, few studies have adjusted for case severity. In this nationwide assessment, we examined relationships between hospital admission time and disabilities at discharge while considering case severity.

Methods and Results—We analyzed 35 685 acute stroke patients admitted to 262 hospitals between April 2010 and May 2011 for ischemic stroke (IS), intracerebral hemorrhage (ICH), or subarachnoid hemorrhage (SAH). The proportion of disabilities/death at discharge as measured by the modified Rankin Scale (mRS) was quantified. We constructed 2 hierarchical logistic regression models to estimate the effect of admission time, one adjusted for age, sex, comorbidities, and number of beds; and the second adjusted for the effect of consciousness levels and the above variables at admission. The percentage of severe disabilities/death at discharge increased for patients admitted outside of regular hours (22.8%, 27.2%, and 28.2% for working-hour, off-hour, and nighttime; $P<0.001$). These tendencies were significant in the bivariate and multivariable models without adjusting for consciousness level. However, the effects of off-hour or nighttime admissions were negated when adjusted for consciousness levels at admission (adjusted OR, 1.00 and 0.99; 95% CI, 1.00 to 1.13 and 0.89 to 1.10; $P=0.067$ and 0.851 for off-hour and nighttime, respectively, versus working-hour). The same trend was observed when each stroke subtype was stratified.

Conclusions—The well-known off-hour effect might be attributed to the severely ill patient population. Thus, sustained stroke care that is sufficient to treat severely ill patients during off-hours is important. **(*J Am Heart Assoc.* 2014;3:e001059 doi: 10.1161/JAHA.114.001059)**

Key Words: hemorrhagic stroke • ischemic stroke • mortality • stroke • weekend effect

Stroke is a major cause of death in Japan, and residual disability after stroke is a heavy societal burden.[1] Death risk tendencies are high for patients hospitalized with serious medical conditions (including stroke) during off hours, especially on weekends.[2–7] Reduced quality of care during off hours because of insufficient physician volume, uneven staffing pattern for urgent procedures, and insufficient management of operative procedures, are among the possible reasons for this tendency.[2,3,6–9] Acute stroke severity is an important prognostic factor,[10] and stroke symptom severity is associated with healthcare-seeking behavior.[11–13] However, only 5 previous studies have

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adjusted for case severity, and these reports included relatively small numbers of hospitals (2 to 28).[14–18] Furthermore, the results of these studies were inconsistent; 2 reported positive relationships between admission hours and outcomes[14,15] and 3 reported negative relationships.[16–18] We examined the relationship between admission time and disabilities/deaths at discharge by adjusting for case severity using data from a nationwide cohort of Japanese hospitals.

Materials and Methods

Database

This study included a nationwide retrospective cohort of stroke patients (J-ASPECT study).[19] Among 749 certified training hospitals of the Japan Neurosurgical Society, the Societas Neurologica Japonica, and/or the Japan Stroke Society, 262 participated in this study. We collected Japanese Diagnosis Procedure Combination/Per Diem Payment System (DPC/PDPS) data, which list the lump-sum system of medical expenses evaluated based on diagnostic and procedural costs beginning in 2002.[20] Subject data were extracted from DPC/PDPS data at each hospital using specially developed computer software.

Inclusion and Exclusion Criteria

We included consecutive patients admitted to 262 hospitals between April 1, 2010 and May 31, 2011 for acute ischemic stroke (IS), non-traumatic intracerebral hemorrhage (ICH), or subarachnoid hemorrhage (SAH) according to the International Classification of Disease 10th revision (ICD-10 codes, I60.0 to I60.9, I61.0 to I61.9, I62.0, I62.1, I62.9, and I63.0 to I63.9). Because of major differences in their typical prognoses, we excluded patients with transient ischemic attack (TIA) (G45). We also excluded patients who experienced in-hospital stroke during treatment for other diseases.

Variables

The outcome measure was the proportion of severe disability/death (score 5 to 6 on the modified Rankin Scale [mRS]) at discharge.[21] We classified admission into (1) working-hour (professed work hours [usually 8 h] in each hospital from Monday to Friday, except for national holidays), (2) off-hour (hours not included in working-hour or nighttime classifications), or (3) nighttime (22:00 to 6:00 on any day) by using calendar time and additional medical billings in case of admission outside of working hours (Figure 1). We could not count the total hours of each admission-hour category.

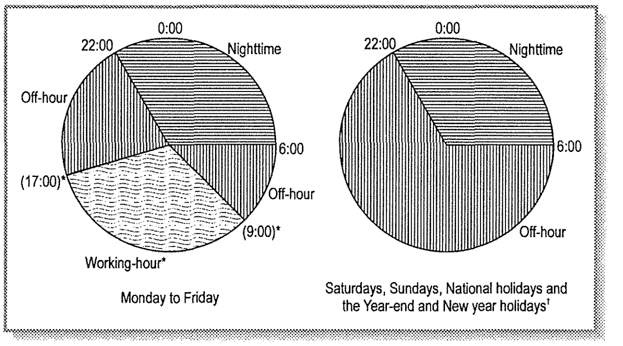

Figure 1. Classification of hospital admission time. *Working-hour was defined as working-hours professed by each hospital on consultation day (from Monday to Friday except for national holiday). †The YEAR-end and New Year holidays are from 29th December to 3rd January.

Proportions of total numbers of hours were hypothesized to be 22.2%, 44.5%, and 33.3% for working-hours, off-hours, and nighttime categories, respectively.

To account for the classical confounding factors for stroke and the capability of stroke care provided by hospitals, we adjusted for the following factors to estimate the effect of admission time: age (categorized as <35 years,

Table 1. Japan Coma Scale for Grading Impaired Consciousness*

Grade	Consciousness Level
1-digit code	The patient is awake without any stimuli, and is:
1	Almost fully conscious
2	Unable to recognize time, place, and person
3	Unable to recall name or date of birth
2-digit code	The patient can be aroused (then reverts to previous state after cessation of stimulation):
10	By easily by being spoken to (or is responsive with purposeful movements, phrases, or words)†
20	With a loud voice or shaking of shoulders (or is almost always responsive to very simple words like yes or no or to movements)
30	Only by repeated mechanical stimuli
3-digit code	The patient cannot be aroused with any forceful mechanical stimuli, and:
100	Responds with movements to avoid the stimulus
200	Responds with slight movements, including decerebrate and decorticate posture
300	Does not respond at all except for changes in respiratory rhythm

*"R" and "I" are added to the grade to indicate restlessness and incontinence of urine and feces, respectively: for example; 100-R and 30-RI.
†Criteria in parentheses are used in patients who cannot open their eyes for any reason.

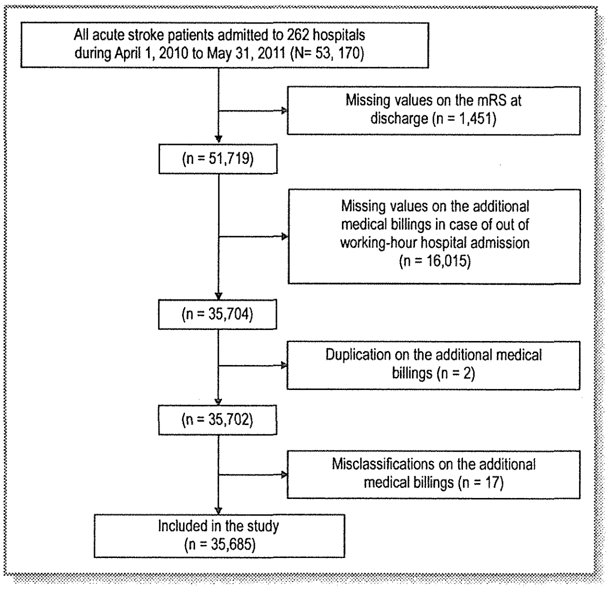

Figure 2. Flow chart for inclusion criteria.

every 5 years from 35 to 100 years, and ≥100 years), sex, comorbidities (hypertension, diabetes mellitus, and hyperlipidemia), and number of hospital beds (<100, 100 to 299, 300 to 499, and ≥500). Comorbidities were assessed from recorded disease name and prescription history in patient medical records.

To adjust effects of baseline consciousness level at admission, we used the Japan Coma Scale (JCS).[22–25] The JCS – originally published in 1974 for the assessment of impaired consciousness of head trauma and stroke patients[22] and published in the same year as the Glasgow Coma Scale[26] – remains one of the most popular scales used among health care professionals and personnel for emergency medical services in Japan.[25] Briefly, a normal level of consciousness is graded as 0. Other levels are graded with 1-, 2-, or 3-digit codes depending on status as shown in Table 1. We treated JCS as a categorical variable and classified patients as grade 0, 1 to 3, 10 to 30, or 100 to 300 for analysis. A 3-digit JCS score is roughly equivalent to a GCS score of ≤7 (≤E1V1M5).

Table 2. Demographics and Clinical Characteristics of Patients Included and Excluded in the Analyses

	Total (n=53 170)		
	Excluded Subjects	Included Subjects	*P* Value
Number, %	n=17 485 (32.9)	n=35 685 (67.1)	
Male, %	58.1	53.8	<0.001
Age mean (SD)	74.0 (12.0)	71.7 (13.6)	<0.001
Stroke subtype, n (%)			
IS	68.1	58.2	<0.001
SAH	5.9	10.9	<0.001
ICH	26.2	31.1	<0.001
Comorbidity, %			
Hypertension	72.7	76.2	<0.001
Diabetes mellitus	28.9	24.3	<0.001
Hyperlipidemia	29.3	27.7	<0.001
Current/past smoking history (n=44 842) (%)	26.7	29.3	<0.001
Japan Coma Scale, %			
0	42.0	34.5	<0.001
1-digit code	34.8	37.2	
2-digit code	11.6	13.8	
3-digit code	11.6	14.6	
Emergency admission by ambulance (%)	51.4	64.5	<0.001
mRS at discharge (n=51 719) (%)			
mRS=6	11.4	12.2	0.014
mRS=5/6	24.1	25.4	0.001
mRS=4 to 6	41.3	44.0	<0.001

ICH indicates intracerebral hemorrhage; IS, ischemic stroke; mRS, modified Rankin Scale; SAH, subarachnoid hemorrhage.

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Table 3. Patient Demographics and Clinical Characteristics by Inclusion in the Analyses for Each Stroke Subtype

	IS (n=32 671)			SAH (n=4934)			ICH (n=15 699)		
	Excluded	Included	P Value*	Excluded	Included	P Value*	Excluded	Included	P Value*
Number, %	11 913 (36.5)	20 758 (63.5)		1035 (21.0)	3899 (79.0)		4588 (29.2)	11 111 (70.8)	
Male, %	59.8	56.3	<0.001	29.1	32.9	0.019	60.4	56.3	<0.001
Age mean (SD)	75.1 (11.4)	74.1 (12.5)	<0.001	67.9 (14.1)	63.8 (14.8)	<0.001	72.5 (12.6)	70.0 (13.8)	<0.001
Comorbidity, %									
Hypertension	69.8	68.5	0.013	82.4	86.6	0.001	78.3	87.2	<0.001
Diabetes mellitus	31.3	27	<0.001	25.6	23.3	0.124	23.6	19.8	<0.001
Hyperlipidemia	34.2	33.9	0.511	26.5	29.2	0.086	17.2	15.7	0.015
Current/past smoking history (n=44 842) (%)	27.6	30.1	<0.001	22.5	28.2	0.001	25.1	28.2	<0.001
Japan Coma Scale, %									
0	48.8	44.4	<0.001	23.4	20.1	<0.001	28.6	20.8	<0.001
1-digit code	35.7	39.2		19.3	23.5		36.2	38.5	
2-digit code	9.9	10.7		14.7	18		15.2	18.1	
3-digit code	5.7	5.7		42.6	38.5		20	22.7	
Emergency admission by ambulance (%)	46.3	57	<0.001	73.8	78.6	0.001	59.7	73.5	<0.001
mRS at discharge (n=51 719) (%)									
mRS=6	7.8	7.2	0.099	29.1	26.8	0.165	17	16.3	0.284
mRS=5/6	19.1	19.5	0.413	46.4	37.8	<0.001	32.1	32.3	0.812
mRS=4 to 6	36.4	37.5	0.061	56.8	47.8	<0.001	50.8	55	<0.001

ICH indicates intracerebral hemorrhage; IS, ischemic stroke; mRS, modified Rankin Scale; SAH, subarachnoid hemorrhage.
*Off-hour and nighttime were compared with working-hours.

Statistical Analysis

We performed descriptive analyses for demographic and clinical characteristics for each group using the working-hour group as the control. Chi-square tests and *t* tests were used to compare categorical and continuous variables, respectively. For outcome analysis, we first compared crude outcome proportions among admission times in the total population, and then analyzed for each stroke subtype (IS, ICH, and SAH). For multivariable analysis, we used unique hospital ID in random-intercept hierarchical regression models to assess the relationships between hospital admission times and outcomes, while adjusting for patient characteristics and the hospitals at which patients received stroke care. This modeling adjusts for hospital-level cluster effects on outcome, which arise from various factors such as geographical location and ageing of the local population. We constructed 2 models to assess the impact of case severity. Model 1 included age, sex, hypertension, diabetes mellitus, hyperlipidemia, and number of beds. Baseline consciousness level was included in model 2 in addition to the variables in model 1. Moreover, to examine whether outcomes were consistent across admission times for patients with the same level of consciousness at admission, we performed subgroup analysis by JCS. To test the sex-specific differences, we performed sex-stratified analysis after the main analysis. Furthermore, to test whether results differ when age is treated as a continuous variable, we performed additional analyses. For sensitivity analyses, we substituted outcomes to death (mRS=6) (sensitivity analysis 1) and moderately severe disability to death (mRS=4 to 6) (sensitivity analysis 2). To confirm the robustness of our results, we also estimated the off-hours effects at admission using the modified Rankin Scale. Unlike JCS, mRS uses 5 categories to assess severity. All statistical analyses were performed using STATA version 12 (StataCorp LP). All tests were 2-tailed, and $P<0.025$ was considered statistically significant in consideration of multiple comparisons.

Ethical Approval

The Institutional Review Board of the National Cerebral and Cardiovascular Center and the University of Tokyo approved this research.

Table 4. Patient Demographic and Clinical Characteristics by Admission Time

	Total (n=35 685)				
	Working-Hour	Off-Hour	*P* Value*	Nighttime	*P* Value*
Number, %	15 084 (42.3)	16 908 (47.4)		3693 (10.4)	
Male, %	54.7	52.8	0.001	54.6	0.957
Age mean (SD)	72.4 (13.3)	71.8 (13.5)	<0.001	68.3 (14.3)	<0.001
Comorbidity, %					
Hypertension	74.8	77.2	<0.001	77.8	<0.001
Diabetes mellitus	24.9	23.8	0.015	24.2	0.329
Hyperlipidemia	29.5	26.5	<0.001	26.1	<0.001
Current/past smoking history (n=30 179) (%)	30	28.3	0.001	31.3	0.191
Japan Coma Scale, %					
0	38.4	32.1	<0.001	29.2	<0.001
1-digit code	37.7	37.6		33.9	
2-digit code	12.4	14.6		15.7	
3-digit code	11.6	15.8		21.3	
Emergency admission by ambulance (%)	54.2	69.9	<0.001	81.4	<0.001

*Off-hour and nighttime were compared with working-hours.

Results

Demographic and Clinical Characteristics

Out of 53 170 patients, we analyzed 35 685 patients. The inclusion criteria are shown in Figure 2. Demographics and clinical characteristics of excluded and included subjects for each stroke subtype are shown in Tables 2 and 3. IS, SAH, and ICH patients accounted for 58.2% (n=20 758), 10.9% (n=3899), and 31.1% (n=11 111), respectively. Overall, 42.3% (n=15 084), 47.4% (n=16 908), and 10.4% (n=3693) of patients were admitted during working hours, off hours, and nighttime, respectively. Patient demographics and clinical characteristics categorized according to admission time are shown in Table 4. Patients admitted during off hours and nighttime had lower baseline consciousness levels, and the percentage of these patients transferred to hospitals by ambulance was higher than that of patients admitted by ambulance during working hours. Patient demographics and clinical characteristics for each stroke subtype are shown in Table 5. The trends for age, baseline consciousness levels, and ambulance use by admission time were the same for each stroke subtype as observed for the total population.

Table 6 shows differences in primary outcomes among the 3 admission times for each stroke subtype. In the total population, increasing proportions of severe disability/death (mRS=5 to 6) at discharge were observed (22.8%, 27.2% and 28.2% for working-hour, off-hour, and nighttime, respectively). This remained the case when results were stratified by stroke subtype, although nighttime IS and off-hour and nighttime SAH patients did not have statistically significant higher disabilities/death at discharge compared with patients admitted during working hours.

Figure 3 shows adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for severe disability/death at discharge depending on stroke subtype and admission time. In model 1, which was adjusted for age, sex, comorbidities, and number of beds, off-hour and nighttime admitted patients had higher risks of severe disability/death than working-hour admitted patients irrespective of stroke subtype (adjusted OR, 1.23; 95% CI, 1.17 to 1.30 for off-hour and adjusted OR, 1.45; 95% CI, 1.33 to 1.58 for nighttime). When we further adjusted for consciousness level at admission (model 2), the effects of admission time were no longer significant (adjusted OR, 1.06; 95% CI, 1.00 to 1.13; P=0.067 for off-hour and adjusted OR, 0.99; 95% CI, 0.89 to 1.10; P=0.851 for nighttime compared with working-hour). The same trends were observed when we stratified by stroke subtype: off-hour and nighttime admission times were associated with significantly higher risks of severe disability/death at discharge in each stroke subtype except for off-hour SAH (adjusted OR, 1.12; 95% CI, 0.95 to 1.32, P=0.168) in model 1, and these effects were no longer significant in model 2 (Figure 3). Table 7 shows the effects of consciousness level at admission using Model 2.

In the subgroup analysis by using JCS at admission, proportions of severe disabilities/death were larger during off hours/nighttime than during working hours among IS and ICH patients with a JCS of 0. Proportions of primary outcome were larger during working hours than off hours/nighttime among

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Table 5. Patient Demographic and Clinical Characteristics by Admission Time for Each Stroke Subtype

Stroke Subtype	IS (n=20 758)					SAH (n=3899)					ICH (n=11 111)				
Admission Time	W	O	P Value*	N	P Value*	W	O	P Value*	N	P Value*	W	O	P Value*	N	P Value*
Number, %	9275 (44.7)	9630 (46.4)		1853 (8.9)		1407 (36.1)	1886 (48.4)		606 (15.5)		4436 (39.9)	5434 (48.9)		1241 (11.2)	
Male, %	56.7	55.2	0.047	60.7	<0.001	33.6	31.9	0.289	34.5	0.705	57.3	55.8	0.134	44.7	0.208
Age mean (SD)	74.2 (12.4)	74.5 (12.5)	0.046	71.4 (13.0)	<0.001	64.0 (14.6)	64.6 (14.7)	0.219	61.2 (15.3)	<0.001	71.3 (13.7)	69.6 (13.6)	<0.001	67.2 (14.3)	<0.001
Comorbidity, %															
Hypertension	68.5	68.6	0.930	67.6	0.411	88.2	86.2	0.085	84.2	0.013	83.5	89.6	<0.001	90.1	<0.001
Diabetes mellitus	28.0	26.1	0.003	26.2	0.111	24.1	23.3	0.610	21.5	0.198	18.9	19.8	0.215	22.6	0.004
Hyperlipidemia	35.9	32.3	<0.001	32.0	0.002	28.8	29.6	0.594	28.7	0.974	16.3	15.1	0.107	15.9	0.734
Smoking history (n=30 179) (%)	30.9	28.8	0.002	33.1	0.092	28.7	27.7	0.550	28.9	0.943	28.5	27.7	0.388	29.6	0.492
JCS, %															
0	47.3	42.1	<0.001	42.2	<0.001	24.5	17.9	<0.001	16.5	<0.001	24.1	19.2	<0.001	16.0	<0.001
1-digit code	38.2	40.2		38.5		24.5	22.9		23.4		40.6	38.2		32.1	
2-digit code	9.6	11.5		11.7		17.8	18.0		18.2		16.4	18.9		20.4	
3-digit code	4.8	6.3		7.7		33.3	41.3		41.9		19.0	23.8		31.5	
Ambulance admission (%)	46.9	62.8	<0.001	77.1	<0.001	72.2	80.9	<0.001	86.6	<0.001	63.9	78.7	<0.001	85.4	<0.001

ICH indicates intracerebral hemorrhage; IS, ischemic stroke; JCS, Japan Coma Scale; SAH, subarachnoid hemorrhage.
*Off-hour (O) and Nighttime (N) were separately compared with Working-hour (W).

Table 6. Crude Primary Outcome Comparisons Between Each Admission Time by Stroke Subtype

Stroke Subtype	Admission Time	N	Severe Disability/Death at Discharge, n (%)	Crude OR (95% CI)	*P* Value
Total population	Working-hour	15 084	3434 (22.8)	—	
	Off-hour	16 908	4597 (27.2)	1.24 (1.18 to 1.31)	<0.001
	Nighttime	3693	1042 (28.2)	1.30 (1.19 to 1.41)	<0.001
IS	Working-hour	9275	1659 (17.9)	—	—
	Off-hour	9630	2039 (21.2)	1.21 (1.13 to 1.31)	<0.001
	Nighttime	1853	355 (19.2)	1.06 (0.93 to 1.21)	0.361
SAH	Working-hour	1407	499 (35.5)	—	—
	Off-hour	1886	733 (38.9)	1.14 (0.99 to 1.32)	0.077
	Nighttime	606	240 (39.6)	1.18 (0.97 to 1.44)	0.105
ICH	Working-hour	4436	1293 (29.2)	—	—
	Off-hour	5434	1842 (33.9)	1.24 (1.13 to 1.35)	<0.001
	Nighttime	1241	449 (36.2)	1.38 (1.20 to 1.58)	<0.001

ICH indicates intracerebral hemorrhage; IS, ischemic stroke; SAH, subarachnoid hemorrhage.

IS and ICH patients who had a 3-digit JCS score (Table 8). Table 9 shows the results of subgroup analysis adjusted for age, sex, comorbidities, and number of hospital beds. Effects of nighttime admission were significantly higher (adjusted OR, 1.59; 95% CI, 1.11 to 2.29; IS and adjusted OR, 2.87; 95% CI, 1.66 to 4.98; for ICH) in patients with a JCS score of 0 and significantly lower (adjusted OR, 0.50; 95% CI, 0.31 to 0.81; for IS and adjusted OR, 0.67; 95% CI, 0.49 to 0.90; for ICH) in patients with a 3-digit JCS score. Furthermore, no sex-based differences were present in these trends. Results obtained with age as a continuous variable were comparable with those obtained when it was treated as a categorical variable.

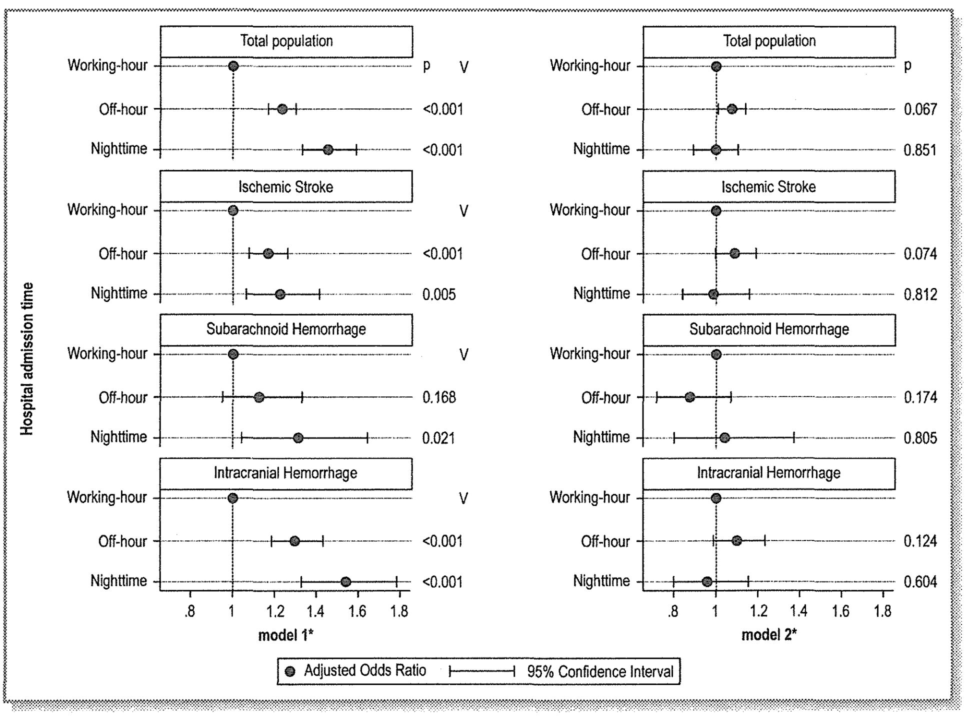

Figure 3. Effects of admission time on primary outcomes (modified Rankin Scale [mRS]=5 to 6) among acute stroke patients with 2 different models. *Model 1 adjusted for age, sex, hypertension, diabetes mellitus, hyperlipidemia, and number of beds. Model 2 further adjusted for Japan Coma Scale.

Table 7. Effects of Consciousness Level at Admission on Primary Outcomes (mRS=5 to 6) Among Acute Stroke Patients Determined Using Model 2

		Total Population		IS		SAH		ICH	
Admission Time	Japan Coma Scale	Adjusted OR (95% CI)	*P* Value	Adjusted OR (95% CI)	*P* Value	Adjusted OR (95% CI)	*P* Value	Adjusted OR (95% CI)	*P* Value
Off-hour	0	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
	1 digit	3.53 (3.18 to 3.90)	<0.001	4.08 (3.60 to 4.62)	<0.001	1.72 (1.22 to 2.44)	0.002	2.87 (2.32 to 3.56)	<0.001
	2 digit	12.31 (11.00 to 13.78)	<0.001	16.70 (14.41 to 19.35)	<0.001	2.68 (1.88 to 3.81)	<0.001	10.33 (8.25 to 12.92)	<0.001
	3 digit	72.27 (64.01 to 81.59)	<0.001	45.98 (38.17 to 55.39)	<0.001	24.79 (17.93 to 34.28)	<0.001	90.05 (71.19 to 113.91)	<0.001
Nighttime	0	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
	1 digit	3.10 (2.72 to 3.53)	<0.001	3.66 (3.10 to 4.31)	<0.001	1.73 (1.13 to 2.64)	0.011	2.28 (1.75 to 2.97)	<0.001
	2 digit	10.89 (9.42 to 12.58)	<0.001	15.89 (13.08 to 19.31)	<0.001	2.96 (1.90 to 4.59)	<0.001	7.79 (5.91 to 10.26)	<0.001
	3 digit	69.17 (59.18 to 80.85)	<0.001	51.80 (40.27 to 66.64)	<0.001	24.79 (16.49 to 37.28)	<0.001	68.28 (51.33 to 90.82)	<0.001

ICH indicates intracerebral hemorrhage; IS, ischemic stroke; mRS, modified Rankin Scale; SAH, subarachnoid hemorrhage.

Two sensitivity analyses that used different outcomes showed almost the same trend observed in the original analysis, except for ICH patients in sensitivity analysis 2 (Figure 4). Here, the effect of admission time was observed in ICH patients even when adjusted for consciousness level at admission (adjusted OR, 1.17; 95% CI 1.06 to 1.30; P=0.003 for off-hour compared to working-hour). Additional sensitivity analyses performed using mRS at admission as a confounder instead of JCS revealed a trend similar to that observed in the original analysis (Figure 5). Here, the effects of admission time were no longer significant even when stratified to each stroke subtype.

Discussion

Using nationwide population data on acute stroke patients, we found that outcome varied with admission time. Patients admitted outside of regular working hours were about 1.2 times more likely to have a poor outcome than those admitted during working hours. The effect of admission time remained significant for almost all stroke subtypes without adjusting for consciousness level at admission, which is similar to what has been reported previously. However, once we adjusted for consciousness level, the effects of admission time were dramatically attenuated; comatose patients were approximately 70 times more likely to suffer severe disabilities or death than lucid patients. Therefore, the different outcomes observed depending upon admission times were because of differences in stroke severity.

This study has several strengths. First, we included a large number of subjects from hospitals certified for training by the Japan Neurosurgical Society, the Societas Neurologica Japonica, and/or the Japan Stroke Society. Therefore, our results accurately reflect current practice in acute stroke care and are not influenced by changes in therapeutic strategy. The second strength is that we highlighted risks associated with nighttime admission. During the nighttime shift, hospital functions are reduced, and we observed a higher percentage of poorer outcomes for nighttime admitted patients. This finding is in accordance with a Dutch study that did not adjust for case severity, but did describe risk among IS patients admitted during the night.[27] Third, we adjusted for case severity at admission by using consciousness level. Case severity is a major confounding factor because it is one of the most important prognosis factors and is related to healthcare-seeking behaviors in stroke patients.[10–13] However, only 5 previous studies adjusted for case severity and they reported inconsistent results.[14–18] Among these, the Canadian study was the only one including a large number of subjects and reported a positive relationship between weekend hospital admission and stroke mortality among 20 000 acute stroke

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Table 8. Crude Primary Outcome Comparisons Between Each Admission Time by Stroke Subtype and Japan Coma Scale

Japan Coma Scale	Admission Time	Total Population		IS		SAH		ICH	
		Admission (n)	Severe Disability/ Death at Discharge, n (%)	Admission (n)	Severe Disability/ Death at Discharge, n (%)	Admission (n)	Severe Disability/ Death at Discharge, n (%)	Admission (n)	Severe Disability/ Death at Discharge, n (%)
0	Working-hours	5793	286 (4.9)	4388	193 (4.4)	345	37 (10.7)	1069	56 (5.2)
	Off-hour	5420	293 (5.4)	4051	203 (5.0)	337	29 (8.6)	1042	62 (6.0)
	Nighttime	1079	78 (7.2)	781	46 (5.9)	100	8 (8.0)	199	25 (12.6)
1-digit	Working-hours	5679	991 (17.5)	3546	664 (18.7)	344	57 (16.6)	1799	276 (15.3)
	Off-hour	6354	1243 (19.6)	3869	831 (21.5)	431	65 (15.1)	2075	355 (17.1)
	Nighttime	1250	202 (16.2)	713	120 (16.8)	142	25 (17.6)	398	57 (14.3)
2-digit	Working-hours	1867	774 (41.5)	894	451 (50.5)	250	55 (22.0)	727	271 (37.3)
	Off-hour	2469	1034 (41.9)	1108	576 (52.0)	340	74 (21.8)	1026	387 (37.7)
	Nighttime	579	195 (33.7)	217	94 (43.3)	110	29 (26.4)	253	73 (28.9)
3-digit	Working-hours	1745	1383 (79.3)	447	351 (78.5)	468	350 (74.8)	841	690 (82.1)
	Off-hour	2665	2027 (76.1)	602	429 (71.3)	778	565 (72.6)	1291	1038 (80.4)
	Nighttime	785	567 (72.2)	142	95 (66.9)	254	178 (70.1)	391	294 (75.2)

ICH indicates intracerebral hemorrhage; IS, ischemic stroke; SAH, subarachnoid hemorrhage.

Table 9. Effects of Admission Time on Primary Outcomes (mRS=5 to 6) Among Acute Stroke Patients by Japan Coma Scale

Japan Coma Scale	Admission Time	Total Population		IS		SAH		ICH	
		Adjusted OR† (95% CI)	*P* Value*	Adjusted OR† (95% CI)	*P* Value*	Adjusted OR† (95% CI)	*P* Value*	Adjusted OR† (95% CI)	*P* Value*
0	Working-hours	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
	Off-hour	1.45 (1.33 to 1.58)	<0.001	1.07 (0.87 to 1.33)	0.515	0.87 (0.48 to 1.56)	0.633	1.29 (0.86 to 1.93)	0.220
	Nighttime	1.45 (1.33 to 1.58)	<0.001	1.59 (1.11 to 2.29)	0.011	0.83 (0.34 to 1.99)	0.672	2.87 (1.66 to 4.98)	<0.001
1-digit	Working-hours	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
	Off-hour	1.20 (1.09 to 1.33)	<0.001	1.20 (1.07 to 1.36)	0.003	1.00 (0.64 to 1.55)	0.998	1.21 (1.00 to 1.45)	0.044
	Nighttime	1.06 (0.89 to 1.26)	0.536	0.98 (0.78 to 1.23)	0.856	1.28 (0.71 to 2.31)	0.416	1.01 (0.73 to 1.41)	0.941
2-digit	Working-hours	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
	Off-hour	1.08 (0.94 to 1.24)	0.295	1.03 (0.85 to 1.25)	0.770	0.93 (0.60 to 1.44)	0.751	1.18 (0.93 to 1.48)	0.170
	Nighttime	0.91 (0.73 to 1.14)	0.406	0.89 (0.63 to 1.25)	0.498	1.56 (0.84 to 2.88)	0.160	0.81 (0.57 to 1.16)	0.250
3-digit	Working-hours	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
	Off-hour	0.81 (0.69 to 0.95)	0.008	0.65 (0.48 to 0.88)	0.006	0.81 (0.60 to 1.10)	0.169	0.89 (0.70 to 1.13)	0.325
	Nighttime	0.70 (0.57 to 0.86)	0.001	0.50 (0.31 to 0.81)	0.005	0.77 (0.51 to 1.15)	0.196	0.67 (0.49 to 0.90)	0.009

ICH indicates intracerebral hemorrhage; IS, ischemic stroke; mRS, modified Rankin Scale; SAH, subarachnoid hemorrhage.
*Off-hour and nighttime were compared with working-hours.
†Adjusted for age, sex, hypertension, diabetes mellitus, hyperlipidemia, and hospital volume.

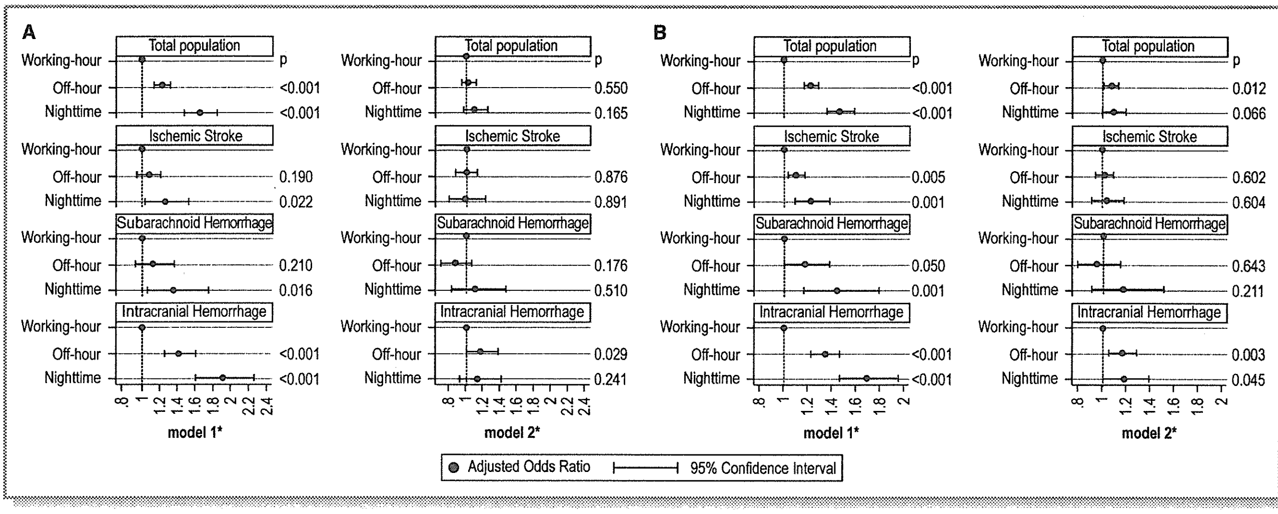

Figure 4. Sensitivity analyses for effects of admission time on modified Rankin Scale (mRS)=6 (A) and mRS=4 to 6 (B) among acute stroke patients with 2 different models. *Model 1 adjusted for age, sex, hypertension, diabetes mellitus, hyperlipidemia, and number of beds. Model 2 further adjusted for Japan Coma Scale.

or TIA patients at 11 hospitals.[14] The major differences of this study and the Canadian study are the number of participating hospitals and the definition of stroke subtypes. The Canadian study did not perform subtype-specific analyses, whereas we evaluated both total population and stroke subtype outcomes. Therapeutic strategies and responses vary with stroke subtypes. Therefore, we considered that stratified analysis by subtype was more appropriate.

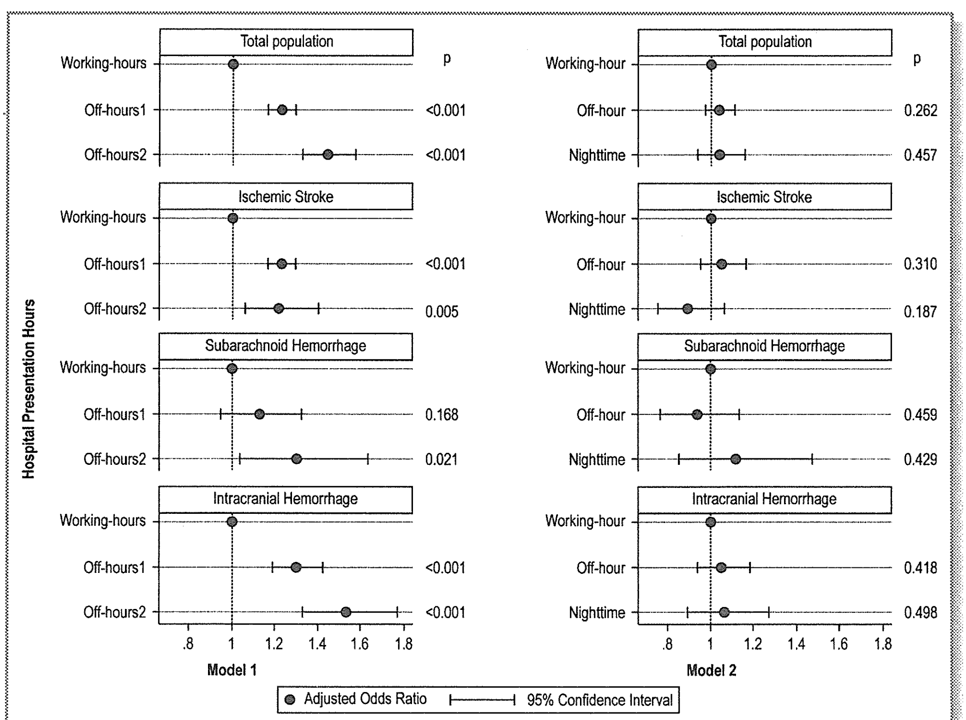

Figure 5. Sensitivity analysis for effects of admission time on primary outcomes (modified Rankin Scale [mRS]=5 to 6) among acute stroke patients with 2 different models using mRS at admission as a confounder instead of JCS. *Model 1 adjusted for age, sex, hypertension, diabetes mellitus, hyperlipidemia, and hospital volume. Model 2 further adjusted for modified Rankin Scale at admission instead of Japan Coma Scale.

The reason why admission outside of working hours is related to case severity remains unknown. A circadian rhythm of stroke has been reported in large studies and may partially explain this phenomenon. Stroke is more frequent in the morning and evening,[28–31] and a surge in blood pressure and altered heart rate may be responsible for diurnal variation in stroke incidence.[32,33] However, the exact effect of circadian rhythm on stroke severity is unclear. Other factors such as limited access, minor symptoms, and age are known to be reasons that patients delay coming to the hospital.[10–12] Larger percentages of patients are admitted at off hours because baseline consciousness levels decrease during nighttime. Delayed perception of stroke symptoms or postponement of hospital consultation until regular working hours by patients with minor symptoms might have caused the perceived diurnal variation in stroke admission, though we could not confirm this from our data. Interestingly, in the subgroup analysis by baseline consciousness level, effects of admission time were reversed to a favorable outcome, as baseline consciousness levels got poorer in IS and ICH patients. These results may be inconsistent with the true values as a result of over stratification. Compared with patients with good consciousness level, patients with poor consciousness level could have been transferred to skilled hospitals by emergency medical services personnel and this may have led to this reverse effect of admission time, although we could not verify whether selective transfers existed in our dataset. Thus, health service managers must ensure that adequate stroke care is provided during off hours to promptly identify and treat severe stroke cases. Moreover, it is important to increase awareness among the general population about the appropriate facilities at Japanese hospitals for receiving stroke treatment in the acute phase.

In the sensitivity analyses, ICH patients admitted outside of working hours did not show robust results, but the effects of admission outside of working hours remained significant even when adjusted for baseline consciousness level among ICH patients. This is an important point because the numbers of hemorrhagic patients who are admitted outside of working hours are increasing. Although we could not measure any metrics of acute stroke care, our results suggest that the quality of acute stroke care provided by hospitals in Japan for hemorrhagic patients during the day are inconsistent. The results of a study published by the Get With The Guidelines-Stroke Program may support these findings; appropriate care and prevention were less frequently provided for ICH and SAH patients than for IS patients.[34] Systematic care processes for ICH and SAH may be poor during off-hours because of impaired healthcare systems, such as differential response times by night-shift workers and the presence of less skilled neurosurgeons, general physicians, residents, and paramedics.

We could not detect outcome differences for SAH patients probably because of the poor clinical prognosis associated with this stroke subtype. However, further studies that measure acute stroke care quality, such as prompt examination or available procedures during working hours and off hours, are necessary to verify this hypothesis.

This study has some limitations. Because the Japanese DPC/PDPS data were used, JCS scores were used to adjust for severity instead of the National Institute of Health Stroke Scale (NIHSS) or GCS.[25,26] However, our findings did not change even when data were adjusted by mRS at admission. Second, we used information on the occurrence of additional billings from the DPC/PDPS data to classify admission time; therefore, some data on the occurrence of additional billings were missing. We excluded subjects with missing values from analysis, and this may have biased our results. However, we believe that this exclusion does not alter our findings because severities of consciousness levels at admission and outcomes at discharge were not significantly different between subjects who were excluded and those who were included. Third, as for the classification of hospital admission time, we could not split the times in a more detailed manner because of data restriction, ie, daytime admissions during weekends and on national holidays were considered to be off-hour admissions. However, if patients admitted during this time exhibited less severe stroke symptoms or if hospitals during this time indeed provided better stroke care than at other off-hour times among off-hour, it could underestimate the effects of differences in severity on relationships between admission time and outcome at discharge. Fourth, although we collected nationwide data, we may have underestimated the relationship between admission time and outcomes because participating hospitals were certified training hospitals, which are considered to offer similar qualities of care. If hospitals that provide fewer resources and less professional stroke care were included in the analysis, stronger relationships may have been identified. Furthermore, we could not follow-up on post-discharge outcomes and we were unable to include multiple metrics representing acute stroke care quality, such as promptness or execution of specific procedures and protocols. Most studies have dealt with the inequality of care between working hours and off hours, such as reduced availability of highly skilled personnel and less access to urgent procedures, as the main reason for outcome disparity.[2,3] Further studies that focus on acute stroke care metrics are needed to better identify variability in care quality between admission times.

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Consciousness Level and Off–Hour Admission Affect Discharge Outcome of Acute Stroke Patients: A J–ASPECT Study

Satoru Kamitani, Kunihiro Nishimura, Fumiaki Nakamura, Akiko Kada, Jyoji Nakagawara, Kazunori Toyoda, Kuniaki Ogasawara, Junichi Ono, Yoshiaki Shiokawa, Toru Aruga, Shigeru Miyachi, Izumi Nagata, Shinya Matsuda, Yoshihiro Miyamoto, Michiaki Iwata, Akifumi Suzuki, Koichi B. Ishikawa, Hiroharu Kataoka, Kenichi Morita, Yasuki Kobayashi and Koji Iihara

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EDITORIAL

Maternal Death Due to Stroke Associated With Pregnancy-Induced Hypertension

Koji Iihara, MD, PhD; Ataru Nishimura, MD

Pregnancy and the postpartum period are associated with an increased risk of ischemic and hemorrhagic stroke and stroke is the leading cause of pregnancy-related disability. There are few long-term prospective studies of the incidence of stroke in pregnancy. The data from multiple retrospective studies about the incidence and mortality of stroke in pregnancy are summarized in Table 1. Various studies estimate the incidence of all types of stroke in pregnancy and puerperium between 25 and 34 per 100,000 deliveries.[1–8] By comparison, the incidence of stroke in non-pregnant women in the 15–45 years age group is 11 per 100,000 women.[5] A population-based retrospective study conducted from 1988 to 1991 found no increase during pregnancy but a relative risk of 8.7 during the first 6 weeks postpartum.[3] Kuklina et al reported their recent analysis of hospital discharge data from the Nationwide Inpatient Sample of the Healthcare Cost and Utilization Project, which is the largest nationwide all-payer inpatient care database in the United States.[4] That report demonstrated that between 1994–1995 and 2006–2007, the rates of antenatal and postpartum hospitalizations for all types of stroke increased by 47% and 83%, respectively.

Article p1835

Risk factors associated with pregnancy-related stroke include hypertension, diabetes, valvular heart disease, hypercoagulable disorders, sickle cell disease, lupus, abuse of tobacco and other substances, and migraines.[1,6] Several studies have demonstrated that hypertensive disorders are the leading cause of both hemorrhagic and ischemic strokes in pregnant and postpartum women.[1–3,6,7] Preeclampsia/eclampsia and pregnancy-induced hypertension (PIH) are the 2 most important hypertensive disorders of pregnancy. Preeclampsia is defined as progressively worsening high blood pressure (BP) in pregnancy, occurring in the setting of proteinuria (≥300 mg of protein in a 24-h urine specimen).[9] Eclampsia is preeclampsia that progresses to seizures. PIH is described as high BP (systolic BP ≥140 mmHg or diastolic BP ≤90 mmHg) after 20 weeks' gestation that occurs without the other signs and symptoms of preeclampsia.

Compared with women without hypertension, women with hypertension complicating pregnancy are 6–9-fold more likely to have a stroke.[5] Therefore, control of PIH is considered to reduce the risk of maternal death from stroke (especially hemorrhagic stroke) during pregnancy. There are few reports about the relationship of maternal death due to stroke and PIH.

In this issue of the Journal, Hasagawa et al review case reports from medical institutions in Japan, and describe the clinical features of maternal death associated with PIH.[10] In this review of maternal deaths in Japan between 2010 and

Table 1. Summary of Studies on the Incidence, Mortality and Morbidity of Pregnancy-Associated Stroke

Study date and first author	Subjects	Incidence (per 100,000 deliveries)	Mortality (%)
Sharshar (1995)[7]	Pregnancy and 2 weeks PP 63 public maternities of the region of Ile de France (1989–1992)	Nonhemorrhagic stroke: 4.3 Hemorrhagic stroke: 4.6	0 (25)
Kittner (1996)[3]	Women aged 15–44 years, pregnancy and 6 weeks PP 46 hospitals in central Maryland and Washington DC (1998–1991)	Ischemic stroke: 11 ICH: 9	
Lanska (1998)[5]	Women aged 15–44 years National Hospital Discharge Survey in the USA (1979–1991)	All strokes: 17.7 CVT: 11.4	3.3 (0)
Lanska (2000)[6]	Women aged 15–44 years National Hospital Discharge Survey in the USA (1993–1994)	All strokes: 13.1 CVT: 11.6	14.7 (0)
Jaigobin (2000)[8]	Pregnancy and 6 weeks PP Tronto Hospital, Canada (1980–1997)	Ischemic stroke: 18 ICH: 8	0 (23)
James (2005)[1]	Pregnancy related discharges Nationwide Inpatient Sample in the USA (2000–2001)	All strokes: 34.2	4.1
Bateman (2006)[2]	Women aged 15–44 years Nationwide Inpatient Sample in the USA (1993–2002)	ICH: 6.1	20.3

CVT, cerebral venous thrombosis; ICH, intracerebral hemorrhage; PP, postpartum.

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Table 2. AHA/ASA Recommendations for Treatment of Hypertension in Pregnancy and PP

Class I recommendation

- Severe hypertension in pregnancy should be treated with safe and effective antihypertensive medications, such as methyldopa, labetalol, and nifedipine, with consideration of maternal and fetal side effects (Level of Evidence A).

Class IIa recommendation

- Consideration may be given to treatment of moderate hypertension in pregnancy with safe and effective antihypertensive medications, given the evidence for possibly increased stroke risk at currently defined systolic and diastolic BP cutoffs, as well as evidence for decreased risk for the development of severe hypertension with treatment (although maternal- fetal risk-benefit ratios have not been established) (Level of Evidence B).
- After giving birth, women with chronic hypertension should be continued on their antihypertensive regimen, with dosage adjustments to reflect the decrease in volume of distribution and glomerular filtration rate that occurs after delivery. They should also be monitored carefully for the development of PP preeclampsia (Level of Evidence C).

Class III recommendation

- Atenolol, angiotensin-receptor blockers, and direct renin inhibitors are contraindicated in pregnancy and should not be used (Level of Evidence C).

BP, blood pressure; PP, postpartum.

2012, 11% of all maternal deaths were associated with PIH. More than 70% of the causes of maternal death associated with PIH were due to stroke, and 12 of 25 deaths (48%) due to stroke were associated with PIH. In this series, the most frequent type of stroke was intracerebral hemorrhage (ICH). Of all stroke types, ICH during pregnancy and the puerperium leads to the highest risk of morbidity and mortality. Pregnancy increases the risk of hemorrhagic more than ischemic stroke (relative risk of 2.5 and 28.5 during pregnancy and the postpartum period).[3] The underlying mechanism of pregnancy-related hemorrhage is likely to be the consequences of physiologic changes, such as blood volume expansion and vascular tissue remodeling in pregnancy, plus the risk from the strain and trauma of labor and delivery. Major causes of pregnancy-related hemorrhage are preeclampsia and eclampsia, which contribute to a large proportion of cases, followed by intracerebral aneurysm, arteriovenous malformation and moyamoya desease.[11,12] The present study revealed that PIH is strongly related with poor outcomes of stroke, especially ICH, associated with pregnancy in Japan.

In February 2014, the American Heart Association and the American Stroke Association released their first guideline focused on stroke prevention in women.[13] Their recommendations are shown in Table 2. Regarding control of hypertension during pregnancy, they recommend that severe hypertension should be treated with safe and effective antihypertensive medications, such as methyldopa, labetalol, and nifedipine, with consideration of maternal and fetal side effects (Class I, Level of Evidence A). For moderate hypertension, consideration may be given with safe and effective antihypertensive medications, given the evidence for possibly increased stroke risk at currently defined systolic and diastolic BP cutoffs, as well as evidence for decreased risk for the development of severe hypertension with treatment (although maternal-fetal risk-benefit ratios have not been established) (Class IIa, Level of Evidence B). In this guideline, high BP during pregnancy is defined as mild (diastolic BP 90–99 mmHg or systolic BP 140–149 mmHg), moderate (diastolic BP 100–109 mmHg or systolic BP 150–159 mmHg), or severe (diastolic BP ≥110 mmHg or systolic BP ≥160 mmHg). They mention that the goal of BP management in pregnancy is to maintain systolic BP between 130 and 155 mmHg and diastolic BP between 80 and 105 mmHg. These recommendations are based on studies of European and American populations. Because there are differences among the races for stroke risk in pregnancy, prospective randomized controlled trials assessing antihypertensive interventions to reduce stroke risk are needed.

An important point in the present study is that although 83% of patients with PIH who died had experienced initial symptoms in a hospital, more than half required medical transport due to lack of local medical resources. They point out that such delays in receiving proper treatment sometimes resulted in maternal death. Although the mortality rate associated with cardiovascular disease such as stroke or acute myocardial infarction is not high in Japan,[10,14] timely transport and treatment of patients who have risk factors in pregnancy, especially PIH, is important for improving the outcome of pregnancy in Japan.

Disclosures

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Comprehensive Stroke Care Capabilities in Japan: A Neurovascular Surgeon's Perspective

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Ladies and gentlemen, it is a great honor for me to give a talk at this annual meeting of the Congress of Neurological Surgeons. The 34th annual meeting of the Japanese Congress was successfully held in Osaka on May 16 to 18, 2014, and >4000 participants exchanged cutting-edge knowledge about neurosurgical techniques and management, clinical and basic science, and social issues related to neurosurgical practice. The theme of the 34th annual meeting of the Japanese Congress was Visionary Approach to Neurosurgery. In this presentation, I wish to briefly review the current status of comprehensive stroke care capabilities in Japan from a neurovascular surgeon's perspective, focusing on healthcare delivery and cutting-edge neurosurgical techniques. This year has afforded me the extraordinary opportunity to work closely with many neurosurgeons across the full spectrum of our specialty. To provide insights into and information for our brighter future, I conducted the first nationwide survey on the real-world setting of neurosurgical practices using data obtained from the Diagnosis Procedure Combination (DPC)–based payment systems. First, I discuss the impact of comprehensive stroke care capabilities on the outcome of ischemic and hemorrhagic stroke revealed by this nationwide study (called the Nationwide Survey of Acute Stroke Capacity for Proper Designation of Comprehensive Stroke Center in Japan, or J-ASPECT Study). Second, I discuss a key role of advanced neuroimaging capabilities in comprehensive stroke centers (CSCs) using our positron emission tomography study for postoperative hyperperfusion in patients with moyamoya disease. Finally, to describe multimodality treatment for complex neurovascular lesions, one of the most important roles and responsibilities of CSCs, I focus on our cutting-edge microsurgical management of partially thrombosed large or giant aneurysms in the posterior circulation.

J-ASPECT STUDY

Increasing attention has been given to defining the quality and value of health care through the reporting of process and outcome measures. In Japan, stroke is the fourth-leading cause of death and a leading cause of long-term disability. Almost 270 000 individuals in Japan have a new or recurrent stroke each year, and nearly 120 000 individuals die after a stroke. In 2000, the Brain Attack Coalition discussed the concept of stroke centers and proposed 2 types of centers: CSCs and primary stroke centers (PSCs).[1,2] Most patients with stroke can be appropriately treated at a PSC, and the Joint Commission has established programs for certifying PSCs and measuring their performance.[3] The concept and recommended key components of CSCs enable intensive care and specialized techniques that are not available at most PSCs. A set of metrics and associated data elements that cover the major types of care distinguishing CSCs from PSCs have been published previously.[1,2]

First, to examine the associations between PSC and CSC capabilities and the impact of CSC capabilities on hospital volume of stroke interventions, we performed the J-ASPECT study, for which a 49-question survey was developed on hospital characteristics (ie, number of beds, academic status, geographic location, and participation in the DPC payment system[4]), PSC and CSC capacity, and hospital volume of stroke interventions.[5] The questionnaire was mailed in February 2011 to the 1369 certified training institutions of the Japan Neurosurgical Society, Japanese Society of Neurology, and Japan Stroke Society. This survey included 25 items related to the 5 major components of CSCs (personnel, diagnostic programs, specific expertise, infrastructure, and educational components) and 5 items related to PSC certification (Tables 1 and 2).[1,2] The availability of personnel was assessed according to 7 categories (eg, board-certified neurologists, board-certified neurosurgeons, and board-certified endovascular physicians). Because the original questions were highly specific, they were modified when necessary. Six advanced neuroimaging capabilities (eg, magnetic resonance imaging [MRI] with diffusion-weighted imaging [DWI] and digital subtraction angiography) were investigated on the basis of their availability 24

TABLE 1. Number (Percentage) of Responding Hospitals (n = 749) With the Recommended Items of Comprehensive Stroke Care Capacity[a]

Components	Items	n (%)
Personnel	Neurologists	358 (47.8)
	Neurosurgeons	694 (92.7)
	Endovascular physicians	272 (36.3)
	Critical care medicine	162 (21.6)
	Physical medicine and rehabilitation	113 (15.1)
	Rehabilitation therapy	742 (99.1)
	Stroke rehabilitation nurses[b]	102 (13.8)
Diagnostic availability 24/7	CT[b]	742 (99.2)
	MRI with diffusion	647 (86.4)
	Digital cerebral angiography[b]	602 (80.8)
	CT angiography[b]	627 (84)
	Carotid duplex ultrasound[b]	257 (34.5)
	TCD[b]	121 (16.2)
Specific expertise	Carotid endarterectomy[b]	603 (80.6)
	Clipping of intracranial aneurysm	685 (91.5)
	Hematoma removal/draining	689 (91.9)
	Coiling of intracranial aneurysm	360 (48.1)
	Intra-arterial reperfusion therapy	498 (66.5)
Infrastructure	Stroke unit[b]	132 (17.6)
	Intensive care unit	445 (59.4)
	Operating room staffed 24/7[b]	451 (60.4)
	Interventional services coverage 24/7	279 (37.3)
	Stroke registry[b]	235 (31.7)
Education	Community education[b]	369 (49.4)
	Professional education[b]	436 (58.6)

[a]CT, computed tomography; MRI, magnetic resonance imaging; TCD, transcranial Doppler; 24/7, 24 h/d, 7 d/wk.
[b]Data missing: stroke rehabilitation nurse, 9; CT, 1; digital cerebral angiography, 4; CT angiography, 3; carotid endarterectomy, 1; carotid duplex, 3; TCD, 3; stroke unit, 1; operating room staffed, 2; stroke registry, 7; community education, 2; and professional education, 5. Reproduced from Iihara et al[5] with permission from the publisher. Copyright © 2014 National Stroke Association.

hours per day, 7 days per week (24/7). The availability of specific expertise for stroke interventions was examined according to 5 categories (eg, carotid endarterectomy and clipping and coiling of intracranial aneurysms). In terms of infrastructure, the availability of 5 items (eg, stroke unit and intensive care unit) was surveyed. Educational/research programs were assessed according to 2 items (community and professional education). Overall organizational and staffing levels of the hospitals in terms of CSC capacity were scored on the basis of the results of a questionnaire referring to 25 items originally recommended by the Brain Attack Coalition (total CSC score).[1] A score of 1 was assigned for each recommended item that was met, resulting in a maximum total CSC score of 25 points. Hospital volume of stroke interventions (eg, tissue-type plasminogen activator [tPA] infusion, removal of intracerebral hemorrhage [ICH], and clipping and coiling of intracranial aneurysms) performed in 2009 was assessed.

Regarding the recommended PSC capabilities, written tPA protocols were available in 85% of hospitals, and the National Institutes of Health Stroke Scale score was routinely documented in 70.7% of hospitals; however, an acute stroke team was available in only 26.5% of hospitals. In terms of the recommended personnel components of CSCs (Table 1), 92.7% of hospitals had a neurosurgeon, 47.8% had a neurologist, and 36.3% had an endovascular physician. The proportions of hospitals with critical care medicine physicians, physical medicine and rehabilitation, and stroke rehabilitation nurses were 21.6%, 15.1%, and 13.8%, respectively. The score for the availability of the personnel component ranged from 0 to 7 points (median, 3; interquartile range [IQR], 2-4).

Computed tomography (CT), MRI with DWI, digital subtraction angiography, and CT angiography (CTA) were available 24/7 in 99.2%, 86.4%, 80.8%, and 84% of institutions, respectively, whereas carotid duplex ultrasonography and transcranial Doppler were available in only 34.5% and 16.2% of hospitals, respectively. The score for the availability of diagnostic components ranged from 0 to 6 points (median, 4; IQR, 4-5).

Carotid endarterectomy, clipping of intracranial aneurysms, and removal of ICH were available in 80.6%, 91.5%, and 91.9% of hospitals, respectively, whereas coiling of intracranial aneurysms and intra-arterial thrombolysis were available in 48.1% and 66.5% of hospitals, respectively. The score for the availability of surgical and interventional components ranged from 0 to 5 points (median, 4; IQR, 3-5).

A stroke unit and an intensive care unit were available in 17.6% and 59.4% of hospitals, respectively. Interventional service coverage on a 24-hour basis was available in 37.3% of hospitals, whereas an operating room staffed 24/7 was available in 60.4% of hospitals. The score of the availability of infrastructure components ranged from 0 to 5 points (median, 2; IQR, 1-3).

Professional and community education was available in 58.6% and 49.4% of institutions, respectively (Table 2). The score of the availability of the educational component ranged from 0 to 2 points (median, 1; IQR, 0-2).

The inclusion of total CSC score, availability of a tPA protocol, and other hospital characteristics in the model revealed that total CSC score, but not availability of a tPA protocol, was significantly associated with the hospital volume of stroke interventions (Figure 1).

UNIQUE ASPECTS OF CSC CAPACITY IN JAPAN

The J-ASPECT study illustrated several unique aspects of CSC capacity in Japan, including higher availability of neurosurgeons (92.7% vs 24%-54% in the United States) and endovascular surgeons (36.3% vs 15%-22% in the United States),[6,7] which was in sharp contrast to the relative shortage of neurologists (47.8% vs 31%-73% in the United States) and other personnel. In the United States, only 7% of neurosurgeons play an active role in nontraumatic cranial emergencies, whereas 59% of the board-certified neurosurgeons in Japan are engaged in stroke care. The

TABLE 2. Characteristics of Comprehensive Stroke Care Capacity According to the Presence or Absence of a Tissue-Type Plasminogen Activator Protocol[a]

Components	Variables	tPA Protocol Present, n (%)	tPA Protocol Absent, n (%)	OR	95% CI	P Value
Personnel	Neurologists	327 (51.3)	31 (27.7)	2.8	1.8-4.3	<.001
	Neurosurgeons	620 (97.3)	74 (66.1)	18.7	10.1-34.8	<.001
	Endovascular physicians	262 (41.1)	10 (8.9)	7.1	3.7-13.9	<.001
	Critical care medicine	151 (23.7)	11 (9.8)	2.9	1.5-5.5	<.001
	Physical medicine and rehabilitation	105 (16.5)	8 (7.1)	2.3	1.2-5.4	.006
	Rehabilitation therapy	632 (99.2)	110 (98.2)	1.14	0.4-12	.36
	Stroke rehabilitation nurses	88 (14)	14 (12.6)	1.1	0.6-2.1	.67
Diagnostic	CT[b]	634 (99.5)	108 (97.3)	5.9	1.2-29.5	.04
	MRI with diffusion	571 (89.6)	76 (67.9)	4.1	2.6-6.6	<.001
	Digital cerebral angiography[b]	554 (87.4)	48 (43.2)	9.1	5.8-14.2	<.001
	CT angiography[b]	566 (89.1)	61 (55)	6.7	4.3-10.5	<.001
	Carotid duplex ultrasound[b]	235 (37)	22 (19.8)	2.4	1.5-3.9	<.001
	TCD[b]	115 (18.1)	6 (5.4)	3.9	1.7-9.1	<.001
Specific expertise	Carotid endarterectomy[b]	554 (87.1)	49 (43.8)	8.7	5.6-13.5	<.001
	Clipping of intracranial aneurysm	619 (97.2)	66 (58.9)	24	13.1-43.7	<.001
	Hematoma removal/draining	621 (97.5)	68 (60.7)	25.1	13.4-46.9	<.001
	Coiling of intracranial aneurysm	344 (54)	16 (14.3)	7	4.1-12.2	<.001
	Intra-arterial reperfusion therapy	465 (73)	33 (29.5)	6.5	4.2-10.1	<.001
Infrastructure	Stroke unit[b]	128 (20.1)	4 (3.6)	6.8	2.5-18.8	<.001
	Intensive care unit	407 (63.9)	38 (33.9)	3.4	2.3-5.3	<.001
	Operating room staffed 24/7	426 (67.1)	25 (22.3)	7.1	4.4-11.4	<.001
	Interventional services coverage 24/7	268 (42.1)	11 (9.8)	6.7	3.5-12.7	<.001
	Stroke registry[b]	229 (36.3)	6 (5.4)	10	4.3-23.1	<.001
Education	Community education[b]	348 (54.8)	21 (18.8)	5.3	3.2-8.7	<.001
	Professional education[b]	413 (65.2)	23 (20.7)	7.2	4.4-11.7	<.001

[a]CI, confidence interval; CT, computed tomography; MRI, magnetic resonance imaging; OR, odds ratio; TCD, transcranial Doppler; tPA, tissue-type plasminogen activator; 24/7, 24 h/d, 7 d/wk.
[b]Data missing: CT, 1; digital cerebral angiography, 4; carotid ultrasound, 3; TCD, 3; carotid endarterectomy, 1; stroke unit, 1; stroke registry, 7; community education, 2; professional education, 5. Reproduced from Iihara et al[5] with permission from the publisher. Copyright © 2014 National Stroke Association.

proportion of Japanese hospitals offering MRI with DWI and CTA corresponded with the gradual increase in the availability of certain special diagnostic tests in the United States, whereas the availability of digital subtraction angiography (80.8%) was in contrast to the temporal decrease in the availability of catheter angiography observed in the state of North Carolina (from 38% in 1998 to 30% in 2008) because of declines in the proportion of hospitals with neurointerventionalists.[8]

A stroke unit/stroke care unit as the critical infrastructure for acute stroke, which has been proven to reduce the number of deaths and long-term dependency,[9] was available in only 17.6% of hospitals in Japan. This was comparable to the proportion observed in hospitals in the United States (6.6%-28%).[6-8]

The implementation of a written tPA protocol as a key item of PSC capacity was used to determine the relationship between PSC and CSC capacity because it is a key step in reducing tPA-related complications[2,10] (Table 2). The availability of a tPA protocol (85%) was comparable to that reported in 2 US statewide studies performed in Illinois in 2000 (72.8%) and North Carolina between 1998 (43%) and 2008 (69%).[6,8] Notably, facilities with a tPA protocol in Japan had a higher availability of nearly all (92%) recommended items of CSC capacity, with the exception of personnel in rehabilitation therapy and stroke rehabilitation nurses. However, in a previous study performed in the United States,[6] no significant differences were noted in the availability of a larger number of critical items corresponding to the CSC items in this study (eg, endovascular physicians, CTA, conventional cerebral angiography, carotid duplex ultrasound, intra-arterial thrombolysis, stroke unit, and community stroke awareness program) based on the presence of a tPA protocol. Therefore, CSC capacity was more likely to coexist in hospitals with PSC capacity in Japan than in the United States, which might be explained by a relatively larger commitment of neurosurgeons in acute stroke care (eg, tPA infusion) in Japan.

IMPACT OF CSC CAPABILITIES ON IN-HOSPITAL MORTALITY IN PATIENTS WITH ISCHEMIC OR HEMORRHAGIC STROKE (J-ASPECT STUDY)

Next, I would like to discuss the impact of CSC capabilities on outcomes in patients with ischemic or hemorrhagic stroke. As

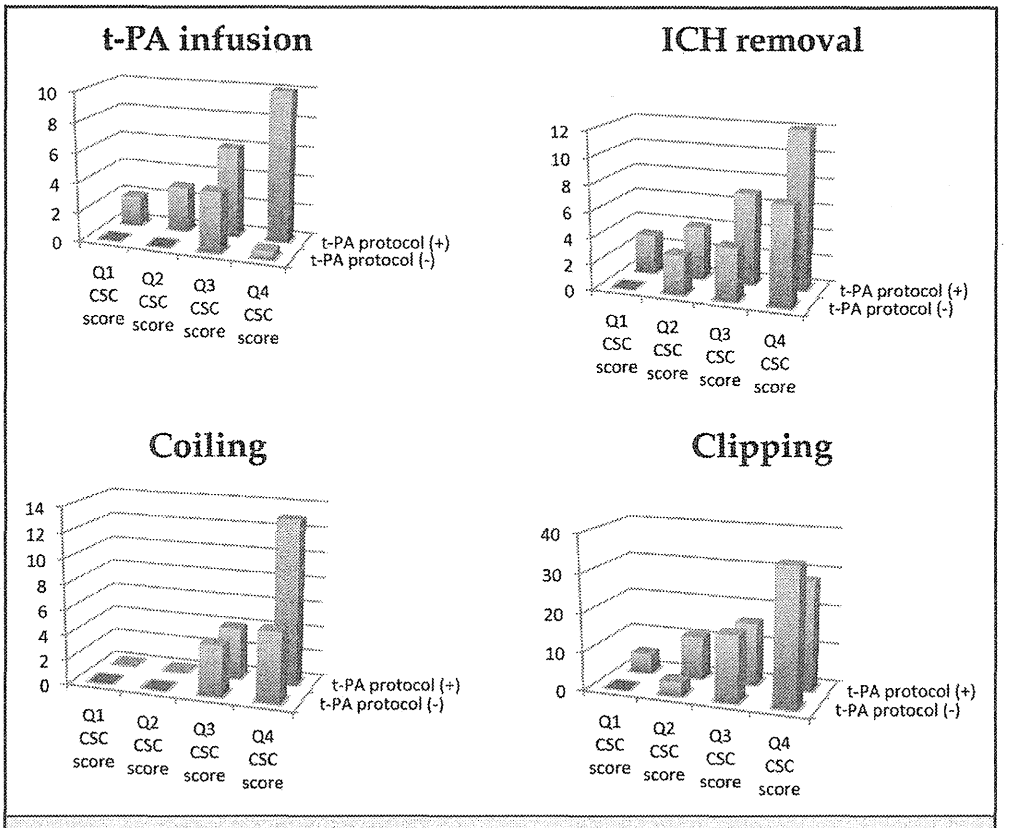

FIGURE 1. *Associations between primary and comprehensive stroke care capabilities and case volume of tissue-type plasminogen activator (tPA) infusion, intracerebral hemorrhage (ICH) removal, and coiling and clipping of intracranial aneurysms in 2009 in Japan. The inclusion of total comprehensive stroke care (CSC) score, availability of a tPA protocol, and other hospital characteristics in the model revealed that total CSC score, but not availability of a tPA protocol, was significantly associated with the hospital volume of stroke interventions. Q, quintile.*

a specialty, we have to step back and ask the very fundamental question, What evidence exists that any of these CSC capabilities have improved stroke outcomes? At the beginning of this project, no evidence existed on the impact of CSC capabilities on outcomes in patients with ischemic or hemorrhagic stroke. Among the institutions that responded to the questionnaire on CSC capacity, data on patients hospitalized for stroke between April 1, 2010, and March 31, 2011, were obtained from the Japanese DPC database.[11] The DPC is a mixed-case patient classification system that was launched in 2002 by the Ministry of Health, Labor, and Welfare of Japan and was linked with a lump-sum payment system.[12] Computer software was developed to identify patients hospitalized because of acute stroke from the annual deidentified discharge database using the *International Classification of Diseases, 10th Revision* diagnosis codes related to ischemic stroke (I63.0-9), nontraumatic ICH (I61.0-9, I62.0-1, and I62.9), and subarachnoid hemorrhage (I60.0-9).[11] The following data were collected from the database: unique identifiers of hospitals, patient age and sex, diagnoses, comorbidities at admission, in-hospital use of medications (antihypertensive agents, oral hypoglycemic agents, insulin, antihyperlipidemic agents, statins, anticoagulant agents, or antiplatelet agents), smoking, arrival by ambulance, level of consciousness at admission according to the Japan Coma Scale, and discharge status. The Japan Coma Scale[13] was originally published in 1974, the same year as the Glasgow Coma Scale,[14] and it remains one of the most popular grading scales among healthcare professionals and emergency medical service personnel in Japan for assessing impaired consciousness. Grading with the 1-, 2-, and 3-digit codes corresponds to the following status: (1) the patient is awake in the absence of any stimulation, (2) the patient can be aroused but reverts to the previous state after the cessation of stimulation, and (3) the patient cannot be aroused even by forceful mechanical stimulation. Zero on the scale indicates normal consciousness. In-hospital mortality was analyzed with hierarchical logistic regression analysis adjusted for age, sex, level of consciousness on admission, comorbidities, and the number of fulfilled CSC items in each component and in total.

Data from 265 institutions and 53170 emergency-hospitalized patients were analyzed (Table 3).[11] The distribution of total CSC