First Impression at Stroke Onset Plays an Important Role in Early Hospital Arrival

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Abstract

Background Treatment for acute ischemic stroke should be administered as soon as possible after symptom onset. The aim of this study was to investigate whether or not the patient's and bystander's first impression at stroke onset was associated with hospital arrival time.

Methods To investigate the factors influencing the prehospital delay, we prospectively interviewed consecutive stroke patients and bystanders about their first impression at the stroke onset and assessed the methods of transportation, and clinical characteristics. Early arrival was defined as a hospital arrival of within 2 h from stroke onset.

Results One hundred thirty patients were enrolled: 82% were ischemic stroke and 18% were cerebral hemorrhage. The median interval between symptom onset and the hospital arrival was 7.5 h and 30% of patients presented within 2 h of stroke onset. First impression of stroke (odds ratios [OR] 4.56, 95% confidence interval [CI] 1.54-13.5, $p=0.006$), presence of consciousness disturbance (OR 4.29, CI 1.39-13.3, $p=0.011$), arrival through other facilities (OR 0.25, CI 0.08-0.76, $p=0.015$), a history of diabetes (OR 0.23, CI 0.06-0.80, $p=0.028$) and nocturnal onset (OR 0.19, CI 0.04-0.88, $p=0.042$) independently contributed to the early arrival.

Conclusions The first impression of patients and bystanders at stroke onset is important in order to reach hospital earlier in Japan. Public educational systems such as those, which advertise stroke warning signs, are necessary

Key words: prehospital interval, first impression, stroke, educational campaign

(DOI: 10.2169/internalmedicine.45.1554)

Introduction

Stroke represents a leading cause of death and serious, long-term disability in Japan, causing 140,000 deaths in 1999. The proportion of deaths from stroke was about 14% of the total national deaths, making this the third most common cause of death following heart disease and cancer (1). The economic burden of stroke on medical expense was estimated to be \$200 billion in 1999 (2).

Effective implementation of early treatment strategies for stroke requires prompt hospitalization. Several studies have demonstrated that age, direct transportation by ambulance, awareness of symptoms, National Institutes of Health stroke scale (NIHSS) score on admission and public awareness of

stroke represented factors influencing the interval from stroke onset to hospital arrival (3-5). In particular, poor public knowledge of the warning signs and risk factors of stroke limits effective stroke intervention and prevention. Unfortunately, public education regarding stroke in Japan has been insufficient and most Japanese might be unlikely to recognize the warning signs and symptoms of stroke at onset. The aim of the present study was to investigate whether patients and witnesses considered the events as representing stroke at stroke onset, and whether the first impression contributed to early presentation to the hospital in Japan.

Method

Between May 1 and October 30, 2004, stroke patients

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Received for publication August 30, 2005; Accepted for publication January 18, 2006

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Table 1. Prehospital Interval after Stroke Onset: Univariate Analysis

Variables	Early group (<2 h) n=39	Late group (>2 h) n=91	p
Age, y, Median (25th-75 percentiles)	68.5 (57.0-78.0)	68 (56.0-73.0)	0.489
Female, n (%)	16 (41)	33 (36)	0.694
Impression Yes*, n (%)	30 (77)	37 (41)	<0.001
Use of EMS**, n (%)	24 (62)	34 (37)	0.013
Arrival through other facilities, n (%)	9 (23)	42 (46)	0.018
Nocturnal onset, n (%)	3 (8)	25 (27)	0.011
Past history			
Transient ischemic attack, n (%)	7 (18)	9 (10)	0.245
Cerebral infarction, n (%)	13 (33)	15 (17)	0.039
Cerebral hemorrhage, n (%)	2 (5)	3 (3)	0.636
Hypertension, n (%)	30 (77)	67 (74)	0.827
Diabetes Mellitus, n (%)	5 (13)	31 (34)	0.018
Hyperlipidemia, n (%)	14 (36)	38 (42)	0.564
Atrial fibrillation, n (%)	8 (21)	7 (8)	0.068
Smoking, n (%)	19 (49)	38 (42)	0.563
Alcohol consumption, n (%)	16 (41)	24 (26)	0.103
Symptoms			
Consciousness disturbance, n (%)	21(54)	14 (15)	<0.001
Headache, n (%)	3(8)	4 (4)	0.428
Dizziness, n (%)	4(10)	8 (9)	0.751
Visual disturbance, n (%)	8(21)	13 (14)	0.437
Speech disturbance, n (%)	18(46)	45 (50)	0.848
Motor disturbance, n (%)	27(69)	54 (59)	0.328
Sensory disturbance, n (%)	13(33)	34 (33)	0.695
NIHSS score at admission	5.4±4.0	6.2±4.6	0.332
NIHSS*** score at admission ≥7	21(54)	63 (69)	0.111

Prehospital interval was defined as follows; the Early group arrived at the hospital ≤2 h after stroke onset; the Late group arrived >2 h after stroke onset.

*Impression Yes; the patients or witnesses considered their events as stroke from symptoms onset.

**EMS: Emergency medical services

***NIHSS: National Institutes of Health stroke scale

presenting to the emergency department (ED) or outpatient clinic of our hospital within 7 days after symptom onset were prospectively enrolled in the study. The diagnosis of stroke was confirmed in each patient using computed tomography or magnetic resonance imaging including diffusion-weighted imaging. Immediately after their hospital arrival, patients or witnesses on hospital visits were interviewed to determine first impressions as to whether the event at the time of onset was considered to be stroke. In addition, the symptoms at onset (disturbance of consciousness, headache, dizziness, visual disturbance, speech disturbance, motor disturbance or sensory disturbance) were investigated. The following data were also assessed in all patients from medical records: 1) age and gender; 2) prehospital interval; 3) use of emergency medical services (EMS); 4) referral from another outpatient clinic or hospital; 5) symptoms upon waking; 6) previous illness (transient ischemic attack (TIA), cerebral infarction or cerebral hemorrhage); 7) risk factors (hypertension, diabetes mellitus, hyperlipidemia,

atrial fibrillation, and smoking and excessive alcohol consumption); and 8) NIHSS score on admission. Patients were divided into two groups: the Yes group considered their events as stroke from symptom onset; the No group did not. Prehospital interval was defined as the interval from symptom onset to arrival at the ED or outpatient clinic of our hospital. Time of symptom onset was defined as the time that patients or witnesses first noticed symptoms. If symptoms occurred during sleep, time of symptom onset was considered to be the time when the patient fell asleep. Furthermore, patients were divided into two subgroups based on the prehospital interval: the Early group arrived at the hospital ≤2 h after stroke onset; the Late group arrived >2 h after stroke onset. The cut-off for prehospital interval (Early group) was set at 2 h because the therapeutic time window for intravenous thrombolysis is only within 3 h from stroke onset. Optimally, patients would arrive at hospital ≤2 h after stroke onset to receive r-PA treatment. Stroke severity was assessed on admission as NIHSS 0-6 (mild) and ≥7 (moderate or severe). NIHSS cut-offs were used in accordance with previous reports (6, 7).

Vascular risk factors were identified as follows: 1) hypertension, use of antihypertensive agents, with systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥80 mmHg at 2 weeks after admission; 2) diabetes mellitus, use of oral hypoglycemic agents, insulin, or glycosylated hemoglobin >6.4%; 3) hypercholesterolemia, use of antihyperlipidemic agents or serum cholesterol level >220 mg/dL; and 4) smoking, any cigarette usage within the 28 days preceding the index stroke.

Significant differences in prehospital interval between Early group and Late group were determined using Mann-Whitney's U-test or Fisher's exact test. Logistic regression was used to analyze factors associated with prehospital interval (≤2 h) and first impression, when applicable. Variables identified from univariate analyses at p<0.2 were considered to represent explanatory variables and were entered together into multivariate analysis. However, we excluded the NIHSS score from independent variables of a multiple regression analysis model because the NIHSS score was strongly affected by consciousness disturbance. All significant tests were 2-tailed, and values of p<0.05 were considered statistically significant. Odds ratios (OR) and 95% confidence interval (CI) were generated for all terms in the final analysis. Data were analyzed using SPSS version 10.0 for Windows (SPSS Inc).

Results

Subjects comprised 130 consecutive patients with stroke. Median time from symptom onset to arrival at the ED or outpatient clinic was 7.5 h (interquartile range, 2.0-31.8 h). A total of 39 (30%) patients presented ≤2 h after symptom onset. While 67 patients (52%) considered the events as representing stroke (Yes group), 63 did not (48%; No group). EMS transported 58 patients (45%) to the hospital. Noctur-

Figure 1. Rate of first impression according to prehospital interval. Impression Yes; patients or witnesses considered their events as stroke from symptom onset. Impression No; they did not consider their illness as stroke at the onset. Early group; patient arrived at the hospital ≤ 2 h after stroke onset. Late group; patient arrived >2 h after stroke onset.

Table 2. Multiple Regression Analysis Model for Probability of Prehospital Interval within 2 h

Variables	OR** (95%CI***)	p
Impression Yes*	4.56 (1.54-13.5)	0.006
Consciousness disturbance	4.29 (1.39-13.3)	0.011
Arrival through other facilities	0.25 (0.08-0.76)	0.015
Diabetes Mellitus	0.23 (0.06-0.80)	0.021
Nocturnal onset	0.19 (0.04-0.88)	0.034
A history of cerebral infarction	2.21 (0.68-7.19)	0.185
Alcohol consumption	1.91 (0.70-5.24)	0.208
Atrial fibrillation	1.88 (0.44-8.14)	0.397
Use of EMS	1.52 (0.51-4.51)	0.451

*Impression Yes; patients or witnesses considered their events as stroke from symptom onset.

**OR: odds ratios

***CI: confidence interval

Table 3. First Impression of Patients and Witnesses: Univariate Analysis

Variables	First Impression at Stroke Onset		p
	Yes group* n=67	No group** n=63	
Age, y, Median (25th-75 percentiles)	67.0 (57.0-73.0)	70.0 (59.0-79.0)	0.173
Female, n (%)	26(39)	23(37)	0.694
Use of EMS, n (%)	33(49)	25(40)	0.294
Arrival through other facilities, n (%)	25 (37)	26 (41)	0.720
Nocturnal onset, n (%)	14(20)	14(22)	1.000
Past history			
Transient ischemic attack, n (%)	7(10)	9(14)	0.597
Cerebral infarction, n (%)	21(31)	7(11)	0.006
Cerebral hemorrhage, n (%)	3(5)	2(3)	1.000
Hypertension, n (%)	52(78)	45(71)	0.429
Diabetes Mellitus, n (%)	16(24)	20(32)	0.334
Hyperlipidemia, n (%)	28(42)	24(38)	0.722
Atrial fibrillation, n (%)	8(12)	7(11)	1.000
Smoking, n (%)	28(42)	29(46)	0.724
Alcohol consumption, n (%)	25(37)	15(24)	0.128
Symptoms			
Consciousness disturbance, n (%)	23(34)	12(19)	0.074
Headache, n (%)	5(8)	2(3)	0.442
Dizziness, n (%)	5(8)	7(11)	0.553
Visual disturbance, n (%)	11(16)	10(16)	1.000
Speech disturbance, n (%)	31(46)	32(51)	0.726
Motor disturbance, n (%)	51(76)	30(48)	0.001
Sensory disturbance, n (%)	26(39)	21(33)	0.585
NIHSS score at admission	6.4 $\pm$ 4.9	5.4 $\pm$ 4.2	0.443
NIHSS score at admission ≥ 7 , n (%)	29(43)	17(27)	0.067

*Yes group considered their events as stroke from symptom onset. **No group did not.

nal onset was observed in 28 patients (22%). Median NIHSS score on admission was 3 (interquartile range, 1-9), and 46 patients (35%) displayed a baseline NIHSS score ≥ 7 . One hundred-seven patients had ischemic cerebrovascular disease. Brain hemorrhage was observed in 23 patients.

Prehospital interval

The Early group comprised 39 patients (30%; 23 men, 16 women; median age, 70.0 years), while the Late group comprised 91 patients (70%; 58 men, 33 women; median age, 68.0 years, Table 1). In the Early group, 30 of the 39 patients (77%) reported a first impression of stroke, compared to 37 of the 91 Late group patients (41%, $p < 0.001$, Fig. 1). EMS was used more frequently in the Early group than in the Late group (62% vs. 37%, $p=0.013$). Forty-two patients (46%) arrived at our hospital via another outpatient clinic or hospital in the Late group. Nocturnal onset was observed in 3 Early group patients (8%) and 25 Late group patients (27%, $p=0.011$).

History cerebral infarction was reported in 13 Early group patients (33%) and in 15 Late group patients (17%, $p=$

0.039). Disturbance of consciousness was experienced by 21 Early group patients (54%) and 14 Late group patients (15%, $p<0.001$). Diabetes was present in 31 Late group patients (34%) and 5 Early group patients (13%, $p=0.018$).

Table 2 shows the factors associated with prehospital interval within 2 h by using multivariate logistic regression analysis. First impression of stroke (OR 4.56, CI 1.54 to 13.5, $p=0.006$), and presence of consciousness disturbance (OR 4.29, CI 1.39 to 13.3, $p=0.011$) were associated with

Table 4. Factors Significantly Associated with First Impression as Stroke

Variables	OR (95%CI)	p
Motor disturbance	3.05 (1.34-6.85)	0.007
A history of cerebral infarction	3.78 (1.39-10.3)	0.009
Alcohol consumption	1.86 (0.81-4.26)	0.143
Consciousness disturbance	1.61 (0.66-3.91)	0.297

prehospital interval ≤ 2 h. Conversely, arrival via other facilities (OR 0.25, CI 0.08 to 0.76, $p=0.015$), a history of diabetes (OR 0.23, CI 0.06 to 0.80, $p=0.021$) and nocturnal onset (OR 0.19, CI 0.04 to 0.88, $p=0.034$) were associated with delayed hospital arrival. Other variables, such as history of hypertension, hyperlipidemia, smoking, alcohol habitation, prior TIA and cerebral hemorrhage, and other symptoms (headache, dizziness, visual, speech, and motor or sensory disturbances) displayed no significant associations with prehospital interval.

Factors associated with first impression of stroke

Table 3 shows the first impression of patients or witnesses and their characteristics. Logistic regression analysis was conducted to investigate factors associated with first impression of stroke (Table 4). Motor dysfunction (OR 3.05, CI 1.34-6.85, $p=0.007$) and history of cerebral infarction (OR 3.78, CI 1.39-10.3, $p=0.009$) represented the only independent variables contributing to the first impression of stroke by the patient or witness.

Discussion

The present study demonstrated that 52% of patients considered their events as stroke, and 77% of these patients and witnesses arrived at hospital ≤ 2 h after symptom onset. Multivariate logistic regression analysis revealed the first impression of stroke as an independent factor associated with early hospital arrival. The first impression of stroke thus represents an important factor for reducing prehospital delay after stroke onset. Many studies have found that nocturnal onset and arrival via other facilities extended the prehospital delay (5, 8). The history of diabetes mellitus contributed to the delayed hospital presentation. We suspect that some of these patients and their witness might misunderstand their event as hypoglycaemic attack.

In the present study, history of cerebral infarction and motor dysfunction as neurological symptoms were the only

independent variables associated with the first impression of stroke among patients and witness. Patients with a history of cerebral infarction were likely to arrive at hospital earlier, because they were already familiar with the warning signs of stroke from their own experiences (9). Motor dysfunction was the most common sign of stroke in a previous hospital-based study (10, 11). When an individual experiences motor dysfunction, many people must consider this as stroke. Conversely, in our study, consciousness disturbance was associated with the early hospital presentation, but not first impression of stroke. These results are similar to the report of Pandian et al; they reports that only 6% of stroke patients and families had recognized loss of consciousness as stroke symptoms (11). Loss of consciousness may be recognized as an emergency sign in spite of illness (12, 13).

What should be done to help individuals to recognize events as stroke? Unfortunately, in our study, stroke symptoms other than motor dysfunction were not recognized as representing stroke. Several studies have suggested that poor recognition of the warning signs of stroke may be at least partially responsible for delays in seeking medical attention (14). Public education is thus needed to familiarize people with the warning signs of stroke (e.g., speech, visual or sensory disturbance) at onset.

The prehospital interval was longer in our study than in previous studies. This is explicable based on differences in the inclusion criteria. The present study included stroke patients who came to the hospital within 7 days after onset. Among the 15,831 acute stroke and TIA patients in the Japan Multi-center Stroke Investigator's Collaboration study (15), which included patients arriving ≤ 7 days after stroke onset, 35% were admitted within 3 h. We thus believe that our study protocols did not result in selection bias.

The present study had some limitations. First, 28% of patients who considered the events as representing stroke did not visit the hospital ≤ 2 h after symptom onset. Reasons as to why patients decided against coming to hospital earlier were not investigated. Secondly, the distance between location of stroke onset and the hospital was not recorded. However, most patients lived in Kurashiki-city, within about 20 km from the hospital. Thirdly, we did not consider the educational level of patients and bystanders because the rate of illiteracy in the Japanese population is quite low.

In conclusion, the first impression at stroke onset should contribute to early hospitalization in Japan. Advertising campaigns to increase public knowledge regarding the warning signs of stroke may be successful for reducing delays in hospital presentation.

References

- Sarti C, Rastenyte D, Cepaitis Z, Tuomilehto J. International trends in mortality from stroke, 1968 to 1994. *Stroke* 31: 1588-1601, 2000.
- Social and economic changes surrounding individuals. Annual Report on Health, Labour and Welfare 2000-2001. In: Health, Labour and Welfare Administration for Providing Life-Long Support to Self-Sufficiency of the People. Gyosei Corporation, Tokyo, Japan, 2002: 163-150.

3. Morris DL, Rosamond W, Madden K, Schultz C, Hamilton S. Pre-hospital and emergency department delays after acute stroke: the Genentech Stroke Presentation Survey. *Stroke* **31**: 2585-2590, 2000.
4. Lacy CR, Suh DC, Bueno M, Kostis JB. Delay in presentation and evaluation for acute stroke: Stroke Time Registry for Outcomes Knowledge and Epidemiology (S.T.R.O.K.E.). *Stroke* **32**: 63-69, 2001.
5. Chang KC, Tseng MC, Tan TY. Prehospital delay after acute stroke in Kaohsiung, Taiwan. *Stroke* **35**: 700-704, 2004.
6. Adams HP Jr., Davis PH, Leira EC, et al. Baseline NIH Stroke Scale score strongly predicts outcome after stroke: A report of the Trial of Org 10172 in Acute Stroke Treatment (TOAST). *Neurology* **53**: 126-131, 1999.
7. DeGraba TJ, Hallenbeck JM, Pettigrew KD, Dutka AJ, Kelly BJ. Progression in acute stroke: value of the initial NIH stroke scale score on patient stratification in future trials. *Stroke* **30**: 1208-1212, 1999.
8. Koga M, Kimura K, Minematsu K, Takenori Y. Factors influencing delayed arrival of acute stroke patients. *Jpn J Stroke* **22**: 301-306, 2000.
9. Williams LS, Bruno A, Rouch D, Marriott DJ. Stroke patients' knowledge of stroke. Influence on time to presentation. *Stroke* **28**: 912-915, 1997.
10. Kothari R, Sauerbeck L, Jauch E, et al. Patients' awareness of stroke signs, symptoms, and risk factors. *Stroke* **28**: 1871-1875, 1997.
11. Pandian JD, Jaison A, Deepak SS, et al. Public awareness of warning symptoms, risk factors, and treatment of stroke in north-west India. *Stroke* **36**: 644-648, 2005.
12. Pancioli AM, Broderick J, Kothari R, et al. Public perception of stroke warning signs and knowledge of potential risk factors. *JAMA* **279**: 1288-1292, 1998.
13. Silver FL, Rubini F, Black D, Hodgson CS. Advertising strategies to increase public knowledge of the warning signs of stroke. *Stroke* **34**: 1965-1968, 2003.
14. Jorgensen HS, Nakayama H, Reith J, Raaschou HO, Olsen TS. Factors delaying hospital admission in acute stroke: the Copenhagen Stroke Study. *Neurology* **47**: 383-387, 1996.
15. Kimura K, Minematsu K, Kazui S, Yamaguchi T. Japan Multicenter Stroke Investigators' Collaboration (J-MUSIC). Mortality and cause of death after hospital discharge in 10,981 patients with ischemic stroke and transient ischemic attack. *Cerebrovasc Dis* **19**: 171-178, 2005.