Factors Influencing Pre-Hospital Delay after Ischemic Stroke and Transient Ischemic Attack

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Abstract

Background and Purpose We investigated which factors influence pre-hospital delay after the onset of stroke and transient ischemic attack (TIA).

Methods A total of 113 patients with ischemic stroke or TIA who were directly transported to the emergency room within 24 hours of onset were entered into the study. We analyzed factors relating to an early arrival at hospital (≤ 2 hours), and factors relating to an early emergency call (≤ 1 hour).

Results The interval between symptom onset and arrival at hospital was within 2 hours in 75 (66%) patients. The interval between symptom onset and call to emergency was significantly related to arrival within 2 hours ($p < 0.001$), whereas time ($p = 0.09$) and distance ($p = 0.32$) for transportation were not. The interval between onset and emergency call was within 1 hour in 68 patients (60%). The presence of a bystander (Odds ratio 3.68) and consciousness disturbance (Odds ratio 2.49) were independently related to an early emergency call.

Conclusion An early emergency call is essential for the timely admission of stroke patients into a hospital. The presence of a bystander and consciousness disturbance are keys to an early emergency call.

Key words: acute stroke, emergency services, pre-hospital delay

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Introduction

Intravenous recombinant tissue plasminogen activator (rtPA) for hyperacute stroke patients was approved in October 2005 in Japan. This drug is effective when applied within 3 hours of stroke onset. However, many patients arrive at a hospital too late to receive thrombolytic therapy. One study has shown that the proportion of stroke patients who arrive at hospital within 3 hours of onset is 17-61% (1); and a nationwide investigation found that it is 36.8% in Japan (2).

Although the time window for intravenous rtPA might be extended from 3 hours to 4.5 hours, it is known that to shorten the time window is important to avoid intracranial hemorrhage (3). To apply timely intravenous rtPA treatment, ideally, patients must arrive at a hospital within 2 hours of onset. However, few studies have investigated the causes of

pre-hospital delay within this 2-hour window (4, 5). The relationship between pre-hospital delay and some factors also remains unknown: the time period between stroke onset and contacting Emergency, or distance that patient is transported (6-9).

We conducted a retrospective study to clarify the factors influencing pre-hospital delay ≥ 2 hours after the onset of ischemic stroke or transient ischemic attack, in patients who were transported by the Emergency Medical Services. Secondly, we investigated the factors influencing the delay of emergency calls after stroke onset, because it might be shortened by efforts of medical staff, such as public education about stroke symptoms.

Subjects and Methods

Kumamoto Rosai Hospital is in the Yatsushiro large municipal area, which covers an area of 713 km² and contains

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Figure 1. Patient selection.

158,000 inhabitants. Approximately 70% of patients with neurological disorders in emergency are transported to our hospital from all over this region.

From April 2004 to September 2005, 350 consecutive patients with acute ischemic stroke or transient ischemic attack (TIA) were admitted to our hospital within 7 days of onset. We excluded patients who were admitted without emergency medical services (N=139) and those admitted at over 24 hours of onset (N=68). We also excluded those who were referred from other clinics or hospitals (N=30) because the elapsed time between onset and arrival at hospital was longer for these patients than for those who were directly transported (4, 5). We finally enrolled 113 patients (69 males and 44 females, aged 75 ± 12 years) in the study (Fig. 1) and assigned them to Early arrival group and Late arrival groups according to whether they arrived at hospital within or after 2 hours of symptom onset, respectively.

Clinical data of the participants were collected from pre-hospital and hospital records. We compared age, gender, vascular risk factors (hypertension, diabetes mellitus and hyperlipidemia), smoking and alcohol consumption within the last month, paroxysmal or chronic atrial fibrillation, history of stroke, stroke type, presence of a bystander at onset, the person who had called for an ambulance and location of onset, period between symptom onset and emergency call, time taken and distance to transport from the location of the emergency call to the hospital. We evaluated all symptoms observed by patients or bystanders before calling for an ambulance as an evidence of stroke.

Onset time was defined as the moment that a patient or witness initially noticed symptoms. When indeterminate, we defined onset time as the last time that the patient had been observed without symptoms. Onset was separated according whether it occurred in the nighttime (between 2400 and 0600 h) or in the daytime (between 0600 and 2400 h). The time of the emergency call and arrival at the hospital were confirmed by pre-hospital records in the emergency department. Distance for transportation was defined as the direct

Figure 2. The gap between onset and arrival. Early arrival group (n=75) shared 66% of 113 patients.

distance between the location of the emergency call and the emergency department at our hospital. Stroke type was determined according to the Classifications of Cerebrovascular Diseases III (NINDS CVD-III) (10): atherothrombotic (stenosis of the corresponding artery or occlusion caused by atherosclerosis), cardioembolic (presence of emboligenic heart diseases), lacunar (small lesion of largest diameter <1.5 cm caused by occlusion of perforating arteries), other, unknown origin, and TIA. Individuals who called for an ambulance were classified as patients, family, neighbor, staff of hospital or nursing home, and others. Locations of onset were categorized as home, outside the home, hospital or nursing home.

Secondarily, we investigated the factors influencing early emergency calls. We assigned 1 hour as a cutoff point for early emergency call from symptom onset, because it enables most patients to arrive at a hospital within 2 hours. Patients were divided into Early call group (time between symptom onset and emergency call ≤ 1 hour) and Late call group (>1 hour). All the previously described factors but transportation time and distance were compared between the two groups. We identified the factors associated with early calls using logistic regression analysis. Variables identified from the univariate analysis at $p < 0.10$ were considered to be explanatory and were entered together into the models in the multivariate analysis.

Significant differences between the two groups were determined using the χ^2 test, Fisher's exact test, Mann-Whitney's U-test. We used Spearman's test to evaluate the association between the time and distance for patients' transportation to hospital. Values of $p < 0.05$ were considered statistically significant. Stat View[®] Version 5.0 (SAS Institute Inc., Cary, NC) was used for all calculations.

Results

A total of 75 (66%) patients were included in the Early arrival group; which accounted for 36% of patients admitted for ischemic stroke or TIA within 7 days of onset (Fig. 2).

Table 1. Characteristics of Early and Late Arrival Groups

	Early arrival (≤2 h)	Late arrival (>2 h)	p
Number	75	38	
Age, y, median (range)	75 (16-97)	75 (45-95)	0.94*
Male / female	45 / 30	24/14	0.75
Hypertension, N (%)	42 (56)	27 (71)	0.12
Diabetes, N (%)	23 (31)	9 (24)	0.43
Hypercholesterolemia, N (%)	15 (20)	10 (26)	0.44
Atrial fibrillation, N (%)	34 (45)	14 (37)	0.39
Stroke history, N (%)	23 (31)	7 (18)	0.16
Smoking, N (%)	14 (19)	10 (26)	0.35
Alcohol consumption, N (%)	25 (33)	13 (34)	0.93
Onset to call, min, median (range)	20 (0-101)	193 (84-593)	<0.001*
Transportation duration, min, median (range)	28 (13-64)	31 (18-87)	0.09*
Distance, km, median (range)	4.2 (0.4-20.0)	5.1 (1.0-21.2)	0.32*
Clinical symptoms			
Consciousness disturbance, N (%)	46 (61)	15 (39)	0.03
Motor disturbance, N (%)	30 (40)	20 (53)	0.20
Sensory disturbance, N (%)	4 (5)	2 (5)	1.00**
Gait disturbance, N (%)	2 (3)	6 (16)	0.02**
Vertigo / dizziness, N (%)	1 (1)	2 (5)	0.26**
Nausea / vomiting, N (%)	11 (15)	4 (11)	0.54
Speech disturbance, N (%)	17 (23)	7 (18)	0.60
Visual disturbance, N (%)	1 (1)	0	1.00**
Convulsion, N (%)	1 (1)	0	1.00**
Headache, N (%)	3 (4)	3 (8)	0.40**
Apraxia / agnosia, N (%)	1 (1)	0	1.00**
Daytime onset, N (%)	69 (92)	32 (84)	0.21**
Location of onset			0.52
Home, N (%)	50 (67)	30 (79)	
Outside home, N (%)	17 (23)	5 (13)	
Hospital or nursing home, N (%)	7 (9)	3 (8)	
Bystander	64 (85)	21 (55)	<0.001
Person who called ambulance			0.17
Patient, N (%)	1 (1)	3 (8)	
Family, N (%)	53 (71)	(74)	
Neighbor, N (%)	10 (13)	3 (8)	
Staff, N (%)	6 (8)	4 (11)	
Other, N (%)	0	5 (13)	
Stroke subtype			0.18
Cardioembolic	39 (52)	15 (39)	
Atherothrombotic	10 (13)	10 (26)	
Lacunar	3 (4)	5 (13)	
Others	6 (8)	3 (8)	
Undetermined	9 (12)	2 (5)	
Transient ischemic attack	8 (11)	3 (8)	
Cardioembolic stroke / Other subtype, N	39 / 36	15 / 23	0.21

P value analyzed by Chi-square test, *Mann-Whitney's U test, or **Fisher's exact test.

The duration between onset and the emergency call was significantly shorter for the Early arrival group, than for the Late arrival group (mean, 20 vs. 193 minutes, $p<0.001$). The time taken to transport the Early arrival group was slightly,

Figure 3. Relationship between transportation duration and distance. Transportation duration was correlated with distance both in the early arrival group and late arrival group ($p < 0.01$, $\rho = 0.65$). All patients arrived at hospital within 90 minutes of emergency call.

but not significantly shorter than that for the Late arrival group (28 vs. 31 minutes, $p = 0.09$). Distance from the location of the emergency call to hospital also did not significantly differ between the two groups (4.2 vs. 5.1 km, $p = 0.32$, Table 1). A consciousness disturbance was significantly frequent among the initial symptoms experienced in the Early arrival group ($p = 0.03$). Gait was frequently disturbed in the Late arrival group ($p = 0.02$). The time required for transportation significantly correlated with distance between the location of the emergency call and the hospital ($p < 0.01$, $\rho = 0.65$ by Spearman's test). Transportation time was within 90 minutes in all of the patients, and was within 1 hour in 97% of them (Fig. 3).

The median interval between onset and emergency call was 44 minutes (range, 0 to 593 minutes), and 68 patients (60.2%) were classified into the Early call group. All of these patients arrived at the hospital within 2 hours of onset, whereas only 7 patients (15.6%) in the Late call group arrived at the hospital within 2 hours. A consciousness disturbance was significantly frequent among the initial symptoms experienced in the Early call group ($p = 0.005$). Gait was frequently disturbed in the Late call group, but the difference did not reach statistical significance ($p = 0.057$). Other symptoms did not significantly differ between the two groups.

Onset time and location, as well as the type of person who called the ambulance did not significantly differ between the two groups. A bystander was present more frequently in the Early call group, than in the Late call group ($p = 0.002$). The proportions of stroke subtypes were similar between the two groups, but cardioembolic stroke was relatively more frequent in the Early group ($p = 0.08$, Table 2).

Logistic regression analysis showed that the presence of a bystander (Odds ratio, 3.68; 95% C.I. 1.42-9.54) and consciousness disturbance (Odds ratio, 2.49; 95% C.I. 1.03-6.02) were independently related to an early emergency call (Table 3).

Discussion

We clarified that the early arrival of stroke patients at a hospital depends on duration between symptom onset and emergency call and not the time or distance involved in transportation. This notion might not be applicable to all hospitals, considering regional characteristics and emergency transportation systems. Nevertheless, we confirmed that an urgent call for an ambulance, in particular, in regions where emergency medical services are developed, represents one of the most important factors involved in providing more patients with intravenous rtPA.

We also found that bystander's awareness of stroke symptoms and an immediate response is important for early call for an ambulance, as previously described (6, 11). The presence of bystanders was also an independent predictor for an early emergency call, which supports the findings of Derex et al (12). Other investigators have found that being part of a large family, residing with others and daytime onset are related to early emergency calls. Most suggest that early awareness of symptoms is critical (13). The increase in the number of nuclear families might accelerate an increase in the numbers of lone residents in rural and urban areas, which might result in a delay of awareness of stroke onset. Some knowledge of cerebrovascular diseases is necessary for immediate awareness of stroke symptoms. Public education about stroke symptoms has already been proven effective for early emergency calls (4, 14-16).

Among stroke symptoms, we found that only consciousness disturbance was independently related to an early emergency call. However, discovering a person with disturbed consciousness might result in a stranger making an emergency call regardless of whether the event was recognized as a stroke. Rather, it would be alarming that no other major symptoms indicating stroke were related to an early emergency call. Only 29% of the general Japanese population can recognize any stroke symptoms (17), compared with 57% of the general American population (13), indicating that public education about stroke symptoms is necessary in Japan.

We did not detect a significant relationship between transportation distance and duration between onset and arrival. A similar relationship has been identified in India (6) and Canada (11), but not in France (12) and Sweden (18). These differences might be associated with the extent or nature of the emergency medical systems in various countries. One reason for rapid transportation in our study might be that emergency personnel are highly trained and emergency response systems have been established. Additionally, the area has few islands or extremely remote rural areas. Although we found a significant relationship between time and distance involved in transportation, this should be more characteristic of rural areas.

In our study, the median interval between symptom onset and the first emergency call was 45 minutes, contrary to

Table 2. Characteristics of Early and Late Call Groups

	Early call (≤ 1 h)	Late call (> 1 h)	p
Number	68	45	
Age (y), mean (range)	75 (48-97)	76 (16-95)	0.88*
Male/female	40/28	29/16	0.55
Hypertension, N (%)	38 (56)	31 (69)	0.17
Diabetes mellitus, N (%)	21 (31)	12 (27)	0.63
Hypercholesterolemia, N (%)	13 (19)	13 (29)	0.23
Atrial fibrillation, N (%)	32 (47)	17 (38)	0.33
Stroke history, N (%)	20 (29)	8 (18)	0.16
Smoking, N (%)	13 (19)	11 (24)	0.50
Alcohol consumption, N (%)	24 (35)	14 (31)	0.65
Clinical Symptoms			
Consciousness disturbance, N (%)	44 (65)	17 (38)	0.005
Motor disturbance, N (%)	29 (43)	22 (49)	0.51
Sensory disturbance, N (%)	2 (3)	3 (7)	0.39**
Gait disturbance, N (%)	2 (3)	6 (13)	0.057**
Vertigo / dizziness, N (%)	1 (1)	2 (4)	0.56**
Nausea / vomiting, N (%)	10 (15)	4 (9)	0.36
Speech disturbance, N (%)	16 (24)	9 (20)	0.66
Visual disturbance, N (%)	1 (1)	0	$>0.99^{**}$
Convulsion, N (%)	2 (3)	4 (9)	0.21**
Headache, N (%)	1 (1)	0	$>0.99^{**}$
Apraxia / agnosia, N (%)	0	1 (2)	0.40**
Daytime onset, N (%)	63 (93)	38 (84)	0.17
Location of onset			0.65
Home, N (%)	61 (90)	42 (93)	
Outside home, N (%)	1 (1)	0	
Hospital or nursing home, N (%)	6 (9)	3 (7)	
Bystander	55 (81)	30 (67)	0.002
Person who called ambulance			0.49
Patient, N (%)	1 (1)	3 (7)	
Family, N (%)	48 (71)	33 (73)	
Neighbor, N (%)	10 (15)	3 (7)	
Staff, N (%)	5 (7)	5 (11)	
Other, N (%)	4 (6)	1 (2)	
Stroke subtype			0.13
Cardioembolic	37 (54)	17 (38)	
Atherothrombotic	9 (13)	11 (24)	
Lacunar	3 (4)	5 (11)	
Others	4 (6)	5 (11)	
Undetermined	9 (13)	2 (4)	
Transient ischemic attack	6 (9)	5 (11)	
Cardioembolic stroke / Other subtype, N	37 / 31	17 / 28	0.08

P value analyzed by Chi-square test, *Mann-Whitney's U test, or **Fisher's exact test.

Table 3. Logistic Regression Analysis for Early Call ≤ 1 Hour

	Odds ratio	95% CI		p
Consciousness disturbance	2.49	1.03	6.02	0.043
Gait disturbance	0.31	0.05	1.85	0.198
Bystander	3.68	1.42	9.54	0.007
Cardioembolic stroke	1.38	0.10	1.06	0.478

previous reports of 2.2 and 3.4 hours for TIA and stroke patients, respectively (13). One reason for this is that we limited the study subjects to those with acute stroke who were admitted to our hospital within 24 hours of onset.

Our investigation has some limitations. First, this is a retrospective study of pre-hospital and hospital records. Therefore, information in the records about symptoms before the emergency call was limited. Secondly, selection bias exists because we excluded patients who did not arrive by ambulance. Since the precise times that patients arrived by means other than an ambulance was not evident in the hospital records, we excluded these patients from the study. Fourth, stroke severity was not evaluated using a quantitative index, such as the National Institutes of Health Stroke Scale. However, consciousness disturbance, motor disturbance, or stroke subtype may serve as some surrogate measures of stroke se-

verity.

In conclusion, we investigated the factors that influence the early arrival of patients with ischemic stroke at a hospital and found that early emergency call was a key rather than distance or time required for transportation. Moreover, consciousness disturbance and the presence of a bystander were closely related to an early emergency call. The general population should be educated about stroke symptoms so that stroke is recognized as an emergency.

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