Prehospital Delay After Acute Stroke in Kaohsiung, Taiwan

Ku-Chou Chang, MD; Mei-Chiun Tseng, PhD; Teng-Yeow Tan, MD

**Background and Purpose**—Successful acute stroke intervention depends on early hospital presentation. Our study aimed to examine the extent of and factors associated with prehospital delays after acute stroke in Taiwan, where people are new to thrombolytic therapy for stroke.

**Methods**—Data were prospectively collected from 196 patients admitted with acute stroke who presented to the emergency department (ED) of the study hospital within 48 hours of symptom onset before intravenous recombinant tissue plasminogen activator was approved. Prehospital delay was defined as time from symptom onset to the ED arrival. Univariate and multivariable regression analyses were conducted to evaluate factors influencing delay in ED presentation and delay in decision to seek medical help.

**Results**—The median interval between symptom onset and decision to seek medical contact was 90 minutes; the median interval between symptom onset and ED arrival was 335 minutes. The time from symptom onset to first call for medical help accounted for 45% (95% confidence interval, 41 to 50) of the prehospital delay. Advanced age delayed the decision to seek medical help, whereas stroke severity reduced the risk for this delay.

**Conclusions**—The time interval between symptom onset and the decision to call for medical care is far from optimal and is the underlying cause of prolonged prehospital delay. Educational efforts to reduce extent of delay are urgently needed.

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**Key Words:** stroke management ■ stroke, acute ■ Taiwan

Six years after approval in the United States, the use of intravenous recombinant tissue plasminogen activator (rtPA) for treatment of patients with acute ischemic stroke was approved in the European Union and in countries outside North America after 2002. The biggest hurdle for administering intravenous rtPA is time; the narrow window of opportunity is within 3 hours after stroke.1 Presentation >3 hours after symptom onset continues to be a primary cause of exclusion from thrombolytic therapy among stroke patients in North America and will be a problem in areas new to this therapy. Several studies have identified factors influencing delays in the treatment of stroke patients in different countries and clinical trials.2,3 According to the revised basic product information of rtPA released September 2002, new treatment recommendations prohibit giving intravenous rtPA to patients >80 years of age or patients with stroke severity of >25 points on the National Institutes of Health Stroke Scale (NIHSS). To the best of our knowledge, with the study of Nedeltchev et al4 as the only exception, stroke severity was often not included in studies reporting prehospital delay for patients with stroke.5–10

In this observational study, we studied the magnitude of and factors associated with prehospital delay in the Kaohsiung metropolitan area of Taiwan before intravenous rtPA was approved, aiming to generate hypotheses for future prospective studies in areas new to this therapy.

**Methods**

The study hospital, a 1900-bed nonprofit proprietary hospital providing medical center–level health care in the Kaohsiung metropolitan area of Taiwan, was the site of patient enrollment. It has a catchment area of ~3 million inhabitants. Other hospitals, including 2 medical centers and 24 community hospitals, provide services to stroke patients in the same area. The study hospital is the main referral hospital for all kinds of stroke in the area. Between September 1998 and March 1999, patients presenting to the emergency department (ED) of the study hospital with symptoms of stroke within 48 hours of onset were included. The diagnosis of each enrolled patient was confirmed by cranial CT scanning to exclude nonstroke causes of the neurological deficits. No public campaigns were performed to shorten time to hospital presentation before and during the study period.

Interviews with patients and their next of kin or witnesses were conducted within 48 hours of hospital admission to collect data regarding demographic characteristics and circumstances from the onset of symptoms to arrival at the ED of the study hospital. All patients had their stroke severity assessed with the NIHSS, with scores ranging between 0 and 38 at admission categorized as mild (0 to 6), moderate (7 to 15), or severe (16 to 38). The NIHSS cutoffs were prespecified and based clinical judgment and suggestion found in the literature.11,12 The design of this study and descriptive analyses have been reported in detail elsewhere.13

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Prehospital delay was defined as time from symptom onset to arrival at the ED of the study hospital. Decision delay, defined as time from the onset of symptoms to decision to seek medical help and thus a component of the prehospital delay, was further examined. Time of symptom onset was defined as the time that patients or bystanders noticed the symptoms. If the symptoms occurred during sleep, the time of symptom onset was considered to be the time when the patient fell asleep. We prospectively chose time windows of different time durations: 27% (95% CI, 20 to 34), 47% (95% CI, 39 to 55), and 53% (95% CI, 47 to 60) for ED arrival within ≤120, 121 to 300, and >300 minutes, respectively (P<0.001 by Kruskal-Wallis test). The relationship between this proportion and the use of EMS or the categorized stroke severity among groups of different arrival times to the ED of the study hospital is described further in the Figure.

Judging from the geographic features, patients could easily present at the ED of the study hospital (or any nearby medical facilities) within 2 hours if they acted to seek medical care within 1 hour of symptom onset. Accordingly, we conducted a logistic analysis, based on the categorization of decision delay within 1 hour or not, to investigate factors significantly affecting decision delay. Table 3 summarizes univariate odds ratios (ORs) for significant factors and adjusted ORs calculated by multivariable logistic regression models. We found that variables that were significantly associated with decision delay in univariate analyses still remained significant in multivariable analyses, but not the other screened explanatory variables.
Because intravenous rtPA is contraindicated for patients 80 years of age in Taiwan, a separated study for patients 18 to 80 years of age was conducted. As shown in Tables 2 and 3, the results did not change materially.

**Discussion**

The results of our study suggest that prehospital delay in patients with acute stroke was considerable in this area (only 26% of patients reached the ED of the study hospital within 2 hours of symptom onset) and that there are long intervals between the onset of symptoms and the initiation of seeking medical help. In particular, we noted that of the 51 patients with prehospital delay within 2 hours, 49 took action to seek medical help within 1 hour. Overall, because this study was conducted before rtPA approval in Taiwan, these findings largely reflect the care-seeking patterns in patients with acute stroke in this area.

Of those 91 patients whose decision delays were <1 hour, 49 patients (54%) arrived at the ED of the study hospital within 2 hours, whereas the proportion was much lower (2 of 105) in patients whose decision delay was >1 hour. Unfortunately, the reasons for the apparent prolonged decision delay were unclear because only limited data were collected. Among the 45 patients who provided this information, 34 (76%) reported that they did not realize the urgency of seeking medical help. Nonetheless, Barber et al. noted that patients who recognized their symptoms might choose not to seek medical attention.

Patients experiencing severe stroke, as measured by NIHSS score at admission, did respond more quickly than patients with less severe stroke. This finding implies that the perceived urgent nature of the illness might be a factor contributing to decreased prehospital delay. Derex et al. reported the same finding in their univariate analysis of admission delay (NIHSS ≥15 versus <15; range, 0 to 42), albeit not in their multivariable analysis. Similar findings

**Table 2. Delay Time by Patient Attributes**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients 18–80 y of Age (n=183)</th>
<th>All Patients (n=196)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Decision Delay</td>
<td>Prehospital Delay</td>
</tr>
<tr>
<td></td>
<td>P*</td>
<td>P*</td>
</tr>
<tr>
<td>Age, y</td>
<td>0.011</td>
<td>0.006</td>
</tr>
<tr>
<td>≥65</td>
<td>120 (45–435)</td>
<td>365 (172–875)</td>
</tr>
<tr>
<td>Arrival through referral</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>60 (30–270)</td>
<td>661 (237–1311)</td>
</tr>
<tr>
<td>No</td>
<td>115 (15–390)</td>
<td>190 (82–517)</td>
</tr>
<tr>
<td>Arrival by EMS</td>
<td>0.044</td>
<td>0.007</td>
</tr>
<tr>
<td>Yes</td>
<td>55 (16–139)</td>
<td>232 (132–754)</td>
</tr>
<tr>
<td>No</td>
<td>120 (30–420)</td>
<td>365 (106–867)</td>
</tr>
<tr>
<td>NIHSS score at admission</td>
<td>0.009</td>
<td>0.046</td>
</tr>
<tr>
<td>&lt;7</td>
<td>180 (30–510)</td>
<td>475 (111–964)</td>
</tr>
<tr>
<td>7–15</td>
<td>60 (15–240)</td>
<td>317 (122–776)</td>
</tr>
<tr>
<td>&gt;15</td>
<td>35 (15–143)</td>
<td>182 (98–428)</td>
</tr>
</tbody>
</table>

Values are median (25th–75th percentile) and are given in minutes.
*Measured by Mann-Whitney U test or Kruskal-Wallis test; only significant values are reported.
have been reported in studies using different measures of stroke severity.16

Many studies have found that the use of EMS could shorten prehospital delay.3,4,6,7,12,13 However, prehospital delay was not influenced by the use of EMS in this study or in another study done in other areas of Taiwan.7 Because of the extensive network of hospitals and clinics in the Taiwan area, the transportation time to medical facilities is minimal. For the 44% of patients referring from other medical facilities, the reported mean transportation time to the first contacted medical facilities was 14 minutes (median, 10 minutes; interquartile range, 5 to 20 minutes). Overall, the reported mean transportation time from the location of onset or the first visited medical facilities (if applicable) to the study hospital was 40 minutes (median, 30 minutes; interquartile range, 20 to 45 minutes). Thus, what made a difference was whether patients or bystanders responded quickly enough in seeking medical care, rather than the use of EMS.

If patients arrived through referral, prehospital delay was, naturally, significantly increased (Table 2). Nevertheless, if the first visited medical facilities could be readily available for acute stroke therapy, ≈50% of the study patients could be screened for thrombolytic therapy because the intravenous thrombolysis has been indicated in Taiwan since November 2002.

In this study, advanced age was significantly associated with increased delay time. In contrast, Lacy et al8 reported that patients ≥65 years of age were more likely to arrive earlier than were younger patients. However, most studies did not find that age was a factor influencing prehospital delay.3,6,7,15,16 Reasons for the increased delay in seeking hospital treatment among the elderly may be due partially to negative previous experiences with hospital treatment. On the other hand, patients ≥65 years of age have been reported to be less likely to know a symptom of stroke than their younger counterpart.17 Consequently, how to help the elderly have timely presentation for rtPA treatment is an unavoidable challenge in this aging society.

Our study indicated that patients who already had a prior stroke did not appear to take quicker action in seeking medical help, nor did patients with comorbidity (ie, hypertension, diabetes mellitus, or hypercholesterolemia). A partial explanation for this may be that, before rtPA was approved for use in ischemic stroke in Taiwan, there were few benefits or incentives for earlier presentation. It could also be due to patients’ misperception of the seriousness of symptoms. Since rtPA therapy has been approved in Taiwan, this finding highlights the urgent need for educating this high-risk group.

In a previous analysis,13 we categorized beforehand prehospital delay >2 hours to examine factors affecting increased delay. In this study, a different approach was taken that allowed us to identify, among others, the crucial role of decision delay. These findings can guide educational strategies to effectively reduce delay time. However, we need to further explore patients’ or caregivers’ general knowledge of stroke, their interpretation of stroke symptoms, and how these affect the decision to seek medical care after rtPA is available.17–19 From our study, because of the medical infrastructure in the Taiwan area, use of EMS is unlikely to have any critical impact on reducing prehospital delay, at least not in the near future. Studies addressing the determinants for stroke patients to use or not to use EMS are essential for the health policy.

In conclusion, the time interval between the onset of symptoms and the decision to call for medical care is far from optimal in patients with acute stroke and is the underlying cause of the prolonged prehospital delay. This is especially true for older patients. Because early presentation is a prerequisite for thrombolysis for acute ischemic stroke, educational programs that increase public awareness of the need to seek medical help promptly after stroke may be most successful in reducing the delay for hospital presentation.

References

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