Factors Associated with the Administration of Tissue Plasminogen Activator for Acute Ischemic Stroke

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Background: The use of intravenous tissue plasminogen activator (t-PA) can be an effective treatment for acute ischemic stroke if administered promptly. Despite its clinical effectiveness, overall use in Japan remains low, and regional variations have been reported. Factors such as ambulance utilization and geographical distance from patients' residences to hospitals may influence t-PA administration rates. The aim of this study is to identify factors associated with the administration of t-PA for acute ischemic stroke while adjusting for casemix using a large-scale administrative database in Japan. *Methods:* We analyzed acute ischemic stroke patients admitted to acute care hospitals between July 2010 and March 2011 using a nationwide database. A logistic regression model was used to analyze the factors influencing t-PA administration. Candidate factors included patient gender, age, stroke severity, direct distance between each patient's residence and admitting hospital, and ambulance utilization. *Results:* Of the 10,615 ischemic stroke patients from 89 hospitals analyzed, 557 (5.2%) received t-PA treatment. Patients aged 75 years and older were found to be associated with decreased t-PA administration. In contrast, severe stroke and ambulance utilization were associated with increased t-PA administration. Distance was not significantly associated with the use of t-PA. *Conclusions:* Our findings suggest that ambulance utilization is an important factor for improving the likelihood of t-PA administration in patients with stroke and may underline a need for educational programs to the general public that promote the use of ambulances for suspected stroke patients. **Key Words:** Stroke—tissue plasminogen activator—health services accessibility—ambulances—risk adjustment.

Introduction

The use of intravenous tissue plasminogen activator (t-PA) was approved as a treatment for acute ischemic stroke in Japan in October 2005. Although utilization rates have gradually increased after its first application, the overall use remains low, and regional variations have been reported.[1] Opportunities to administer t-PA are limited as guidelines recommend the use of intravenous t-PA

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only to patients within a few hours of acute ischemic stroke onset.[2-5]

Because the use of t-PA is dependent on the elapsed time after stroke onset, emergency medical service infrastructure and geography are important factors to consider in an analysis of this treatment. Variations in these factors can directly affect the time duration from onset to treatment and may result in regional health disparities that need to be addressed from a public health perspective. Although the factors that influence t-PA administration have been previously investigated, these studies have generally been conducted using relatively small sample sizes.[6-8] A previous study has reported an association between the use of ambulance transportation and acute stroke intervention in young adults,[7] with the stated caveat that the limitations of small sample size and lack of stroke severity data may have affected the observed results. Additionally, the association between the distance from patient's residence to hospital and t-PA utilization has also been reported.[8-10] However, the results concerning the relationship between patient's travel distance and delayed hospital arrival are inconclusive as other researchers have reported no association between these 2 factors.[11] Understanding the effects of ambulance use and geographical distance between patient's residence and hospital on the likelihood of t-PA use is essential to improve stroke care from political and social perspectives. To do so, an analysis based on a relatively large sample size comprising numerous hospitals of different sizes and infrastructures that are located throughout various regions would yield results with greater external validity.

Since the introduction of the hospital reimbursement system known as the Diagnosis Procedure Combination (DPC) per-diem payment system in Japan in 2003, hospitals using this system routinely generate the DPC data for each patient per hospitalization for reimbursement purposes. From July 2010 onward, the DPC per-diem payment system has required the collection of additional information such as patient's residence postal code, neurologic deficits, and date of stroke onset for patients admitted for stroke. These data are uniformly formatted, which allows researchers to collect, manage, and analyze large quantities of administrative data from numerous hospitals located nationwide. Furthermore, the recent inclusion of factors reflecting disease severity such as patient consciousness and physical impairment levels in this database supports analyses that take into account critical differences in patient casemix.

An extensive investigation of the associations between t-PA use and the factors of ambulance use and geographical distance from patient's residence to hospital in Japan has not yet been conducted. Therefore, the objective of this study was to investigate the influence of these and other factors on t-PA administration using a large administration database in Japan.

Methods

Study Design and Setting

We used a nationwide database maintained by the government and public research funds. This database comprises data from more than 300 hospitals distributed across Japan and includes a variety of public and private hospitals, with varying teaching statuses, case volumes, casemix, and specialties. In addition to hospital identifier codes, patient identifier codes, and DPC codes, the DPC data also include items such as principal diagnosis and other medical and demographic information such as gender, date of ischemic stroke onset, consciousness and physical impairment levels at admission, postal code of patient's residence, and information regarding whether the patient arrived at the hospital by ambulance. The postal code for each patient's residence and the address for the hospital to which they were admitted were geocoded to longitudinal and latitudinal co-ordinates using MarketPlanner 2.5.1 (PASCO Corporation, Tokyo, Japan) and Geocoding Tools & Utilities (Center for Spatial Information Science, Tokyo, Japan)[12]; the direct distances between the 2 were then calculated. We estimated the average error of the distance when using the postal code as a substitute for patients' addresses to be less than 1 km, by applying the following formula for each city:

$$\sqrt{\frac{(\text{inhabitable area})}{3.14 \times (\text{number of postal codes})}}$$

The average radius of each postal code was calculated to be .68 km (±.34 SD).

Data Selection

Using the DPC database, we identified and extracted acute ischemic stroke cases discharged between July 2010 and March 2011. The criteria for identification of acute ischemic stroke were cases with (1) "010060" as the first 6 digits of the 14-digit DPC code; (2) an *International Classification of Diseases, Tenth Revision*, "I63$" as the principal diagnosis code; and (3) stroke onset occurring either on the day before or on the day of admission. We limited the analysis to patients residing within 50 km from the admitting hospital. Cases that were administered t-PA were identified by the number "4" in the 12th digit of the DPC code. Because not all hospitals are equipped to provide t-PA treatment,[2] we further limited our analysis to include only hospitals that had administered t-PA to 1 or more patients during the study period. Only cases with complete information for the variables of interest were retained for analysis. Consequently, a total of 10,615 cases from 89 hospitals were included in the analysis.