Hospital-Based Study of the Care and Cost of Acute Ischemic Stroke in Japan

Yukihiro Yoneda, MD; Toshiyuki Uehara, MD; Hiroshi Yamasaki, MD; Yasushi Kita, MD; Masayasu Tabuchi, MD; Etsuro Mori, MD

Background and Purpose—To evaluate the current status of care and cost of acute ischemic stroke in Japan, we performed a hospital-based analysis at a tertiary emergency hospital with a 24-hour neurology-neurosurgery team and care unit.

Methods—During the 12-month period of October 2000 to September 2001, we collected data on 179 patients consecutively hospitalized with acute ischemic stroke within 7 days of onset. We examined demographic data, in-hospital care, length of hospital stay, outcome at discharge, and hospital costs. The medical cost data were collected from official hospital medical cost charts, which calculated direct medical costs for beds, staff, examinations, medications, and rehabilitation.

Results—The mean age was 70 years, and 69% were male. Hospital arrival was within 3 hours of onset in 30% of the patients. A history of stroke was present in 37%. The mean initial National Institutes of Health Stroke Scale score was 8.3 points (median, 6 points). Using the Trial of Org 10172 in Acute Stroke Treatment classification, 25% were lacunar, 27% were atherothrombotic, 33% were cardioembolic, and 15% were of unknown origin. All patients underwent neuroimaging studies during hospitalization; 96% and 92% underwent CT and MRI with MR angiography, respectively. Antithrombotic medications were given in 94%, none of whom received thrombolysis. A newly licensed neuroprotective agent, edaravone, was given in 16%. More than half of the patients (55%) were initially admitted to the neurological intensive care unit. Overall, 64% received in-hospital rehabilitation. Mean length of stay was 33 days. In-hospital mortality rate was 3%. On the modified Rankin Scale (mRS), 63% were independent (mRS, 0 to 2) and 34% were dependent (mRS, 3 to 5) at discharge. Two thirds of the patients (65%) went directly back home. The mean hospital cost per patient was $6887 ($209/d), of which 69% was attributable to the costs for beds and staff, 12% for medications, 7% for rehabilitation, 6% for imaging studies, 5% for laboratory examinations, and 1% for other costs.

Conclusions—Despite the single hospital-based analysis, this study provided current, precise data on short-term inpatient care and costs of acute ischemic stroke in Japan. Because stroke often carries a permanent dependence, long-term cost-effective stroke care should be established. (Stroke. 2003;34:718-724.)

Key Words: costs and cost analysis ■ economics ■ Japan ■ stroke
onset. The median delay from hospital arrival to initial diagnostic CT was 32 minutes, which was a relatively acceptable figure for accessing immediate clinical diagnosis and treatments. In this study, together with referral systems, we examined the latest 12-month data on hospital care, outcomes, and costs for acute ischemic stroke at our hospital.

**Methods**

This study was carried out during the 12-month period between October 2000 and September 2001 at the Neurology Service of the Hyogo Brain and Heart Center at Himeji, Japan. The Institutional Review Board approved this study without assessment because the study design maintained patient anonymity and did not affect human rights.

**Subjects**

During the study period, a total of 222 patients with a final diagnosis of acute ischemic stroke (n = 194) or transient ischemic attack (n = 28) seen within 7 days of symptom onset were admitted to Neurology Service for treatment and evaluation. Among ~600 patients admitted annually to Neurology Service for various neurological disorders, stroke is the leading cause. Of the 222 patients, 28 patients with transient ischemic attack and 15 with in-hospital ischemic stroke were excluded from this study. Therefore, this study comprised 179 patients with acute ischemic stroke.

**Hospital Characteristics**

Our hospital with 350 beds is a 24-hour–service tertiary emergency hospital for acute cardiovascular and cerebrovascular diseases situated in Himeji, which has a population of nearly half a million and an area of 275 km². Our hospital covers Himeji and surrounding smaller cities and towns. The 24-hour neurology-neurosurgery team consisted of 7 neurology and 5 neurosurgery staff members with access to 4 neurological intensive care beds and 48 neurology and 43 neurosurgery ward beds. In-hospital rehabilitation included physiotherapy and speech therapy. One neurologist and 1 neurosurgeon are on duty and on call outside working hours. At least 1 technician is on night duty, and neuroradiological facilities available 24 hours include CT and angiographic system. MRI with the capability of MR angiography and single photon emission CT are available only during working hours.

**Prehospital Delay and Mode of Transportation**

The prehospital delay was evaluated by time from symptom onset to arrival at the emergency room or outpatient clinic. For patients with unknown time of stroke onset (eg, nocturnal onset of stroke), onset time was conservatively defined as the time that the patient last was neurologically asymptomatic. The mode of transportation was evaluated as follows: direct ambulance transportation by Emergency Medical Service, referral from general practitioners or hospitals, and individual visits (alone or accompanied) by means of public transport or family car.

**Stroke Severity**

Stroke severity on admission was assessed by an attending neurologist using the National Institutes of Health Stroke Scale (NIHSS), ranging from 0 (asymptomatic) to 42 points (maximum score).

**Subtype of Ischemic Stroke**

Based on the clinical, neuroradiological, cardiac, and hematological profiles, the subtype of ischemic stroke was classified according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) categories: small-artery (lacunar) atherosclerotic; large-artery atherosclerotic (atherothrombotic), including artery-to-artery embolism; cardioembolic; and unknown origin or unclassified. The subtype of ischemic stroke was determined by agreement of all neurologists.

**In-Hospital Care**

Measures of hospital care included delayed time from hospital arrival to initial diagnostic brain CT, type of wards that the patient was admitted to in either the neurological intensive care unit or the neurology-neurosurgery wards, medications, rehabilitation programs, and length of hospital stay.

For patients with suspected acute ischemic stroke on the initial CT, antithrombotic medications were initiated as early as possible, unless antithrombotic medications were contraindicated. The anticoagulant medications included intravenous unfractionated heparin, intravenous argatroban (a selective thrombin inhibitor), and warfarin. The antiplatelet medications included intravenous sodium oxagrel (an inhibitor of thromboxane A₂ synthetase), aspirin, and occasionally ticlopidine. In Japan, thrombolysis with tissue plasminogen activator has not yet been approved. In June 2001, edaravone, an antioxidant neuroprotector that inhibits free radicals, was approved for acute ischemic stroke within 24 hours of onset. In-hospital rehabilitation was given according to the patient’s neurological deficits by the neurologist in charge. The team, consisting of neurologists, rehabilitation staff, a social worker, and experienced nurses, had weekly meetings about patient care and discharge plans. In calculations of the length of hospital stay for patients who were subsequently transferred to other in-hospital departments, the stay in other departments was included.

**Outcomes at Discharge**

Functional outcomes at discharge were evaluated by the modified Rankin Scale (mRS) and discharge destinations. Favorable outcome was defined as independence (mRS, 0 to 2); poor outcome was defined as dependence (mRS, 3 to 5) and death (mRS, 6).

**Hospital Costs**

Data on hospital cost were collected from the official hospital medical cost charts. These charts calculated direct medical costs for beds, staff, examinations, medications, rehabilitation, and miscellaneous expenses such as commissions for official medical certificates. Costs for meals were not included. Costs for intensive care beds, ward beds, and staff were officially fixed according to the hospital category; our hospital was in the highest class. Regardless of the hospital class, the costs for laboratory examinations, imaging studies, and medications were also officially fixed. Rehabilitation costs were determined according to the classification of rehabilitation unit; our rehabilitation unit was in the second class. Physician fees were included separately in each component of medical costs. As in other studies, the costs calculated in the Japanese yen (¥) were then converted to the US dollar by use of an exchange rate of $1 = ¥150 according to the purchasing power parities of the 2001 fiscal year on the OECD. The purchasing power parities index is an international currency exchange rate that eliminates the difference in value of the products.

**Statistical Analysis**

Pearson’s correlation test was used to examine the correlation between costs and other variables. The significance level was set at P < 0.05. Patients were then divided into 4 groups according to the TOAST clinical categories. To compare variables among groups, Kruskal-Wallis test with posthoc Mann-Whitney U test, 1-way analysis of variance with posthoc Sheffe’s test, or χ² test was computed with Bonferroni’s correction for multiple comparisons. The analyses were computed with StatView version 5.0 (SAS Inc).

**Results**

Demography, hospital care, outcomes, and costs for 179 patients are summarized in Tables 1 through 3.

**Demography and Prehospital Care**

The mean age was 70 years, and 117 (69%) patients were male. Fifty-four patients (30%) arrived within 3 hours of onset, and overall, 69 patients (39%) and 115 patients (65%)...
arrived within 6 and 24 hours, respectively. See Table 1 for details.

### Stroke Severity and Subtype of Ischemic Stroke

The mean and median NIHSS scores on admission were 8.3 and 6 points, ranging from 1 to 38 points, respectively (Table 1). From the TOAST clinical categories, 44 patients (25%) were lacunar, 49 (27%) were atherothrombotic, 59 (33%) were cardioembolic, and 27 (15%) were unknown or unclassified origins of stroke.

### In-Hospital Care

Of the 179 patients, 142 (80%) were initially transferred to the emergency room, and the remaining 37 (20%) arrived at the outpatient clinic (Table 2). The mean and median delays from hospital arrival to initial CT were 39 and 30 minutes, respectively. By decision of an attending neurologist, 99 patients (55%) were initially admitted to the neurological intensive care unit (mean length of stay, 4.7 days) but subsequently transferred to the neurology ward.

During hospitalization, all patients underwent neuroimaging studies of CT, MRI, or both; 171 (96%) and 164 (92%) underwent CT and MRI with MR angiography, respectively. Overall, 142 patients (80%) underwent transthoracic or transesophageal echocardiography during hospitalization (n = 107) or previously (n = 35) at our hospital.

Antithrombotic medications were given in 172 patients (94%), and a newly licensed neuroprotector, edaravone, was given in 29 (16%). Overall, 114 patients (62%) received in-hospital rehabilitation.

The mean and median lengths of hospital stay were 33 and 24 days, respectively. Overall, 12 patients (7%) were transferred to other departments for concomitant disorders after acute treatment in the neurology service.

### Outcome at Discharge

In-hospital mortality (mRS, 6) was 3% (6 patients) (Table 2). One hundred twelve patients (63%) were independent (mRS, 0–2) and 12 (6%) were dependent (mRS, 3–5).

### Costs

The mean cost per patient was $6887 (¥1 033 120) (Table 3), with a range of $469-$34 415. The mean daily cost per patient was $209 (¥31 340).

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**TABLE 1. Demography for 179 Patients**

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Male (%)</th>
<th>Female (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HT/DM/HL/AF</td>
<td>66%</td>
<td>34%</td>
</tr>
<tr>
<td>History of stroke</td>
<td>66 (37%)</td>
<td>43 (63%)</td>
</tr>
</tbody>
</table>

**TABLE 2. Hospital Cares and Outcomes for 179 Patients**

<table>
<thead>
<tr>
<th>NIHSS, mean (median)</th>
<th>CT, min</th>
<th>NICU/wards, %</th>
<th>Thrombolysis/thrombectomy, %</th>
<th>Neuroprotection, %</th>
<th>Rehabilitation, %</th>
<th>Discharge destinations, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.3 (6)</td>
<td>39 (30)</td>
<td>99 (55%)</td>
<td>0%</td>
<td>29 (16%)</td>
<td>114 (64%)</td>
<td>56 (31%)</td>
</tr>
</tbody>
</table>

**TABLE 3. Direct Medical Costs for 179 Patients**

<table>
<thead>
<tr>
<th>Cost Category</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>For beds and staffs</td>
<td>$4747</td>
</tr>
<tr>
<td>For medications</td>
<td>$853</td>
</tr>
<tr>
<td>For imaging studies</td>
<td>$426</td>
</tr>
<tr>
<td>For laboratory exams</td>
<td>$335</td>
</tr>
<tr>
<td>For miscellaneous</td>
<td>$45</td>
</tr>
<tr>
<td>Mean daily cost</td>
<td>$209</td>
</tr>
</tbody>
</table>

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AF indicates atrial fibrillation; DM, diabetes mellitus; GP, general practitioner; HL, hyperlipidemia; and HT, hypertension.
0 to 2) at discharge, and 61 (34%) were dependent (mRS, 3 to 5). One hundred seventeen patients (65%) went directly back home, and 56 (31%) were transferred to other hospitals or care homes.

### Hospital Costs

The mean and median hospital costs per patient were $6887 and $5017, respectively (Table 3). The mean daily cost per patient was $209. Of the total costs, $4747 (69%) was attributable to the costs for beds and staff, $853 (12%) for medications, $481 (7%) for rehabilitation, $426 (6%) for imaging studies, $335 (5%) for laboratory examinations, and $45 (1%) for other costs. Total hospital costs were correlated strongly with length of stay (r = 0.894, P = 0.0001) and moderately with initial NIHSS score (r = 0.484, P = 0.0001) but not with age (r = 0.137, P = 0.67).

### Variables among Stroke Subtype

Table 4 summarizes data on the TOAST clinical categories. The following variables were significantly different among the 4 groups: arrival within 3 hours of onset, initial NIHSS score, type of admission ward, proportion of rehabilitation, and mean and daily costs. The proportion of arrival within 3 hours of onset was significantly higher in cardioembolic stroke than lacunar (P = 0.001) or atherothrombotic (P < 0.001) stroke. The initial NIHSS score was significantly higher in cardioembolic stroke (P < 0.001) than lacunar stroke. The admission rate to the neurological intensive care unit was significantly higher in cardioembolic (P = 0.001) and atherothrombotic (P < 0.001) stroke than in lacunar infarction. More patients with atherothrombotic stroke (P < 0.001) received rehabilitation than those with lacunar infarction. The mean hospital cost in cardioembolic stroke was significantly higher (P = 0.001) than in lacunar infarction.

### Discussion

This study is, to the best of our knowledge, the first to systematically examine hospital care, outcomes, and costs of acute ischemic stroke in Japan.

### Prehospital Referral Systems

Of the 179 patients with acute ischemic stroke within 7 days of onset, 30% and 39% overall arrived at our hospital within 3 and 6 hours, respectively. In our previous study that surveyed during an 18-month period (January 1998 through June 1999), 32% and 40% overall, including 3% with in-hospital ischemic stroke, arrived within 3 and 6 hours, respectively. Because the therapeutic time window for acute ischemic stroke is very narrow in the first few hours, further efforts are necessary to reduce the prehospital delay in our community as described previously.

### In-Hospital Care

Stroke care in our hospital would be classified as a type of stroke unit, fulfilling the guidelines for a primary stroke center proposed by the Brain Attack Coalition in the United States. Our hospital is equipped with a 24-hour neurology-neurosurgery team with access to neurological intensive care.
beds and facilities such as CT, angiograms, and routine laboratory examinations available 24 hours a day. The mean delay time from hospital arrival to initial CT was 39 minutes (median, 30 minutes), which was comparable to or even shorter than that in stroke centers in the United States,29,30 and Europe.13,18,22

In this study, 55% of the patients were initially admitted in the neurological intensive care unit with the mean length of stay of 4.7 days. The criteria to admit stroke patients to the neurological intensive care unit were not clearly predefined, but patients with severely reduced level of consciousness, those who required continuous cardiac monitoring, and those with massive infarction were usually admitted in the neurological intensive care unit. Further studies are necessary to establish the role of the intensive care unit in acute stroke, including the cost-effectiveness.41

**Length of Stay**

The mean length of hospital stay in this study was 33 days, which was considerably longer than that in academic and community hospitals in the United States17,21,26 (Table 5) and comparative to or slightly longer than that in stroke centers in Europe,13,18,22–24 A difference in hospital type or healthcare systems between Japan and other communities may largely account for the difference in length of stay. In Japan, stroke centers have generally provided care for the acute and subacute phases of stroke. Furthermore, application of the diagnosis-related group and prospective payment system may limit a longer hospitalization in the United States, whereas the healthcare system in Japan principally covers the hospital costs with limited patient fees, regardless of length of stay or type of diseases.

**Outcomes**

In this study, 63% of the patients became functionally independent (mRS, 0 to 2) at discharge, and 65% went directly back home. In-hospital mortality was only 3%. Although initial stroke severity was relatively mild (8.3 points on the mean NIHSS), functional outcomes were favorable in this study. This may indicate relative feasibility in the management of acute ischemic stroke at our hospital.

**Insurance Systems and Costs**

In Japan, all residents are insured primarily by either the National Healthcare Insurance or the Social Healthcare Insurance.9 The National Healthcare Insurance is a semigovernmental organization, whereas the Social Healthcare Insurance is company-based insurance systems. The 2 main medical insurance systems have reimbursed 70% to 90% of the hospital medical costs to hospitals in accordance with the type of healthcare insurance. Thus, any individuals can receive medical care with limited charges. Currently in Japan, patients ≥70 years of age are principally charged 10% of total hospital costs with a monthly ceiling fee of $250 (¥37,500), although previously the services were free. On the other hand, patients <70 years of age are charged 20% to 30% of the total costs with a monthly ceiling fee of $417 (¥62,500), according to the type of healthcare insurance and economic status.

Although a direct comparison is not possible, total and daily medical costs of acute ischemic stroke in our study were lower than those in the United States, which in previous studies, in which stroke severity influenced medical costs, the milder stroke severity in our study may partly account for the differences. However, a difference in other factors such as medical care and healthcare systems would be also involved. In this study, the cost for beds and staffs was 69% of the total direct medical costs compared with 50% in an academic center in the United States.21 In contrast, the cost for imaging studies was only 6% in our study, compared with 19% in the United States.21 The higher proportion of the unit costs in our study may be explained by the longer hospitalization (33 days).

In this study, total hospital costs were correlated strongly with length of stay and moderately with initial stroke severity. As in a previous study,14 an effort to decrease the length of hospital stay may contribute to a reduction in hospital costs. However, because stroke patients often are permanently dependent after acute hospitalization, a cost analysis of

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**TABLE 5. Comparison of Hospital Cares and Costs for Acute Ischemic Stroke Between This Study and Hospitals in the United States**

<table>
<thead>
<tr>
<th></th>
<th>Japan</th>
<th>United States</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HBHC</td>
<td>St Louis17</td>
</tr>
<tr>
<td>No. of patients</td>
<td>179</td>
<td>191</td>
</tr>
<tr>
<td>Mean age, y</td>
<td>70</td>
<td>71</td>
</tr>
<tr>
<td>Mean initial NIHSS</td>
<td>8.3</td>
<td>10.4</td>
</tr>
<tr>
<td>Mean LOS, days</td>
<td>33</td>
<td>8</td>
</tr>
<tr>
<td>Discharge to home</td>
<td>65%</td>
<td>42%</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Mean hospital cost per patient, US$</td>
<td>6887 (4408)</td>
<td>12,626*</td>
</tr>
<tr>
<td>Mean daily cost per patient, US$</td>
<td>209 (551)</td>
<td>1323*</td>
</tr>
</tbody>
</table>

HBHC indicates Hyogo Brain and Heart Center at Himeji; LOS, length of hospital stay. Parentheses indicate median figures of the costs are only available.21

*Adjusted figures26 using the Medical Component of the Consumer Price Index of 1998 from the original data of 1992.27
long-term care would be necessary, as pointed out in other studies.\textsuperscript{12,13,15,20,22–25}

In other studies,\textsuperscript{12,15,19,25} indirect costs estimating a loss of productivity were analyzed with the direct costs. In this study, however, we did not examine the indirect costs because calculation of the indirect costs should be based on estimation, which is complex and difficult.\textsuperscript{12} Even direct costs were estimated in the analyses in some studies,\textsuperscript{12–15,18,19,22,23} whereas the hospital costs in our study were actually direct medical costs, including physician fees.

In this study, we did not examine data on patients with hemorrhagic stroke because such patients are treated in the neurosurgical department at our hospital. The costs for patients with hemorrhagic stroke have been reported to be higher than for those with ischemic stroke.\textsuperscript{15,17,26}

**Subtype of Ischemic Stroke**

In this study, we used the TOAST classification for clinical categorization of ischemic stroke.\textsuperscript{32} During hospitalization, all patients underwent neuroimaging with CT and/or MRI scans, and 92\% underwent vascular imaging with MR angiography and/or angiograms. Overall, 80\% underwent echocardiography to document potential sources of emboli. This indicates a high accuracy in the classification of ischemic stroke in this study.

The proportion of cardioembolic stroke in this study was considerably higher than that in other studies (up to 25\% of all ischemic strokes).\textsuperscript{32} This is probably due to the fact that our hospital is classified as a tertiary medical center for brain and heart diseases. Despite the earlier presentation to hospital, patients with cardioembolic stroke had more severe neurological deficits and poorer outcomes with higher medical costs, as in a previous study.\textsuperscript{22} More severe initial neurological deficits may account for more resource utilization, relatively longer hospitalization, and the higher costs in cardioembolic stroke.

**Study Limitations**

This study was a single hospital-based analysis of care and costs of acute ischemic stroke in Japan. Because community-based or nationwide studies are apparently more representative, further studies are necessary to evaluate general clinical data of stroke care and cost in Japan. In this study, we could not exclude some unintentional bias in patient care because all physicians involved in this study were fully aware of the study designs. In addition, we did not have strict guidelines for examinations, medications, rehabilitation, and discharge, which depended primarily on the decision of the physician in charge. To minimize variations, we performed weekly multidisciplinary meeting on care and discharge planning.

**Conclusions**

Despite the single hospital-based analysis, this study provided current precise data on short-term inpatient care and costs for acute ischemic stroke in Japan. Although the management of acute ischemic stroke in our hospital appears reasonable, nationwide studies and community-based surveys are necessary in Japan. Because stroke often results in permanent dependence, long-term, cost-effective stroke care should be established.

**Acknowledgments**

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**References**


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