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Original Article

# Risk Factors for In-Hospital Mortality among Ischemic Stroke Patients in Southern Taiwan☆

Cheung-Ter Ong [1,3*], Sheng-Feng Sung [1], Yi-Sin Wong [2], Chi-Shun Wu [1], Yung-Chu Hsu [1], Yu-Hsiang Su [1], Chen-Hsien Li [1], Ling-Chien Hung [1]

[1] Department of Neurology, [2] Department of Family Medicine, Ditmanson Medical Foundation Chia-Yi Christian Hospital, [3] Department of Nursing, Chung Jen Junior College of Nursing, Health Science and Management, Chia-Yi, Taiwan, ROC

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SUMMARY

*Background/purpose:* The in-hospital mortality rates of patients with acute ischemic stroke remain between 3% and 18%. For improving the quality of stroke care, we investigated the factors that contribute to an increased risk of in-hospital mortality in patients with acute ischemic stroke.
*Methods:* A total of 2556 patients with acute ischemic stroke, who were admitted to a stroke unit between January 1, 2007 and December 31, 2011, were included in this study. Factors such as demographic and clinical characteristics, comorbidities, and complications related to in-hospital mortality were assessed.
*Results:* Of the 2556 ischemic stroke patients, 157 received thrombolytic therapy. Eighty of the 2556 patients (3.1%) died during hospitalization, which included 14 (8.9%) patients who received thrombolytic therapy. A history of heart disease ($p < 0.01$) and stroke severity ($p < 0.01$) were independent risk factors, whereas herniation, sepsis, and basilar artery occlusion were the most common causes of in-hospital mortality. Approximately 70% of in-hospital mortality was found to be related to stroke severity (total middle cerebral artery occlusion with herniation, basilar artery occlusion, and hemorrhagic transformation). The remaining 30% of in-hospital mortality is attributable to sepsis, heart disease, and other complications.
*Conclusion:* Nearly 30% of in-hospital mortality is associated with preventable factors. The prognosis of acute stroke can be improved by increased focus on reducing serious complications after stroke, particularly on the prevention of infection, heart disease, and increased intracranial pressure.


## 1. Introduction

Stroke is one of the chief causes of death and disability worldwide. A study conducted in Taiwan showed that the in-hospital mortality rates of patients with ischemic and hemorrhagic strokes were approximately 6–8% and 22–45%, respectively[1], whereas the corresponding rates were 8.8% and 29.8%, respectively, according to another study conducted in Asia[2]. These studies, however, were conducted prior to the optimization of stroke units and before intravenous recombinant-tissue plasminogen activator (rt-pa) was approved for use in acute stroke patients.

In recent years, important advances have been made in the management of acute stroke patients, including the availability of stroke units in several hospitals[3,4] and administering rt-pa to stroke patients who are compatible with thrombolytic therapy guidelines[5,6]. Previous studies have reported significant improvements in patient outcome and in-hospital mortality rates upon treatment of patients in stroke units[3,4]. However, intravenous rt-pa is known to improve outcome in stroke patients but not stroke-associated mortality[5]. Despite these advances in stroke management, the in-hospital mortality rate of stroke patients remains between 3% and 18%[4,6–10].

The purpose of the current study was to identify the predictors of in-hospital mortality among ischemic stroke patients who were treated in stroke units, and to analyze the medical and neurological complications associated with in-hospital fatality.

☆ Conflicts of interest: All contributing authors declare that they have no conflicts of interest.

* Correspondence to: Dr Cheung-Ter Ong, Department of Neurology, Chia-Yi Christian Hospital, 539 Chung-Shao Road, Chia-Yi, Taiwan 600, ROC.
*E-mail address:* ctong98@yahoo.com.tw (C.-T. Ong).

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## 2. Materials and methods

### 2.1. Data collection

Data were prospectively collected during stroke registration from patients with acute ischemic stroke, who were admitted to the Department of Neurology in Chia-Yi Christian Hospital between January 1, 2007 and December 31, 2011. Chia-Yi Christian Hospital is a 1000-bed acute-care teaching hospital in southern Taiwan, where more than 750 patients with acute ischemic stroke are treated every year. All patients with acute neurological symptoms were initially attended to in the emergency department. After neurological evaluation, cranial computed tomography (CT) scan or magnetic resonance imaging (MRI) was performed, and stroke patients were admitted to the stroke unit, which is part of the Department of Neurology. Complete blood count, biochemistry profile, chest radiography, and 12-lead electrocardiography were performed at the emergency department. Fasting blood sugar, cholesterol, and triglycerides were evaluated on the day following admission, and neurological examination was performed every day. The National Institutes of Health Stroke Score (NIHSS) and modified Rankin score (mRS) were used for evaluating stroke severity and outcome, respectively. Good and poor outcomes were defined as mRS $\leq$ 2 and mRS > 2, respectively. The four subtypes of stroke include large artery atherosclerosis ($n = 634$), small vessel occlusion ($n = 922$), cardioembolism ($n = 387$), and undetermined etiology ($n = 613$). Only patients with ischemic stroke were included in the current study, and those presenting with transient ischemic attack, intracerebral hemorrhage, and subarachnoid hemorrhage were excluded. Other exclusion criteria were not applied during patient selection in the present study.

The following information was recorded for each patient: demographic data (age, sex, and body mass index), vascular risk factors (hypertension, diabetes mellitus, atrial fibrillation, hyperlipidemia, smoking, and heart disease), stroke severity score (NIHSS), neuroimaging, carotid duplex, and outcome. Variables that affect the outcome of stroke were assessed. Age was categorized as <65 years, 65–74 years, 75–84 years, or >85 years. Hypertension was defined by systolic blood pressure of $\geq$140 mmHg, diastolic blood pressure of >90 mmHg, a self-reported history of hypertension, or use of an antihypertensive agent. Diabetes mellitus was defined by elevated fasting blood glucose, a self-reported patient history of diabetes mellitus, or regular use of antidiabetic medications. Atrial fibrillation was defined by a history of atrial fibrillation or identification of transient atrial fibrillation from an electrocardiogram. Hyperlipidemia was defined by total serum cholesterol levels of >200 mg/dL, or low-density lipoprotein levels of >130 mg/dL, as measured during the acute stage of stroke. Heart disease was defined by a history of ischemic heart disease or congestive heart failure. Increased intracranial pressure (IICP) was defined by the evidence of brain edema, mass effect, or brain shift syndrome in cranial CT or MRI scans, showing an association with clinical deterioration[9]. Transtentorial herniation was defined by brain edema, as seen in cranial CT or MRI scans, associated with acute onset of unilateral or bilateral papillary dilation, loss of reactivity to light, and decline of $\geq$2 points in the Glasgow coma scale score[11]. Hemorrhagic transformation was defined by a sign of hemorrhage on cranial CT or MRI scans[12]. Outcome variables included infection, cardiac or vascular events, and respiratory disease. The causes of death were categorized as transtentorial herniation, pneumonia, cardiac event, sudden death, septicemia, brain stem infarction, unknown, or other causes[13]. For patients who had presented with signs of herniation and sepsis, the cause of death was considered to be stroke (IICP) related if death resulted within 1 week of stroke onset and as sepsis if death occurred after 1 week of stroke onset. The data used in the current study were collected from the acute stroke registry of Chia-Yi Christian Hospital; this study was approved by the Ethics Committee of the hospital.

### 2.2. Statistical analyses

Chi-square and independent (Student) *t* tests were employed for univariate analysis; a $p$ value < 0.05 was considered statistically significant. Logistic regression was used for identifying independent risk factors of in-hospital mortality. Analysis was performed using MedCalc statistical software version 12.3 (MedCalc Software, Ostend, Belgium).

## 3. Results

During the 5-year period covered by this study, 3107 patients with ischemic stroke were admitted to the hospital, and 451 of them were excluded due to a final diagnosis of transient ischemic attack; a total of 2556 patients, therefore, were included in this study. CT scan was performed for all the 2556 patients, whereas both CT and MRI scans were performed for 1362 patients. Clinical characteristics of the enrolled patients are shown in Table 1. The age of the patients ranged from 23 years to 101 years, with a mean age of 69.6 ± 11.9 years; of them, 814 (31.8%), 781 (30.5%), 732 (28.7%), and 229 (9%) patients belonged to the age groups of <65 years, 65–74 years, 75–84 years, and >85 years, respectively. Moreover, 1482 (58%) of the total 2556 patients were men, and the rest (1074 or 42%) were women. Of the 2556 patients, 109 (4.3%) lacked a risk factor, and 432 (16.9%), 755 (29.5%), 664 (26.0%), and 596 (23.3%) had one, two, three, or more than three risk factors of stroke, respectively. The most common risk factors were hypertension (80.3%), followed by hyperlipidemia (55.4%), diabetes mellitus (44%), heart disease (29.5%), stroke history (27.5%), and atrial

**Table 1**
Characteristics of the study population ($n = 2556$).

| Characteristics | Total ($n = 2556$) | Alive ($n = 2476$) | Dead ($n = 80$) | $p$ |
|---|---|---|---|---|
| Age (y), mean (SD) | 69.57 (11.99) | 69.42 (11.98) | 74.12 (12.09) | <0.01 |
| Age (y) | | | | |
| <65 | 818 (32.0) | 805 (32.5) | 13 (16.2) | |
| 65–74 | 779 (30.5) | 760 (30.7) | 19 (23.8) | |
| 75–84 | 730 (28.6) | 695 (28.1) | 35 (43.8) | |
| >85 | 229 (8.9) | 216 (8.7) | 13 (16.2) | |
| Gender | | | | |
| Men | 1482 (58.0) | 1446 (58.4) | 36 (45.0) | 0.02 |
| Women | 1074 (42.0) | 1030 (41.6) | 44 (55.0) | |
| Comorbidity | | | | |
| Diabetes mellitus | 1126 (44) | 1089 (44.0) | 37 (46.3) | <0.01 |
| Hypertension | 2051 (80.3) | 1985 (80.2) | 66 (82.5) | <0.01 |
| Atrial fibrillation | 437 (17.1) | 398 (16.1) | 39 (48.8) | <0.01 |
| Previous stroke | 703 (27.5) | 678 (27.4) | 25 (31.3) | 0.04 |
| Heart disease | 753 (29.5) | 697 (28.2) | 56 (70.0) | 0.08 |
| Hyperlipidemia | 1417 (55.4) | 1384 (55.9) | 33 (41.3) | 0.01 |
| Stroke severity (NIHSS) | | | | |
| ≤5 | 1394 (54.5) | 1388 (56.1) | 6 (7.5) | <0.01 |
| 6–15 | 745 (29.1) | 736 (29.7) | 9 (11.3) | |
| 16–25 | 272 (10.7) | 248 (10.0) | 24 (30.0) | |
| >25 | 145 (5.7) | 104 (4.2) | 41 (51.3) | |
| IICP | 108 (4.2) | 73 (2.9) | 35 (43.8) | 0.2 |
| Stroke subtype | | | | |
| LAA | 634 (24.8) | 607 (24.5) | 27 (33.8) | <0.01 |
| CE | 387 (15.1) | 359 (14.5) | 28 (35.0) | |
| SVO | 922 (36.1) | 920 (37.2) | 2 (2.5) | |
| UN | 613 (24.0) | 590 (23.8) | 23 (28.7) | |

Data are presented as $n$ (%), unless otherwise indicated.
CE = cardioembolism; IICP = increased intracranial pressure; LAA = large artery atherosclerosis; NIHSS = National Institutes of Health Stroke Scale; SVO = small vessel occlusion; UN = undetermined etiology.