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Improving the One-Year Mortality of Stroke Patients: An 18-Year Observation in a Teaching Hospital

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Long-term follow-up and comparison of serial changes in the one-year mortality after stroke are important in assessing the quality of stroke management. This study determined the one-year survival rate and prognostic factors of hospitalized hemorrhagic and ischemic stroke patients from 1991 to 2008 in a teaching hospital in Taiwan. We also evaluated the improvements in the one-year mortality after stroke during an 18-year study period. Patients admitted for cerebral hemorrhage (n = 3,678) and cerebral infarction (n = 16,010), identified from an in-patient electronic database, were linked to the National Death Registry of Taiwan. Actuarial analysis was used to determine the one-year survival rates, and Cox proportional hazard regression model was used to investigate the predictors for the one-year mortality of stroke patients. For patients with cerebral hemorrhage and infarction and who were admitted from 1991 to 2008, the one-year survival rates were 71% and 84%, respectively. In addition, stroke patients who also suffered from myocardial infarction, chronic renal illness, and pneumonia and had high Charlson comorbidity index scores showed increased risks of mortality due to cerebral hemorrhage and infarction. Compared with the patients admitted from 1991 to 1996, those admitted from 1997 to 2002 and from 2003 to 2008 showed 15%-20% and 20%-25% reduction in one-year mortality risk in cerebral hemorrhage and infarction, respectively. This result demonstrates the continuous quality improvement of stroke management in the hospital from 1991 to 2008. Further reduction in one-year mortality can be achieved by early recognition and prompt treatment of certain comorbidities.

Keywords: cerebral hemorrhage; cerebral infarction; mortality; stroke; Taiwan
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Introduction

Stroke is a debilitating condition that has a detrimental effect on the health-related quality of life of patients and also has high economic costs (Norrving and Kissela 2013). This condition has been the third leading cause of death in Taiwan (Ministry of Health and Welfare 2012). The incidence of first-time stroke among Taiwanese over 36 years of age is 330 per 100,000; this value is higher than those reported for the United Kingdom and the United States but is comparable to those of Japan and Mainland China (Hu et al. 1992). A number of studies have reported one-month (Hu et al. 1992; Jeng et al. 1998) or 3-month (Chang et al. 2006) mortality rates of stroke; however, the one-year mortality remains to be investigated in Taiwan. Moreover, previous studies have determined the risk factors for the one-year mortality of stroke in Australia (Anderson et al. 1994), Greece (Vemmos et al. 2000), and Hong Kong (Wong and Li 2003); however, the studies involved only a limited number of study participants. Although a study based on a hospital in Hong Kong (Wong and Li 2003) has reported follow-up studies on patients for a maximum of 42 months, the extent of quality improvement in the one-year mortality of stroke over a long period could not be assessed. The Charlson comorbidity index (CMI) (Charlson et al. 1987) is more than adequate in predicting the functional outcome of stroke patients after case-mix adjustments (Tessier et al. 2008). However, most of the CMI adjusted stroke outcome studies included either ischemic stroke (Goldstein et al. 2004; Fischer et al. 2006) or hemorrhagic stroke (Bar and Hemphill 2011) rather than including both two diseases in the studies.

This hospital-based analysis aims to calculate the one-year mortality rates of hospitalized ischemic and hemor-

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rhagic stroke patients in Far Eastern Memorial Hospital (FEMH), New Taipei City, Taiwan from January 1, 1991 to December 31, 2008, as part of the audit of quality of care delivered to these patients. Particular focus was given to determining whether the one-year mortality rate has improved over the 18-year study period. Moreover, this study attempted to explore the effects of various prognostic factors, such as patient demographics, underlying comorbidities (e.g., CMI), and different years of treatment characteristics, on the one-year mortality risk of stroke patients.

Materials and Methods

FEMH is a 1000-bed teaching hospital in northern Taiwan and has been accredited as a medical center since 2006. From January 1, 1991, this hospital has established an in-patient electronic database, which includes information about patient age, sex, hospital chart number, personal identification number, dates of admission and discharge, and durations of hospital stay. The database also included up to six International Classification of Diseases (ICD-9) discharge diagnosis codes and five ICD-9 procedure codes. We used the electronic database for all patients hospitalized for cerebral hemorrhage (ICD-9: 430, 431) and cerebral infarction (ICD-9: 433, 434, 436), irrespective of the diagnosis (primary or secondary), between January 1, 1991 and December 31, 2008. We extracted each patient's age, sex, length of hospital stay, and underlying diseases ascertained from ICD-9 discharge diagnosis codes. Access to the research data was approved by the Institutional Review Board of FEMH.

To assess the underlying comorbidities for each patient, we used the translation of CMI by Deyo et al. (1992), which was conducted using an ICD-9 administrative database (Charlson et al. 1987). The CMI was calculated by obtaining the sum of the risk weights across the disease categories (Roos et al. 1997). For the potential determinants of mortality risks in patients with cerebral hemorrhage and infarction, we also assessed the common underlying comorbidities and complications for each patient, including diabetes (ICD-9: 250), myocardial infarction (ICD-9: 410, 412), congestive heart failure (ICD-9: 428), chronic obstructive pulmonary disease (ICD-9: 490-496, 500-505, 506.4), chronic renal disease (ICD-9: 582, 583.0-583.7, 585, 586, 588), pneumonia (ICD-9: 480-487, 510, 511.1, 513), and urinary tract infection (ICD-9: 590, 595, 597-599).

From the unique personal identification numbers, we linked the electronic database to the National Death Registry of Taiwan, which contains information on age, sex, dates, and causes of death of the deceased. The mortality registry is considered accurate and complete because of the mandatory registration of all deaths in Taiwan; all death certificates were completed by physicians (Lu et al. 2000). The first day of patient admission to the hospital was used as the index dates for all patients. When the patients were hospitalized for more than one occasion during the study period, the index dates were the first day of the first admission due to each type of stroke. The study endpoint was the death within one-year post-stroke admission. When the patients did not encounter any mortality before 365 days from their admissions, they were censored on the 365th day from the first admissions. The study period was from January 1, 1991 to December 31, 2008.

Actuarial analysis was used to determine the one-year survival rates associated with hemorrhagic and ischemic strokes during the study period. In addition, we divided the 18-year period into three consecutive 6-year periods (1991 to 1996, 1997 to 2002, and 2003 to 2008) and compared the one-year mortality of cerebral hemorrhage and infarction over the study period. To determine the determinants of the one-year survival of either hemorrhagic or ischemic stroke patients, we used the Cox proportional hazard regression model and simultaneously adjusted the age, sex, CMI, and different calendar years. All statistical analyses were performed with SAS (version 9.1, SAS institute, Cary, NC, USA). A p-value < 0.05 was considered statistically significant.

Results

Over the 18-year study period, a total of 3,678 and 16,010 patients were admitted to the study hospital because of cerebral hemorrhage and infarction, respectively. The mean (± S.D.) age of the cerebral hemorrhage patients was 58.8 (± 14.6) years, whereas that of cerebral infarction patients was 67.1 (± 12.5) years. The elderly (> 65 years) accounted for 35% and 61%, of the total number of patients, respectively. Male predominance existed in both types of stroke. For patients with cerebral hemorrhage and infarction, the mean durations of hospital stay were 19.2 (± 30.6) and 11.9 (± 25.1) days, respectively. In addition, the mean CMI was higher in the patients with cerebral infarction than that in patients with cerebral hemorrhage. The detailed characteristics of the study participants are listed in Table 1.

The 30-day, 90-day, 180-day, and one-year survival rates of cerebral hemorrhage patients were 81%, 77%, 75%, and 71%, respectively. The corresponding values for cerebral infarction were higher at 96%, 92%, 89%, and 84%, respectively. The factors affecting the one-year mortality of patients with cerebral hemorrhage and cerebral infarction are presented in Tables 2 and 3. No difference in the mortality risk was found between patients aged < 45 and 45 to 65 years; however, those aged > 65 years had a significantly increased risk of mortality from cerebral hemorrhage [hazard ratio (HR) = 1.68, 95% confidence interval (CI) = 1.38-2.02] and cerebral infarction (HR = 3.35, 95% CI = 2.56-4.39). Other determinants, such as sex and underlying diabetes, did not significantly increase the risk of mortality of both types of stroke. However, patients that also suffered from myocardial infarction, chronic renal illness or pneumonia and who also exhibited higher CMI scores all had increased HRs for both cerebral hemorrhage and infarction. By contrast, certain comorbidities, including heart failure, chronic obstructive pulmonary disease, and urinary tract infection, increased the mortality risk only of patients with cerebral infarction.

An increased risk in the one-year mortality was also noted in patients with cerebral infarction who had hospital stays that exceeded 14 days; this result was not observed in patients with cerebral hemorrhage. However, higher CMI scores were associated with significantly higher mortality HRs in both cerebral hemorrhage and cerebral infarction patients. Compared with the patients admitted for cerebral hemorrhage from 1991 to 1996, those admitted for the same illness from 1997 to 2002 and from 2003 to 2008 had one-

Table 1. Characteristics of the study subjects.

Characteristics[a]	Cerebral hemorrhage		Cerebral infarction	
	n	%	*n*	%
Age				
< 45	603	16.4	866	5.4
45-65	1,789	48.6	5,381	33.6
> 65	1,286	35.0	9,763	61.0
Mean (years ± S.D.)	58.8	(14.6)	67.1	(12.5)
Sex				
Male	2,250	61.2	9,190	57.4
Female	1,428	38.8	6,819	42.6
Diabetes				
No	3,147	85.6	12,359	77.2
Yes	531	14.4	3,651	22.8
Myocardial infarction				
No	3,624	98.5	15,764	98.5
Yes	54	1.5	246	1.5
Heart Failure				
No	3,646	99.1	15,670	97.9
Yes	32	0.9	340	2.1
Chronic renal illness				
No	3,521	95.7	15,304	95.6
Yes	157	4.3	706	4.4
Pneumonia				
No	3,384	92.0	15,227	95.1
Yes	294	8.0	783	4.9
Chronic obstructive pulmonary disease				
No	3,528	95.9	14,898	93.1
Yes	150	4.1	1,112	6.9
Urinary tract infection				
No	3,324	90.4	14,580	91.1
Yes	354	9.6	1,430	8.9
Year group				
1991-1996	1,042	28.4	4,611	28.8
1997-2002	944	25.7	5,222	32.7
2003-2008	1,682	45.9	6,155	38.5
Length of stay				
Mean (days ± S.D.)	19.2	(30.6)	11.9	(25.1)
Charlson index				
Mean (± S.D.)	1.5	(1.0)	1.7	(1.0)
Total[b]	3,678	100.0	16,010	100.0

[a] Data are Mean (± S.D.) or *n* (%) unless otherwise indicated.

[b] Inconsistency between total population and population summed for individual variables was due to missing information.

year mortality rate reductions of 15% (HR = 0.84, 95% CI = 0.71-0.98) and 20% (HR = 0.77, 95% CI = 0.67-0.89), respectively. In a similar manner, patients admitted for cerebral infarction from 1997 to 2002 and from 2003 to 2008 had one-year mortality risks reductions of 20% (HR = 0.81, 95% CI = 0.73-0.89) and 25% (HR = 0.72, 95% CI = 0.66-0.80), respectively, compared with those admitted from 1991 to 1996.

Discussion

Direct comparisons of the survival rates of the stroke patients in this study and those of previous studies are diffi-

Table 2. Predictors for one-year mortality among cerebral hemorrhage (ICD-9: 430, 431).

	Survivors during one year	Fatalities during one year [a]	
	n (%)	*n* (%)	Adjusted HR (95% CI) [b]
Age			
< 45	459 (17.5)	144 (13.7)	1.0
45-65	1,380 (52.6)	409 (38.8)	0.91 (0.75-1.11)
> 65	785 (29.9)	501 (47.5)	1.68 (1.38-2.02)**
Sex			
Male	1,612 (61.4)	638 (60.5)	1.0
Female	1,012 (38.6)	416 (39.5)	0.97 (0.86-1.10)
Diabetes			
No	2,254 (85.9)	893 (84.7)	1.0
Yes	370 (14.1)	161 (15.3)	0.99 (0.84-1.18)
Myocardial infarction			
No	2,601 (99.1)	1,023 (97.1)	1.0
Yes	23 (0.9)	31 (2.9)	2.20 (1.53-3.15) **
Heart failure			
No	2,606 (99.3)	1,040 (98.7)	1.0
Yes	18 (0.7)	14 (1.3)	1.07 (0.63-1.83)
Chronic renal illness			
No	2,572 (98.0)	949 (90.0)	1.0
Yes	52 (2.0)	105 (10.0)	2.70 (2.16-3.38) **
Pneumonia			
No	2,453 (93.5)	931 (88.3)	1.0
Yes	171 (6.5)	123 (11.7)	1.49 (1.24-1.81) **
Chronic obstructive pulmonary disease			
No	2,519 (96.0)	1,009 (95.7)	1.0
Yes	105 (4.0)	45 (4.3)	0.74 (0.54-1.00)
Urinary tract infection			
No	2,343 (89.3)	981 (93.1)	1.0
Yes	281 (10.7)	73 (6.9)	0.58 (0.46-0.74) **
Length of stay			
< 7 days	659 (25.1)	504 (47.8)	1.0
7-14 days	873 (33.3)	213 (20.2)	0.32 (0.28-0.38) **
> 14 days	1,092 (41.6)	337 (32.0)	0.36 (0.31-0.41) **
Charlson index			
< 2	2,483 (94.6)	908 (86.2)	1.0
2-4	132 (5.0)	113 (10.7)	1.79 (1.47-2.18) **
> 4	9 (0.4)	33 (3.1)	3.77 (2.66-5.35) **
Calendar years			
1991-1996	711 (27.2)	331 (31.4)	1.0
1997-2002	670 (25.6)	274 (26.0)	0.84 (0.71-0.98) *
2003-2008	1,234 (47.2)	448 (42.6)	0.77 (0.67-0.89) **
Total	2,624 (100.0)	1,054 (100.0)	

[a] Inconsistency between total population and population summed for individual variables was due to missing information.

[b] Based on Cox proportional hazard regression with adjustment for age, sex, Charlson index, and different calendar years.

HR, hazard ratio; CI, confidence interval.

* $p < 0.05$ and ** $p < 0.01$.

Table 3. Predictors for one-year mortality among cerebral infarction (ICD-9: 433, 434, 436).

	Survivors during one year	Fatalities during one year [a]	
	n (%)	*n* (%)	Adjusted HR (95% CI) [b]
Age			
< 45	811 (6.0)	55 (2.2)	1.0
45-65	4,936 (36.6)	445 (17.6)	1.26 (0.95-1.66)
> 65	7,739 (57.4)	2,024 (80.2)	3.35 (2.56-4.39)**
Sex			
Male	7,763 (57.6)	1,427 (56.5)	1.0
Female	5,722 (42.4)	1,097 (43.5)	0.96 (0.88-1.05)
Diabetes			
No	10,438 (77.4)	1,921 (76.1)	1.0
Yes	3,048 (22.6)	603 (23.9)	1.06 (0.97-1.17)
Myocardial infarction			
No	13,325 (98.8)	2,439 (96.6)	1.0
Yes	161 (1.2)	85 (3.4)	1.95 (1.56-2.43)**
Heart failure			
No	13,253 (98.3)	2,417 (95.8)	1.0
Yes	233 (1.7)	107 (4.2)	1.80 (1.46-2.22)**
Chronic renal illness			
No	13,029 (96.6)	2,275 (90.1)	
Yes	457 (3.4)	249 (9.9)	1.91 (1.66-2.20)**
Pneumonia			
No	13,103 (97.2)	2,124 (84.2)	1.0
Yes	383 (2.8)	400 (15.9)	4.27 (3.83-4.76)**
Chronic obstructive pulmonary disease			
No	12,637 (93.7)	2,261 (89.6)	1.0
Yes	849 (6.3)	263 (10.4)	1.18 (1.04-1.35)*
Urinary tract infection			
No	12,386 (91.8)	2,194 (86.9)	1.0
Yes	1,100 (8.2)	330 (13.1)	1.47 (1.31-1.66)**
Length of stay			
< 7 days	5,888 (43.7)	762 (30.2)	1.0
7-14 days	5,502 (40.8)	752 (29.8)	1.00 (0.90-1.10)
< 7 days	2,096 (15.5)	1,010 (40.0)	2.68 (2.43-2.95)**
Charlson index			
< 2	11,681 (86.6)	1,889 (74.8)	1.0
2-4	1,707 (12.7)	527 (0.9)	1.83 (1.66-2.02)**
> 4	98 (0.7)	108 (4.3)	4.94 (4.07-6.01)**
Calendar years			
1991-1996	3,822 (28.4)	789 (31.3)	1.0
1997-2002	4,339 (32.2)	883 (35.1)	0.81 (0.73-0.89)**
2003-2008	5,309 (39.1)	846 (33.6)	0.72 (0.66-0.80)**
Total	13,486 (100.0)	2,524 (100.0)	

[a] Inconsistency between total population and population summed for individual variables was due to missing information.
[b] Based on Cox proportional hazard regression with adjustment for age, sex, Charlson index, and different calendar years.
* $p < 0.05$ and ** $p < 0.01$.

cult or even nearly impossible to achieve because of the different study designs, dissimilar baseline demographic characteristics, and variations in outcome ascertainments and follow-up periods. Generally, the 30-day survival rates of cerebral hemorrhage (81%) and cerebral infarction (96%) patients in this study were higher than those of previous reports from a community (Hu et al. 1992) and medical center-based studies in Taiwan (Jeng et al. 1998). In addition, the 90-day survival rates of ischemic stroke patients noted in this study (92%) were slightly higher than those obtained from another medical center in Taiwan (Chang et al. 2006). The one-year survival rates for cerebral hemorrhage (71%) and cerebral infarction (84%) in this study were higher than those of studies conducted in Perth, Australia (Anderson et al. 1994) and in the Arcadia region of Greece (Vemmos et al. 2000) but comparable to those conducted in Hong Kong (Wong and Li 2003), Canada (Saposnik et al. 2008), and Sweden (Eriksson and Olsson, 2001).

Age appears to be the most important predictor of the one-year mortality of stroke patients; however, a number of previous studies (Anderson et al. 1994; Vemmos et al. 2000; Eriksson and Olsson 2001; Wong and Li 2003) have not reported the exact risk estimates for various age levels. In the current study, patients aged > 65 years had the highest risk of mortality, whereas those aged 45 years to 65 years had a risk estimate similar to that of patients aged < 45 years in both cerebral hemorrhage and infarction. On the other hand, the study by the Nanjing Stroke Registry (Liu et al. 2006) has reported that stroke patients aged > 45 years had increased risk of one-year mortality, with the risk increasing with age.

Diabetes mellitus did not appear to be a significant predictor of the one-year mortality of stroke based on a study conducted in Greece (Vemmos et al. 2000). However, previous studies have shown that diabetes can increase the risks of 3.5-year (Wong and Li 2003) and 5-year mortality (De Wit et al. 2012) as well as the recurrence of stroke with a prolonged follow-up. Although stroke patients with prior histories of heart failure and myocardial infarction did not show increased risk of one-year mortality in a previous research (Vemmos et al. 2000), our study showed a significantly increased risk of one-year mortality in both types of stroke with myocardial infarction. A study in Italy (Alberti et al. 2011) has also reported that myocardial infarction is a significant predictor of mortality. Our study also showed that heart failure may also be a predictor of the one-year mortality of patients with cerebral infarction but not of those with cerebral hemorrhage. Previous studies (Eriksson and Olsson 2001; Koton et al. 2010) similarly reported that congestive heart failure is a significant predictor of mortality in stroke patients. A small number of heart-failure patients with cerebral hemorrhage may have underpowered the statistical analysis in this study.

Infection complications occur in 30% of acute stroke patients, and 10% of stroke patients suffer from pneumonia and urinary tract infection (Westendorp et al. 2011). A number of studies have suggested that both pneumonia (Vermeij et al. 2009; Westendorp et al. 2011) and urinary tract infection (Westendorp et al. 2011) increase the risk of an unfavorable outcome in stroke patients. In the current study, pneumonia was found to increase the one-year mortality of both types of stroke, whereas urinary tract infection affected only patients with cerebral infarction. The relationship between chronic kidney disease and stroke mortality was rarely reported in literature. Ovbiagele (2011) reported that the presence of chronic kidney disease is independently associated with a higher odds ratio of death during stroke hospitalization regardless of index stroke type; however, the researchers did not further correlate the long-term mortality of stroke and chronic renal illness. In the current study, the risks of one-year mortality in both types of stroke complicated with chronic renal insufficiency both exhibited a nearly two-fold increase.

A number of studies assessed the effects of the CMI score on the long-term functional outcome of patients with cerebral hemorrhage (Bar and Hemphill 2011) and cerebral infarction (Goldstein et al. 2004). Every one-point increase in CMI was found to be independently associated with a 15% increase in the odds of a poor outcome at discharge as well as with a 29% increase in the odds of death within 1-year post stroke ($p < 0.001$; Goldstein et al. 2004). In a similar manner, our study found that increased CMI scores could predict the one-year mortality of both types of stroke, with a higher hazard ratio noted in cerebral hemorrhage. Stroke patients with a CMI score > 4 showed the highest risk of one-year mortality and should therefore be given increased attention.

Over an 18-year study period, we found that patients with both stroke types admitted in later years, particularly in the last six years (i.e., from 2003 to 2008) had a significantly reduced risk of one-year mortality. Establishment of a stroke registry (George et al. 2011) accompanied by aggressive treatment of accompanying comorbidities (e.g., hyperglycemia, hyperlipidemia, hypertension, and atrial fibrillation) (Furie et al. 2011), widespread dissemination of a community education program for public awareness of early stroke symptoms, and collaboration with the Radiology department to optimize the management of acute ischemic stroke (Biller et al. 2012) using intravenous or intra-arterial recombinant tissue plasminogen activator reperfusion therapy, angioplasty, stent, or carotid endartrectomy, may have accounted for the observed improvements in stroke mortality.

This study possessed several strengths. One is the 18-year study coverage that allowed analysis of the secular trends in the one-year mortality of patients with cerebral hemorrhage and cerebral infarction. Another is that we used an in-patient electronic database and thus minimized the probability of obtaining erroneous information on disease histories. Moreover, we linked this database to the National Death Registry of Taiwan and thus may have

effectively reduced the chances of loss to follow-up and of selection (non-response) bias.

However, this study also had several limitations. One is that the FEMH electronic database has not been systematically reviewed for validity. Thus, our exclusive reliance on the electronic database could have resulted in disease misclassification bias. However, the data used in this study were retrieved from hospital records and are considered to be relatively valid compared with those directly reported by the patients. In addition, the potential disease misclassification would likely be non-differential and would thus bias our results toward the null (Gordis 2000). The electronic database does not contain imaging studies such that we were unable evaluate the validity of the disease status in relation to one-year mortality risk. Article 70 (Ministry of Health and Welfare 2009) of the Medical Care Act of Taiwan states that all medical institutions should retain medical records only for seven years. Thus, we were unable to review all medical records to obtain essential clinical data. Another limitation is that because of the lack of subtypes and severities of cerebral hemorrhage and infarction (e.g., the baseline National Institute of Health Stroke scale, educational level, and socioeconomic variables in the electronic database), we could not adjust for the potential confounding factors that may have been important contributors to stroke mortality. Lastly, after the patients were discharged from the hospital, their stroke recovery may have depended on medical care, rehabilitation programs (Hu et al. 2013), availability and adherence to medical therapy for preventing stroke recurrence (Li et al. 2013), and sufficient social support. Absence of these factors in the analysis may have led to some degree of information bias.

In conclusion, the one-year survival rates in the study hospital were estimated at 71% and 84% for cerebral hemorrhage and cerebral infarction, respectively. These values are lower or comparable to the figures reported in previous studies. An improvement in the one-year mortality rate was found in the later years of the study period, particularly between 2003 and 2008. Prompt recognition and treatment of certain comorbid medical problems may reduce the number of stroke-related complications and subsequently lead to a further reduction of one-year mortality in stroke patients.

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Conflict of Interest

The authors declare no conflict of interest.

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