Epidemiological Studies of Cerebrovascular Diseases and Carotid Atherosclerosis in Taiwan

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Abstract- Cerebrovascular disease (CVD) or stroke has been always one of the first three leading causes of death in the past four decades in Taiwan. CVD is also the most important cause of disability in the elderly. For decreasing case-fatality of stroke, modest alterations of age-specific stroke incidences, and an ageing population, CVD will still prevail in the future decades in Taiwan. There have been many studies concerning about CVD in Taiwan, especially in recent 20 years. This article focuses on reviewing epidemiological studies of CVD in Taiwan. The review includes mortality, prevalence, and incidence of stroke, hospital-based stroke registry studies, risk factor studies of stroke and carotid atherosclerosis, young stroke, and outcome and survival of CVD.

Key Words: Carotid atherosclerosis, Epidemiology, Risk factors, Stroke, Taiwan

INTRODUCTION

Stroke or cerebrovascular diseases (CVD) had been the first cause of death during 1963-1981, and has been the second leading cause of death for persons of all ages and the leading cause of death for those aged 65 years or over since 1982 in Taiwan except 2004 (the 3rd leading cause of death), despite a steady decline in standardized stroke mortality over the past three decades[1]. CVD is also important in physical and mental disability in adults, particularly in the elderly, and possesses an enormous burden on healthcare expenditure in developed and developing countries[2].

Epidemiology is the study of the distribution and determinants of diseases in human population. The distribution of CVD is dealt with the incidence, prevalence, mortality and outcome by age, gender and geographic areas. Studies of the determinants of CVD are mainly the etiologies, risk factors and implication for prevention of CVD. This review aimed to summarize past epidemiological studies of CVD and carotid atherosclerosis in Taiwan. An electronic relevant papers was searched through Medline or PubMed (1980 to June 2007). Electronic search key words included: cerebrovascular diseases, stroke, ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage, transient ischemic

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attack, carotid arteries, and carotid stenosis in combination with Taiwan or Taiwanese. The references lists of selected articles were also reviewed.

Stroke mortality

In Taiwan, the most common source of stroke mortality estimation is the vital statistics system. It is obligatory to report any death event with information of underlying causes, largely by physicians, and there is nearly 100% coverage of all death events. However, it is unattainable to report death rates of stroke subtypes through the vital statistics. Of 13,139 reported stroke deaths during 2005 in Taiwan[1], 7,976 (60.7%) were uncertain stroke subtypes, including "acute but ill-defined CVD" (28.8%, ICD-9: 436), "other and ill-defined CVD" (4%, 437), and "late effects of CVD" (27.9%, 438). The situation is similar in other countries, such as in the United States[3]. Besides, there is inconsistency for the causes of death between official coding and physician panel coding[4]. Therefore, it should be cautious in interpretation of stroke mortality, especially the subtypes of stroke, by vital statistics. However, we still could observe the stroke trends across the periods by vital statistics data.

The earliest stroke mortality description in Taiwan can be traced back to the reports by Ri in 1938[5,6], followed by Chang et al. in 1973[7], Ko et al. in 1980[8], and Hu et al. in 1986[9]. The mortality rates for cerebral hemorrhage (CH) were always higher than those for cerebral infarct (CI). The age-adjusted stroke mortality decreased 17.5% for men and 18.5% for women during 1972-83, and had a geographic difference with more prominent decrease in the urban areas[9]. An age-period-cohort analysis of stroke mortality during 1974-88 was reported by Chang and Chen[10]. There was a consistent change of a decline in the CH/CI ratio. Higher CH/CI ratios were observed among younger age groups. The analysis also revealed that the decline of mortality rates from CH after 1974 was persistently greater than those from CI[10]. A longer period analysis of stroke mortality in Taiwan during 1957-1987 was reported by Hung in 1993[11]. The stroke mortality rates were consistently higher in men than in women. The age-adjusted stroke mortality increased from 1957 to 1972, reached the peak in 1972,

and decreased afterward[11]. In an analysis of mortality in the elderly, there was a sharp decline of stroke mortality for both sexes during 1974-94 in Taiwan[12]. In the past one more decades, there has been lack of systematic analysis of stroke mortality in Taiwan. To better understand the secular trends of stroke mortality, a detailed new analysis is warranted.

There are substantial international variations of stroke mortality[13]. Results from the World Health Organization Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (WHO MONICA) Project showed 10-year trends in stroke mortality differed within study populations from several countries[14]. In most of these populations, changes in stroke mortality rates were mainly attributable to changes in case fatality rates, rather than incidence rates[15], alike the situation in Taiwan.

Stroke prevalence

Previous stroke prevalence studies in Taiwan are shown in Table 1. The earliest prevalence study of stroke in Taiwan was reported by Tseng[16]. In adult residents aged 40 years or more in Taipei, the prevalence of stroke was 1.2% in the urban area and 1.7% in the rural area. Hu et al. conducted an epidemiological study of stroke, and used a cluster sampling of 4 urban and 4 rural communities in Taiwan[17]. Of 8,705 people aged 36 years or older, the stroke prevalence was $1,642 \times 10^{-5}$ and was higher in the northern Taiwan and in urban communities. The distribution of stroke subtypes included CI in 67%, CH in 14%, subarachnoid hemorrhage (SAH) in 4%, and unclassified in 15%. People with stroke had higher comorbidity of hypertension, diabetes mellitus (DM), and heart disease than people without stroke.

A cross-sectional survey of old population in 4 communities in Taiwan was carried out by Lee et al[18]. Of 2,600 people aged 65 years or more, 155 had stroke (prevalence, 5.96%; CI, 74%; CH, 14%; unclassified, 12%). Smoking was more important than alcohol drinking for stroke and CI. Lee YT and his study team conducted a longitudinal cohort study in Chin-Shan community since 1990 (Chin-Shan Community Cardiovascular Cohort, CCCC)[19]. There were 3,602 residents aged 35

years or older participated in this cohort. The prevalence of stroke was 2.2% for overall, 2.5% for men, and 1.9% for women. Chiou et al. investigated the effect of inorganic arsenic exposure on cardiovascular diseases in Ilan area[20]. Of 8,102 adults aged ≥ 40 years, the stroke prevalence was 1.58% for men and 1.32% for women. There was a significant dose-relationship between arsenic concentration in well water and prevalence of CVD. Fuh et al. conducted an epidemiological survey of neurological diseases in Kinmen[21]. Of residents aged 50 years or older, the prevalence of stroke was 2.45%. People with stroke had higher frequencies of hypertension, DM, and cardiac arrhythmia than people without stroke.

Findings from the 1994 National Health Interview Survey in Taiwan showed that the stroke prevalence was 5.95×10^{-3} and increased steadily with age, from 0.51% in persons aged 35-44 years to 11.36% in persons aged 85 years and over[22]. The ratio of CI to CH was 1.33; and hypertension, DM, and heart disease increased the risk of stroke. In an analysis of the data of 200,000 sample of National Health Insurance in 2000, the prevalence of stroke was 2.07% for males and 1.98% for females[23]. In a survey of stroke prevalence in type 2 DM patients in Taiwan, 939 out of 12,531 (7.5%) patients had strokes[24]. The age-standardized stroke prevalence in DM patients was 2.3% which was higher than that (0.6%) in the general population. Based on results from previous prevalence studies, the prevalence of stroke in the year 2005 among the general Taiwan population older than 35 years (the population number of 11,272,514) was estimated at 1.5%, yielding a total of around 169,000 stroke sufferers in Taiwan.

Stroke incidence

Previous stroke incidence studies in Taiwan were not many (Table 1). The first reported study was investigated in 8 communities in Taiwan by Hu et al.[25]. During a 4-year follow-up, there were 104 1st-ever stroke cases out of 8,562 people aged 36 years or older. The incidence of stroke was 329×10^{-5} and it was higher in men, eastern Taiwan, and rural area. The stroke subtypes were CI in 71%, CH in 22%, SAH in 1%, and unclassified in 6%. Chang et al. conducted a hospital-based community study to explore the stroke incidence during 1991 in

Table 1. *Prevalence and incidence studies of stroke in Taiwan*

Authors	Study period	Study area	Study population	Rate ($\times 10^{-3}$) Total	Male	Female
Prevalence						
Tseng[16]	1973	Taipei city	1,067 adults aged ≥40 years	12	18	4
	1974	San-chi community	Adults aged ≥40 years	17	--	--
Hu et al.[17]	1986	4 urban and 4 rural communities	8,705 adults aged ≥36 years	16.4	20.6	11.9
Lee et al.[18]	1989-1991	Taipei, Taichung, Kaoshung, Hualien	2,600 adults aged ≥65 years	59.6	68.8	50.1
Lee et al.[19]	1990	Chin-Shan community	3,602 adults aged ≥35 years	22	25	19
Chiou et al.[20]	1991-1994	Ilan county	8,102 adults aged ≥40 years	--	15.8	13.2
Fuh et al.[21]	1993	Kinmen island	3,915 adults aged ≥50 years	24.5	26.4	22.6
Huang et al.[22]	1994	58 townships in Taiwan	4,972 adults aged ≥35 years	14.3	15.3	13.3
Liao et al.[23]	2000	National Health Insurance databank	200,000 population aged ≥1 year		20.7	18.9
Tseng et al.[24]	2001-2002	A national sample of diabetic patients	12,531 diabetic patients	74.9	83.9	67.6
Incidence						
Hu et al.[25]	1986-1990	4 urban and 4 rural communities	8,562 adults aged ≥36 years	3.29	3.48	3.01
Chang et al.[26]	1991	Ilan county	45,152 adults aged ≥45 years	3.38	3.42	3.28
Fuh et al.[27]	1993-1996	Kinmen island	3,081 adults aged ≥50 years	5.27	6.56	3.98
Chien et al.[28]	1990-1998	Chin-Shan community	3,602 adults aged ≥35 years	--	4.67	3.32
Liao et al.[23]	2000	National Health Insurance databank	200,000 population aged ≥1 year		6.64	6.71

southern Ilan[26]. Excluding the referral patients, the incidence of 1st-ever stroke for age 45-79 years was 3.38×10^{-3} (male, 3.42×10^{-3}; female, 3.28×10^{-3}), including 66% of CI and 34% of CH. By a population-based stroke survey in Kinmen by Fuh et al.[27], the incidence of 1st-ever stroke in people aged 50 years or more was 5.27×10^{-3}. The 28-day case fatality was 24.5% for 1st-ever stroke and 60% for recurrent stroke. The CCCC study found 97 incident stroke cases during 1990-98 in 3602 adults aged >35 years in the Chin-Shan community[28]. The incidence of stroke was 4.7×10^{-3} for men and 3.3×10^{-3} for women. The stroke incidence rates were higher in men for age <65 years and in women for age ≥65 years. Estimation based on incidence studies revealed an incidence of 0.33% means that about 37,200 new stroke patients diagnosed in the year 2005. In the National Health Insurance databank analysis in 2000, the incidence of stroke was slightly higher in women than in men (6.71×10^{-3} vs. 6.64×10^{-3}), and there no significant difference of stroke risk between urban and rural area in Taiwan[23].

Stroke registries

Stroke registry or stroke data bank can provide more thorough understanding of etiologies, clinical manifestation, risk factors and outcome in different types of stroke and transient ischemic attack (TIA) patients. The pioneer well-known stroke registry study was the Harvard Cooperative Stroke Registry issued in 1978[29]. Another important stroke registry conducted in Europe is the Lausanne Stroke Registry published in 1988[30]. Some proposed criteria for an optimal stroke data bank suitable for clinical research, including well-designed diagnostic criteria, separate analysis of first-ever and recurrent strokes, high rate of CT (or MRI) investigations, autopsies whenever possible, prospective data correction, pilot phase and interrater studies, consistent screening procedures, collection of a large spectrum of clinical and investigative data, follow-up investigations, and baseline papers[31].

The first stroke registry in Taiwan was Ryu's "Chang Gung Stroke Registry" in 1980[32]. This registry recruited 854 patients with acute stroke; and consisted of CI in 59%, CH in 30%, SAH in 8%, and unclassified in 3%. One-month case fatality was higher in CH (43%) and SAH (33%) than in CI (10%). Lie analyzed changing pattern of CH during 1981-88 at the Cathay General Hospital[33]. The case-fatality rates for CH decreased from 23.4% (1981-82) to 18.9% (1987-88). The CI to CH ratio increased from 1.5 (1981-82) to 2.7 (1987-88). The second Chang Gang Stroke Registry was carried out in 1994-95 and a total of 885 hospitalized patients were recruited[34].

Hung had conducted some large retrospective and prospective collaborative studies at many hospitals during the period of 1984-92[35-37]. The registries included 6,790 acute stroke patients from 26 centers in Taiwan during 1985, 3,982 acute stroke patients from 3 teaching hospitals in Taipei during 1984-86, and 23,910 acute stroke patients from the Prospective Survey and Registry of Stroke in Taiwan Area (PSRST) during 1988-92. The PSRST has been the largest stroke registry study ever performed in Taiwan up to now. Of all 23,910 registered stroke patients, 14,413 (60.3%), 7,250 (30.3%), 892 (3.7%) were categorized as CI, CH, and SAH (including aneurysm rupture), respectively[37]. Hypertension was the most risk factors associated with stroke patients: 76.1% in CH, 63.3% in CI, and 51.1% in SAH. Diabetes mellitus was found in 27.4% of CI and 13.3% of CH patients. The 1-month case-fatality rates for CI, CH and SAH were 8.2%, 27.1%, and 35%, respectively. During a long-term follow-up, the 1-year survival rates were 81.6% for CI and 74.3% for CH.

Howng et al analyzed SAH and intracranial aneurysm of 28,763 stroke patients registered from Taiwan Neurological Society[38]. Among 409 patients with recorded aneurysmal sites, the most common site was anterior communicating artery (26.7%), followed by posterior communicating artery (22.0%), internal carotid artery (20.1%), and middle cerebral artery (19.6%). Lee et al. also did a similar analysis and the most common site of aneurysmal rupture was posterior communicating artery (32%), followed by anterior communicating artery (30%), and middle cerebral artery (18%)[39]. Chang et al. conducted a stroke registry in 2 hospitals in southern Ilan during 1991 and a total of 258 patients were regis-

tered[25].

The National Taiwan University Hospital (NTUH) Stroke Registry was launched in 1995 and is an ongoing registry with study more than 10 years. The NTUH stroke registry in 1995 analyzed 995 patients (aged 1 to 98 years, 575 men and 420 women)[40,41]. Of these patients, 676 (67.9%), 41 (4.1%), 228 (22.9%), and 50 (5%) were categorized as CI, TIA, CH, and SAH, respectively[40]. Hypertension remained one of the most important risk factors for CI, CH, and TIA patients. Severe extracranial carotid artery (ECCA) stenosis (>50%) was found in 12% of the CI patients and 27% of the TIA patients. The 30-day case-fatality rates were higher in SAH (30%) and CH (24.1%) than in CI (5.6%). Of the CI patients, 17%, 29%, 20%, 6% and 29% were classified as sufferers of large-artery atherosclerosis, lacunae, cardioembolism, other determined causes, and undetermined cause subtypes, respectively[41]. The Kaohsiung Veterans General Hospital stroke registry in 1999 was reported by Lin et al and a total of 578 patients with acute stroke were registered[42]. Table 2 lists previous stroke registries performed in Taiwan. It shows a trend of increasing CI/CH ratios in Taiwan from 1980 to 2005.

Since August 2006, more than 30 teaching hospitals in Taiwan have participated a multi-center stroke registry, i.e. Taiwan Stroke Registry. This registry was well-designed and put emphasis on study quality and follow-up. Up to 25,000 acute stroke patients will be recruited till the mid-year of 2008. This registry will provide valuable information about stroke etiologies, risk factors, management, and outcome, and enhance stroke researches in Taiwan.

Risk factors of stroke

Table 3 summarizes previous published articles concerning stroke risk factors in Taiwan. In almost papers, conventional risk factors, particularly hypertension and diabetes mellitus, were still important risk factors for stroke and its subtypes. In the study of the relation between lipids and lipoproteins in CVD, Hwang et al. showed that serum apoB was more related to CI than other lipids and lipoproteins[43]. Chung et al. revealed that low-density lipoprotein cholesterol was significantly related to CI[44]. Results from the CCCC, Chien et al. found that apoA-1, but not apoB, as an effect modifier of hypertension for the risk of stroke events[28]. Chen et al. showed that apoB polymorphisms with emphasis on A+ allele, were associated with CI[45]. Lin et al. analyzed the association between apoE polymorphisms and CI/vascular dementia and found apoEε4 was not related to CI, but ApoEε2 had a protective effect on the development of CI[46]. Pan et al. gave a review of plasma lipid profiles and epidemiology of atherosclerotic diseases, including

Table 2. *Hospital-based stroke registry in Taiwan*

Authors, year	Study period	Study hospitals	No of patients	CI to CH ratio
Ryu, 1986[32]	1980	Chang Gang Memorial Hospital	854	1.96
Lee et al., 1989[33]	1981-1982	Cathay General Hospital	817	1.50
Hung et al., 1987[34]	1985	26 teaching hospitals in Taiwan	7,355	1.54
Hung et al., 1987[35]	1984-1987	3 teaching hospitals in northern Taiwan	3,982	1.63
Lee et al., 1989[33]	1987-1988	Cathay General Hospital	901	2.80
Chang et al., 1995[26]	1991	Lotung Poh-Ai Hospital and St Mary's Hospital	258	2.01
Hung et al., 1992[37]	1988-1992	Prospective Survey and Registry of Stroke in Taiwan	23,910	1.99
Hsu et al., 1995[34]	1994-1995	Chang Gang Memorial Hospital	885	2.58
Jeng et al., 1998[40]	1995	National Taiwan University Hospital	995	2.96
Lin et al., 2005[41]	1999	Kaohsiung Veterans General Hospital	578	2.40
Jeng et al., (unpublished)	2006	National Taiwan University Hospital	1,179	3.70

CI: cerebral infarct; CH: cerebral hemorrhage.

Table 3. *Studies on risk factors of stroke in Taiwan*

Author, year	Study design	Study population	Main results
Hwang et al., 1993[43]	Case-controls study	367 CI patients and 71 controls	ApoB and HDL-C are related to CI
Chung et al, 1994[44]	Case-controls study	138 CI patients and 80 controls	LDL-cholesterol and hypertension are related to CI
Pan et al., 1995[47]	Vital statistics	Vital statistics during 1981-91	A U-shaped relation between temperature and CI mortality
Chen et al., 1995[49]	Stroke registry	517 acute stroke patients	CH, but not CI, occurs more frequently on cooler days
Lee et al., 1995[18]	Cross-sectional study	2,600 adults aged ≥65 years	Smoking as a more important risk factor for stroke and CI than alcohol drinking
Chiou et al., 1997[20]	Community-based cross-sectional study	8,102 residents in community	Exposure to inorganic arsenic is associated with an increased stroke prevalence
Chen et al., 1997[45]	Case-control study	159 CI patients and 44 controls	ApoB gene polymorphism is associated with CI
Yang et al., 1998[50]	Ecological correlation study	17,133 fatal stroke cases and 17,133 fatal non-stroke cases	Protective effect of magnesium from drinking water on the risk of CVD
Lin et al., 2000[55]	Case-control study	306 stroke patients and 300 controls	Angiotensin-I converting enzyme gene deletion polymorphism is not associated with stroke
Chien et al., 2002[28]	Community based incidence study	3,602 community residents	ApoA-1 but not apoB levels as an effect modifier of hypertension for the risk of stroke events
Tsai et al., 2003[52]	Ecological correlation study	23,179 stroke admissions	Exposure to air pollution is associated with hospital admission for stroke
Chen et al., 2003[56]	Case-control study	100 CI patients and 150 controls	PAI-1 4G/5G promoter polymorphism is not associated with CI
Lin et al., 2004[46]	Case-control study	277 CI patients, 49 vascular dementia patients	No association between ApoEε4 and CI; protective effect of ApoEε2 on CI
Chen et al., 2004[57]	Case-control study	157 young CI patients and 157 controls	No association of platelet glycoprotein Ia, Ib, and IIIa polymorphisms to CI
Yeh et al., 2004[58]	Case-control study	231 young CI patients and 200 controls	No influence of prothrombotic gene polymorphism on prognosis of CI
Tan et al., 2004[65]	Case-control study	228 first-ever CI patients and 228 controls	Hypertension, atrial fibrillation, left ventricular hypertrophy, ischemic heart disease, and smoking are related to CI
Lin et al., 2005[59]	Case-control study	234 CI patients and 223 controls	No association of Toll-like receptor 4 gene polymorphism with CI
Chien et al., 2005[62]	Community based incidence study	3,602 community residents	Hyperuricemia increases the risk of occurrence of cardio vascular events and stroke
Chan et al., 2006[53]	Ecological correlation study	8,582 emergency admission for CVD	Emergency admission for CVD is associated with increasing air pollution levels of O_3 and CO
Chen et al., 2006[60]	Cohort study	3,453 adults followed-up for a 10.4 years with 132 incident CI patients	Metabolic syndrome increases the occurrence of CI
Chiu et al., 2006[64]	Case-control study	238 CI patients and 238 controls	Electrocardiographic findings of atrial fibrillation, myocardial ischemia, and left ventricular hypertrophy are related to CI
Lien et al., 2006[63]	Case-control study	273 CI patients and 181 controls	Elevated anticardiolipin antibody titer is related to CI
Peng et al., 2007[54]	Case series study	524 1st-ever acute stroke patients	Male heavy drinkers with mild liver disorder increase risk of CH
Chien et al., 2007[61]	Community based incidence study	3,602 community residents	Metabolic syndrome is associated with increased risks of coronary heart disease and stroke

CI: cerebral infarct; CH: cerebral hemorrhage; CVD: cerebrovascular disease.

stroke, in Taiwan[47].

In the study of the influence of environment on stroke, there were several environmental factors, including weather, air pollution and well water, been investigated in Taiwan. Pan et al. showed a temperature mortality relation in the elderly. Higher or lower temperature may increase CI mortality, and decreasing temperature may increase CH mortality[48]. Chen et al. also found that CH, not CI, occurred more frequently on cooler days[49]. Yang approached the relationship between water hardness and CVD mortality and found that magnesium from drinking water has a protective effect on CVD risk[50]. On the contrast, Chiou et al. found that ingestion of high arsenic drinking water was associated with an increased prevalence of CVD[20]. Chiu et al. revealed that mortality due to primary CH mortality declined gradually after the improvement of drinking water supply system in an arseniasis-endemic area in southwestern Taiwan[51]. Two studies have disclosed the association between air pollution and stroke. Tsai et al. showed an association between air pollution and stroke admission in Kaohsiung[52]. Chan et al. revealed that emergency admission for CVD was associated with increasing air pollution levels of O_3 and CO in Taipei[53].

In the studies of smoking and alcohol drinking habits on the occurrence of stroke, Lee et al. found that cigarette smoking was a more important risk factor than excessive drinking of alcohol for stroke occurrence[18]. Peng et al. showed that heavy alcohol drinking with mild liver disorder increased the risk of CH[54].

In the analysis of the association between genetic factors and CVD, some case-control studies were reported. Lin et al. found there was no association between angiotensin-I converting enzyme gene deletion polymorphism and stroke[55]. Coagulation and thrombosis related gene study showed PAI-1 4G/5G promoter polymorphism, platelet glycoprotein Ia, Ib, and IIIa polymorphisms, and prothrombotic gene polymorphism had no significant relation with CVD[56-58]. Lin et al. showed that toll-like receptor 4 gene polymorphism was associated with CI[59].

Metabolic syndrome was found by two community studies, the CCCC and the Cardiovascular Diseases Risk Factor Two-Township Study, to be an important risk for the occurrence of stroke[60,61]. The CCCC study also showed that hyperuricemia as a risk factor for the development of cardiovascular diseases[62].

In addition, Lien et al. investigated the association between anticardiolipin antibody and stroke and found elevated titer of anticardiolipin IgG antibody was independently associated with 1st-ever ischemic stroke[63]. Chiu et al. studied the correlation of electrocardiographic findings with stroke and showed atrial fibrillation, myocardial ischemic changes, and left ventricular hypertrophy on electrocardiography were related to CI[64]. Tan et al. found hypertension, atrial fibrillation, ischemic heart disease, smoking, and left ventricular hypertrophy as risk factors of ischemic stroke from a case-control study[65].

Risk factors of carotid atherosclerosis

ECCA atherosclerosis serves as a reliable marker of systemic atherosclerosis as well as a major risk factor for ischemic stroke. Increased intima-media thickness (IMT) of the carotid arteries and the presence of ECCA atherosclerotic plaques have been identified as important indices for prediction of CVD morbidity and mortality. Previous studies about risk factors of carotid atherosclerosis in Taiwan are listed in Table 4. In an analysis of carotid stenosis and risk factors in CI patients, severe ECCA stenosis ≥50% was found in 12% of CI patients[66]. Age, male sex, and left ventricular hypertrophy on electrocardiogram were related to the severity of ECCA atherosclerosis. Another study also showed age and smoking were related to carotid stenosis ≥50% in patients with 1st-ever ischemic stroke[67].

Pan et al. studied the association between vascular risk factors, particularly coagulation profiles, and carotid atherosclerosis. The OR of highest tertile to the lowest tertile of factor VIIIc for carotid atherosclerosis was 3.35. There was a positive correlation between factor VIIIc and the presence of carotid plaques[68]. The results from the CCCC showed there was a significant dose-response relationship between hypertension status and the severity of ECCA atherosclerosis[69]. Compared with the normotensive subjects, the ORs for the hypertensive

Table 4. *Studies on risk factors of carotid atherosclerosis in Taiwan*

Author, year	Study design	Study population	Main results
Jeng et al., 1994[66]	Case series study	367 CI patients	Age, male sex, and left ventricular hypertrophy are related to CA
Pan et al., 1997[68]	Community-based cross-sectional study	147 CI patients	Factor VIIIc, hypertension and cholesterol is associated with CA
Li et al., 2001[75]	Case-control study	333 CI patients and 257 controls	Thrombomodulin G-33A promoter mutation is associated with CA
Su et al., 2001[69]	Community-based nested case-control study	263 hypertensive patients and 270 normotensive subjects	Hypertensive status is related to CA
Huang et al., 2001[71]	Case-control study	1,185 adult non-smokers	Increased leukocyte counts are associated with CA in male non-smokers, but not in female nonsmokers
Sun et al., 2002[73]	Case series study	1,781 people free of stroke	Age, systolic blood pressure, and blood sugar are related to CA
Wang et al., 2002[74]	Community based cohort study	463 residents in arsenic endemic village	A dose-response relationship between exposure to ingested inorganic arsenic and CA
Chang et al., 2006[67]	Case series study	541 CI patients	Age and smoking is related to carotid stenosis >50%
Su et al., 2006[75]	Case-control study	57 postmenopausal vegetarians and 61 omnivores.	No difference of CA between vegetarians and omnivores.
Su et al., 2006[70]	Case-control study	263 hypertensive patients and 270 normotensive subjects	Higher pulse pressure is associated with CA in patients with hypertension
Huang et al., 2007[72]	Case-control study	1,554 people	Males have higher CA than females in the presence of hypertension

CA: carotid artery atherosclerosis; CI: cerebral infarct.

patients to develop ECCA atherosclerosis were 5.0 indexed by maximal IMT of the common carotid artery ≥75th percentile, 3.7 by carotid plaque score >6, and 4.8 by carotid stenosis ≥50%. In terms of risk stratification, pulse pressure is more important in hypertensives than in normotensives which seem to imply that pulsatile hemodynamic component of BP is crucial in association with carotid atherosclerosis[70].

The results from a physical check-up study showed the increase in the leukocyte counts was significantly related to ECCA atherosclerosis in males, but not in females[71]. Males had higher risk of developing carotid atherosclerosis if presence of hypertension[72]. Another study in physical check-up subjects, the mean IMT was 0.68 ± 0.12 mm for males and 0.66 ± 0.11 mm for females. Age, systolic BP and fasting blood sugar were independent risk factors related to ECCA atherosclerosis[73]. Long-term exposure to ingested arsenic was significantly associated with prevalence of carotid atherosclerosis in a dose-response relationship in 463 adult resi-

dents from the southwestern area of endemic arseniasis in Taiwan[74]. The multivariate-adjusted OR was 3.1 for those who had a cumulative arsenic exposure of ≥20 mg/L-years compared with those without exposure to arsenic from drinking artesian well water. In a study of the effect of long-term vegetarianism on atherosclerosis, 57 healthy postmenopausal vegetarians and 61 age-matched omnivores were investigated[75]. There was no significant difference in ECCA atherosclerosis between postmenopausal vegetarians and omnivores. The findings of elevated homocysteine and soluble vascular cell adhesion molecule-1 in vegetarians indicated highly possible B_{12} deficiency.

Studies on the association between genetic factors and carotid atherosclerosis in Taiwan were few. Li et al. investigated the association between the G-33A promoter mutation of thrombomodulin gene and carotid atherosclerosis[76]. Multiple regression showed only diabetes mellitus and G-33A mutation (OR=2.46) were associated with carotid atherosclerosis in young subjects.

Young stroke studies

Chang et al. analyzed 206 young stroke patients aged 15-45 years, including CH in 44.2% and CI in 55.8%[77]. Lu et al. studied 157 young stroke patients aged 15-45 years in southern Taiwan[78]. CI, CH, and SAH comprised 42%, 67%, and 11% respectively. Hypertension (60%) was the most common risk factors, followed by hyperlipidemia (18%), vascular anomaly (16%), and heart disease (11%). Lee et al. investigated 264 young adults aged 18-45 years with CI[79]. Stroke subtypes included lacune in 21%, large artery atherosclerosis in 7%, cardioembolism in 18%, other determined etiologies in 22% (including dissection in 9% and antiphospholipid syndrome in 5%), and undetermined etiology in 24%.

For nontraumatic hemorrhagic stroke in young adults in Taiwan, there were four reported studies[80-83]. These studies investigated hospitalized CH patients aged 15-45 years and analyzed the CH etiologies and case-fatality. Male was predominant and comprised from 62% to 76%. Hypertension was the major etiology in young CH patients (30~50%), followed by vascular anomaly (10~28%), coagulopathy (5~10%), and tumor bleeding (1~7%). Undetermined etiology was still present in 15~25% of young CH patients. The 1-month case-fatality was 18~35%.

Previously, there were three studies concerning stroke complicating pregnancy and the puerperium in Taiwan[84-86]. The incidence rates ranged from 15.2 to 46.2 $\times 10^{-5}$. Cerebral venous thrombosis and cardioembolism were the major causes for CI; and vascular anomaly and preeclampsia/eclampsia were the major causes for CH. Compared to young female patients with stroke unrelated to pregnancy, patients with stroke related to pregnancy had higher frequency of cerebral venous thrombosis (39% vs. 7%, P<0.001), particularly during postpartum[87].

Outcome and survival of stroke

Recognition of the determinants of outcome among first-ever stroke patients is an important step towards better secondary prevention. A study among elderly stroke patients from a nationally representative sample in Taiwan showed that patients receiving continuous DM therapy had much lower mortality than those discontinuing DM therapy[88]. Besides, patients with both cognitive and mobility impairments had higher mortality than those with only one impairment. In a study assessing the relationship in women between age at first birth, parity and SAH mortality, the risk of SAH mortality increased with age at first birth and decreased with multiparity[89].

Stroke severity on admission, measured as National Institute of Health Stroke Scale (NIHSS), can predict outcome of CI patients[90]. For 1st-ever acute CI patients, initial NIHSS, heart diseases, and posterior circulation infarct can predict 3-month mortality[91]. The location and size of infarcts in noncardioembolic patients were prognostic factors of functional outcome[92]. For stroke inpatients receiving rehabilitation, admission functional scale, measures as Functional Independence Measure, can predict functional outcome at discharge[93]. The discharge functional status, measured as Barthel Index, may predict functional outcome 18 months after stroke[94].

Some studies assessing prognostic factors for acute CH patients. The results showed 3rd ventricle midline shift evaluated by transcranial sonography[95], QTc dispersion on the electrocardiogram[96], and abnormal hematology parameters (prolonged prothrombin time, low platelet and high leukocyte counts)[97] had higher short-term poor outcome.

Furthermore, an international prospective study involving 36 hospitals in Asia, including 2 hospitals in Taiwan identified atrial fibrillation, ischemic heart disease, DM, and smoking for CI patients and DM for CH patients as risk factors of early death after stroke[98].

In a study of 466 noncardioembolic patients, the annual recurrence rate of stroke was 4.2%[99]. The basal ganglia had higher recurrence rate than other sites of infarct. Lin et al. followed up 146 TIA and 376 acute CI patients and assessed 3-month risk of vascular events[100]. Large artery atherosclerosis group had the highest vascular event rates. Of patients with hypertensive CH, 4.8% to 5.3% had recurrent CH and the median interval between events was 1.9 to 2.4 years[101,102].

CONCLUSIONS

Effective primary and secondary prevention of stroke would not be possible without a thorough understanding of the relevant risk factors. Apart from numerous epidemiological studies that have provided considerable amounts of useful data, it is likely that future research in the areas of molecular biology, vascular imaging, and genetic epidemiology will further enhance the ability to evaluate the risk of stroke occurrence and recurrence. Previous population studies of CVD were few in Taiwan. A well-designed population study may provide valuable information for understanding incidence, prevalence, and risk factors of CVD, particularly long-term cohort studies. Identification of modifiable risk factors associated with more severe stroke may also help to reduce the health burden that stroke imposes on patients.

REFERENCES

1. Statistical Yearbook of the Republic of China 2006: Directorate General of Budget, Accounting and Statistics, Executive Yuan, Republic of China, 2006.
2. Martinez-Vila E, Irimia P. The cost of stroke. Cerebrovasc Dis 2004;17(Suppl 1):124-9.
3. Howard G, Howard VJ. Distribution of stroke: heterogeneity of stroke by age, race, and sex. In: Mohr JP, eds. Stroke: Pathophysiology, Diagnosis, and Management. 4th ed. Churchill-Livingstone, 2004:3-12.
4. Lu TH, Chang HY, Hwu CM, et al. Comparisons of official coders versus physician panel in assignment of underlying cause of death. J Formos Med Assoc 2001;100:365-9.
5. Ri T. Statistical observations on the mortality rates and the causes of death among the Formosans. J Formos Med Assoc 1938;37:581-628. [In Japanese; English abstract]
6. Ri T. Statistical observations on the mortality rates and the causes of death among the Formosans. J Formos Med Assoc 1938;37:702-60. [In Japanese; English abstract]
7. Chang PY, Chen KP, Lin RS. Geographical distribution of mortality from cerebrovascular disease in Taiwan. J Formos Med Assoc 1974;73:277-88.
8. Ko TS, Chen KP. A statistical study on mortality rate and causes of death by locality in Taiwan area. J Formos Med Assoc 1980;79:802-13.
9. Hu HH, Chu FL, Wong WJ, et al. Trends in mortality from cerebrovascular disease in Taiwan. Stroke 1986;17:1121-5.
10. Chang CC, Chen CJ. Secular trend of mortality from cerebral infarction and cerebral hemorrhage in Taiwan, 1974-1988. Stroke 1993;24:212-8.
11. Hung TP. Changes in mortality from cerebrovascular disease and clinical pattern of stroke in Taiwan. J Formos Med Assoc 1993;92:687-96.
12. Leung KK, Tang LY, Chie WC, et al. Mortality trends of elderly people in Taiwan from 1974 to 1994. Age Ageing 1999;28:199-203.
13. Sarti C, Rastenyte D, Cepaitis Z, et al. International trends in mortality from stroke, 1968 to 1994. Stroke 2000;31:1588-601.
14. Truelsen T, Mähönen M, Tolonen H, et al. Trends in stroke and coronary heart disease in the WHO MONICA Project. Stroke 2003;34:1346-52.
15. Sarti C, Stegmayr B, Tolonen H, et al. Are changes in mortality from stroke caused by changes in stroke event rates or case fatality? Results from the WHO MONICA Project. Stroke 2003;34:1833-41.
16. Tseng WP. Report of Epidemiologic Study of Atherosclerotic Heart Disease and Stroke in Chinese. Department of Health, Executive Yuan, ROC, 1977. [In Chinese]
17. Hu HH, Chu FL, Chiang BN, et al. Prevalence of stroke in Taiwan. Stroke 1989;20:858-63.
18. Lee TK, Huang ZS, Ng SK, et al. Impact of alcohol consumption and cigarette smoking on stroke among the elderly in Taiwan. Stroke 1995;26:790-4.
19. Lee Y, Lin RS, Sung FC, et al. Chin-Shan Community Cardiovascular Cohort in Taiwan--baseline data and five-year follow-up morbidity and mortality. J Clin Epidemiol 2000;53:838-46.
20. Chiou HY, Huang WI, Su CL, et al. Dose-response relationship between prevalence of cerebrovascular disease and ingested inorganic arsenic. Stroke 1997;28:1717-23.
21. Fuh JL, Wang SJ, Larson EB, et al. Prevalence of stroke in Kinmen. Stroke 1996;27:1338-41.
22. Huang ZS, Chiang TL, Lee TK. Stroke prevalence in Taiwan. Findings from the 1994 National Health Interview

Survey. Stroke 1997;28:1579-84.

23. Liao CC, Li TC, Lin RS, et al. Urban and rural difference in prevalence and incidence of stroke in 2000 in Taiwan. Taiwan J Public Health 2006;25:223-30.

24. Tseng CH, Chong CK, Sheu JJ, et al. Prevalence and risk factors for stroke in Type 2 diabetic patients in Taiwan: a cross-sectional survey of a national sample by telephone interview. Diabet Med 2005;22:477-82.

25. Hu HH, Sheng WY, Chu FL, et al. Incidence of stroke in Taiwan. Stroke 1992;23:1237-41.

26. Chang SF, Su CL, Chen ZY, et al. Stroke incidence in Ilan, Taiwan. J Formos Med Assoc 1995;94:30-6.

27. Fuh JL, Wang SJ, Liu HC, et al. Incidence of stroke in Kinmen, Taiwan. Neuroepidemiology 2000;19:258-64.

28. Chien KL, Sung FC, Hsu HC, et al. Apolipoprotein A-I and B and stroke events in a community-based cohort in Taiwan: report of the Chin-Shan Community Cardiovascular Study. Stroke 2002;33:39-44.

29. Mohr JP, Caplan LR, Melski JW, et al. The Harvard Cooperative Stroke Registry: a prospective registry. Neurology 1978;28:754-62.

30. Bogousslavsky J, Van Melle G, Regli F. The Lausanne Stroke Registry: analysis of 1,000 consecutive patients with first stroke. Stroke 1988;19:1083-92.

31. Brainin M. Overview of stroke data banks. Neuroepidemiology 1994;13:250-8.

32. Ryu SJ. The Chang Gung Stroke Registry: 1980. Chang Gung Med J 1986;9:204-16.

33. Lie SK. Changes in the pattern of cerebral hemorrhage: 8-year experience at Cathay General Hospital. J Formos Med Assoc 1989;88:546-9. [In Chinese]

34. Hsu WC, Chen ST, Chang HS, et al. The Chang Gung Stroke Registry: 1994. Acta Neurol Sin 1995; 4:171-9.

35. Hung TP, Chen ST, Lie SK. Final report of collaborative study group on stroke in Taipei region, 1984-1987, Taipei, Department of Health, ROC, 1987. [In Chinese; English abstract]

36. Hung TP and Study Group on Stroke. Epidemiology and clinical profiles of stroke in Taiwan: report of a stroke registry of 26 teaching hospitals in Taiwan, 1985, Taipei, Department of Health, ROC, 1987. [In Chinese; English abstract]

37. Hung TP and Study Group on Stroke. Prospective survey and registry of stroke in Taiwan Area, Taipei, Department of Health, ROC, 1992. [In Chinese; English abstract]

38. Howng SL, Hung TP, Kwan AL, et al. Intracranial aneurysm in Taiwan. J Formos Med Assoc 1995;94:S73-80.

39. Lee LS, Huang SL. Aneurysmal subarachnoid hemorrhage in Taiwan. Neurol Med Chir (Tokyo) 1998;38:122-3.

40. Jeng JS, Lee TK, Chang YC, et al. Subtypes and case-fatality rates of stroke: a hospital-based stroke registry in Taiwan (SCAN-IV). J Neurol Sci 1998;156:220-6.

41. Yip PK, Jeng JS, Lee TK, et al. Subtypes of ischemic stroke. A hospital-based stroke registry in Taiwan (SCAN-IV). Stroke 1997;28:2507-12.

42. Lin YT, Lo YK, Kuo HC, et al. Stroke registry in Kaohsiung Veterans General Hospital. Chin Med J (Taipei) 2002;65:307-13.

43. Hwang WJ, Lai ML, Cheng CJ. Serum apolipoprotein and lipid levels in patients with cerebral infarction. Acta Neurol Sin 1993;2:294-8.

44. Chung MY, Jeng JS, Yip PK, et al. Study on blood lipids, lipoproteins and apolipoproteins in different types of ischemic stroke. Acta Neurol Sin 1994;3:194-9.

45. Chen CH, Lai ML, Lai MD, et al. Apolipoprotein B gene polymorphisms in Taiwanese ischemic stroke patients. J Formos Med Assoc 1997;96:499-502.

46. Lin HF, Lai CL, Tai CT, et al. Apolipoprotein E polymorphism in ischemic cerebrovascular diseases and vascular dementia patients in Taiwan. Neuroepidemiology 2004; 23:129-34.

47. Pan WH, Chiang BN. Plasma lipid profiles and epidemiology of atherosclerotic diseases in Taiwan- a unique experience. Atherosclerosis 1995;118:285-95.

48. Pan WH, Li LA, Tsai MJ. Temperature extremes and mortality from coronary heart disease and cerebral infarction in elderly Chinese. Lancet 1995;345:353-5.

49. Chen ZY, Chang SF, Su CL. Weather and stroke in a subtropical area: Ilan, Taiwan. Stroke 1995;26:569-72.

50. Yang CY. Calcium and magnesium in drinking water and risk of death from cerebrovascular disease. Stroke 1998;29:411-4.

51. Chiu HF, Lin MC, Yang CY. Primary intracerebral hemorrhage mortality reduction after installation of a tap-water supply system in an arseniasis-endemic area in southwest-

ern Taiwan. J Toxicol Environ Health A 2007;70:539-46.

52. Tsai SS, Goggins WB, Chiu HF, et al. Evidence for an association between air pollution and daily stroke admissions in Kaohsiung, Taiwan. Stroke 2003;34:2612-6.

53. Chan CC, Chuang KJ, Chien LC, et al. Urban air pollution and emergency admissions for cerebrovascular diseases in Taipei, Taiwan. Eur Heart J 2006; 27:1238-44.

54. Peng GS, Yin SJ, Cheng CA, et al. Increased risk of cerebral hemorrhage in Chinese male heavy drinkers with mild liver disorder. Cerebrovasc Dis 2007;23:309-14.

55. Lin JJ, Yueh KC, Lin GY, et al. Lack of association between angiotensin I-converting enzyme gene deletion polymorphism and cerebrovascular disease in Taiwanese. J Formos Med Assoc 2000;99:895-901.

56. Chen CH, Eng HL, Chang CJ, et al. 4G/5G promoter polymorphism of plasminogen activator inhibitor-1, lipid profiles, and ischemic stroke. J Lab Clin Med 2003;142:100-5.

57. Chen CH, Lo YK, Ke D, et al. Platelet glycoprotein Ia C807T, Ib C3550T, and IIIa Pl (A1/A2) polymorphisms and ischemic stroke in young Taiwanese. J Neurol Sci 2004;227:1-5.

58. Yeh PS, Lin HJ, Li YH, et al. Prognosis of young ischemic stroke in Taiwan: impact of prothrombotic genetic polymorphisms. Thromb Haemost 2004;92:583-9.

59. Lin YH, Chang YM, Yu JM, et al. Toll-like receptor 4 gene C119A but not Asp299Gly polymorphism is associated with ischemic stroke among ethnic Chinese in Taiwan. Atherosclerosis 2005;180:305-9.

60. Chen HJ, Bai CH, Yeh WT, et al. Influence of metabolic syndrome and general obesity on the risk of ischemic stroke. Stroke 2006;37:1060-4.

61. Chien KL, Hsu HC, Sung FC, et al. Metabolic syndrome as a risk factor for coronary heart disease and stroke: an 11-year prospective cohort in Taiwan community. Atherosclerosis 2007;194:214-21.

62. Chien KL, Hsu HC, Sung FC, et al. Hyperuricemia as a risk factor on cardiovascular events in Taiwan: The Chin-Shan Community Cardiovascular Cohort Study. Atherosclerosis 2005;183:147-55.

63. Lien LM, Chen WH, Chiu HC, et al. High titer of anticardiolipin antibody is associated with first-ever ischemic stroke in Taiwan. Cerebrovasc Dis 2006;22:225-30.

64. Chiu EH, Tan TY, Chang KC, et al. Risk factors for ischemic stroke: electrocardiographic findings. Acta Neurol Taiwan 2006;15:232-6.

65. Tan TY, Tseng MC, Chang KC. Risk factors for first-ever ischemic stroke: a hospital based case-control study in Kaohsiung, Taiwan. Chang Gung Med J 2004;27:801-7.

66. Jeng JS, Chung MY, Yip PK, et al. Extracranial carotid atherosclerosis and vascular risk factors in different types of ischemic stroke in Taiwan. Stroke 1994;25:1989-93.

67. Chang CH, Chang YJ, Lee TH, et al. Risk factors of carotid stenosis in first-ever ischemic stroke in Taiwan: a hospital-based study. Acta Neurol Taiwan 2006;15:237-43.

68. Pan WH, Bai CH, Chen JR, et al. Associations between carotid atherosclerosis and high factor VIII activity, dyslipidemia, and hypertension. Stroke 1997;28:88-94.

69. Su TC, Jeng JS, Chien KL, et al. Hypertension status is the major determinant of carotid atherosclerosis: a community-based study in Taiwan. Stroke 2001;32:2265-71.

70. Su TC, Chien KL, Jeng JS, et al. Pulse pressure, aortic regurgitation and carotid atherosclerosis: a comparison between hypertensives and normotensives. Int J Clin Pract 2006;60:134-40.

71. Huang ZS, Jeng JS, Wang CH, et al. Correlations between peripheral differential leukocyte counts and carotid atherosclerosis in non-smokers. Atherosclerosis 2001;158:431-6.

72. Huang ZS, Wu TH, Jeng JS, et al. Male predominance of hypertension-associated atherosclerosis in the internal carotid artery. Formosan J Med 2007;11:337-44. [In Chinese; English abstract]

73. Sun Y, Lin CH, Lu CJ, et al. Carotid atherosclerosis, intima media thickness and risk factors--an analysis of 1781 asymptomatic subjects in Taiwan. Atherosclerosis 2002;164:89-94.

74. Wang CH, Jeng JS, Yip PK, et al. Biological gradient between long-term arsenic exposure and carotid atherosclerosis. Circulation 2002;105:1804-9.

75. Su TC, Jeng JS, Wang JD, et al. Homocysteine, circulating vascular cell adhesion molecules, and carotid atherosclerosis in postmenopausal vegetarian women and omnivores. Atherosclerosis 2006;184:356-62.

76. Li YH, Chen CH, Yeh PS, et al. Functional mutation in the promoter region of thrombomodulin gene in relation to carotid atherosclerosis. Atherosclerosis 2001;154:713-9.

77. Chang CW, Lay HJ, Horng YS, et al. Evident risk factors

for young stroke patients in Taiwan. J Stroke Cerebrovasc Dis 1995;5:158-62.

78. Lu CH, Chang WN, Chee CY. Young stroke in southern Taiwan. Acta Neurol Taiwan 1997;6:295-9.

79. Lee TH, Hsu WC, Chen CJ, et al. Etiologic study of young stroke in Taiwan. Stroke 2002;33:1950-5.

80. Fuh JL, Liu HC, Wang SJ, et al. Nontraumatic hemorrhagic stroke in young adults in Taiwan. J Stroke Cerebrovasc Dis 1994;4:101-5.

81. Lin CL, Howng SL. Nontraumatic intracerebral hemorrhage in young adult. Kaohsiung J Med Sci 1997;13:237-42.

82. Chen CH, Lai ML. Nontraumatic intracerebral hemorrhage in young adults: analysis of 214 cases. Acta Neurol Taiwan 1999;8:96-101.

83. Lai SL, Chen ST, Lee TH, et al. Spontaneous intracerebral hemorrhage in young adults. Eur J Neurol 2005;12:310-6.

84. Wang KC, Chen CP, Yang YC, et al. Stroke complicating pregnancy and the puerperium. Chin Med J (Taipei) 1999; 62:13-9.

85. Jeng JS, Tang SC, Yip PK. Incidence and etiologies of stroke during pregnancy and puerperium as evidenced in Taiwanese women. Cerebrovasc Dis 2004;18:290-5.

86. Liang CC, Chang SD, Lai SL, et al. Stroke complicating pregnancy and the puerperium. Eur J Neurol 2006;13:1256-60.

87. Jeng JS, Tang SC, Yip PK. Stroke in women of reproductive age: comparison between stroke related and unrelated to pregnancy. J Neurol Sci 2004;221:25-9.

88. Wang SL, Pan WH, Lee MC, et al. Predictors of survival among elders suffering strokes in Taiwan: observation from a nationally representative sample. Stroke 2000;31:2354-60.

89. Yang CY, Chang CC, Kuo HW, et al. Parity and risk of death from subarachnoid hemorrhage in women: evidence from a cohort in Taiwan. Neurology 2006;67:514-5.

90. Tseng MC, Chang KC. Stroke severity and early recovery after first-ever ischemic stroke: results of a hospital-based study in Taiwan. Health Policy 2006;79:73-8.

91. Chang KC, Tseng MC, Tan TY, et al. Predicting 3-month mortality among patients hospitalized for first-ever acute ischemic stroke. J Formos Med Assoc 2006;105:310-7.

92. Pan SL, Wu SC, Wu TH, et al. Location and size of infarct on functional outcome of noncardioembolic ischemic stroke. Disabil Rehabil 2006;28:977-83.

93. Lin JH, Hsieh CL, Lo SK, et al. Prediction of functional outcomes in stroke inpatients receiving rehabilitation. J Formos Med Assoc 2003;102:695-700.

94. Hu MH, Hsu SS, Li CC, et al. Correlation between duration of rehabilitation and functional outcome at discharge and at follow-up in stroke patients. Formosan J Med 2006;10:248-55. [In Chinese]

95. Tang SC, Huang SJ, Jeng JS, et al. Third ventricle midline shift of spontaneous supratentorial intracerebral hemorrhage evaluated by transcranial color-coded sonography. J Ultrasound Med 2006;25:203-9.

96. Huang CH, Chen WJ, Chang WT, et al. QTc dispersion as a prognostic factor in intracerebral hemorrhage. Am J Emerg Med 2004;22:141-4.

97. Fang HY, Lin CY, Ko WJ. Hematology and coagulation parameters predict outcome in Taiwanese patients with spontaneous intracerebral hemorrhage. Eur J Neurol 2005;12:226-32.

98. Wong KS. Risk factors for early death in acute ischemic stroke and intracerebral hemorrhage: a prospective hospital-based study in Asia. Asian Acute Stroke Advisory Panel. Stroke 1999;30:2326-30.

99. Wu TH, Chen HH, Lee TK. Factors affecting the first recurrence of noncardioembolic ischemic stroke. Thromb Res 2000;97:95-103.

100. Lin HJ, Yeh PS, Tsai TC, et al. Differential risks of subsequent vascular events for transient ischemic attack and minor ischemic stroke. J Clin Neurosci 2007;14:17-21.

101. Chen ST, Chiang CY, Hsu CY, et al. Recurrent hypertensive intracerebral hemorrhage. Acta Neurol Scand 1995;91:128-32.

102. Chen CH, Huang CW, Chen HH, et al. Recurrent hypertensive intracerebral hemorrhage among Taiwanese. Kaohsiung J Med Sci 2001;17:556-63.