ORIGINAL ARTICLE

Outcomes after first-ever stroke

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Objectives To determine the outcomes after first-ever stroke, including mortality, dependence, and recurrence.

Design Retrospective study on a prospectively collected cohort.

Setting Regional hospital, Hong Kong.

Patients A cohort of 755 patients presented to our hospital from 1996 to 1998 with their first-ever stroke.

Main outcome measures Mortality and stroke recurrence rate at 30 days, 1 year, and 5 years from the onset of the stroke. Dependence in activity of daily living at 5 years from the onset of stroke.

Results The mortality rate was 15.1% at 30 days, 22.5% at 1 year, and 39.7% at 5 years from the onset of the first-ever stroke. The rate of stroke recurrence was 0.9% at 30 days, 7.0% at 1 year, and 21.2% at 5 years from the onset of first-ever stroke. Among patients presenting with ischaemic strokes, 109 (20.6%) had a recurrence, of which 92 (84%) were ischaemic strokes and 17 (16%) were haemorrhagic. Among patients presenting with intracerebral haemorrhage, 25 (23.1%) had a recurrence, of which 12 (48%) were haemorrhagic strokes and 13 (52%) patients were ischaemic. After 5 years, 11% of the patients were dependent in terms of activity of daily living.

Conclusions The long-term prognosis after first-ever stroke is poor—5 years after their stroke, 39.7% of patients had died and 10.7% were dependent in terms of activity of daily living; 136 (21%) who survived at least 30 days after the initial stroke, had a recurrence within 5 years.

Introduction

Until 2003, stroke was the third leading cause of death (after neoplasm and heart diseases) in Hong Kong,[1] and since then it has become the fourth leading cause of death[2] (pneumonia being the third). We have witnessed a secular change in stroke pattern and significant improvement in stroke case fatality rate locally in the past two decades.[3-5] The proportion of ischaemic strokes increased from 62% in 1984 to 84% in 2002.[3-5] The 30-day fatality rate decreased from 25% in 1989 to 11% in 2002.[4,5] However, data on long-term prognosis after stroke, including mortality and recurrence, are scarce. The burden of stroke can only be meaningfully evaluated if we have reliable data on its long-term outcomes. The purpose of this study was to explore the long-term outcomes of patients with first-ever stroke.

Methods

In our hospital, all patients with acute stroke attending the accident and emergency department would be admitted to the department of medicine. Acute stroke is defined as stroke with onset of symptoms within 5 days from the date of admission. The patients would be transferred to the neurosurgical team only if neurosurgery was needed. From July 1996 onwards, the neurology team assessed all acute stroke patients under the care of our department. We entered the data of all acute stroke patients into a stroke registry, which included: demographic data, risk factors for stroke, and stroke type (ischaemic, intracerebral haemorrhage, subarachnoid haemorrhage) and subtype for ischaemic stroke according to the Oxfordshire Community Stroke Project Classification.[6] The ischaemic stroke subtypes are classified into total anterior circulation infarction, partial anterior circulation infarction, posterior circulation infarction, and lacunar infarction. Non-contrast computed tomography (CT) of the brain was performed in all acute stroke patients within 24 hours of admission. The attending neurologist classified the stroke

Key words
Cerebrovascular accident; Ischemic attack, transient; Prognosis; Recurrence; Treatment outcome

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首次中風後的結果

目的 探討首次中風後的結果，包括死亡率、生活依賴程度和復發率。

設計 利用前瞻性搜集到的資料，對一批病人進行回顧性研究。

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患者 1996年至1998年期間因首次中風而送院的病人，共755人。

主要結果測量 首次中風後的死亡率和復發率（三十日內、一年內和五年內）；首次中風後五年內的日常生活依賴程度。

結果 首次中風後三十日內、一年內和五年內的死亡率，分別為15.1%、22.5%和39.7%，而上述時段的復發率則為0.9%、7.0%和21.2%。對於缺血性中風病人，109人（20.6%）再次病發，其中92人（84%）屬缺血性中風，17人（16%）屬出血性中風。對於臚內出血的病人，25人（23.1%）再次病發，其中12人（48%）屬出血性中風，13人（52%）屬缺血性中風。病發五年內，須依賴他人照顧日常生活的病人有11%。

結論 中風後五年內的長期預後情況並不樂觀——中風後五年有39.7%病人死亡，10.7%病人須依賴其他人照顧日常生活；病發三十日後仍存活的病人中，136人（21%）在五年內會復發。

type and subtype after reviewing all the information upon discharge. All patients enrolled in the first 2 years of our stroke registry with first-ever stroke were identified for recruitment into the present study. Recurrent stroke was defined as new neurological deficit in a different vascular territory or after a period of neurological stability or improvement. All patients with recurrent stroke had CT brain confirmation. Deterioration due to oedema or haemorrhagic transformation was excluded.

Patients' data in the registry, in-patient hospital records, out-patient follow-up notes, and subsequent hospital admission records were retrieved and retrospectively reviewed at 5 years or more after the index stroke episode. For patients followed up in other hospitals, their electronic hospital records including discharge summary and out-patient progress notes were traced. Patients were followed up in the medical clinics, integrated clinics of our hospital, and government out-patient clinics. Some patients were also followed up by doctors in the rehabilitation hospital or in other hospitals (when they change their residence).

Based on the information retrieved, the occurrence of recurrent stroke, dependence in terms of activity of daily living, and mortality were determined. The Modified Rankin Scale score (to assess dependence in the activity of daily living) was determined for each patient after reviewing all available information from hospital data.

The type of recurrent stroke was classified into ischaemic, intracerebral haemorrhage, and subarachnoid haemorrhage. Chi squared test by the Statistical Package for the Social Sciences (Windows version 12.1; SPSS Inc, Chicago [IL], US) was used to analyse the data, if relevant. Any difference with a $P<0.05$ (two-sided) was regarded as statistically significant.

Results

A total of 1057 acute stroke episodes were enrolled in our stroke registry for the 2-year period from 28 July 1996 to 27 July 1998. Of these, 783 were first-ever strokes and 274 were recurrent strokes. There were 28 first-ever stroke patients whose outcome could not be traced at the time of review. The remaining 755 patients were included in the study. The baseline characteristics of these patients are shown in Table 1.

The mortality rates of the whole cohort, the rate of vascular and non-vascular cause, the rates of different stroke types and subtypes of ischaemic stroke are shown in Table 2. Mortality rate at 30 days was significantly higher in patients with haemorrhagic stroke than in patients with ischaemic stroke. Among patients with ischaemic stroke, mortality rate at 30 days was significantly higher in those with more severe stroke (such as total anterior

TABLE 1. Baseline characteristics of the whole cohort, and patients with and without recurrent stroke

Characteristic	Whole cohort	Patients with recurrent stroke in 5 years	Patients without recurrent stroke in 5 years
No. of patients	755	136	619
Mean age (range) [years]	71.1 (27-98)	71.0 (42-92)	71.1 (27-98)
Male:female	390:365	71:65	319:300
No. of patients with atrial fibrillation	97 (13%)	23 (17%)	74 (12%)
No. of patients with diabetes mellitus	167 (22%)	36 (26%)	131 (21%)
No. of patients with hypertension	362 (48%)	80 (59%)	282 (46%)
No. of patients with ischaemic heart disease	87 (12%)	15 (11%)	72 (12%)
No. of patients with hypercholesterolaemia	70 (9%)	17 (13%)	53 (9%)
No. of smokers	180 (24%)	36 (26%)	144 (23%)

TABLE 2. Mortality rates in the whole cohort, different types of stroke, and in different subtypes of ischaemic stroke

Type of index stroke	No. of patients	Mortality rate		
		At 30 days	At 1 year	At 5 years
Whole cohort	755	15.1%	22.5%	39.7%
Vascular cause	-	15.0%	15.0%	21.0%
Non-vascular cause	-	0.1%	7.5%	18.7%
Different types of stroke				
Subarachnoid haemorrhage	18	72.2%*	83.3%	94.4%
Intracerebral haemorrhage	171	36.8%*	41.5%	56.1%
Ischaemic	566	6.7%	14.8%	33.0%
Total anterior circulation infarction	21	52.4%*	71.4%	80.9%
Partial anterior circulation infarction	188	9.6%	20.7%	37.8%
Posterior circulation infarction	38	7.9%	21.1%	31.6%
Lacunar infarction	319	1.9%	6.9%	27.3%

* **P<0.001 (compared to total ischaemic stroke mortality)**

TABLE 3. Rates of recurrent stroke according to stroke type among patients surviving more than 30 days

Type of index stroke	No. of patients	Rate (No.) of recurrent strokes at 1 year	Cumulative rate (No.) of recurrent strokes at 5 years
Ischaemic	528	6.8% (36)	20.6% (109)
Subarachnoid haemorrhage	5	20.0% (1)	40.0% (2)
Intracerebral haemorrhage	108	7.4% (8)	23.1% (25)
Total	**641**	**7.0% (45)**	**21.2% (136)**

TABLE 4. Number of patients with fatal and non-fatal recurrent stroke

Recurrent stroke	No. of patients died in <30 days	No. of patients died in >30 days to 1 year	No. of patients died in >1 year to 5 years
Fatal recurrent stroke	2	7	15
Non-fatal recurrent stroke	4	32	76

circulation infarction) than in the remainder.

The rates of recurrent stroke in patients surviving more than 30 days and in the different stroke types are shown in Table 3. The number of fatal and non-fatal recurrent strokes are shown in Table 4.

In terms of the activity of daily living, 16 (2.1%) patients followed up in the other hospitals could not have their Modified Rankin Scale score determined because of insufficient information. Eighty-one (10.7%) of the whole cohort were dependent in activity of daily living at 5 years.

Among 566 patients with initial ischaemic stroke, 528 were alive 30 days after the initial stroke; of these survivors 109 had a recurrent stroke. The recurrent episode was ischaemic in 92 (84%) patients and haemorrhagic stroke in 17 (16%). Among 171 patients with initial cerebral haemorrhage, 108 patients were alive 30 days after the initial stroke and 25 of them had recurrent stroke. Among them, 12 were haemorrhagic and 13 ischaemic.

After excluding patients who died within 30 days, patients with recurrent stroke were associated with higher mortality rate at 5 years (37.8% vs 26.9%; P=0.014) as shown in Table 5, but not with respect to dependence in terms of activity of daily living.

Discussion

This was a hospital-based study. Thus, patients with very minor deficits (and not admitted), those who refused admission, those who died before admission (often with severe deficits), and those who were admitted to private hospitals were not included. The stroke registry in our hospital had been started since 1996. Only the basic demographic data, stroke type and subtype, and risk

TABLE 5. Mortality rates at 5 years in patients surviving the first 30 days

Patients	No.	Died within 5 years	Mortality rate
With recurrent stroke	136	51	37.5%*
Without recurrent stroke	506	135	26.7%

* **P=0.014 (when compared to patients without recurrent stroke)**

factors were collected. We performed a retrospective analysis of the data during the period from 1996 to 1998, information including how the risk factors were controlled, subtype of ischaemic stroke of the recurrent stroke, might not be available if the patients were not followed up or admitted to our hospital. Patients were treated with anti-platelet agents (or anticoagulants for embolic stroke). Their risk factors were also managed even if they were followed up in different hospitals or clinics.

Previous studies showed the 30-day fatality rate to be declining in the past two decades, both locally[4,5] and in other countries.[7-10] The rate was 25.4% in 1989 in a study from the Prince of Wales Hospital in Hong Kong. In this study the figure was 15.1% for the period from 1996 to 1998 and was down to 11% in a study performed in 2004 done by the authors and using the same stroke registry.[5]

There have been relatively few long-term studies on the prognosis after a first-ever stroke. Despite the promising improving trend, our results show that for the whole cohort the outlook is still dismal; 33.0% of patients with ischaemic strokes, 56.1% with cerebral haemorrhage, and 94.4% with subarachnoid haemorrhage were dead at 5 years. In patients with ischaemic stroke, those with total anterior circulation infarction had a much worse outcome; 80.9% were dead at 5 years. The mortality rate in patients with stroke recurrence was significantly higher than those with no recurrence. This is similar to the experience in Australia where 25% of recurrent stroke patients died within 28 days.[11] It is therefore of utmost importance to prevent recurrent stroke to improve long-term outcomes.

In our study for 30-day survivors of ischaemic stroke, the recurrence rate at 5 years was 20.6% and for cerebral haemorrhage it was 23.1%, these rates are similar though somewhat lower than those reported elsewhere.[11-14] However studies which excluded patients with a new stroke within the first 21 days of the initial stroke reported lower recurrence rates.[15,16]

Among our patients with initial intracerebral haemorrhage, 52% (13) of the 25 patients with recurrent stroke were ischaemic in nature. Notably, intracerebral haemorrhage patients in our study tended not to have multiple risk factors for ischaemic stroke. Thus, investigation for large vessel disease may not be cost-effective in this population. Three previous studies[12-14] had also found that ischaemic strokes may occur among survivors of cerebral haemorrhage. It is therefore possible that non-lacunar ischaemic strokes were due to development of atherosclerotic large vessel disease only in long-term survivors of cerebral haemorrhage.

For individuals with an initial ischaemic stroke, subsequent stroke was also more likely to be ischaemic, although it was haemorrhagic in nature in a sizable proportion of patients (15.6%). Stroke recurrence (whether ischaemic or haemorrhagic) was more likely in the first year. In our series, recurrence of cerebral haemorrhage among ischaemic stroke survivors was similar although somewhat higher than the cumulative results in three other overseas studies (15.6% vs 10.5%).[12-14]

In a long-term follow-up of patients after a minor stroke,[17] the presence of prior myocardial infarction, non-valvular atrial fibrillation and hypercholesterolaemia conferred a higher mortality rate. In the same study, hypertension and prior myocardial infarction was associated with stroke recurrence. In another study in 297 patients with ischaemic stroke,[13] the recurrence rate was 7.4% at 90 days. The authors found that major hemispheric stroke, the atherothrombotic stroke mechanism (cryptogenic [unknown], large-vessel, small-vessel [lacunar] and cardioembolic stroke, of which large-vessel stroke conferred the highest risk of early recurrence), and the presence of atrial fibrillation were independent predictors of early recurrence. Information on the pattern and mechanisms of recurrent stroke is very useful for formulating an effective stroke prevention strategy.

These studies indicate that overemphasis on subtype-specific risk factor control, such as antithrombotic treatment for ischaemic stroke, has inadequacy. Thus, for patients with initial haemorrhagic stroke, we do not prescribe any antithrombotic drugs even in patients with multiple risk factors for atherosclerosis, yet 54% of them subsequently developed ischaemic stroke. After the first year, in fact, ischaemic stroke became more likely even for those whose initial stroke was haemorrhagic. It is advisable that thrombogenic risk factors should be looked for and treated vigorously even among patients presenting with cerebral haemorrhage. The choice and and timing of antithrombotic interventions and the risk benefit ratio in this population are also issues for future study.

For patients with ischaemic stroke, prescribing antiplatelet agents or anticoagulants is a usual practice. However, it may contribute to 4.9-15.6% of recurrent strokes. The problem of cerebral haemorrhage also

needs to be better studied. The presence of microbleeds on gradient echo magnetic resonance imaging sequence may be a marker of a higher chance of cerebral haemorrhage.[18] A case control study showed that patients with recurrent haemorrhagic stroke while taking aspirin had increased numbers of asymptomatic microbleeds.[19] However, microbleeds are also seen with many recurrent ischaemic strokes and may even be predictive of recurrent ischaemic stroke.[20,21] Thus, prospective studies are necessary to clarify whether microbleeds portend higher haemorrhagic risk or a greater need for antithrombotic agents. In clinical practice, it does not seem appropriate to suspend prophylactic antithrombotic agents just because of the presence of microbleeds.

As recurrent stroke is much more likely when multiple risk factors are present, until we can have better method to identify patients who are likely to develop recurrent strokes of a specific type, meticulous control of risk factors for both ischaemic and haemorrhagic strokes is necessary.

Conclusions

Outcomes of first-ever stroke are poor; 21% of the patients surviving more than 30 days had recurrent stroke, 39.7% died and another 10.7% became dependent in activity of daily living within 5 years of the first-ever stroke. Patients with recurrent stroke had a higher mortality. A significant percentage of patients had recurrent strokes of a different type to their primary event. Improvement in secondary prevention is clearly needed.

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