

Stroke in the Very Old

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One of the problems the world has been facing at present is a demographic transition of the population which results from a decrease in fertility and lengthening of life expectancy. The number of people aged 80 or above is growing faster than any other age group. In 2006, the percentage of people aged 80 and over is approximately 19 per cent in developed countries and around 10 per cent in developing countries. In 2050, these figures are projected to be 29 and 18 per cent in developed and developing countries respectively.¹ Life expectancy at the age of 60 for men and women is 17 and 19 years in the less developed countries compared to 19 and 23 years in the more developed countries.

The aged often have multiple diseases; one of which is stroke. Stroke is the leading cause of morbidity and mortality in the elderly and strikes more frequently and more severely in this group. However, only a few patients aged over 80 have been included in the large trials of thrombolysis in acute stroke. Moreover, the evidence of stroke prevention in terms of statins, antidiabetic medications, antiplatelets and carotid endarterectomy in the very old is scant and needs more trials to be approved. Nevertheless, physicians will be forced by this demographic change to re-consider various preventive and therapeutic strategies for patients aged 80 or older in the near future.

Clinical differences between stroke in younger old age and very old age

Patients aged 80 and over account for one fifth to one third of stroke patients.² The incidence of both ischaemic and hemorrhagic strokes rises correspondently with increasing age. As females have a longer life expectancy, stroke in this age group is predominantly female compared to the younger counterpart (67% of females 80 or over versus 43% of females under 80). For hemorrhagic stroke, cerebral amyloid angiopathy accounts for up to one third of the causes in elderly patients and its incidence increases dramatically in octogenarians compared to the younger population. Many medical diseases are more commonly present in the very old such as hypertension, atrial fibrillation, ischaemic heart disease, congestive cardiac failure and prior stroke.²⁻⁸ As a consequence of the higher incidence of heart diseases in this group, the cardio-embolic etiology of stroke is more common in patients aged 80 or over. Table 1 summarizes the clinical differences between stroke in patients aged 80 or over and aged less than 80.

Clinical presentations show some different points

TABLE 1. The clinical differences between stroke in patients aged 80 or over and aged less than 80.²⁻⁸

Clinical characteristics	≥ 80 yrs	< 80 yrs
% female	67%	43%
Pre-stroke independence (mRS 0-1)*	55%	80%
Previous stroke	18%	11%
HT, AF, CCF, IHD [#]	More	Less
NIHSS ⁺	15	13
Cardio-embolic stroke	More	Less

* mRS: Modified Rankin Scale, # HT: hypertension, AF: atrial fibrillation, CCF: congestive cardiac failure, IHD: ischaemic heart disease, + NIHSS: National Institute of Health Stroke Scale

between the two age groups. The very old tend to have more severe stroke as assessed with the National Institute of Health Stroke Scale (NIHSS) and also tend to present more frequently with coma, paralysis, language degradation, swallowing problems, and urinary incontinence.² Furthermore, a lot of patients live alone as their partner has passed away long beforehand. The percentage of the elderly living alone is 19 and 39 per cent for men and women respectively in developed countries respectively and 5 and 9 per cent respectively in developing countries.¹ Though these figures in Thailand in the year 2006 are only 3 and 6 percent for men and women respectively, the figures tend to climb up gradually. Thus, some of these patients arrive in hospitals and receive the treatment far later than the younger old patients as no family member is present to detect their symptoms and bring them to a hospital immediately.

Stroke outcome

The European BIOMED study comparing stroke in patients aged 80 or over and aged less than 80 reported a

TABLE 2. Natural outcome of stroke in patients aged ≥ 80 years and < 80 years.²⁻³

Outcome	≥ 80 years (%)	< 80 years (%)
In-hospital mortality rate	23-32	9-12
3 months mortality rate	31-45	15-21
mRS * 0-2	30	52
Discharge to long term nursing care facilities	17	5

* mRS: Modified Rankin Scale

TABLE 3. The studies regarding thrombolysis in stroke patients aged 80 or older.^{3-8,10-12}

Year	Authors	Patients Included		SICH (%)		Fatal ICH (%)		In-hospital Death rate (%)		Favourable Outcome at 3 months		Mortality after 3 months	
		≥80	<80	≥80	<80	≥80	<80	≥80	<80	≥80	<80	≥80	<80
2000	Tanne, et al	30	159	3	6	3	2	20	8*	NA	NA	NA	NA
2004	Simon, et al	62	0	9.7	-	8	-	24.2	-	19.7	-	32.8	-
2005	Vatankhah, et al	16	13#	0	3.4	0	0	0	6.9	NA	NA	25	20.7
2005	Engelter, et al	38	287	13	8	5	3	NA	NA	29	37	32	12*
2005	Mouradian, et al	31	65	9.7	6.2	NA	NA	32.3	9.2*	NA	NA	32.3	10.8*
2005	Berrouschoot, et al	38	190	2.6	2.6	NA	NA	NA	NA	26.3	46.8*	21.1	5.3*
2005	Chen, et al	56	127	7.1	6.3	3.5	3.9	20	11	NA	NA	NA	NA
2006	Oostenbrugge, et al	45	139	11.1	2.9*	NA	NA	NA	NA	27	45*	NA	NA
2006	Sylaja, et al	270	865	4.4	4.6	4.1	3.6	NA	NA	26	40*	35.3	18.2*

* Statistically significant (p<0.05), NA: non available data, # Patients aged 76-80 years only

23% versus 10% in-hospital and 45% versus 21% 3-month mortality in the two groups respectively.² Compared to the patients aged less than 80, the very old were less often discharged home (46% versus 20% respectively) and were significantly discharged to long term nursing care facilities (5% versus 17% respectively).³

The favourable outcome as assessed by modified Rankin Scale and Barthel index among those who survived after three months clearly shows the better outcome in the younger age group compared to the older one as shown in Table 2.

Thrombolytic treatment in patients aged 80 and over

Most of the rt-PA stroke trials have excluded patients aged over 80; there are only 42 patients in the National Institute of Neurologic Disorders and Stroke (NINDS) records who were randomized to thrombolytic treatment. The point of most concern in giving thrombolysis in the extreme age is the intracranial bleeding which might lead to death. The possible causes of this risk are cerebral amyloid angiopathy, frail cerebral vasculature, and the decrease in renal clearance of the thrombolytic agent.⁹

Several trials have tried to answer questions regarding the safety of the drug and its clinical effectiveness to improve the clinical outcomes in very old patients as tabulated in Table 3. Overall, the rate of symptomatic intracerebral hemorrhage (SICH) and fatal hemorrhage were the same in each group.^{3-8,10-12} The clinical predictors for SICH were previous hypertension and aspirin use whereas age was not. The favourable outcome at three months as assessed by modified Rankin Scale (mRS) was poorer at an advanced age. The mortality rates both in hospital and at 3 months in the octogenarians were significantly higher than that of the younger age group.^{3-8,10,12} However, both favourable outcomes and mortality rates seem to be similar to the natural outcome of stroke without thrombolysis summarized in Table 2.² The systematic review regarding stroke thrombolysis in the elderly shows that if thrombolized, the older patients have a 3.09 times higher 3-month mortality and were less likely to regain a favourable outcome with the odds ratio 0.53. The likelihood for SICH was similar in both age groups.¹³ Some studies which yielded a conflicting result showed that old age was a factor predicting hospital death with the odds ratio of 1.6 for each 10-year increment in age. Moreover, the rate of ICH after rt-PA use increased with age from 4.9 per cent in patients aged under 55 years and 10.3 per cent in patients age 75 years and over.¹⁴

Most of these studies have a tendency to support the

use of thrombolysis in the octogenarian stroke. However, they are not randomized controlled trials and some are retrospective or cohort data, hence the implementation of these results should be done very cautiously. However, at least most of the study results do not advise against the use of thrombolysis in octogenarian stroke.

Prognostic factors for stroke outcome and ICH after thrombolysis

Several studies tried to find factors to predict the outcome of stroke. These factors predicting poor clinical outcome are severity of stroke (National Institute of Health Stroke Scale: NIHSS), old age, high blood glucose, high blood pressure, abnormal baseline CT scan, delayed time to thrombolysis, and some co-morbid diseases such as diabetes mellitus, coronary heart disease and atrial fibrillation.^{5,8,10, 15-16} Some factors might predict the risk of ICH following thrombolysis such as stroke severity (NIHSS), high blood glucose, high systolic blood pressure, hypodensity at basal ganglia on the CT scan, heperdensed middle cerebral artery, and a large volume of ischaemic tissue on diffusion weighted imaging (DWI).^{14,17-22} Though some factors are controversial, identifying these predictors might help in clinical decisions.

CONCLUSION

Currently, the octogenarian population has an average annual growth rate twice as high as the growth rate of the population over 60 years of age. Stroke will unavoidably be a major problem of this age as one third of it strikes this group. Acute medical treatment, especially thrombolysis in carefully selected ischaemic stroke patients, might be beneficial and should not be limited solely on the grounds of age alone. However, evidence-based treatment regarding thrombolysis in octogenarians requires randomized controlled trials and might be provided by the MRC Third International Stroke Trial (IST-3) as a consequence of there being no upper age limit in that trial.

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