

Editorial

The thrombolysis era: from heart attack to brain attack

溶解血栓的年代：從心臟病發至腦中風

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In this issue there are three articles on stroke, attesting to the recent global interest in stroke care. Yun et al presented "a retrospective study on intracerebral haemorrhage reduction by MRI versus CT in intravenous thrombolysis for acute ischaemic stroke". Üstündağ et al studied "the role of serum ferritin, pro-brain natriuretic peptide and homocysteine levels in determining ischaemic stroke subtype, severity and mortality". Kavalci et al discussed the "association of renal dysfunction with stroke subtypes in acute stroke patients".

Stroke is the 4th leading cause of death in Hong Kong. It accounted for 8.9% of the total deaths in 2008.¹ The incidence has been rising in the past five years, with 16,122 strokes (231 per 100,000 population) and 1360 transient ischaemic attacks registered by the Hospital Authority in 2008. Stroke is the leading cause of permanent disability requiring nursing home or institutional care. After stroke, about 1/3 patients die, 1/3 recover and 1/3 suffer from permanent disability.²

The presentation of the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico (GISSI-1) study results in late 1985 and their publication in early 1986 have been widely recognised as the opening of the thrombolytic era: intravenous streptokinase reduces

acute myocardial infarction inhospital mortality.³ Intravenous thrombolysis for acute myocardial infarction is now a standard practice in all the 16 public emergency departments in Hong Kong.

Similarly, the 1995 National Institute of Neurological Disorders and Stroke (NINDS) trial opened a new era for acute ischaemic stroke: intravenous tissue plasminogen activator (tPA) reduces long-term disability.⁴ The use of tPA for acute ischaemic stroke was approved by the US Food and Drug Administration (FDA) in 1996 and subsequently by regulatory agencies in Canada, Europe, South America, and Asia. The Cochrane Database of Systematic Reviews 2009 on tPA thrombolysis for acute ischaemic strokes concluded that there were: (1) non-significant excess of early deaths; (2) non-significant excess of deaths by end of follow-up; (3) significant excess of symptomatic intracranial haemorrhages; (4) significant reduction in disability in survivors; and (5) instability of data.⁵

Because of the unique susceptibility of neurons to ischaemia and the availability of new therapeutic interventions with tPA, minute counts. In a typical middle cerebral artery ischaemic stroke, two million nerve cells will be lost for each minute passed without reperfusion.⁶ In acute cerebral ischaemia, time lost is brain lost and the sooner tPA is given, the greater the benefit. A pooled analysis of all 2775 patients enrolled in the first six intravenous tPA trials provided clear and convincing evidence of a time-dependent benefit of thrombolytic therapy ($p=0.005$). Treatment within the first 90 minutes of symptom onset increased the odds of a favourable 3-month outcome for the tPA

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group by 2.8-folds (95%CI 1.8-4.5), 1.6 (1.1-2.2) for treatment between 91-180 min, and 1.4 (1.1-1.9) for treatment between 181-270 min, while treatment between 271-360 min did not improve outcome in a statistically significant manner – 1.2 (0.9-1.5).⁷

A study by Siu et al in an emergency department in Hong Kong 10 years ago showed that there was a mean delay in computed tomography of 4.9 hours for acute stroke patients. Only 7.3% and 27.1% of the patients had CT brain done within one and two hours respectively, and only 10.5% could meet the three-hour criteria.⁸ The leisurely approach to acute ischaemic stroke management in the past should now be replaced by an approach that treats stroke as a true medical emergency.

The American Heart Association highlights the major steps in diagnosis and treatment and the key points at which delays can occur: the 7D's of stroke care – detection, dispatch, delivery, door (arrival and urgent triage in the emergency department), data (CT/MRI), decision, and drug administration.⁹ Patients at high risk for stroke must be taught to recognise early symptoms (such as the acronym FAST – face, arm, speech and time), and hospitals should organise clinical protocols and pathways for the efficient implementation of stroke therapies. However, it is disappointing to see that emergency departments in Hong Kong are in general ill-prepared for this medical emergency! (Table 1)

Table 1. Arrangement of thrombolysis for acute ischaemic stroke in emergency departments in Hong Kong

Available during office hours	Not available
POH	AHNS
PWH	CMC
PMH	KWH
QEH (24 hours)	NDH
QMH	PYNEH
RH	SJH
TMH	TKOH
UCH	YCH

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