

Intra-arterial revascularisation therapy for acute ischaemic stroke: initial experience in a Hong Kong hospital

Edward HC Wong 王浩中
 Simon CH Yu 余俊豪
 Alexander YL Lau 劉玉麟
 Venus SW Hui 許詩韻
 Cecilia SF Leung 梁淑芳
 Joyce WY Hui 許慧儀
 Deyond YW Siu 蕭容媛
 Jill M Abrigo
 KT Lee 李國棟
 Colin A Graham 簡家簾
 Lawrence KS Wong 黃家星
 Thomas WH Leung 梁慧康

Key words

Brain ischemia; Magnetic resonance angiography; Stroke; Tissue plasminogen activator; Treatment outcome

Hong Kong Med J 2013;19:135-41

Prince of Wales Hospital, Shatin, Hong Kong;

Department of Medicine and Therapeutics

EHC Wong, MB, ChB, FHKAM (Medicine)

AYL Lau, MB, ChB, FHKAM (Medicine)

VSW Hui, MSc, RN

CSF Leung, MSc, RN

LKS Wong, MD, FHKAM (Medicine)

TWH Leung, MB, ChB, FHKAM (Medicine)

Department of Imaging and Interventional Radiology

SCH Yu, MD, FHKAM (Radiology)

JWY Hui, MB, ChB, FHKAM (Radiology)

DYW Siu, MB, ChB, FHKAM (Radiology)

JM Abrigo, MD

KT Lee, MSc

Accident and Emergency Medicine Academic Unit, The Chinese University of Hong Kong

CA Graham, MD, FHKAM (Emergency Medicine)

Correspondence to: Dr EHC Wong
 Email: dr_eddie Wong@yahoo.com.hk

Objectives To assess the outcome of acute ischaemic stroke patients who received intra-arterial therapy in our unit.

Design Case series.

Setting A tertiary hospital in Hong Kong.

Patients Patients with ischaemic stroke due to large artery occlusion treated within 6 hours from symptom onset between January 2007 and May 2011.

Intervention Acute intra-arterial revascularisation therapy.

Main outcome measures Primary outcome was functional independence (modified Rankin Scale score of ≤ 2) at 3 months. Secondary outcome was rate of recanalisation. Safety outcomes were symptomatic intracranial haemorrhage and 3-month mortality.

Results Twenty-one patients with a mean age of 67 years fulfilled the inclusion criteria. Their mean National Institutes of Health Stroke Scale score was 18. The mean onset-to-puncture time was 212 minutes. Nine received intra-arterial tissue plasminogen activator alone, 11 had an adjunctive mechanical thrombectomy, and one received balloon angioplasty without tissue plasminogen activator. At the end of the procedure, thrombolysis grade 2a or better was attained in 18 (86%) of the patients, and 8 (38%) achieved functional independence at 3 months. Rates of symptomatic intracranial haemorrhage and 3-month mortality were 10% and 24%, respectively.

Conclusion In this setting, intra-arterial revascularisation therapy appeared safe and efficacious for this selected group of ischaemic stroke patients with large artery occlusions. Experience gained from this pilot study may help improve clinical outcomes of such patients.

New knowledge added by this study

- Intra-arterial intervention is at the forefront of treatment for patients with acute ischaemic treatment under intense investigation worldwide.
- Its utilisation in Hong Kong, however, has been sparse and data on clinical outcomes in a local setting are lacking.

Implications for clinical practice or policy

- This study will raise the awareness of the limited local availability of this procedure at this stage, and its feasibility as an option for treating acute ischaemic stroke.
- These results may have important implications for future stroke management in Hong Kong, especially the development of an infrastructure for primary and comprehensive stroke centres dedicated to improve patient outcomes.

Introduction

Intravenous (IV) tissue plasminogen activator (TPA) given within 4.5 hours from onset is an effective treatment for acute ischaemic stroke (AIS).^{1,2} However, some patients are ineligible due to delayed presentation or medical contra-indications. Furthermore, expected recanalisation rates with IV TPA are low for patients with large artery occlusions, ranging from 10% for the internal carotid artery (ICA) to 30% for the middle cerebral artery (MCA).³

急性缺血性中風的動脈內血運重建治療： 香港一間醫院的初步經驗

目的	評估本院為急性缺血性中風患者進行動脈內治療的結果。
設計	病例系列。
安排	香港一間提供第三層醫療服務的醫院。
患者	2007年1月至2011年5月期間因大血管閉塞而出現急性中風，並於中風6小時內接受治療的患者。
介入治療	急性動脈內血運重建治療。
主要結果測量	主要療效指標為術後三個月的功能獨立性（根據改良了的Rankin Scale得分為2或以下）。次要療效指標為血栓再通率。安全療效指標為具病徵的顱內出血及三個月的死亡率。
結果	21名病人符合標準而被列入研究範圍。病人平均67歲。根據美國國衛院腦中風評估表，病人的平均得分為18。從病發至手術的時間為212分鐘。9例只接受組織型纖維溶酶原激活物，11例接受輔助式機械血栓切除術，1例僅接受氣囊血管成形術。術後18例（86%）達溶栓治療2a級別或以上，三個月後有8例（38%）達至功能獨立。10%病人出現具病徵的顱內出血，三個月的死亡率為24%。
結論	對於因大血管閉塞而出現急性中風的患者來說，動脈內血運重建治療似乎是一個安全及有效的治療方法。從治療這些病例得出的初步經驗有助改善急性中風患者的臨床結果。

Intra-arterial therapy (IAT) is an alternative with several theoretical advantages. First, it allows direct delivery of the thrombolytic agent to the occlusion at lower overall total dosage. Second, endovascular mechanical devices may be used for recanalisation, which in some cases spare recourse to thrombolytic agents. Third, the recanalisation rate from IAT is higher than after IV TPA.^{4,5} These cumulate to a potentially longer therapeutic window (beyond 4.5 hours). Momentum is gaining for the establishment of IV stroke thrombolysis service in major public hospitals of Hong Kong, whereas IAT remains a non-standard treatment offered in some tertiary centres only. For patients deemed ineligible to IV TPA, our unit also accepts urgent patient referrals from other regional hospitals. Here we report our initial experience with IAT between January 2007 and May 2011.

Methods

Prospectively collected data in our stroke registry were reviewed. Consecutive patients who underwent IAT for AIS due to large artery occlusion within 6 hours (defined by the time of arterial puncture from stroke onset) were identified. Large arteries were

defined as the ICA, the M1 or M2 segments of the MCA, the vertebral artery, and the basilar artery (BA). Patients with uncertain onset times, wake-up stroke with last-seen-well time of more than 6 hours earlier, endovascular procedure-related AIS, and rescue IAT after failed IV TPA were excluded.

Treatment selection

The stroke thrombolysis service in our hospital has previously been described.⁶ In brief, an expedited stroke triage was set up in October 2008 to provide urgent review of potential thrombolysis-eligible AIS patients. While there was no formal mechanism prior to October 2008, ad-hoc urgent consultations were made by emergency physicians and an on-call general medical team to neurologists. Clinical presentation, medical history, stroke onset time, National Institutes of Health Stroke Scale (NIHSS) scores, and brain computed tomography (CT) were reviewed to determine eligibility for thrombolysis. Within 3 hours of onset, IV TPA remained the standard treatment for eligible patients. In 2009, we extended the cut-off to 4.5 hours based on ECASS-III (The European Cooperative Acute Stroke Study III) results.²

On a case-by-case basis, IAT was considered during office hours (9 am to 6 pm). Thus it was contemplated for patients seen within 3 hours of symptom onset with a moderate or severe deficit (NIHSS score ≥ 8) attributable to a large artery occlusion based on clinical or CT angiography (CTA) findings but in whom IV TPA was contra-indicated. It was also contemplated for ischaemic stroke patients presenting between 3 and 6 hours after symptom onset. Consideration for IAT was also given to patients with low Alberta Stroke Programme Early CT Scores (ASPECTS) of ≤ 7 on presentation, which are predictive of poor outcome and an increased intracranial haemorrhage (ICH) risk even if IV TPA is given within 3 hours.⁷ Finally, selection for IAT took into account the patient's premorbid status and practical constraints, such as immediate availability of neuro-interventionists and angiograph. Computed tomography perfusion results, if available, were used to aid treatment but not mandate decisions.

Procedural and perioperative management

All IAT was performed under local anaesthesia and conscious sedation with femoral artery access. Angiography of the occluded artery was followed by placement of a 6-French guiding catheter and bolus IV heparin of 2000 to 3000 units according to body weight. The assembly consisting of a microcatheter and microwire was advanced to within the culprit thrombus, or as close as possible. The TPA (up to 0.3 mg/kg) was infused through the microcatheter

at 1 mg/min as the initial means of recanalisation. If there was no satisfactory recanalisation, one or more mechanical device-assisted procedures followed. The devices used included the Penumbra (Penumbra Inc, Alameda [CA], US), the Merci (Concentric Medical, Mountain View [CA], US), the Wingspan stent (Boston-Scientific, Natick [MA], US), the Gateway angioplasty balloon (Boston-Scientific), and the Trevo retrievable stent (Concentric Medical). Selection of these devices was at the discretion of the neuro-interventionists. Postoperatively, patients were monitored in a high dependency bed of the acute stroke unit or intensive care unit. No antiplatelet agent or anticoagulation was given for 24 hours unless a permanent stent was used. Follow-up CT or magnetic resonance imaging (MRI) brain was performed on day 1 postoperatively to assess the infarct size and detect ICH. All patients were evaluated by stroke neurologists; risk factors were treated and multidisciplinary rehabilitation was provided as needed.

Data collection

Patient characteristics including age, gender, vascular risk factors, time of onset, accident and emergency department (AED; “door”) arrival and CT brain, baseline NIHSS score, CT ASPECTS and occlusion site were recorded prospectively. Also recorded were treatment characteristics including type of intervention, time of puncture, and first IAT at the clot. Angiographic results were classified according to thrombolysis in cerebral infarction (TICI) grades⁸: grade 0 (no reperfusion), grade 1 (minimal reperfusion), grade 2a (partial filling of less than two thirds of vascular territory), grade 2b (complete but slow filling of entire vascular territory), and grade 3 (complete filling). The time of the first sign of recanalisation was defined by the first angiograph run with TICI 2a flow.

The primary outcome was functional independence at 3 months, defined as a modified Rankin Scale (mRS) score of ≤2. The secondary outcome was recanalisation defined as TICI 2a or better. Safety outcomes were symptomatic intracranial haemorrhage (SICH) according to ECASS⁹ (any ICH plus neurological deterioration of NIHSS score of ≥4 within 7 days or leading to death) and 3-month mortality.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (Windows version 16.0; SPSS Inc, Chicago [IL], US). Continuous variables were presented as means ± standard deviations (SDs) unless otherwise specified. The independent sample *t* test was used to compare continuous variables

TABLE 1. Baseline characteristics of patients

Characteristic*	No. of patients (n=21) [§]
Mean (± SD) age (years)	67 ± 14
Male sex	12 (57%)
Diabetes mellitus	7 (33%)
Hypertension	15 (71%)
Hyperlipidaemia	4 (19%)
Atrial fibrillation	12 (57%)
Congestive heart failure	1 (5%)
Valvular heart disease	3 (14%)
Ischaemic heart disease	4 (19%)
Prior ischaemic stroke	3 (14%)
Carotid stenosis	2 (10%)
Stroke subtype [†]	
Cardioembolic	14 (67%)
Atherothrombotic	3 (14%)
Lacunar	0 (0%)
Undetermined or others	4 (19%)
Mean (± SD) NIHSS score	18.0 ± 7.0
Mean (range) NIHSS score according to occlusion site	
Extracranial ICA (n=1)	19
Intracranial ICA (n=3)	20 (15-29)
MCA M1 (n=12)	18.9 (7-29)
MCA M2 (n=4)	15 (8-28)
BA (n=1)	12
Median (range) ASPECTS [‡]	7.0 (1-10)

* SD denotes standard deviation, NIHSS National Institutes of Health Stroke Scale, ICA internal carotid artery, MCA middle cerebral artery, BA basilar artery, and ASPECTS Alberta Stroke Programme Early CT score

[†] According to Trial of Org 10172 in Acute Stroke Treatment (TOAST)

[‡] Applicable in 20 patients with anterior circulation ischaemic stroke

[§] Unless otherwise stated

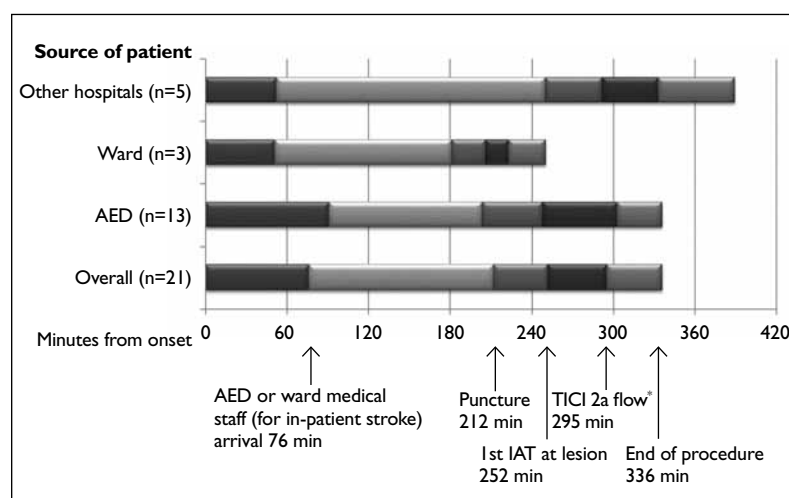


FIG 1. Mean time frame of intra-arterial therapy

AED denotes accident and emergency department, IAT intra-arterial therapy, and TICI thrombolysis in cerebral infarction grade

* TICI 2a time for 18 patients attaining recanalisation

(age, NIHSS score, timing of treatment in minutes, and ASPECTS), and Chi squared or Fisher's exact tests for categorical variables (mRS and extent of recanalisation) between patient groups treated in 2007-08 and 2009-11.

Results

Between January 2007 and May 2011, 21 eligible patients from our unit underwent emergency IAT. There were 12 (57%) males, with a mean (\pm SD) age of 67 ± 14 years. The mean baseline NIHSS score was 18 ± 7 . Five were referred from other regional hospitals, three were in-hospital strokes, and the rest were admitted through the AED of our hospital. Their baseline characteristics and stroke subtypes are outlined in Table 1.

All but one patient had an initial NIHSS score of ≥ 8 ; the exception (with MCA occlusion) had an initial NIHSS score of 7 and a large penumbra detected on CT perfusion that was deemed highly likely to suffer clinical deterioration. Overall, IV TPA was contra-indicated in eight of these patients as they presented outside the time window of 3 hours ($n=4$), had had a recent ischaemic stroke ($n=2$), myocardial infarction ($n=1$), or major surgery ($n=1$). Ten others had CT ASPECTS of ≤ 7 on presentation. The three remaining patients had no absolute contra-indication to IV TPA; IAT was chosen to achieve a higher recanalisation rate for their proximal MCA or BA occlusion.

The mean time frame of our IAT cases is illustrated in Figure 1. The mean (\pm SD) onset-to-door time was 80 ± 57 minutes for 18 patients presenting from the community. For the three in-patient stroke patients, they were attended by ward medical staff at 15, 50, and 90 minutes after symptom onset. The mean door-to-CT time was 37 ± 18 minutes for 19 patients, and could not be measured in two; one developed symptoms during a scheduled CT brain, and the other was a ward patient who had a CT brain in the evening prior to a transient ischaemic attack symptoms. The mean door-to-puncture time was 135 ± 53 minutes, which included times for the five patients transferred from other hospitals. As expected, their mean door (defined as regional hospital AED arrival)-to-puncture time was longer compared to the 16 patients from our centre (198 ± 57 minutes vs 116 ± 35 minutes; $P=0.03$). Overall, the mean onset-to-puncture time of the 21 patients was 212 ± 60 minutes.

The mean time from puncture to initiation of IAT at clot was 40 ± 24 minutes. Nine patients had intra-arterial TPA only. Adjunct mechanical devices (sometimes more than one) were used in 11 patients, and included balloon angioplasty in 7, a clot aspiration device in 4, intracranial stents in 3, clot-retrieval devices in 2, and a carotid stent in 1. One patient had balloon angioplasty only, as TPA was contra-indicated due to major thoracic surgery 1 day earlier. The mean dose of TPA used for the 20 patients was 13 ± 4 (range, 5-20) mg.

Recanalisation, defined as TICl 2a or better, was achieved in 18 (86%) patients at a mean of 295 ± 69 minutes from onset, or 90 ± 48 minutes after puncture. The final angiographic outcomes were

TABLE 2. Comparison of performance in 2007-2008 versus 2009-2011*

Characteristic/variable†	2007-08 (n=10)	2009-11 (n=11)	P value
Baseline characteristic			
Age (years)	69.2 \pm 14.1	65.6 \pm 13.5	0.55
NIHSS score	16.0 \pm 8.2	19.8 \pm 5.5	0.23
ASPECTS‡	8.0 (1-10)	6 (3-9)	0.20
Favourable ASPECTS‡ 8-10	6 (60%)	2 (20%)	0.17
Onset-to-door (mins)	78 \pm 56	74 \pm 56	0.89
Performance variable			
Door-to-CT (mins)	48 \pm 19	28 \pm 9	0.01
Door-to-puncture (mins)	153 \pm 64	120 \pm 37	0.19
Puncture-to-1st IAT (mins)	54 \pm 27	29 \pm 13	0.02
Onset-to-1st IAT (mins)	285 \pm 69	224 \pm 57	0.04
Puncture-to-TICl 2a (mins)	111 \pm 68	75 \pm 34	0.13
Onset-to-TICl 2a (mins)	334 \pm 71	270 \pm 57	0.055
Final TICl 2b or 3	4 (40%)	10 (91%)	0.02
Favourable 3-month mRS (≤ 2)	2 (20%)	6 (55%)	0.18

* Data are shown as mean \pm standard deviation, median (range), or No. (%)
 † NIHSS denotes National Institutes of Health Stroke Scale, ASPECTS Alberta Stroke Programme Early CT score, CT computed tomography, IAT intra-arterial therapy at clot, TICl thrombolysis in cerebral infarction grade, and mRS modified Rankin Scale
 ‡ Applicable in 20 patients with anterior circulation ischaemic stroke

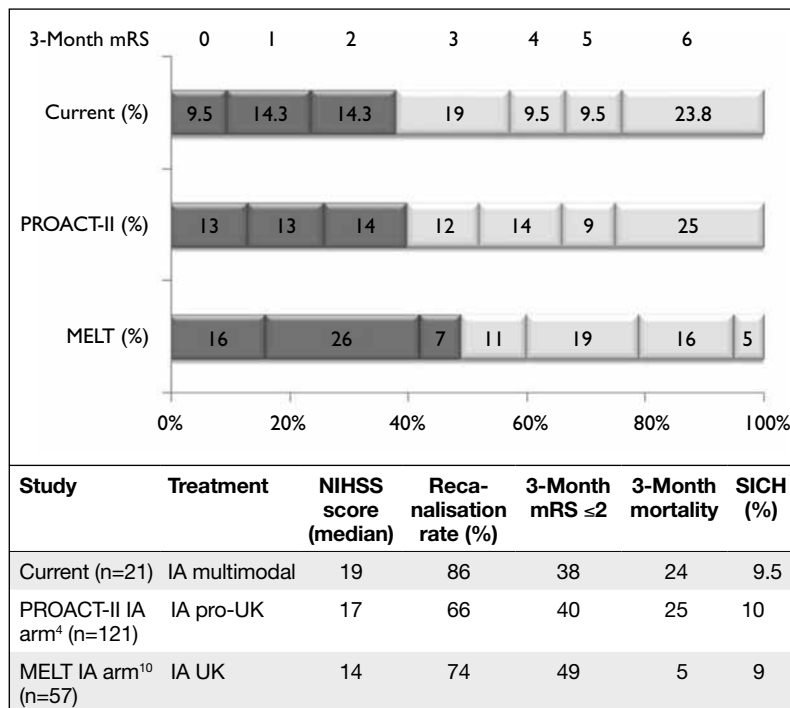


FIG 2. Distribution of 3-month modified Rankin Scale score and comparison with previous studies^{4,10}
 mRS denotes modified Rankin Scale, NIHSS National Institutes of Health Stroke Scale, IA intra-arterial, SICH symptomatic intracranial haemorrhage, and UK urokinase

as follows: two had TICl 0, one had TICl 1, four had TICl 2a, 10 had TICl 2b, and four had TICl 3. Eight (38%) patients achieved the favourable outcome of functional independence (mRS score ≤ 2) at 3 months, and six (29%) were directly discharged home after a mean of 8 (range, 4-11) days. Their mean NIHSS score decreased from 16 (range, 11-22) on admission to 2 (range, 1-3) on discharge.

Follow-up CT or MRI brain scans were available in 20 of the 21 patients. One patient with poor neurological recovery following IAT was moribund with a severe chest infection, and hence had no follow-up CT. Among the rest, five had ICHs, two of which were symptomatic (extensive subarachnoid haemorrhage [SAH] and intra-ventricular haemorrhage [IVH] immediately post-procedure; haemorrhagic transformation with mass effect). Thus, the SICH rate was 10%. Five (24%) patients were deceased at 3 months; as noted above one died of SAH and IVH. Three died of massive cerebral infarction, two of whom had no recanalisation and one died despite full recanalisation (after 340 minutes). One other patient died from chest infection 2 months later.

Post-hoc analysis showed that a favourable outcome was associated with onset-to-first sign of recanalisation of ≤ 5 hours (67% vs 17%, $P=0.032$) and final angiographic outcome of TICl 2b or better (57% vs 0%, $P=0.018$). A trend to more favourable outcomes was noted for procedures performed in the later years of 2009-2011 (55% vs 20%, $P=0.18$; Table 2). However, favourable outcomes were not associated with a younger age of ≤ 70 years ($P=0.39$) or a moderate stroke with NIHSS score ≤ 15 ($P=0.65$). The mean door-to-CT time decreased from 48 ± 19 minutes in 2007-2008 to 28 ± 9 minutes in 2009-2011 ($P=0.01$). Excluding the five patients referred from other hospitals, the mean door-to-puncture time decreased from 131 ± 41 to 101 ± 23 minutes ($P=0.10$). The mean time from puncture to initiation of IAT at clot decreased from 54 ± 27 to 29 ± 13 minutes ($P=0.02$). The mean onset-to-TICl 2a time of 18 patients (three did not attain TICl 2a) decreased from 334 ± 71 to 270 ± 57 minutes ($P=0.055$). Four (40%) of 10 patients in earlier years had satisfactory recanalisation of TICl 2b or better, versus 10 (91%) of 11 in later years ($P=0.02$).

Discussion

In this group of moderate-to-severe AIS patients with a mean NIHSS score of 18 treated with IAT, 38% achieved functional independence at 3 months. This was comparable to overseas series reporting similar treatment time frames and stroke severity (Figure 2),^{4,10} although our series differed in terms of the patient-selection process as the decision to perform IAT was at the treating-neurologist's discretion. Despite our higher recanalisation rate, there remained a mismatch with favourable clinical

outcomes (Figures 3 and 4). We postulate this was due to relatively late recanalisation times (mean, 334 minutes) for patients treated in 2007-2008. As with all new treatments, there was a learning curve to overcome. For IAT, good outcomes do not depend solely on the procedure itself, but on every step in the 'chain of survival'. Such progress was observed in our patients treated in 2009-2011. The door-to-puncture time was reduced through the concerted effort of upgrading the stroke triage category from III to II at the AED, prioritised CT and CTA by radiologists, and more efficient preoperative preparation by stroke nurses. Improvements in catheter profiles and tractability, and experience gained from elective intracranial stenting at our centre during the same period appeared to halve the time taken to reach the site of thrombosis. Not only did these changes result in higher recanalisation rates, but they also occurred about 60 minutes earlier, both of which significantly affect outcome.^{11,12}

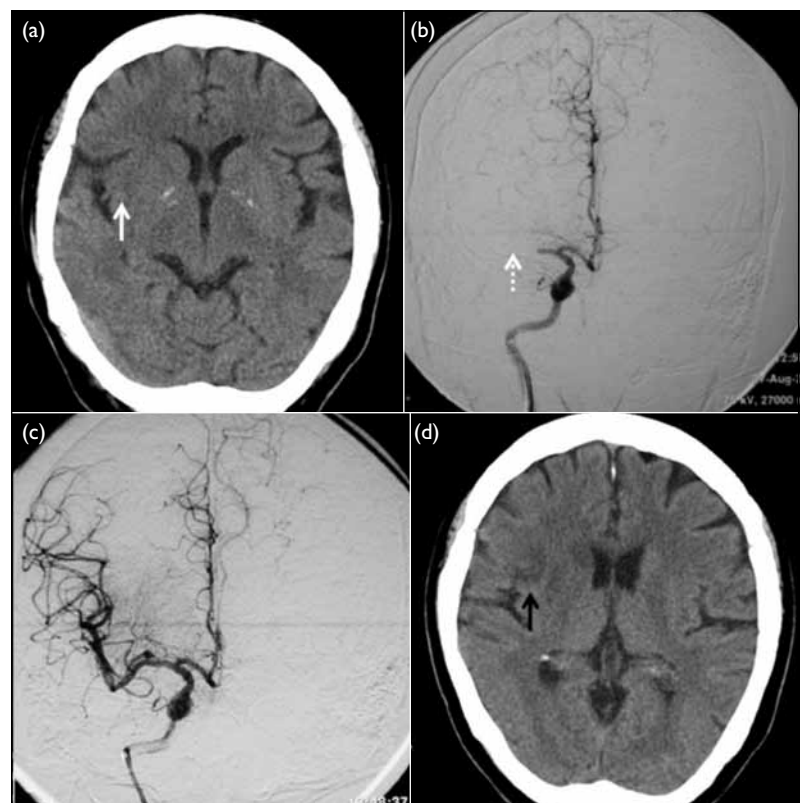


FIG 3. Illustrative case 1

An 80-year-old female developed dense left hemiparesis and neglect day 1 following major thoracic surgery. National Institutes of Health Stroke Scale (NIHSS) score was 22. (a) Computed tomography (CT) brain at 45 minutes after onset shows early ischaemic changes at right insular cortex and lentiform nucleus (white arrow). (b) Digital subtraction angiogram 180 minutes from symptom onset confirmed an occluded proximal right middle cerebral artery M1 segment (dashed white arrow). (c) Recanalisation was achieved by angioplasty balloon (Gateway, Boston-Scientific) at 210 minutes. No tissue plasminogen activator was given due to recent surgery. (d) Day 3 CT brain shows small infarcts at right insular cortex and lentiform nucleus only (black arrow). NIHSS score was 3

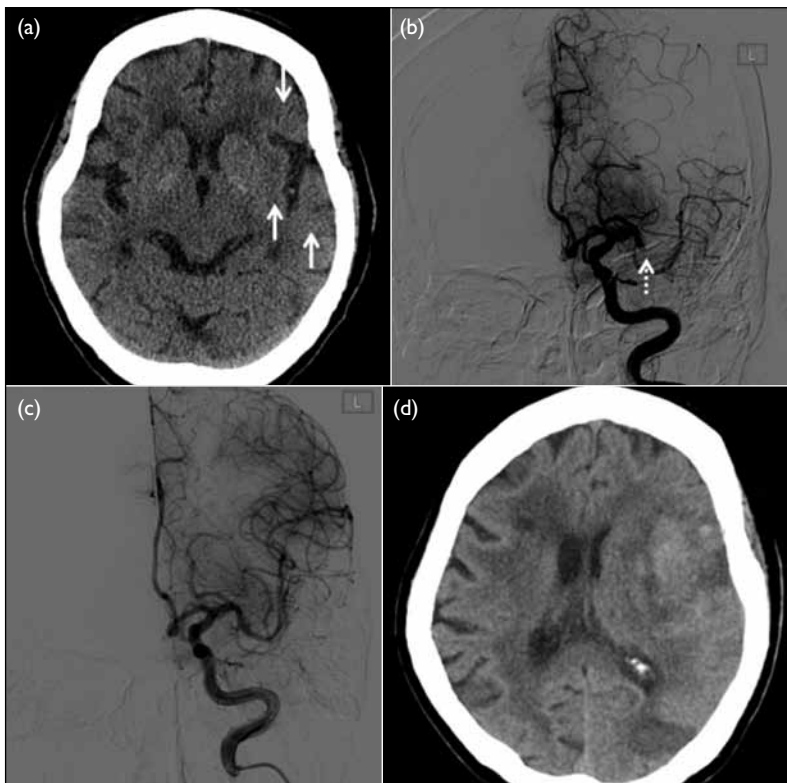


FIG 4. Illustrative case 2

A 78-year-old female presented with dense right hemiparesis and aphasia to a regional hospital at 100 minutes after onset. National Institutes of Health Stroke Scale (NIHSS) score was 29. (a) Computed tomography (CT) at 120 minutes shows early ischaemic changes at left insula, anterior middle cerebral artery and opercular cortex (white arrows). Intra-arterial therapy was performed due to low ASPECTS (Alberta Stroke Programme Early CT Scores) of 7 and high NIHSS score. (b) Digital subtraction angiogram at 270 minutes shows complete occlusion of left middle cerebral artery M1 mid-segment (dashed white arrow). (c) Complete recanalisation at 340 minutes with clot retrieval device (Trevo, Concentric) after poor response to 15-mg intra-arterial tissue plasminogen activator. (d) Despite full recanalisation, day 2 CT shows left middle cerebral artery territory infarct with haemorrhagic transformation. This patient succumbed on day 10

Recanalisation failed in three of our first five patients, but all subsequent patients achieved TICI 2a or better at the end of the procedure. Still, IAT remains technically demanding and carries procedural risk. Ultimately, procedural safety is more important than the speed of recanalisation. Although our overall SICH rate was acceptable, one patient developed procedure-related fatal SAH from attempted recanalisation with TPA, the clot-retrieval device, and balloon angioplasty for terminal ICA occlusion.

Due to the heterogeneity of mechanical devices used and small number of patients, no conclusion could be drawn from this study regarding the safety and efficacy of each device or in comparison to TPA as the primary recanalisation tool. In general, we used TPA as a first-line treatment based on best available evidence.⁴ This was followed by further recanalisation attempts with US Food and Drug Administration-

approved devices (Penumbra, Merci),^{13,14} or stenting and angioplasty if no satisfactory recanalisation was attained after IA TPA up to 0.3 mg/kg. The choice of device was at the neuro-interventionist's discretion, taking into account occlusion site, vessel size and tortuosity, time since onset, presumed stroke mechanism, plus pragmatic considerations such as familiarity with and availability of the device at the time.

Awareness of thrombolysis as an effective AIS treatment by AED and frontline medical staff were heightened after the setup of expedited stroke triage. In fact, three patients in this study were rendered ineligible for IV TPA due to late CT and neurology assessment. This ensued before establishment of the stroke thrombolysis service. Their 3-month mRS scores were 3, 3, and 6. This was in contrast to two patients who similarly developed stroke during their admission in 2010. The assessment and treatment process for the latter was fast-tracked, resulting in onset-to-full recanalisation times of 210 and 240 minutes, and better 3-month mRS scores of 1 and 0.

Although not uncommonly practised in Europe and the US, transferral of AIS patients from regional hospitals to tertiary centres for urgent IAT is still a rarity in Hong Kong. While the number was limited, such transfer appeared feasible. Despite the extra transportation time, two of the five patients from other hospitals had favourable outcomes at 3 months. Their early presentation to their regional hospital AED (after 30 and 35 minutes) prompted expedited neurological evaluation, and efficient ambulance transfer resulting in onset-to-puncture times of 200 and 215 minutes, which were comparable to those reported in European centres.¹⁵ Another treatment strategy, so called 'drip-and-ship', entailing commencement of IV TPA by the regional hospital or primary stroke centre before transferral to a tertiary or comprehensive stroke centre for IAT, has also been utilised overseas.¹⁶ This strategy of bridging IV TPA before IAT is a frontier in AIS treatment currently under intense investigation.¹⁷ Adaptation of more aggressive treatment approaches in Hong Kong hinges on a well-coordinated infrastructure comprising paramedics, AEDs, neurology, and radiology services in regional and tertiary centres throughout the territory. Due to limitation of resources and expertise, it is unlikely that IAT will become universally available in all public hospitals. Thus it may be more practical to designate public hospitals as primary stroke centres for IV thrombolysis,¹⁸ and a few as IAT-capable comprehensive stroke centres.¹⁹ The feasibility of providing such measures territory-wide (24 hours per day) should be further investigated.

Conclusion

Despite our sparse experience, our results suggest

that IAT within 6 hours is probably safe and efficacious for AIS patients in Hong Kong, and clinical outcomes were largely comparable to those reported overseas. This strategy offers patients unsuitable for IV thrombolysis a second chance of

achieving meaningful neurological recovery. Its more widespread use in Hong Kong will depend on the results from on-going trials, as well as the availability of multi-disciplinary expertise, and an infrastructure committed to the improvement of stroke outcomes.

References

1. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med* 1995;333:1581-7.
2. Hacke W, Kaste M, Bluhmki E, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. *N Engl J Med* 2008;359:1317-29.
3. Lee KY, Han SW, Kim SH, et al. Early recanalization after intravenous administration of recombinant tissue plasminogen activator as assessed by pre- and post-thrombolytic angiography in acute ischemic stroke patients. *Stroke* 2007;38:192-3.
4. Furlan A, Higashida R, Wechsler L, et al. Intra-arterial prourokinase for acute ischemic stroke. The PROACT II study: a randomized controlled trial. *Prolyse in Acute Cerebral Thromboembolism*. *JAMA* 1999;282:2003-11.
5. Moonis M. Intraarterial thrombolysis within the first three hours after acute ischemic stroke in selected patients. *Stroke* 2009;40:2611-2.
6. Lau AY, Soo YO, Graham CA, et al. An expedited stroke triage pathway: the key to shortening the door-to-needle time in delivery of thrombolysis. *Hong Kong Med J* 2010;16:455-62.
7. Barber PA, Demchuk AM, Zhang J, Buchan AM. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. ASPECTS Study Group. *Alberta Stroke Programme Early CT Score*. *Lancet* 2000;355:1670-4.
8. Higashida R, Furlan A, Roberts H, et al. Trial design and reporting standards for intraarterial cerebral thrombolysis for acute ischemic stroke. *J Vasc Interv Radiol* 2003;14 (9 Pt 2):S493-4.
9. Hacke W, Kaste M, Fieschi C, et al. Intravenous thrombolysis with recombinant tissue plasminogen activator for acute hemispheric stroke. The European Cooperative Acute Stroke Study (ECASS). *JAMA* 1995;274:1017-25.
10. Ogawa A, Mori E, Minematsu K, et al; MELT Japan Study Group. Randomized trial of intraarterial infusion of urokinase within 6 hours of middle cerebral artery stroke: the middle cerebral artery embolism local fibrinolytic intervention trial (MELT) Japan. *Stroke* 2007;38:2633-9.
11. Khatri P, Abruzzo T, Yeatts SD, et al. Good clinical outcome after ischemic stroke with successful revascularization is time-dependent. *Neurology* 2009;73:1066-72.
12. Rha JH, Saver JL. The impact of recanalization on ischemic stroke outcome: a meta-analysis. *Stroke* 2007;38:967-73.
13. Gobin YP, Starkman S, Duckwiler GR, et al. MERCI 1: a phase 1 study of mechanical embolus removal in cerebral ischemia. *Stroke* 2004;35:2848-54.
14. Bose A, Henkes H, Alfke K, et al. The penumbra system: a mechanical device for the treatment of acute stroke due to thromboembolism. *AJNR Am J Neuroradiol* 2008;29:1409-13.
15. Nedeltchev K, Arnold M, Brekenfeld C, et al. Pre- and in-hospital delays from stroke onset to intra-arterial thrombolysis. *Stroke* 2003;34:1230-4.
16. Martin-Schild S, Morales MM, Khaja AM, et al. Is the drip-and-ship approach to delivering thrombolysis for acute ischemic stroke safe? *J Emerg Med* 2011;41:135-41.
17. Khatri P, Hill MD, Palesch YY, et al. Methodology of the interventional management of Stroke III Trial. *Int J Stroke* 2008;3:130-7.
18. Alberts MJ, Hademenos G, Latchaw RE, et al. Recommendations for the establishment of primary stroke centers. *Brain attack coalition*. *JAMA* 2000;283:3102-9.
19. Alberts MJ, Latchaw RE, Selman WR, et al. Recommendations for comprehensive stroke centers: a consensus statement from the brain attack coalition. *Stroke* 2005;36:1597-616.