Kingston Health Sciences Centre

Centre des sciences de la santé de Kingston

Guidelines for Use of Intravenous (IV) Thrombolysis, or Endovascular Thrombectomy (EVT), or IV Thrombolysis +EVT in the Treatment of Acute Ischemic Stroke at Kingston Health Sciences Centre-Kingston General Hospital Site

If Age < 18 years, Neurology-Stroke Service + Paediatric Intensive Care Service to jointly decide on next steps (e.g., consider contacting The Hospital for Sick Children in Toronto)

Rationale

IV Thrombolysis (thrombolytic therapy):

The use of recombinant tissue plasminogen activator (rt-PA) has been the standard thrombolytic therapy for ischemic stroke. The AcT randomized control trial (June, 2022) combined with evidence to date, demonstrate that tenecteplase (TNK) is a reasonable choice of thrombolytic therapy for ischemic stroke. The use of either thrombolytic agent, when administered within four and a half hours of onset of an acute ischemic stroke, has been shown to reduce morbidity, mortality and improve functional outcome. Evidence indicates that **time is brain** - administration of IV thrombolysis as early as possible post stroke is associated with better outcomes.

Endovascular Thrombectomy (EVT):

In select cases, use of EVT with or without IV thrombolysis may be utilized for patients with an acute ischemic stroke. The procedure consists of arterial catheterization and mechanical clot retrieval or thrombectomy, using stent retriever and/or clot aspiration devices.
5 landmark trials demonstrated strong evidence for improved functional outcomes & reduced mortality with EVT. Benefits of EVT were significantly greater in patients with a small infarct core with proximal large vessel occlusion (LVO) in the anterior circulation, and moderate-to-good collateral circulation. As a result of the impact of these trials, the Canadian Stroke Best Practice Guidelines were revised to recommend EVT for eligible patients who meet select criteria. Recent systematic review and meta-analysis of posterior circulation LVO trials suggest potential benefit of EVT versus medical therapy; decision-making is still on a case-by case basis for EVT with posterior circulation stroke.

In certain circumstances, rt-PA by IA route may continue to be utilized for large vessel occlusion in the posterior territory (e.g., basilar artery).

Who to decide use of IV thrombolysis +/-EVT for the treatment of ischemic stroke?

The decision to administer IV thrombolysis is made by the treating Neurologist. The decision for EVT with or without IV thrombolysis is made jointly between the treating Neurologist and the Interventional Radiologist.
When a potential candidate for treatment with IV thrombolysis +/-EVT is identified in the Emergency Department, the Charge Nurse ***must*** contact the KGH Switchboard to activate the "Stroke Team".
The physician who prescribes IV thrombolysis must provide a ***written order*** to staff.

Essential investigations prior to the use of IV TNK or rt-PA (+/-EVT)

1. Blood work-use tubes in ASP package (**Not Mandatory to wait for all results to make decision for IV thrombolysis+/-EVT; decision at discretion of treating Neurologist)**
    a. Routine hematology (include platelets)
    b. PT/ INR, PTT
    c. Electrolytes, creatinine, glucose, troponin
    d. ßHCG (pregnancy test) if indicated
2. CT head without contrast +/- CT Angiography (CTA). For patients who could be eligible for EVT, CT perfusion (CTP) with RAPID is required

Table 1: Inclusion and Exclusion Criteria for IV Thrombolysis (TNK OR rt-PA)

Inclusion criteria	Absolute Exclusion	Relative Exclusion
1. Diagnosis of ischemic stroke causing measurable neurological deficit. 2. Deficit severity that, should it persist, would lead to a significant compromise of the patient's quality of life 3. Time of the onset must be reliably known, either from the patient, or a credible witness. 4. Duration of the stroke from the time of onset, to the beginning of administration of IV thrombolysis, must be less than **4.5 hours** (including the time required to complete all essential investigations). 5. Informed verbal consent obtained from the patient, or substitute decision maker. 6. Pregnancy is NOT a contraindication but requires special consideration e.g. may require consult to obstetrics 7. Age less than 18 years, page Paediatric Intensivist Care Service.	1. Hemorrhage on brain imaging. 2. Any source of bleeding or condition that could increase risk of major bleeding post thrombolysis.	1. Major surgery during previous 14 days. 2. History of intracranial hemorrhage. 3. Puncture of a non-compressible artery or biopsy site within 7 days, including lumbar puncture. 4. Major cerebral infarct/spinal injury in past 90 days. 5. Blood pressure systolic greater than 180 mmHg, and/or diastolic greater than 105 mmHg at the time of IV thrombolysis administration (see Appendix A: Management of Hypertension). 6. Serious co-morbidity with limited lifespan, (e.g. advanced cancer, renal failure, hepatic failure). 7. Stroke symptoms due to another non-ischemic acute neurological condition such as seizure with post-ictal Todd's paralysis or focal neurological signs due to severe hypo- or hyperglycemia. 8. INR greater than 1.7, increased PTT, or platelet count less than 100,000. 9. Taking a direct non-vitamin K oral anticoagulant. 10. Blood glucose less than 2.7 mmol/L or greater than 22.2 mmol/L.

Table 2: Inclusion & Exclusion Criteria for EVT

Specific Inclusion Criteria for EVT:

☐ If IV thrombolysis is given in conjunction with EVT, refer to Table 1 (inclusion/exclusion criteria for IV thrombolysis (TNK or rt-PA)). Some exceptions will apply for EVT as noted with the following criteria:

☐ Age 18 years or greater

☐ Candidacy determined on a case-by-case basis based on best available evidence and using:

- Preadmission function
- NIHSS
- Non-Contrast CT with ASPECTS
- CTA (arterial phase from aortic arch to vertex of the head) with intracranial large proximal artery occlusion
- CT Perfusion Parameters using RAPID

☐ Time to treatment should be within 24 hours from stroke symptom onset to time of initiation of procedure (puncture).

Other time parameter targets:

☐ Time from first slice of non-contrast CT to revascularization should be 90 minutes or less.

☐ Time from the first slice of non-contrast CT to groin puncture should be 60 minutes or less.

Specific Exclusion Criteria for EVT:

☐ Complete resolution of neurological signs (TIA)

☐ Serious comorbidity with limited lifespan (e.g., advanced cancer, advanced dementia)

For Patient Care Guidelines up to 24 hours see pages 4 - 6.

Care of the Patient during Treatment with IV Thrombolysis +/-EVT (see Table 3 for care if patient candidate for EVT)

1. Patients should have two IV sites, one for IV Thrombolytic Therapy (TNK or rt-PA) and the second for other medications and in reserve.
2. Draw blood work (see pg. 1) if not done before CT.
3. No medication to be co-administered with TNK or rt-PA through IV lines.
4. Administration Guidelines (see Appendices D & E):

   TNK (tenecteplase)-

   TNK is administered as a **bolus IV** dose: 0.25 mg/kg IV push over 5 seconds with a maximum dose of 25 mg (50mg vial diluted with 10 ml of sterile water). Consent for the use of off-label tenecteplase (TNK) in acute ischemic stroke must be obtained.

   rt-PA (alteplase)-

   a. rt-PA is administered **IV** at a dose of **0.9 mg/kg** (maximum dose of 90 mg) using rt-PA 1 mg/mL injection
   b. **10%** of total dose is given as IV push over one minute and the remainder as an IV infusion by pump **over one hour**
5. Vitals (BP, HR, RR) and neurological assessment [Canadian Neurological Scale (CNS)] q 15 min during drug administration. (If EVT: NIHSS or CNS to be done post EVT)
6. If an automated cuff is used, it should be loosened between readings, and position changed q 2 hours.
7. Continuous cardiac monitoring and SpO_2 monitoring.
8. ECG post initiation of IV thrombolysis. If patient for EVT and IVR room is ready, ECG to be done post EVT.
9. If sudden deterioration in neurological function should occur (i.e., ↓ LOC, ↑ weakness & aphasia), stop infusion and notify physician.
10. Observe tongue and oropharynx at 30 min, 45 min, 60 min and 75 min after onset of TNK bolus or rt-PA infusion. If facial, tongue and/or pharyngeal angioedema, stop rt-PA infusion and notify physician (See Appendix C for management guidelines).

Table 3: Additional Specific Care of the Patient for EVT

Prep: 1. If time permits, patient in hospital gown, no underwear 2. Insert foley catheter (if received notification that patient is potential candidate for EVT) 3. 2 working IVs 4. Shave prep both groins only if absolutely necessary-don't delay procedure for shave prep
Care during procedure: 1. Follow standard IVR care processes 2. IVs infusing (consider 1 IV N/S at least 125cc/hr) 3. Continuous cardiac monitoring 4. Continuous BP monitoring Target SBP above 150 mmHg during the procedure until reperfusion achieved 5. Avoid intubation & general anesthesia if possible for anterior circulation cases. Intubation is often considered appropriate for posterior circulation cases. Conscious procedural sedation as per Procedural Sedation Policy & Procedural Sedation/Analgesia Order set is usually sufficient. Continuous SpO_2 monitoring & titrate O_2 as per Oxygen Therapy Protocol 6. If IV thrombolytic therapy is administered (see above)-continue to observe for bleeding & angioedema

Care of the Patient for the first 24 hours following IV thrombolysis +/- EVT (see Table 4 on next page for additional post EVT care)

1. Transfer to D4-ICU as soon as possible.
2. Vitals and neurological assessment (Canadian Neurological Scale (CNS)) q 15 min x 2 hours then q 60 minutes x 22 hours. Notify physician if CNS >1 or change in neurological status.
3. Continuous cardiac monitoring and O_2 sat monitoring.
4. Monitor for bleeding/hematoma (see Table 4 & Appendix B).
    - Internal bleeding (GI, GU), oozing IV sites, oral bleeding, skin, groin site
5. Monitor for angioedema at 30, 45, 60 and 75 mins, then q4-6 h for 24 hours (See Appendix C).
6. Bed rest-No TEDs.
7. IV 0.9 NaCl @ 75 cc/hr or as directed by physician.
8. NPO including no oral medications until swallowing ability has been determined.
9. Report systolic BP > 180 mmHg or diastolic BP > 105 mmHg (See Appendix A for suggested management). Report systolic BP <110mmHg or diastolic BP < 60 mmHg.
10. Report HR< 50 bpm
11. Report temperature > 37.5°C.
12. Acetaminophen 650 mg PO/PR q4 h prn for temperature > 37.5°C or pain.
13. Report RR > 24/minute, or SpO_2 less than 88%.
14. If sudden deterioration in neurological function or evidence of systemic hemorrhage, consider:
    - Stat CT scan
    - Stat CBC, PTT, PT, INR, fibrinogen
    - Cryoprecipitate
15. Monitor for seizure-related activity such as: decreased level of consciousness, focal motor activity, extensor posturing, or tonic-clonic posturing.
16. Repeat serum glucose if first random blood glucose is greater than 10 mmol/L.
17. Notify physician for blood glucose less than 5 mmol/L or greater than or equal to 10 mmol/L.
18. ALT, lipid profile (total cholesterol, HDL/LDL ratio, triglycerides), & HbA1c next morning.
19. Hold patient's PO medications as previously prescribed since patient is NPO for 24 hours.
20. No antiplatelet agents (ASA, clopidogrel, ticlopidine, dipyridamole) for 24 hours & until 1 brain image shows no evidence of hemorrhage. No anticoagulant agents (e.g., warfarin, enoxaparin, dalteparin, heparin, & DOACs (e.g., dabigatran, rivaroxaban, apixaban, edoxaban) for at least 24 hours & until 1 brain image shows no evidence of hemorrhage.
21. No arterial punctures, intramuscular injections or invasive procedures for 24 hours.
22. If arterial sheath in place, remove in accordance with physician orders (see below).
23. Repeat CT at 24 hours or if sudden deterioration in neurological status.
24. Assess removal of indwelling urinary catheter at 24 hours, if in place.

Table 4: Care of the patient for first 24 hours post EVT

Pre Femoral Sheath Removal:

1. Check ACT & remove sheath per IVR Arterial Sheath Removal Nursing Policy & Procedure & Arterial Sheath Removal Order Set

Post Sheath Removal:

1. Follow IVR Arterial Sheath Removal Policy/Procedure & Arterial Sheath Removal Order Set
2. Apply bandage to puncture site
3. Monitor sheath site for bleeding or hematoma, distal pulses and limb viability q 15 min for 1 hour then q 30 min for 3 hours, then q shift until discharge.
4. Maintain supine with HOB no more than 30^{o} with punctured limb (sheath site) at rest, and puncture site visible for 6 hours post sheath removal. If radial or brachial site is used: Maintain arm elevated at level of heart for 2 hours
5. Follow **Care of the Patient for the first 24 hours Following IV Thrombolysis +/- EVT** (above)

Post EVT if Sheath Remains In Situ:

1. Sheath to arterial line.
2. Bedrest-roll q 1-2 h. Keep punctured limb (sheath site) at rest and visible. Elevate HOB no more than 30^{0}.
3. Monitor sheath site for bleeding or hematoma, HR, BP, distal pulses and limb viability q 15 min for 1 hour then q 30 min while sheath in situ
4. Consider peripheral IV N/S 75-125 cc/hr overnight

During Manual Compression of Arterial Site (if Angio-Seal is not used):

1. IVR nurse only to remove sheath wherever the patient is located
2. Follow Sheath Removal Policy & Procedure and Arterial Sheath Removal Order Set which includes:
    a. Normal saline 250 cc fluid bolus if ordered
    b. Monitor blood pressure q 5 min
    c. Monitor HR continuously
    d. Monitor sheath site and vascular status of affected limb (colour, pulses, temp) q 5-10 min

General:

1. All patients post EVT are to be transferred to D4ICU or Kidd 2ICU as soon as possible for at least 24 hours
2. Repeat CT at 24 hours or if sudden deterioration in neurological status
3. Follow the ***Care of the Patient for the first 24 hour following IV thrombolysis +/- EVT*** (above)
4. Follow the ***Acute Ischemic Stroke Thrombolysis/EVT QBP Order Set***

During first 24 hours, the patient should transition to Acute Stroke Collaborative Care Plan

Appendix A:	Management of Arterial Hypertension for Patients Undergoing IV Thrombolysis +/EVT for Acute Ischemic Stroke.
Appendix B:	Management of Hemorrhagic Complications with Use of IV Thrombolysis +/- EVT for Ischemic Stroke.
Appendix C:	Management of Angioedema with Use of IV Thrombolysis.
Appendix D:	rt-PA 1 mg/ml Infusion for Acute Ischemic Stroke Dosing Chart.
Appendix E:	TNK for Acute Ischemic Stroke Dosing Chart

tPA Protocol approved by Pharmacy & Therapeutics April 2001
Protocol last updated: May 28, 2024

Appendix A

Management of Arterial Hypertension for Patients Undergoing IV Thrombolysis and/or EVT for Acute Ischemic Stroke

Rationale:

The acute hypertensive response commonly seen in ischemic stroke does not normally require emergent treatment, because the higher pressure may actually be beneficial, and a rapid fall in pressure may extend the infarct volume. However, for patients receiving thrombolysis and/or EVT, very high pressures (180-230 systolic or 105-125 mm Hg diastolic) are associated with increased risk of hemorrhagic complication and justify careful antihypertensive therapy prior to receiving thrombolytic, and for 24 hours afterwards.

Recommended Treatment:

If the systolic blood pressure is 180 mmHg or greater and/or the diastolic is 105 mmHg or greater:

- Give labetalol 10 mg IV over 2 minutes
- Repeat labetalol 10-20 mg IV over 2 minutes every 10-20 minutes PRN to aim for BP less than 180 mmHg systolic and/or 105 mmHg diastolic. If patient receives greater than 3 doses of labetalol within 2 hour period, start labetalol IV infusion (usual starting dose is 0.5-1 mg/min). The maximum cumulative dose of labetalol is 300 mg in a 24 hour period.

OR

- Give hydralazine 10 mg IV q4-6 h PRN to aim for BP less than 180 mmHg systolic and/or 105 mmHg diastolic (Consider for use if HR less than 50 beats/min)

- Monitor BP q 15 min or more frequently during initial management. * Report hypotension (systolic BP less than 110 mmHg or diastolic BP less than 60)

- * BP monitoring must be frequent in order to detect dramatic changes in pressure. The risk of bleeding secondary to an arterial puncture must be weighed against the difficulties in monitoring rapid changes in pressure.

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Appendix B

Management of Hemorrhagic Complications with Use of IV Thrombolysis and/or EVT for Ischemic Stroke

The use of rt-PA or TNK carries the risk of hemorrhagic complications either intracranial or systemic.

1. Intracranial Hemorrhage:

- Clear neurologic deterioration during or within 24 hours of rt-PA infusion or TNK bolus +/- EVT should be assumed to be due to intracranial hemorrhage.
- If deterioration occurs during rt-PA infusion. Stop infusion.
- Emergent CT scan
- Consider urgent neurosurgical consultation
- Consider cryoprecipitate

2. Systemic Hemorrhage (thrombolysis only):

- The management of systemic hemorrhage will depend upon the location and size of the hemorrhage, and the likelihood the bleeding can be controlled mechanically.
- If systemic bleeding is identified or suspected, stat CBC, INR, PTT, fibrinogen
- If transfusion is considered cross-match and type for 4 units packed red cells,
- 15-20 units of cryoprecipitate and 1 unit of single donor platelets.
- If further bleeding occurs, consider repeat of cryoprecipitate
- Monitor vital signs q 15 min
- Consider neuro-imaging studies
- Consider surgical consultation.
- Active bleeding around intravenous and arterial puncture sites may be controlled by direct pressure

Appendix C

Management of Angioedema with Use of IV Thrombolysis (TNK or rt-PA) for Ischemic Stroke

Angioedema has been reported in 1.3% (8 of 596; 95% CI 0.6-2.6%) of patients treated with IV rt-PA therapy for acute stroke. It has been associated with previous angiotensin converting enzyme (ACE) inhibitor therapy and with a past history of angioedema reactions. The reaction has been observed approximately 45-90 minutes after the rt-PA infusion was started. Patients reported dysphagia and inspection of the tongue revealed hemilingual (ipsilateral to the side of the hemiplegia) tongue swelling. Progression to the entire tongue and oropharynx may occur.

Risk Assessment

- Inquire if patient has ever experienced angioedema in past.
- Take **ACE inhibitor** history. The following is a list of currently marketed ACE inhibitors to facilitate in their identification:

Benazepril (Lotensin®)	Lisinopril (Zestril®)
Captopril (Capoten®, generic brands)	Perindopril (Coversyl®)
Cilazapril (Inhibace®)	Quinapril (Accupril®)
Enalapril (Vasotec®)	Ramipril (Altace®)
Fosinopril (Monopril®)	Trandolapril (Mavik®)

- Although **angiotensin II (ATII) receptor antagonists** have not been implicated in the angioedema reaction, caution is advised in patients reporting a history of ATII antagonist use. Currently marketed ATII antagonists include:

Candesartan (Atacand™)	Epoprosartan (Teveten™)
Irbesartan (Avapro™)	Telmisartan (Micardis™)
Valsartan (Diovan™)	Losartan (Cozaar™)

- Note: Combination diuretic and ACE inhibitor or ATII formulations are also currently marketed and should be noted.

Monitoring Parameters

- Observe for facial, tongue, and/or pharyngeal angioedema 30 minutes, 45 minutes, 60 minutes and 75 minutes after initiation of IV thrombolysis and q4-6 h for 24 hours afterwards
- Continuous O_2 monitoring during rt-PA IV infusion or post TNK bolus and for 24 hours afterward

Management

Treat angioedema aggressively with the following agents until resolution:

- Diphenhydramine (Benadryl) 50 mg IV Q4H
- Ranitidine 50 mg IV Q8H or Famotidine 20 mg IV q12 h
- If severe, consider Hydrocortisone 100 mg IV or Methylprednisolone 80 mg IV Q8H
- Avoid use of epinephrine due to possibility of increasing risk of intracerebral hemorrhage secondary to sudden rise in blood pressure

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Reference: Hill M et al. Anaphylactoid reactions and angioedema during alteplase treatment of acute ischemic stroke. *CMAJ* 2000; 162(9):1281-4.

Appendix D
Rt-PA (alteplase) Dosage Guideline

rt-PA 1 mg/ml Infusion for Acute Ischemic Stroke

Patient weight (kg)	Patient weight (lbs)	10% bolus (mL)	Infusion Dose Over One Hour Where 1mg = 1cc	Total t-PA dose: 0.9 mg/kg
50	110	5	40	45
51	112	5	41	46
52	115	5	42	47
53	117	5	43	48
54	119	5	44	49
55	121	5	45	50
56	123	5	45	50
57	126	5	46	51
58	128	5	47	52
59	130	5	48	53
60	132	5	49	54
61	134	6	49	55
62	137	6	50	56
63	139	6	51	57
64	141	6	52	58
65	143	6	53	59
66	146	6	53	59
67	148	6	54	60
68	150	6	55	61
69	152	6	56	62
70	154	6	57	63
71	157	6	58	64
72	159	7	58	65
73	161	7	59	66
74	163	7	60	67
75	165	7	61	68
76	168	7	62	68
77	170	7	62	69
78	172	7	63	70
79	174	7	64	71
80	176	7	65	72
81	179	7	66	73
82	181	7	66	74
83	183	8	67	75
84	185	8	68	76
85	187	8	69	77
86	190	8	70	77
87	192	8	70	78
88	194	8	71	79
89	196	8	72	80
90	198	8	73	81
91	201	8	74	82
92	203	8	75	83
93	205	8	75	84
94	207	9	76	85
95	209	9	77	86
96	212	9	78	86
97	214	9	79	87
98	216	9	79	88
99	218	9	80	89
100 +	220 +	9	81	90

Instructions: Administer 10% bolus dose IV over one minute and the remainder as an IV infusion over one hour. The maximum dose is 90 mg.

Appendix E

TNK (tenecteplase) Dosage Guideline:

Intravenous tenecteplase (TNK; 0.25 mg/kg, maximum 25 mg) Dosing Information (50 mg Vial diluted with 10 mL Sterile Water)			
Patient Weight (kg)	**Patient Weight (lbs)**	**TNK dose (mg)**	**Volume TNK to be administered (mL)**
Less than 60	Less than 132	15	3
60 to less than 70	132 to less than 154	17.5	3.5
70 to less than 80	154 to less than 176	20	4
80 to less than 90	176 to less than 198	22.5	4.5
90 or more	198 or more	25	5