Canadian Stroke Best Practices

CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Acute Stroke Management during Pregnancy Consensus Statement

Acute Ischemic Stroke Treatment:

Thrombolysis and Endovascular Therapy

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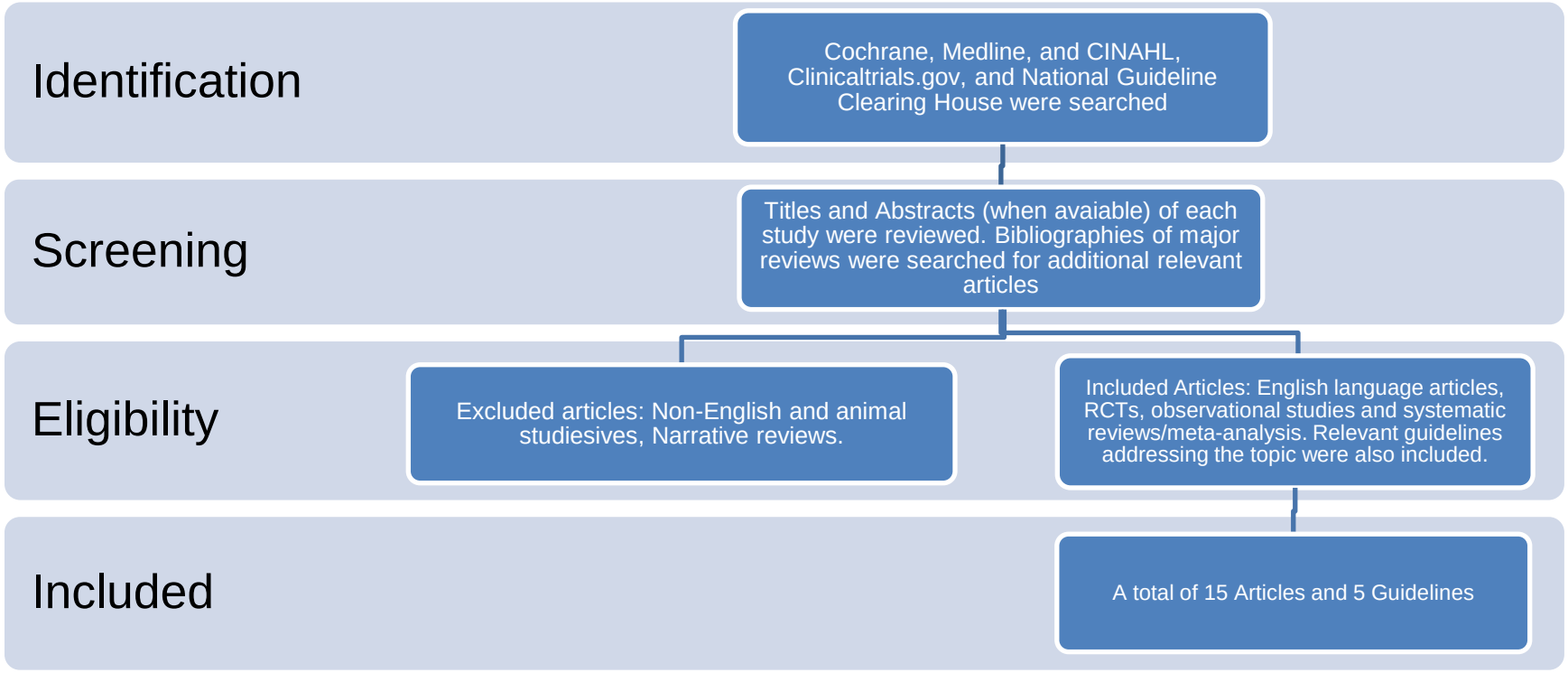
Search Strategy



Search terms included: “brain ischemia”, “brain infarction” or “stroke”, AND “tissue plasminogen activator” OR “endovascular therapy” OR “mechanical thrombectomy” AND “pregnancy” OR “obstetric*” OR “post-partum” OR “puerperium”. A total of 15 articles and 5 guidelines were included and were separated into separate categories designed to answer specific questions.

Published Guidelines

Guideline	Recommendations
Demaerschalk BM, Kleindorfer DO, Adeoye OM et al. Scientific Rationale for the Inclusion and Exclusion Criteria for Intravenous Alteplase in Acute Ischemic Stroke: A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke* 2016;47(2): 581-641. **selected**	1. Intravenous alteplase administration for ischemic stroke may be considered in pregnancy when the anticipated benefits of treating moderate to severe stroke outweigh the anticipated increased risks of uterine bleeding (Class IIb; Level of Evidence C). 2. The safety and efficacy of intravenous alteplase in the early postpartum period (<14 days after delivery) have not been well established (Class IIb; Level of Evidence C). 3. Urgent consultation with an obstetrician-gynecologist and potentially a perinatologist to assist with management of the mother and fetus is recommended (Class I; Level of Evidence C).
Toni D, Mangiafico S, Agostoni E, Bergui M, Cerrato P, Ciccone A, Vallone S, Zini A. and Inzitari D. (2015), Intravenous thrombolysis and intra-arterial interventions in acute ischemic stroke: Italian Stroke Organisation (ISO)-SPREAD guidelines. International Journal of Stroke, 10: 1119–1129 Intravenous thrombolysis and intra-arterial interventions in acute ischemic stroke: Italian Stroke Organisation (ISO)-SPREAD guidelines	1. Pregnancy listed as an exclusion for intravenous thrombolysis 2. No statements related to intra-arterial thrombolysis
Jauch EC, Saver JL, Adams HP, Jr. et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2013;44:870-947.	Recent experience suggests that under some circumstances—with careful consideration and weighting of risk to benefit—patients may receive fibrinolytic therapy despite 1 or more relative contraindications. Consider risk to benefit of IV rtPA administration carefully if any of these relative contraindications are present: Only minor or rapidly improving stroke symptoms (clearing spontaneously), **Pregnancy,** Seizure at onset with postictal residual neurological impairments, Major surgery or serious trauma within previous 14 days, Recent gastrointestinal or urinary tract hemorrhage (within previous 21 days), Recent acute myocardial infarction (within previous 3 months) (Table 10).
Lansberg MG, O'Donnell MJ, Khatri P, Lang ES, Nguyen-Huynh MN, Schwartz NE, Sonnenberg FA, Schulman S, Vandvik PO, Spencer FA, Alonso-Coello P, Guyatt GH, Akl EA. Antithrombotic and thrombolytic therapy for ischemic stroke: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice	No statements related to treatment with intravenous or intra-arterial thrombolysis during pregnancy or the puerperium

Guideline	Recommendations
guidelines. Chest 2012 Feb;141(2 Suppl):e601S-36S.	
Management of patients with stroke or TIA: assessment, investigation, immediate management and secondary prevention. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2008.	No statements related to treatment with intravenous or intra-arterial thrombolysis during pregnancy or the puerperium

Evidence Tables

Thrombolytic Therapy

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
Landais et al. 2017 **France** **Case study**	32-year-old, right-handed woman, 13 weeks pregnant, with no significant history, presenting to the ER with brutal onset aphasia (blurred understanding, speaking disorders) and numbness of the right hand. Baseline NIHSS score was 3. MRI showed L MCA infarct, of presumed cardioembolic origin. She was treated with intravenous rt-PA (dose unspecified) 240 minutes after symptom onset.	NA	NA	Aphasia was improved significantly. She was transferred to a rehabilitation day center for speech therapy. Aspirin was later switched to subcutaneous low molecular weight heparin 2 weeks before delivery. Six months after her stroke she gave birth to a healthy, term baby without complications.
Leffert et al. 2016 **USA** **Retrospective study**	24,641 women, aged 18-44 years admitted to one of 1,991 hospital following acute ischemic stroke from 2008-2013, who were included in the Get with the Guidelines Stroke Registry. Among them, 338 women were pregnant or <6 weeks postpartum at the time of stroke and 24,303 were nonpregnant.	The characteristics and outcomes of women: i) who were pregnant/postpartum vs. nonpregnant were compared and ii) who received any form of reperfusion therapy (n=40) were compared with those who did not (n=2,545)	Medical history, LOS, discharge destination	**Pregnant vs. nonpregnant women:** Women who were pregnant/postpartum were significantly younger (median 31 vs. 39 years, p<0.0001). A significantly higher proportion of nonpregnant women had a previous history of stroke or TIA (20.5% vs. 7.4%, p<0.001), coronary heart disease or previous MI (5.6% vs. 1.2%, p<0.0004), a history of diabetes (21.5% vs. 6.5%, p<0.001), HTN (42.5% vs. 17.5%, p<0.0001), smoker (32.9% vs. 22.9%, p<0.0001), dyslipidemia (16.4% vs. 3.3%, p<0.0001), heart failure (3.1% vs. 1.2%, p=0.041). Median admission SBP/DBP were significantly higher among nonpregnant women (139 vs. 127 mm Hg, p<0.0001 and 84 vs. 78 mm Hg, p<0.0001, respectively). A significantly higher proportion of nonpregnant women were taking antiplatelet/anticoagulant and antihypertensive medications. There were no significant differences between groups for discharge outcomes. Overall, 3.7% of all women died in hospital, 72.9% were discharged home and 70.9% were independent in ambulation at D/C. A higher proportion of pregnant/postpartum women had hospital LOS>4 days (45% vs. 395, p=0.046).

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				Women who did/did not received reperfusion therapy by pregnancy status: The percentage of pregnant/postpartum vs. nonpregnant women who received reperfusion therapy was similar (11.4% vs. 10.5%, p=0.42). Significantly fewer pregnant women received i.v t-PA monotherapy (4.4% vs. 7.95, p=0.03). Women who were pregnant/postpartum were significantly younger (median 31 vs. 39 years, p<0.0001). Medical histories were similar between groups, except a significantly higher proportion of nonpregnant women had a previous history HTN (35.4% vs. 17.5%, p=0.02). Median NIHSS score at admission was significantly lower among nonpregnant women (9 vs. 13, p=0.01). A significantly higher proportion of nonpregnant women were taking cholesterol-lowering medication (10.6% vs. 0%, p=0.03). Complications, including symptomatic ICH, serious hemorrhages and other complications were similar between groups. Discharge outcomes were similar between groups.
Tversky 2016 **USA** **Case report and review**	31-year- old woman, 5 months pregnant. presenting to the local ER with a chief complaint of sudden onset slurred speech, mild right hemiparesis, and hemisensory loss. NIHSS was 5. She had a medical history of ischemic stroke, associated with a prior pregnancy, with documented protein C and S deficiencies. She had decided to discontinue daily LMWH therapy and had not followed up with her primary physician. MRI revealed a left thalamic and internal capsular infarct. She was treated with intravenous rt-PA (dose unspecified)	NA	NA	By hospital day 2, her neurological symptoms completely resolved. PFO was thought to be the likely source of embolism. Obstetrical evaluation did not reveal any complications with the placenta or fetus. The patient was discharged home on daily LMWH therapy for the remainder of the pregnancy.
Ritchie et al. 2015 **UK**	28-year-old woman with a previous normal vaginal delivery presenting in her third trimester with a sudden onset of dense left hemiparesis. Baseline NIHSS score was 11. Patient was treated with	NA	NA	A post-thrombolysis MRI revealed a lacunar-type stroke (LACS) involving the right MCA. 24 hours post-thrombolysis, NIHSS score had improved to 6.

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
Case report	intravenous rt-PA within 2 hours of stroke onset.			Labour was induced at 48 hours post thrombolysis. Patient made a full recovery after normal delivery of a healthy infant. Post-delivery, she was initiated on clopidogrel and prophylactic tinzaparin, and LMWH
Mantoan Ritter et al. 2014 **UK** **Case report**	32-year old women at 36 weeks' gestation during her first pregnancy presented to the ER within 40 minutes of symptom onset of L MCA stroke. There were no (other) stroke risk factors. NIHSS score was 22 on admission. She received 0.9 mg/kg intra-arterial rt-PA within 2 hours of stroke onset.	NA	NA	2 hours post thrombolysis, NIHSS score was 13. Investigations were normal with 2 slightly abnormal blood levels (total chol 5.4 mmol/l, Hgb 10.6 g/dl) A healthy baby was delivered by caesarean section, at term. The mother was discharged from rehabilitation 4 month after stroke onset. Final mRS was 2.
Tassi et al. 2013 **Italy** **Case report**	28-year old woman, who was 16 weeks pregnant, presenting to the ER within 1 hour of onset of stroke symptoms. Initial NIHSS score of 20. She was treated with intravenous rt-PA (0.9 mg/kg)	NA	NA	Within 1 hour of treatment her NIHSS score was 1, with slight aphasia. No evidence of ICH at 24 hours. Following discharge, a healthy infant was delivered without complication following an uneventful pregnancy.
Li et al. 2012 **USA** **Case report and review**	24-year-old woman at 11 weeks' gestation with ischemic stroke (NIHSS score of 13) was treated with 25 mg dose total of intra-arterial rtPA. The authors review 10 additional cases where t-PA was used in the first (n=5), second (n=2) and third (n=3) trimesters of pregnancy for ischemic stroke. In 7 of these cases intravenous t-PA was used (doses not specified), and in 3, the IA route.	NA	Narrative descriptive of status of mother and infant following treatment and incidence of ICH	The mother's status in the present case was described as complete recovery. The infant was healthy and there was no evidence of ICH. In the 10 remaining cases, the mother's outcome was described as complete recovery (n=1), recovered well (n=3), marked improvement (n=4), good (n=1), and death (n=1). ICH was reported in 4 cases. 7 infants were born healthy, 2 pregnancies were terminated, and the fetus died in 1 case.
Ronning et al. 2010 **Norway** **Case report**	29-year old woman whose delivery was induced at 38 weeks due to pre-eclampsia. During the next 3 days she developed chest pain, tachycardia and orthopnea and was diagnosed with peripartum cardiomyopathy. She was treated with an ACE inhibitor and a diuretic and received unfractionated heparin. She then developed right-sided hemiplegia and global aphasia and was diagnosed with a L MCA stroke. NIHSS score was 14. She received 20 mg of intra-arterial rt-PA.	NA	NA	Neurological status improved rapidly over the next few hours. By the following day she had only a mild right facial paralysis, reduced tempo of the right hand, a partial non-fluent aphasia, but normal comprehension. There was no evidence of carotid atherosclerosis, coagulopathy or immunological disease. 4 months after stroke NIHSS was 1 and a mRS was 1.

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
DeKoninck et al. 2008 **Netherlands** **Case report**	33-year old woman was admitted to hospital after resuscitation for cardiac arrest, 19 days after the birth of her second child. Emergency CT demonstrated extensive ischemic damage throughout the brain. A thrombus in left internal carotid artery and right vertebral artery and a complete occlusion of the basilar artery was found on cerebral angiography. She was treated with intra-arterial thrombolysis (dosage not reported).	NA	NA	The patient deteriorated neurologically. Clinical brain death was confirmed by isoelectric electroencephalography the following day.
Mendez et al. 2008 **Spain** **Case report**	37-year-old woman developed sudden onset of left arm/leg weakness with facial droop, homonymous hemianopsia, and slight dysarthria. Symptoms occurred 15 hours after delivery of a healthy baby at 36 weeks by cesarean delivery. She was diagnosed with a R MCA infarction. NIHSS score was 16. She received 100,000 U of urokinase over 15 minutes.	NA	NA	Patient's neurological status improved rapidly. Final angiogram demonstrated complete recanalization of entire R MCA. Day 2 after treatment, NIHSS score was 1. Patient was discharge home 9 days post stroke, with only minimal facial weakness. At 3 months, there were no residual deficits.
Wiese et al. 2006 **USA** **Case report**	33-year-old woman, 13 weeks gestation, admitted to a community hospital within 30 min of left MCA stroke, who received intravenous t-PA (0.9 mg/kg). She was then transferred to a tertiary-care facility. NIHSS score at the time of arrival to tertiary care facility was 13.	NA	NA	Patient was transferred to a rehabilitation facility. Final NIHSS score was 4. There was no mention of complications associated with the treatment. Delivered healthy baby at 37 weeks.
Johnson et al. 2005 **USA** **Case report**	39-year-old woman, 37 weeks' gestation admitted within 40 minutes of MCA stroke. NIHSS score at baseline was 20. 15 mg of intra-arterial t-PA was administered	NA	NA	NIHSS score was 7 at 9 hours following treatment. There was no mention of complications associated with the treatment. Healthy baby was delivered 3 days following treatment.
Elford et al. 2002 **Canada** **Case report**	28-year-old woman with a 7-year history of infertility underwent in vitro fertilization. 7 days after embryo transfer she was admitted to hospital with severe ovarian hyperstimulation syndrome. 7 hours after acute treatments, she developed a R MCA stroke. NIHSS score was 11. She received 15.5 mg of intra-arterial rt-PA	NA	NA	After treatment her neurological status improved (NIHSS score 3). She developed a hematoma in the right basal ganglia which grew to 3.0 cm. Symptoms resolved over 3 weeks following treatment with fluids and drainage of pleural effusions. By 3 months she had only a mild incomplete left inferior

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
				quadrantanopia, normal strength, slight subjective sensory alteration in the left leg, and mild circumduction when ambulating. She was maintained on low-dose dalteparin for until the last 2 months of her pregnancy and delivered a healthy baby at term by spontaneous vaginal delivery.

Mechanical Thrombectomy

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
Bhogal et al. 2017 **Germany** **Case reports**	Case 1: 38-year-old woman in 24th gestational week admitted to hospital with sudden right-sided hemiparesis and global aphasia, confirmed as L MCA infarct. NIHSS score 15. Was not treated with t-PA, as presentation outside of therapeutic window. Patient was treated with thrombectomy using Solitaire device + 9 mg intra-arterial t-PA. The total time to recanalization after symptom onset was 11 h 25 min, the time from symptom onset to initial imaging was 3 h 52 min and the total duration of the interventional procedure was 6 h 7 min. Case 2: 36-year-old woman in 25th gestational week, of her 4th pregnancy admitted to hospital, after rapid deterioration of consciousness, preceded by headache, blurred vision, nausea, and vomiting. NIHSS could not be assessed. The past medical history was significant for operative reconstruction of the ascending aorta after type A dissection. CT/CTA showed a distal occlusion of the basilar artery. Initial treatment was 36 mg rt-PA followed by thrombectomy using Penumbra and Phenox devices. The duration of the procedure was 2 h 30 min, and the total time to recanalization from symptom onset was 5 h 52 min.	NA	NA	Case 1: After 48 h of monitoring in the ICU, the patient was transferred to the stroke unit. Aphasia and right hemiparesis improved markedly after physical therapy and speech therapy. 8-years after treatment, there was only mild residual paresis of the right hand (mRS score 1). Most likely source of embolism was a PFO. Healthy infant delivered vaginally, at term. Case 2: The patient was weaned successfully on the first postinterventional day, and apart from mild internuclear ophthalmoplegia there were no residual neurological symptoms (mRS score 1). Pregnancy was ongoing at the time of publication.
Aaron et al. 2016	Case 1: 24-year-old woman in 3rd trimester of first pregnancy, admitted	NA	NA	Case 1: Immediately after the procedure, motor power improved to grade 3, hemi neglect resolved and

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
India **Case reports**	within one hour of symptoms (acute L hemiparesis, neglect and altered sensorium). Previous medical history was significant for mitral valve replacement associated with rheumatic heart disease. Within the previous week, she had been switched from OAC to LMWH therapy. Baseline NIHSS was 20. MRI showed infarct involving the right lateral lenticulostriate territory. Underwent thrombectomy using Penumbra system, with partial recanalization. Total procedure time was 15 minutes. Case 2: 28-year-old woman, 37 weeks gestation of first pregnancy admitted to hospital for an elective cesarean section. After her admission for the planned procedure she developed a sudden dense left hemiplegia and became drowsy. Baseline NIHSS score was 21. Previous medical history was significant for mitral valve replacement, done 9 years previously, associated with rheumatic heart disease. She had been switched from OAC to LMWH therapy recently. MRI showed infarct involving the right putamen. Underwent thrombectomy using Penumbra system, with partial recanalization. Total procedure time was 30 minutes.			sensorium became normal. NIHSS was 12. Power improved to grade 4 over next 3 days. NIHSS was 1 at the time of discharge. Normal vaginal delivery. mRS 0. Case 2: Post procedure, she became fully conscious. Power grade 3. After 10 days, she underwent cesarean section and delivered a normal baby. At discharge, NIHSS score was 4. At six months follow-up, she had slight disability (mRS 2) and was unable to carry out all previous activities, but able to look after own affairs without assistance.

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