MAYO CLINIC

STROKE IN YOUNGER ADULTS

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DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIP(S) WITH INDUSTRY

- Nothing to disclose

REFERENCES TO OFF-LABEL USAGE(S) OF PHARMACEUTICALS OR INSTRUMENTS

- Nothing to disclose

LEARNING OBJECTIVES

- Review epidemiology, risk factors, diagnostic approach and management in stroke in young adults
- Discuss specific causes of stroke in younger population on a case-based format

EPIDEMIOLOGY – STROKE IN 18 TO 50-55 YO

- Incidence is rising and accounts for up to 15-18% of all stroke
- 2005 GCNKSS study, age 20-54 years
  - ischemic 69%, intracranial hemorrhage 17%, subarachnoid hemorrhage 10%, unknown 5%
- Varied incidence:
  - 8 per 100,000 person-years in Europe
  - >100 per 100,000 person-years in sub-Saharan Africa
- Case-fatality, FUTURE study, age 18-50
  - 1 year mortality 2.4% ischemic, 3% hemorrhagic
  - 9 years: 32% had modified Rankin score >2
  - young survivors: risk of seizure and neuropsychiatric syndromes

Putaala J, et al. Stroke 2009; 40:2698-2703
Kissela BM, et al. Neurology 2012; 79: 1781–1787
Singhal AB, et al. Neurology 2013; 81: 1089–1097
Mayte E van Alebeek et al. Journal of Cerebral Blood Flow & Metabolism 2018, Vol. 38(9) 1631–1641

YOUNG ADULTS' CHALLENGES

- longer inpatient stay
- longer need for rehabilitation
- higher cost of care
- loss of productivity
- social and emotional impact
- higher chance of surviving
- despite extensive workup, about 30% are still deemed cryptogenic

MODIFIABLE RISK FACTORS

- Tobacco smoking
- Illicit drug use
- Physical inactivity
- Obesity
- Hypertension
- Dyslipidemia
- Diabetes mellitus
- Cardiovascular disease
- Obstructive sleep apnea
- High-risk alcohol use
- Uncontrolled migraine disorder, especially migraine with aura
- Social isolation, loneliness

SPECIFIC RISK FACTORS

- Oral contraceptives and hormone replacement therapy
- Pregnancy and early postpartum state
- Patent foramen ovale
- Thrombophilia: inherited or acquired hypercoagulable states
- Venous sinus thrombosis
- Specific arterial diseases
- Inherited conditions

TOAST ETIOLOGICAL CLASSIFICATION FOR ISCHEMIC STROKES IN YOUNG ADULTS

- large artery disease 9.8%
- likely large artery disease 15.5 %
- small-vessel disease 13.1%
- cardioembolism 13.1%
- other determined etiology 14.6%
- multiple etiologies 2.6%
- unknown cause 34.5%

Mayte E van Alebeek et al. Risk factors and mechanisms of stroke in young adults: The FUTURE study. Journal of Cerebral Blood Flow & Metabolism 2018, Vol. 38(9) 1631–1641

INTERNATIONAL PEDIATRIC STROKE STUDY ETIOLOGICAL CLASSIFICATION

IPSS Risk factor category No. (%)	<35 years 138 (21.1)	≥35 years 518 (78.9)	Men 309 (47.1)	Women 347 (52.9)
Arteriopathy,[a] *n*/total (%)	10/73 (13.7)	35/295 (11.9)	17 (5.5)	28 (8.1)
Cardiac disorders, *n* (%)	18 (13.0)	73 (14.1)	35 (11.3)	56 (16.1)
Chronic systemic conditions, *n* (%)	45 (32.6)*	81 (15.6)	12 (3.9)	114 (32.9)*
Prothrombotic states, *n* (%)	15 (10.9)	36 (6.9)	18 (5.8)	33 (9.5)
Chronic head and neck disorders, *n* (%)	23 (16.7)	73 (14.1)	26 (8.4)	70 (20.2)*
Acute head and neck disorders, *n* (%)	4 (2.9)	4 (0.8)	5 (1.6)	3 (0.9)
Pregnancy related,[b] *n*/total (%)	15/94 (16.0)*	5/253 (2.0)	N/A	20 (5.8)
≥1 RF for early atherosclerosis,[c] *n*/total (%)	113/127 (89.0)	473/488 (96.9)*	277/288 (96.2)	309/327 (94.5)

Mayte E van Alebeek et al. Risk factors and mechanisms of stroke in young adults: The FUTURE study. Journal of Cerebral Blood Flow & Metabolism 2018, Vol. 38(9 1631–1641

LARGE OR MEDIUM-SIZED VESSEL DISEASE

- Carotid and vertebral artery dissection (spontaneous or traumatic)
- Premature atherosclerosis
- Reversible cerebral vasoconstriction syndrome: postpartum angiopathy, thunderclap headache, drug-induced
- Inherited metabolic causes: homocystinuria, MELAS syndrome
- Other genetic or inherited: Moyamoya, Sickle cell, Fabry, Fibromuscular dysplasia
- Infectious:
  - TB, syphilis, HIV, bacterial, herpes zoster
- Inflammatory
  - Takayasu, giant cell arteritis, collagen vascular disease (SLE, Sjogren's, etc)
- Toxic
  - cocaine, heroine, phencyclidine, therapeutic drugs such as cytosine arabinosine

SMALL VESSEL DISEASE

- Inflammatory
  - PACNS, PAN, SLE, Bechet, Scleroderma, Churg-Strauss, Susac
- Infectious
  - Herpes zoster, cysticercosis
- Genetic or inherited
  - CADASIL, HERNS, COL4A1 mutation

INTRACEREBRAL HEMORRHAGE

- arteriovenous malformation
- neoplasm
  - primary CNS, metastatic, leukemia
- hematologic
  - thrombocytopenia, sickle cell disease
- moya-moya disease/syndrome
- drug use
  - warfarin, vitamins, cocaine
- iatrogenic
  - peri-procedural
- cerebral venous thrombosis

RISK FACTORS SPECIFIC FOR WOMEN

- Natural menopause <42 yo (2=fold risk increase)
- Estrogen plus progestin and estrogen alone (> 50 micrograms)
- Migraine with aura

- Pregnancy
- Peri-partum and post-partum state (up to 6 weeks)

- Preeclampsia is a risk factor for subsequent ischemic strokes

MIGRAINE INCREASED STROKE RISK

- Overall, migraine with aura and without aura: 70% increased stroke risk
- OR is 2.3 in migraine with aura
- High-risk for women <45
- Higher-risk if smoking (10-fold greater), combined OCP (17 X), and all 3 (30 X)
- Migraine with aura associated with TIA/ischemic stroke, good outcome
- Migraine with aura
  - risk for subclinical MRI white matter lesion
  - increased cardiovascular risk

Spector JT, Kahn SR, Jones MR, et al. Migraine headache and ischemic stroke risk: an updated meta-analysis. Am J Med 2010;123(7):612–624.
Bousser MG. Estrogens, migraine, and stroke. Stroke 2004;35(11 suppl 1):2652–2656.

DIAGNOSTIC APPROACH

- V
- I
- T
- A
- M
- I
- N
- C
- P

DIAGNOSTIC APPROACH

- V – vasculopathy (athero and non atherosclerotic) and vasculitis. RCVS (reversible cerebral vasoconstriction syndrome)
- I – infectious
- T – toxic, trauma
- A – autoimmune/inflammatory
- M – metabolic and migraine
- I – idiopathic
- N – neoplastic
- C – cardiac embolism, coagulation
- P – pregnancy, post-partum

INHERITED HYPERCOAGULABLE STATES

- Protein S deficiency (1/1000)
- Protein C deficiency (1/200)
- Antithrombin III deficiency (1/2000)
- Activated protein C resistance (factor V Leiden)(1/25)
- Prothrombin gene mutation [20210 G/A](1/50)
- Dysfibrinogenemia
- C677T mutation (homocysteinemia)(1/15)

Population prevalence of top 5 is ~10% but varies by race/ethnicity.

ACQUIRED HYPERCOAGULABLE STATES

- Antiphospholipid antibodies / lupus anticoagulants
- Elevated factor VIII, IX or XI
- Pregnancy
- Post-operative / trauma / burns
- Cancer (marantic endocarditis)
- Nephrotic syndrome
- Myeloproliferative (polycythemia vera, thrombocythemia)
- Thrombotic thrombocytopenic purpura & HUS
- Diffuse intravascular coagulation (DIC)
- Falciparum malaria
- Severe hyperglycemia
- Macroglobulinemia & cryofibrinogenemias
- Scorpion stings (certain species)

MEDICATION-INDUCED HYPERCOAGULABLE STATES

- Estrogens (oral contraceptives & HRT)
- Tamoxifen
- L-Asparaginase
- Heparin-induced thrombocytopenia
- IVIG (vasospasm?)
- Topiramate ? (Neurology. 2003 Aug 26;61(4):456-64)

STAGED THROMBOPHILIA WORK-UP

- To evaluate for causes of increased venous and arterial thrombosis risk, the baseline evaluation should consist of the following tests:

  - ✓Hypercoagulation panel 1st tier: Factor V Leiden, Antithrombin III, Protein C, Protein S, Prothrombin gene mutation, fibrinogen, Anticardiolipin antibodies IgM and IgG, Beta 2 glycoprotein antibodies, LA)
  - ✓Homocysteine level
  - ✓CBC
  - ✓PT/INR and APTT

STAGED THROMBOPHILIA WORK-UP

Second Tier Testing

- If the only abnormalities are positive antiphospholipid Abs (lupus anticoagulant, anticardiolipin or beta2 glycoprotein antibodies) then the abnormal study/studies should be repeated in about 12 weeks. Sometimes positive for only a short period of time and can normalize spontaneously.
- If the patient has any coagulation abnormality (Prot C or S deficiency, Factor V Leiden or Prothrombin gene abnormality [either homo or heterozygous], etc.) they should be referred to Hematology for further evaluation to help plan long term therapy; e.g., should they be on lifelong antithrombotic agent, and which one?

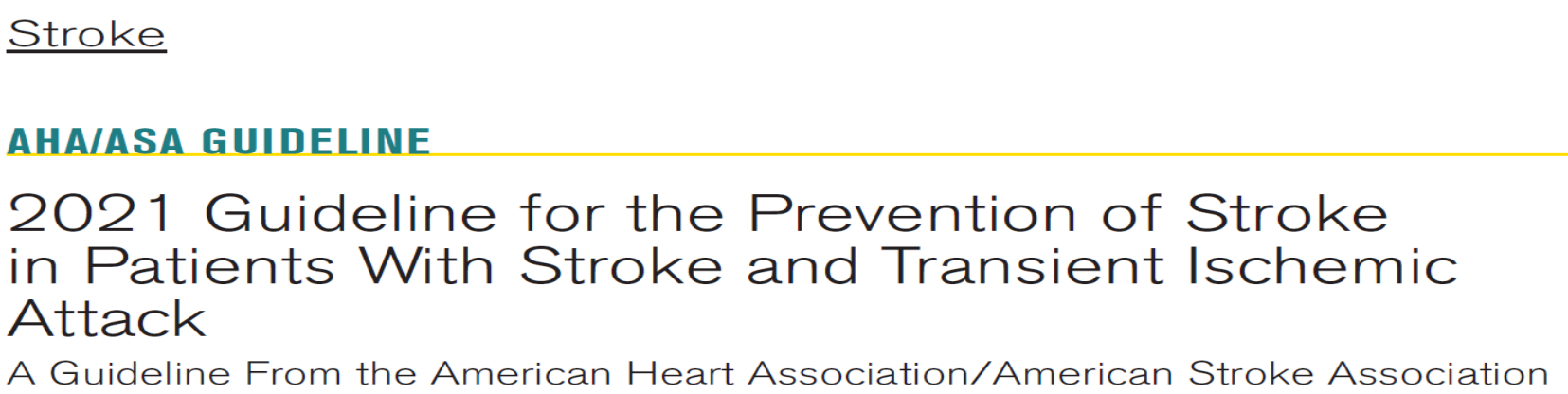
STAGED THROMBOPHILIA WORK-UP

Third Tier Testing

1. If the labs from the first and second tiers of testing are negative, and the homocysteine level is increased, then obtain a genetic study to determine if the patient has an MTHFR abnormality.

2. If all the baseline tests are negative, and there is an indication to pursue further coagulation testing (e.g., the presence of a PFO or a history of cerebral vein/sinus thrombosis), then consider ordering the following:

- Factor VIII, IX, and XI Activity Assays.
- Protein electrophoresis
- Paraneoplastic panel
- Paroxysmal nocturnal hemoglobinuria



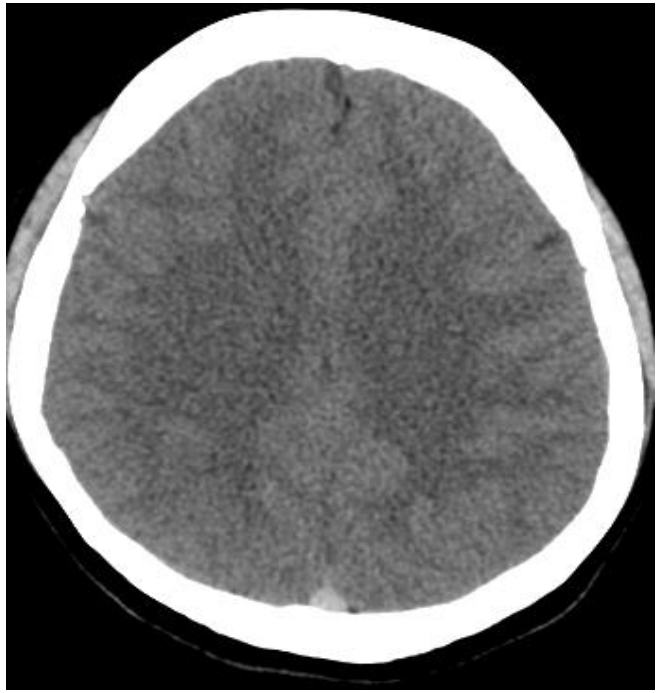
- In patients with cryptogenic stroke, tests for inherited or acquired hypercoagulable state, bloodstream or cerebral spinal fluid infections, infections that can cause central nervous system (CNS) vasculitis (eg, HIV and syphilis), drug use (eg, cocaine and amphetamines), and markers of systemic inflammation and genetic tests for inherited diseases associated with stroke are reasonable to perform as clinically indicated to identify contributors to or relevant risk factors for stroke (Class 2a, LOC C)
- In patients with ischemic stroke or TIA of unknown source despite thorough diagnostic evaluation and no other thrombotic history who are found to have prothrombin 20210A mutation, activated protein C resistance, elevated factor VIII levels, or deficiencies of protein C, protein S, or antithrombin III, **antiplatelet therapy is reasonable** to reduce the risk of recurrent stroke or TIA (Class 2a, LOC C)

Kleindorfer DO, et al. 2021 Guideline for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack. Stroke. 2021;52:00–00.

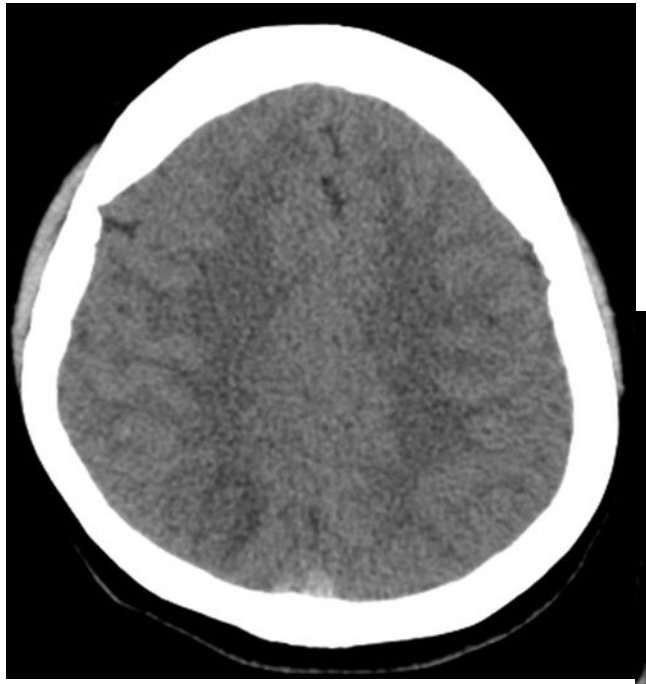
- Testing for protein C, protein S, or antithrombin levels should be deferred or repeated at least 4 to 6 weeks (or up to 6 months for factor VIII) after the acute stroke given that these protein levels may be altered during the acute stroke phase
- The risk of stroke recurrence among stroke survivors with thrombophilic traits is less well established.
- The ideal treatment (antiplatelet versus anticoagulation) remains unknown
- Isolated antiphospholipid antibody without fulfilling the criteria for antiphospholipid syndrome: antiplatelet therapy alone is recommended to reduce the risk of recurrent stroke
- Confirmed anti phospholipid syndrome: warfarin with goal INR 2-3, avoid rivaroxaban (higher risk of thrombotic events compared to warfarin)

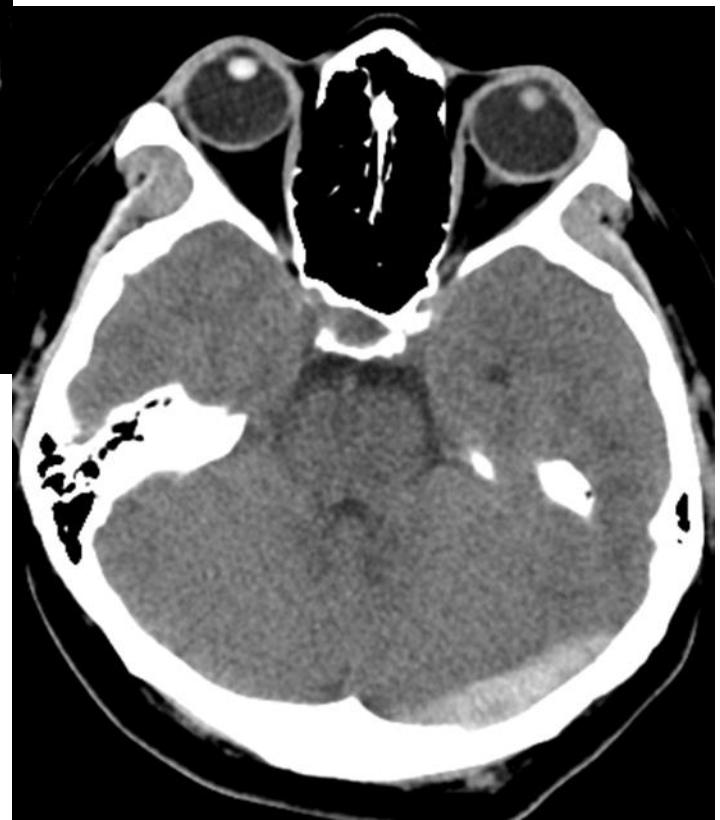
32 F develops thunderclap headache and emesis while driving home from work. HA persists at moderate intensity w repeated episodes of emesis over the next 2 days. On day #3 she wakes up with left- sided weakness, unable to walk independently & presents to the ED.
Medications: OCP, started 1 week prior.
In the ED she is witnessed to have a GTC seizure. BP 136/66, HR 103, T 37.3.
Neuro exam: depressed level of consciousness & flaccid left hemiplegia. CTH w/o contrast shown below.
Which of the following diagnostic tests is the most appropriate next step?

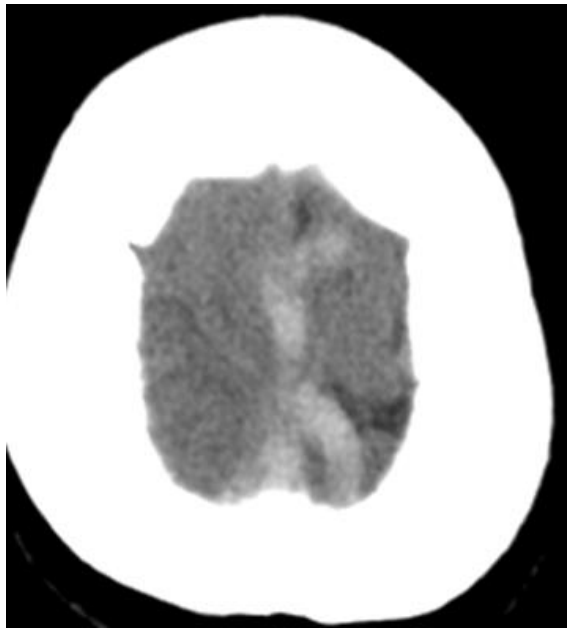
- A. Lumbar Puncture
- B. MRI Brain
- C. MRA Neck
- D. MR Venogram



VENOUS INFARCT RIGHT PARIETAL, EXTENSIVE VENOUS SINUS THROMBOSIS SUPERIOR SAGITTAL, LEFT TRANSVERSE SINUS







CEREBRAL VENOUS THROMBOSIS (CVT)

- Cerebral venous sinus thrombosis: thrombosis of the dural sinuses and/or deep cerebral veins
- Cortical vein thrombosis: occlusion of small veins on the surface of the cortex (rarer)
- 0.5-1% of all strokes, more common in young individuals

- COVID-19 considerations
  - CVT as a direct complication of SARSC-COV2 infection
  - Vaccine-induced immune-mediated thrombotic thrombocytopenia (VITT)

Stam J. Thrombosis of the cerebral veins and sinuses. N Engl J Med. 2005;352:1791–1798.

SAPOSNIK G, ET AL. STROKE. 2011;42:1158-1192

AHA/ASA Scientific Statement

Diagnosis and Management of Cerebral Venous Thrombosis

A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists.

The American Association of Neurological Surgeons and Congress of Neurological Surgeons have reviewed this document and affirm its educational content.

The Ibero-American Stroke Society (Sociedad Iberoamericana de Enfermedad Cerebrovascular) endorses the recommendations contained in this report.

Endorsed by the Society of NeuroInterventional Surgery

FERRO JM, ET AL. EUROPEAN JOURNAL OF NEUROLOGY 2017, 24:1203–1213

European Stroke Organization guideline for the diagnosis and treatment of cerebral venous thrombosis – endorsed by the European Academy of Neurology

J. M. Ferro[a,b], M.-G. Bousser[c], P. Canhão[a,b], J. M. Coutinho[d], I. Crassard[c], F. Dentali[e], M. di Minno[f,g], A. Maino[h], I. Martinelli[h], F. Masuhr[i], D. Aguiar de Sousa[a] and J. Stam[d], for the European Stroke Organization

CVT DIAGNOSIS

Ropper AH, Klein JP. Cerebral venous thrombosis, N Engl J Med 2021;385:59-64

Lindgren E, et al. Neurology 2020;95(12): e1706-e1715.

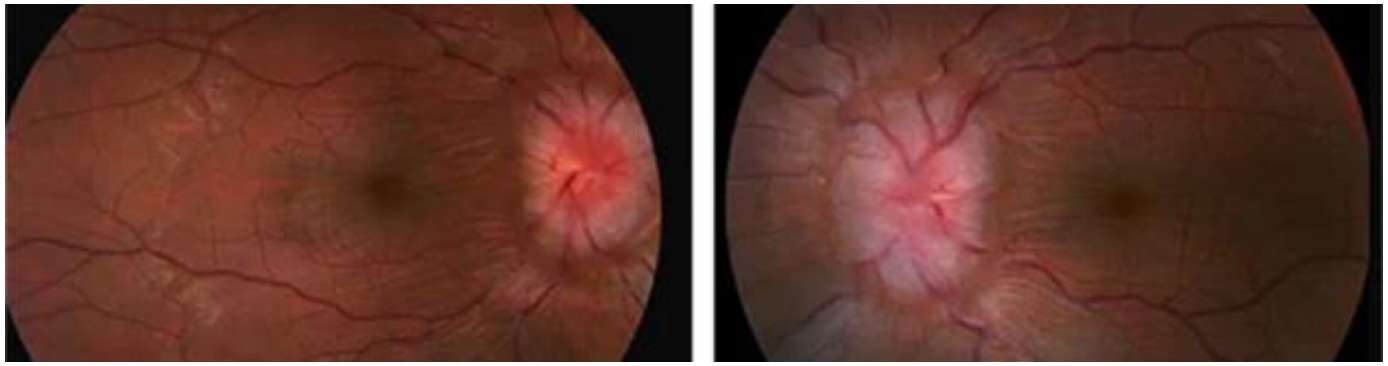
Ferro JM, et al.Stroke 2004; 35: 664-70.

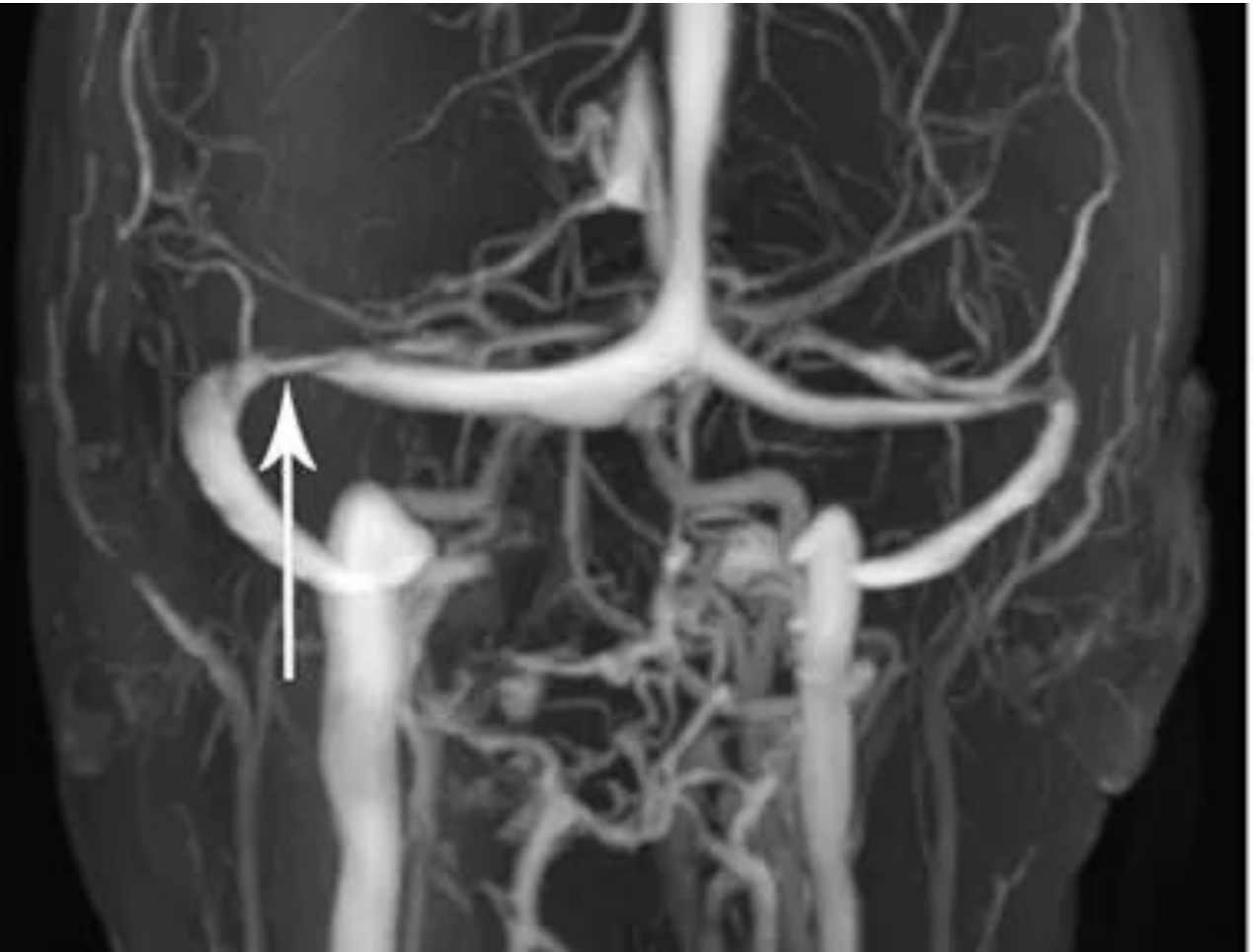
- **1. Clinical suspicion**

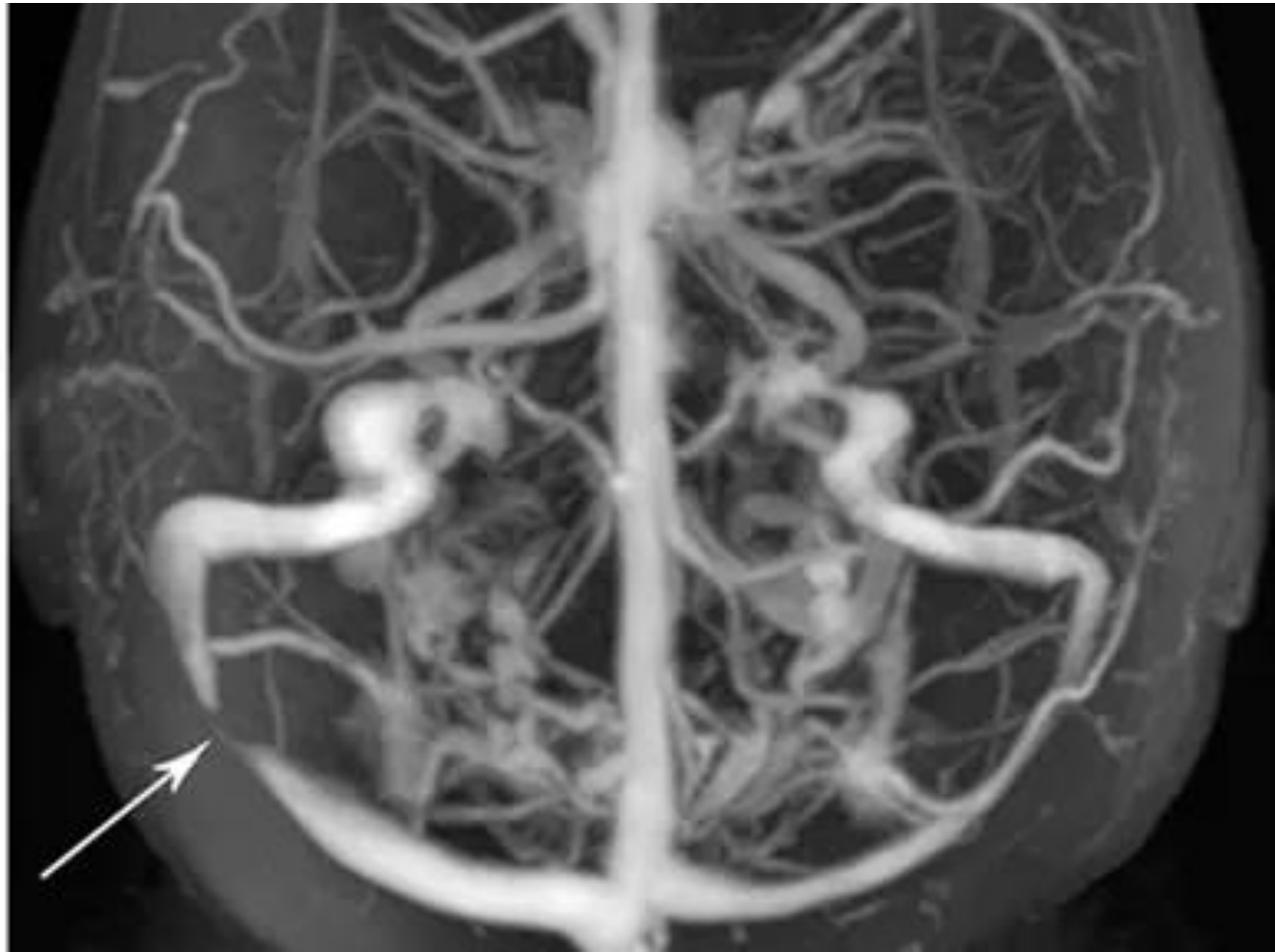
- 2 major and distinct clinical and pathophysiological entities:
  - Focal brain injury from venous ischemia/infarction or hemorrhage
  - Intracranial hypertension due to impaired venous drainage

- Clinical manifestations of CVT may also depend on the location of the thrombosis

- 2**. Neuro-imaging confirmation**







CVT CLINICAL PRESENTATIONS

Ropper AH, Klein JP. Cerebral venous thrombosis, N Engl J Med 2021;385:59-64

Lindgren E, et al. Neurology 2020;95(12): e1706-e1715.

Ferro JM, et al.Stroke 2004; 35: 664-70.

1. **Subacute headaches**, with normal neurological examination
2. **Seizures**, usually focal
3. **Focal neurological deficits** (if venous infracts develop)

Occur over hours or days after the headache in about 50% of cases

Paresis of one or both legs or hemiparesis from frontoparietal infarcts (V. Trolard)

Aphasia from temporal lobe infarcts (V. Labbe)

The symptoms/syndromes don’t respect arterial stroke territories

4. **Blurry vision/double vision** from papilledema and increased ICP
5. **Encephalopathy or coma**

CLINICAL PRESENTATIONS

- **Deep cerebral vein thrombosis**: drowsiness and stupor from b/l thalamic dysfunction and obstructive hydrocephalus; motor symptoms(bl and fluctuating paresis)
- **Cavernous sinus thrombosis**: periorbital and forehead pain, ocular chemosis, and palsies of cranial nerves that pass through the structure (the third, fourth, and sixth cranial nerves and the ophthalmic and maxillary divisions of the fifth cranial nerve
- **Sigmoid sinus**: pain in the mastoid, 6, 7, 8 nerve palsy
- **Petrosal sinuses**: brainstem and cerebellar signs and symptoms
- **Jugular vein or lateral sinus**: Pulsatile tinnitus
- **Transverse sinus thrombosis: i**solated HA/intracranial HTN, aphasia, motor
- **Sagittal sinus occlusion:** motor deficits, bilateral deficits, seizures, IH
- **Cortical veins:** focal neuro deficits, seizures

Ropper AH, Klein JP. Cerebral venous thrombosis, N Engl J Med 2021;385:59-64
Lindgren E, et al. Neurology 2020;95(12): e1706-e1715.
Ferro JM, et al.Stroke 2004; 35: 664-70.

CVT MANAGEMENT

CVT confirmed by neuroimaging: initiate anticoagulation, parenteral route initially (UFH or LMWH), followed by oral anticoagulants

Rationale:

to prevent thrombus growth
to facilitate recanalization
to prevent DVT or PE

Other considerations :

- ✓ oral anticoagulation choice and duration – depending on etiology and thrombophilia risk stratification
- ✓ endovascular therapy indications- TO-ACT terminated early due to futility in high-risk CVT, low risk excluded; only if clinical deterioration despite intensive anticoagulation
- ✓ decompressive craniectomy indications – if impending herniation to prevent death
- ✓ intracranial hypertension therapy – acetazolamide, monitor for progressive visual loss; avoid dehydration
- ✓ when to use corticosteroids – only in inflammatory diseases causing CVT
- ✓ anti-seizure medications – for seizure at CVT onset and not prophylactically in the absence of seizures
- ✓ pregnancy: LMWH in full anticoagulant dose
- ✓ ENT or CNS infections: antibiotics and surgical drainage or purulent collections

LONG-TERM MANAGEMENT

- **Depends on Thrombophilias and Risk Stratification**
- AHA: the overall risk of recurrence of any thrombotic event (CVT or systemic) after a CVT is 6.5%
- In patients with provoked CVT (associated with a transient risk factor), vitamin K antagonists may be continued for 3 to 6 months
- In patients with unprovoked CVT, vitamin K antagonists may be continued for 6 to 12 months
- A study comparing short-term (3–6 months) versus long-term (12 months) anticoagulation after CVT (Extending oral antiCOAgulation treatment after acute Cerebral Vein Thrombosis) is ongoing.
- For patients with recurrent CVT, VTE after CVT, or first CVT with severe thrombophilia (ie, homozygous prothrombin G20210A; homozygous factor V Leiden; deficiencies of protein C, protein S, or antithrombin; combined thrombophilia defects; or antiphospholipid syndrome), indefinite anticoagulation may be considered

Miranda B et al. Int J Stroke 2018;13:771–4
Saposnik G, et al. Stroke. 2011;42:1158-1192

JAMA Neurology | Original Investigation

Effect of Endovascular Treatment With Medical Management vs Standard Care on Severe Cerebral Venous Thrombosis
The TO-ACT Randomized Clinical Trial

Jonathan M. Coutinho, MD, PhD; Susanna M. Zuurbier, MD, PhD; Marie-Germaine Bousser, MD, PhD; Xunming Ji, MD, PhD; Patricia Canhão, MD, PhD; Yvo B. Roos, MD, PhD; Isabelle Crassard, MD; Ana Paiva Nunes, MD, PhD; Maarten Uyttenboogaart, MD, PhD; Jian Chen, MD; Bart J. Emmer, MD, PhD; Stefan D. Roosendaal, MD, PhD; Emmanuel Houdart, MD, PhD; Jim A. Reekers, MD, PhD; René van den Berg, MD, PhD; Rob J. de Haan, PhD; Charles B. Majoie, MD, PhD; José M. Ferro, MD, PhD; Jan Stam, MD, PhD; for the TO-ACT investigators

- First multicenter, open-label, blinded end point, randomized clinical trial conducted in 8 hospitals in 3 countries
- Evaluated safety and efficacy of EVT in severe CVT
- Adult patients with radiologically confirmed CVT who had at least 1 risk factor for a poor outcome (mental status disorder, coma state, intracerebral hemorrhage, or thrombosis of the deep venous system)
- The study was prematurely terminated because of futility: EVT with medical management did not improve functional outcome in patients with severe CVT, and had greater mortality rates
- Because of the small sample size, the possibility that future studies, using other methods of patient selection and endovascular techniques, may identify better recovery rates after EVT for patients with severe CVT, is not excluded

Coutinho JM, et al. JAMA Neurology 2020; 7798):966-973

CVT ORAL MANAGEMENT – RE-SPECT CVT

JAMA Neurology | Original Investigation

Safety and Efficacy of Dabigatran Etexilate vs Dose-Adjusted Warfarin in Patients With Cerebral Venous Thrombosis
A Randomized Clinical Trial

José M. Ferro, MD, PhD; Jonathan M. Coutinho, MD, PhD; Francesco Dentali, MD; Adam Kobayashi, MD, PhD; Andrey Alasheev, MD, PhD; Patrícia Canhão, MD, PhD; Denis Karpov, MD, PhD; Simon Nagel, MD; Laura Posthuma, MD; José Mário Roriz, MD; Jorge Caria, MD; Mandy Frässdorf, PhD; Holger Huisman, MSc; Paul Reilly, PhD; Hans-Christoph Diener, MD, PhD; for the RE-SPECT CVT Study Group

- Exploratory, prospective, randomized (1:1), open-label, multicenter clinical trial with blinded end-point adjudication, 51 tertiary sites in 9 countries
- Acute CVT in pts stable on IV heparin day 5-15: randomized to Dabigatran, 150 mg twice daily, or dose-adjusted warfarin for a treatment period of 24 weeks

CVT MANAGEMENT – RE-SPECT CVT RESULTS

- In 120 pts with CVT, no recurrent venous thrombotic events were observed in patients randomized to either the dabigatran or warfarin treatment group. Similar rates of recanalization (60 vs 67%).
- 1 major bleeding event (GI) was recorded among users of dabigatran and 2 (SDH) among users of warfarin.
- Any bleeding, irrespective of its severity, occurred in 20% of patients, with the same frequency in both treatment groups
- Both dabigatran and dose-adjusted warfarin may be safe options to prevent recurrent venous thrombotic events in patients with cerebral venous thrombosis.
- Because of the limited sample size, the noninferiority or superiority of either treatment could not be demonstrated

Stroke

ORIGINAL CONTRIBUTION

Direct Oral Anticoagulants Versus Warfarin in the Treatment of Cerebral Venous Thrombosis (ACTION-CVT): A Multicenter International Study

- Observational, real-world comparison of DOAC to Warfarin in a multicentric CVT cohort
- International retrospective study, 845 CVT patients across 27 centers

66.6% (271) used apixaban
18.2% (74) used rivaroxaban
13.5% (55) used dabigatran
1.7% (7) used other or multiple DOACs

ACTION-CVT

- When compared with warfarin, DOAC treatment was associated with similar risk of:

-recurrent venous thrombosis (aHR, 0.94 [95% CI, 0.51–1.73]; P=0.84)
-death (aHR, 0.78 [95% CI, 0.22–2.76]; P=0.70)
-rate of partial/complete recanalization (aOR, 0.92 [95% CI,0.48–1.73];P=0.79)

-but a lower risk of major hemorrhage (aHR, 0.35 [95% CI, 0.15–0.82]; P=0.02)

- Ongoing studies
- DOAC-CVT study (Direct Oral Anticoagulants in the Treatment of Cerebral Venous Thrombosis; https://clinicaltrials.gov; NCT04660747) - large prospective international observational study
- Randomized SECRET trial (Study of Rivaroxaban for Cerebral Venous Thrombosis; https://clinicaltrials.gov; NCT03178864).

IMPORTANT CONSIDERATIONS ACTION-CVT

1. **Patients with antiphospholipid antibody syndrome were excluded**, as DOACs are contraindicated after 2 randomized trials have demonstrated an increase in arterial thrombotic events in patients treated with rivaroxaban compared with VKAs

Ordi-Ros J et al. Ann Intern Med. 2019;171:685–694
Pengo V, et al. Blood. 2018;132:1365–1371

2. **Pregnant patients and those with active cancer were excluded**, as VKAs are generally contraindicated in these scenarios

In patients with cancer-associated VTE at typical sites, DOACs have recently been shown to be a viable option, noninferior to low molecular-weight heparins. CVT was excluded in those studies

Agnelli G et al. Thromb Haemost. 2018;118:1668–1678
Raskob GE et al. N Engl J Med. 2018;378:615–624

3. **Only 6 pts out of 845 had COVID-associated CVT**

34yo F presents to the ED within 2 hours of an abrupt onset headache, neck pain, vertigo, emesis. NIHSS is 3 for sensory loss & incoordination of L upper & lower extremity. A lateral medullary stroke is suspected. CT head is normal; no evidence of acute ischemic changes & no ICH. CT angio head & neck reveals a vertebral artery dissection. Blood pressure is 161/92. INR 1.0, PTT 27.2, platelets 256

Would you consider IV recombinant tissue-type plasminogen activator (rtPA) in this patient?

- YES
- Vertebral artery dissection is **NOT** a contraindication to receive IV tPA

AHA/ASA Scientific Statement

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

"IV alteplase in acute ischemic stroke known or suspected to be associated with extracranial cervical arterial dissection is reasonably safe within 4.5 hours and is probably recommended"

Both IA tPA & mechanical thrombectomy are used to tx acute ischemic stroke in the setting of dissection

Demaerschalk et al. Stroke 2016

ARTERIAL DISSECTION

- Common cause of stroke in the young, but may occur at any age
  - Mean age = 45 yrs
  - all ages, but 2/3 btw 35-50 yrs

- Approx 2% of all ischemic strokes and **10-25% of strokes in young pts**
- **Internal carotid 3x** more common than vertebral
- **Extracranial** > intracranial
- Men = women

- Dissection occurs when structural integrity of arterial wall is compromised
  - allowing blood to collect btw layers as an intramural hematoma
-

Schievink et al. NEJM 2001

PREDISPOSING FACTORS FOR DISSECTION

Genetic:

- Fibromuscular **dysplasia—most common**
- Ehlers–Danlos syndrome type IV
- Marfan's syndrome
- Type 1 collagen point mutation
- Osteogenesis imperfecta type 1
- Cystic medial necrosis
- Autosomal dominant polycystic kidney disease
- Alpha-1 antitrypsin deficiency
- Pseudoxanthoma elasticum
- Moyamoya
- Reticular fiber deficiency
- Homocystinuria

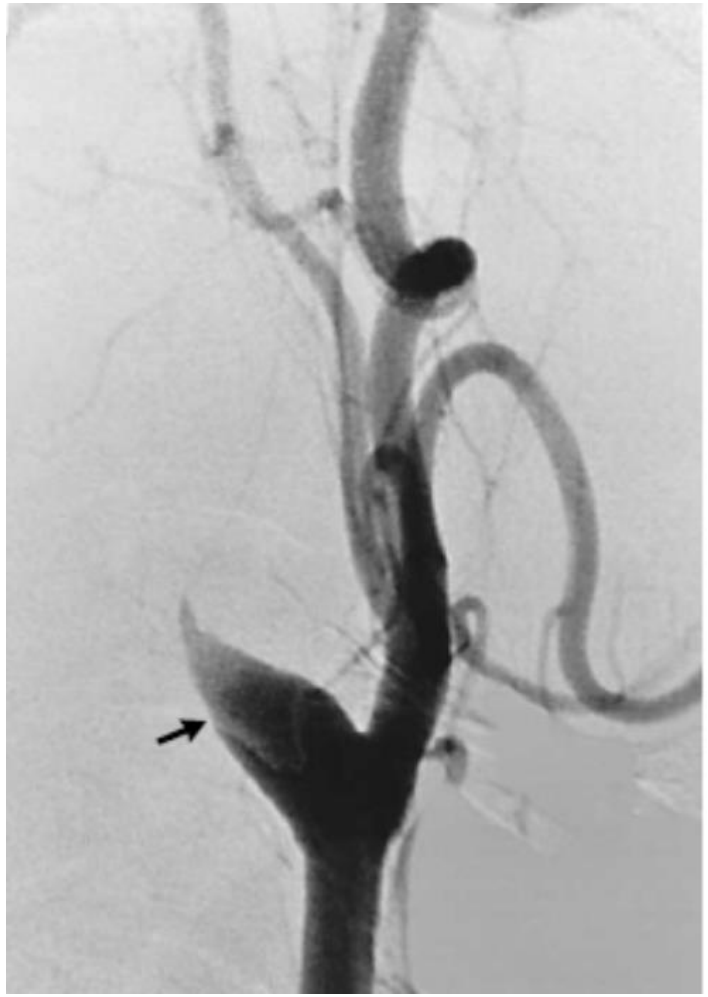
- **Trauma**: MVA, vigorous coughing, chiropractic manipulation, iatrogenic

- **Other**: infection (URTI), smoking, HTN, OCP

- RCVS

DISSECTION OF INTERNAL CAROTID

- Pain head, face, neck with partial Horner's (miosis & ptosis)
- Headache, gradual or thunderclap
- 12% have lower cranial nerves palsies (hypoglossal)
- Pulsatile tinnitus in 25%
- Cerebral or retinal ischemia symptoms in 50-95%
    - Transient monocular blindness



Tapered, flame-like occlusion typical of acute dissection

DISSECTION OF VERTEBRAL ARTERY

- Neck pain
- Occipital headache but can be holocephalic
- **90% have ischemic symptoms**
  - Dizziness, dysarthria, ataxia
  - Lateral medullary syndrome is common

MANAGEMENT OF EXTRACRANIAL ARTERIAL DISSECTION

- Traditionally **anticoagulation with heparin as immediate tx & warfarin as subsequent tx** had been the most suggested approach

- Anticoagulation may **prevent occlusion of a stenotic vessel and minimize distal embolization** (artery-to-artery embolization, from thrombus at the dissection site)

- But…

CADISS (CERVICAL ARTERY DISSECTION IN STROKE STUDY)

- Randomized controlled trial 2006-2013
- 250 pts extracranial carotid & vertebral dissection assigned to **antiplatelet** or **anticoagulan**t tx for **3 months**
- 1° endpoint: ipsilateral stroke or death w/in 3 mos

- **No significant difference btw 2 treatment groups**
  - ipsi ischemic stroke occurred in 2% antiplatelet group & 1% anticoagulant group (OR 0.34, P= 0.63)
  - **No deaths** in either group

- Rate of recurrent stroke 2% at 3 months

Lancet Neurol. 2015;14:361–367.
Neurology. 2017;88:646–652

JAMA Neurology | Original Investigation

Antiplatelet Therapy vs Anticoagulation Therapy in Cervical Artery Dissection

The Cervical Artery Dissection in Stroke Study (CADISS) Randomized Clinical Trial Final Results

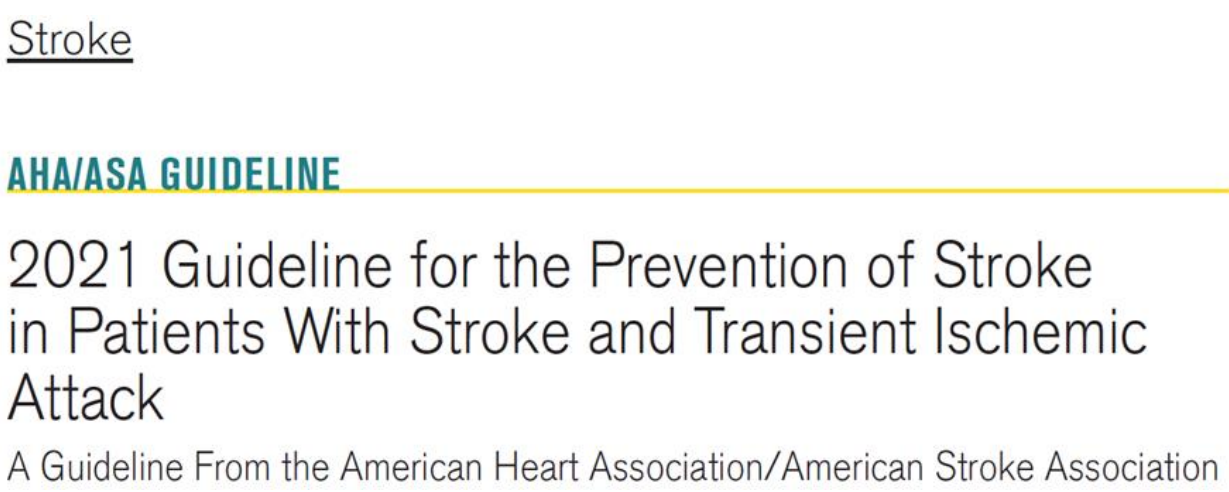
- Risk of **recurrent stroke** at 1 year was **2.5%**
- **No difference in recurrence** rates with antiplatelets or anticoagulants
- **No difference** in rates of angiographic **recanalization**

- **Conclusion**:
  - Risk of recurrent stroke after dissection is low
  - No evidence that antiplatelets or anticoagulants were more effective at reducing this risk

Markus HS, et al. Antiplatelet Therapy vs Anticoagulation Therapy in Cervical Artery Dissection. JAMA Neurol. 2019 Jun; 76(6): 657–664

DISSECTIONS GUIDELINES

- In patients with ischemic stroke or TIA after an extracranial carotid or vertebral arterial dissection, **treatment with antithrombotic therapy for at least 3 months** is indicated to prevent recurrent stroke or TIA.
- In patients with ischemic stroke or TIA who are <3 months after an extracranial carotid or vertebral arterial dissection, it is reasonable to **use either aspirin or warfarin** to prevent recurrent stroke or TIA.
- In patients with stroke or TIA and extracranial carotid or vertebral artery dissection who have **recurrent events despite antithrombotic therapy, endovascular therapy** may be considered to prevent recurrent stroke or TIA.



33yo F develops an explosive 10/10 holocephalic headache while having sexual intercourse . The 10/10 HA is associated with dysarthria & left UE weakness lasting 2 hours. She had been drinking heavily all evening & smoking marijuana. She went to sleep and woke up in the morning with persistent 8/10 HA but no weakness or dysarthria. She has history of migraine (PRN sumatriptan), but this HA is different than her usual migraines thus she presents to the ED.

On exam T 37.5 °C , BP 112/62 , HR 70, RR 14.

Neuro exam non-focal. A CT head is normal. Results of a lumbar puncture are: RBCs 8, Nuc 2, Glu 60, protein 40; opening pressure 19

Which of the following is the most appropriate next step in management?

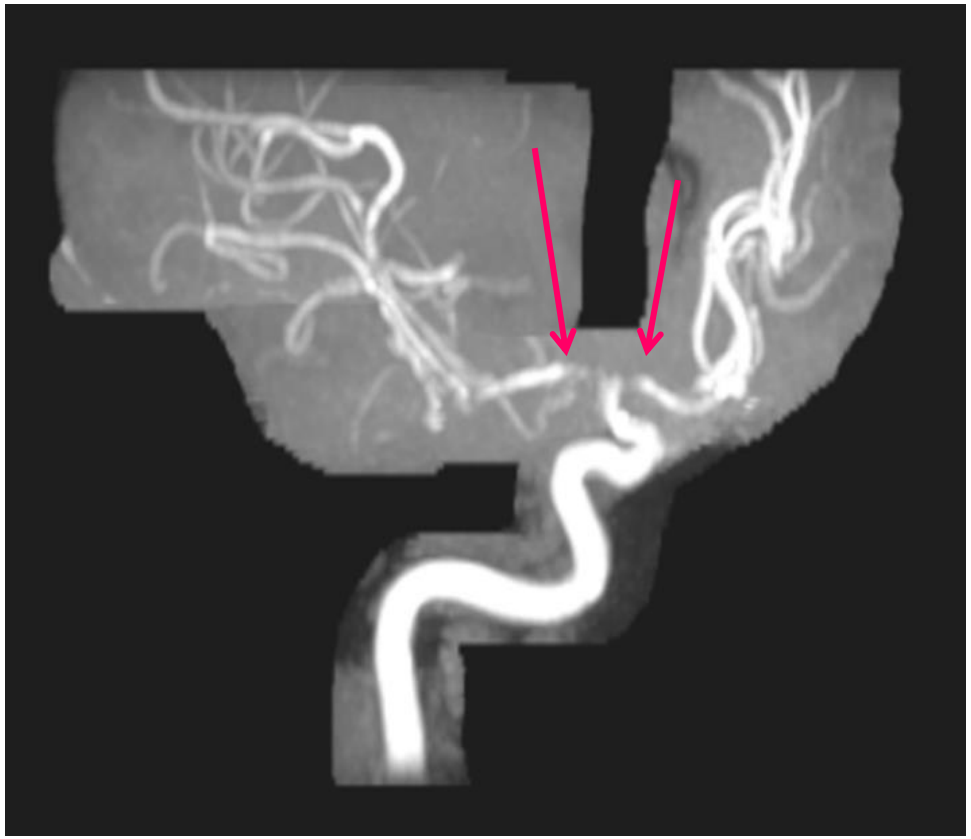
A. IV thrombolysis

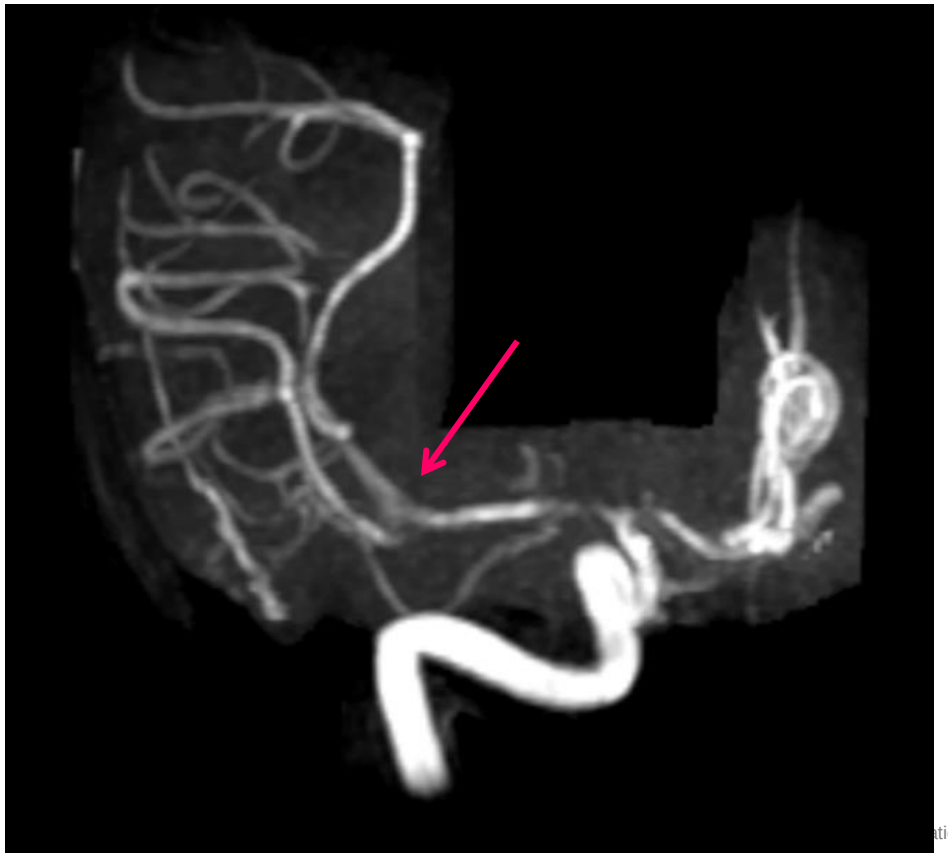
B. Cerebrovascular imaging (CTA, MRA)

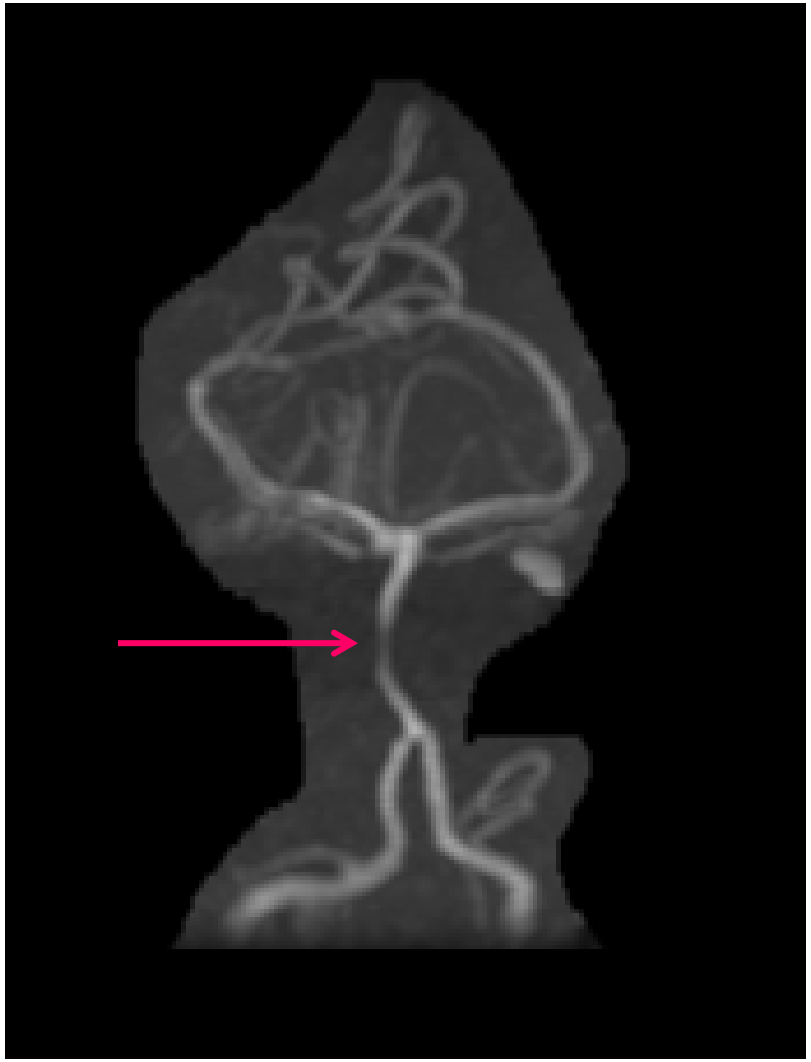
C. Indomethacin

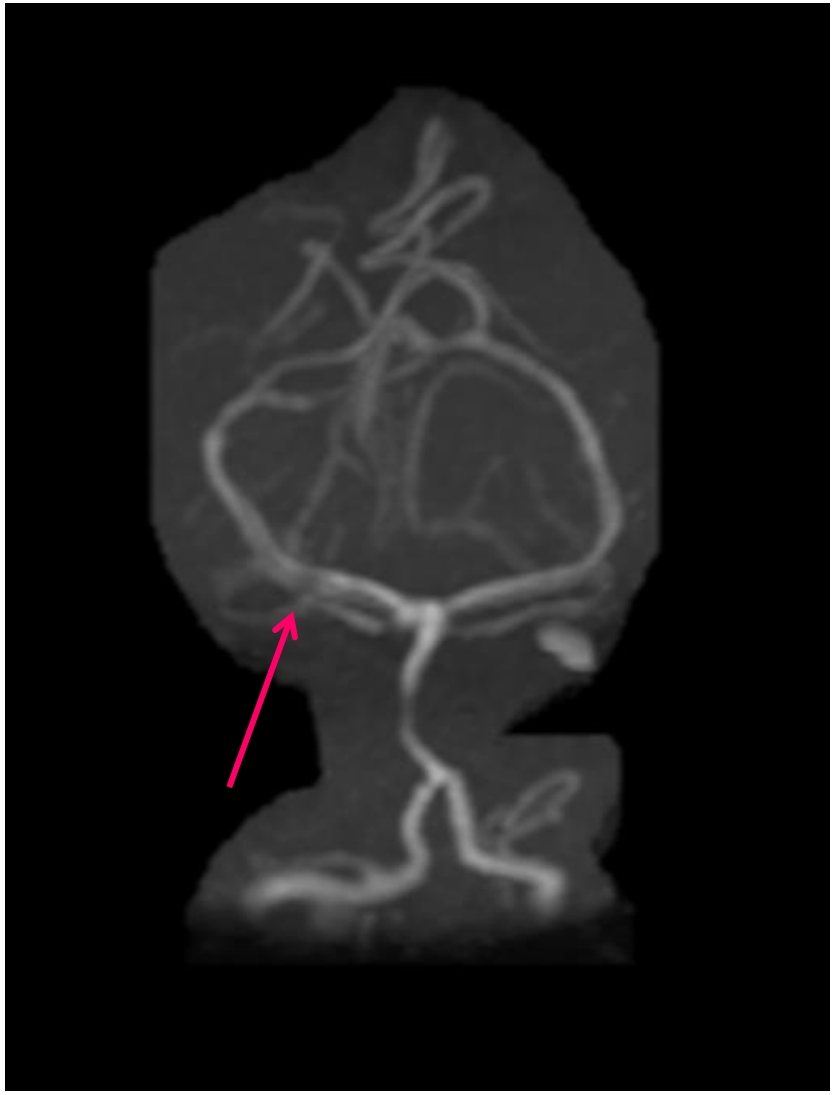
D. Sumatriptan

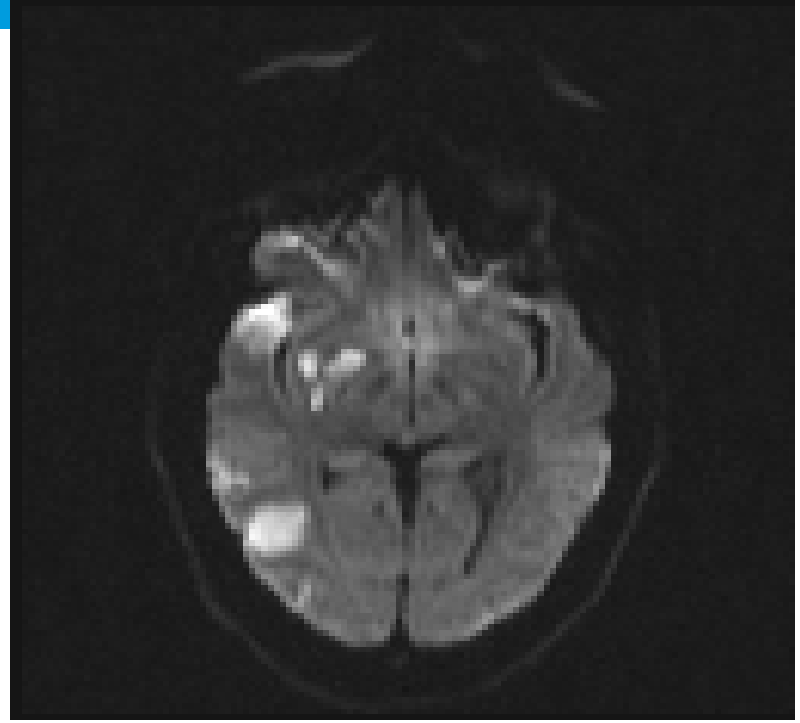
E. Dexamethasone

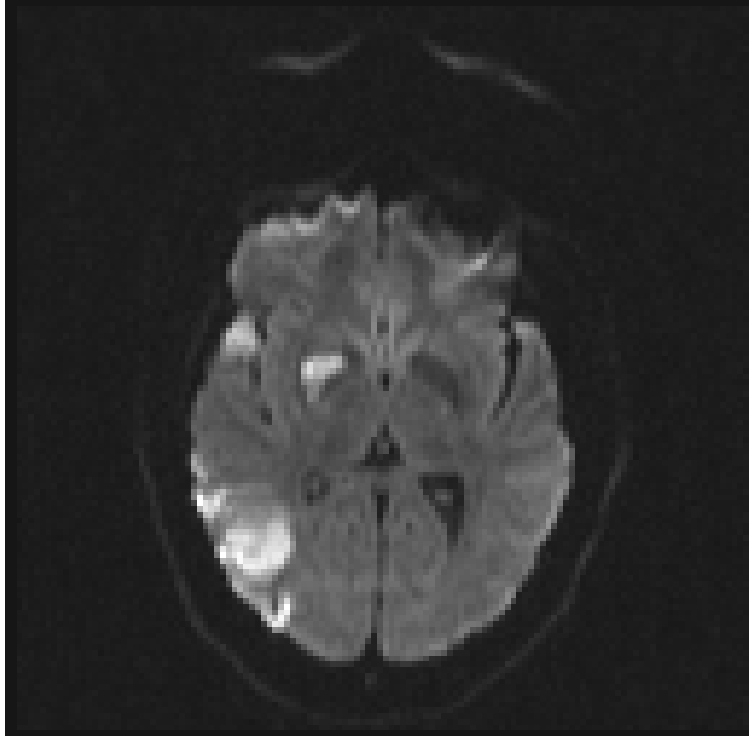


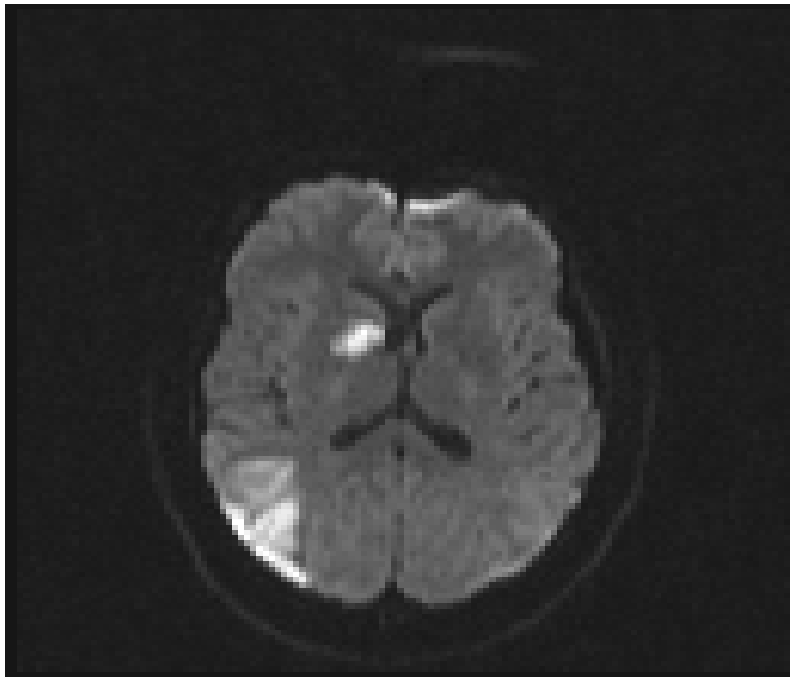


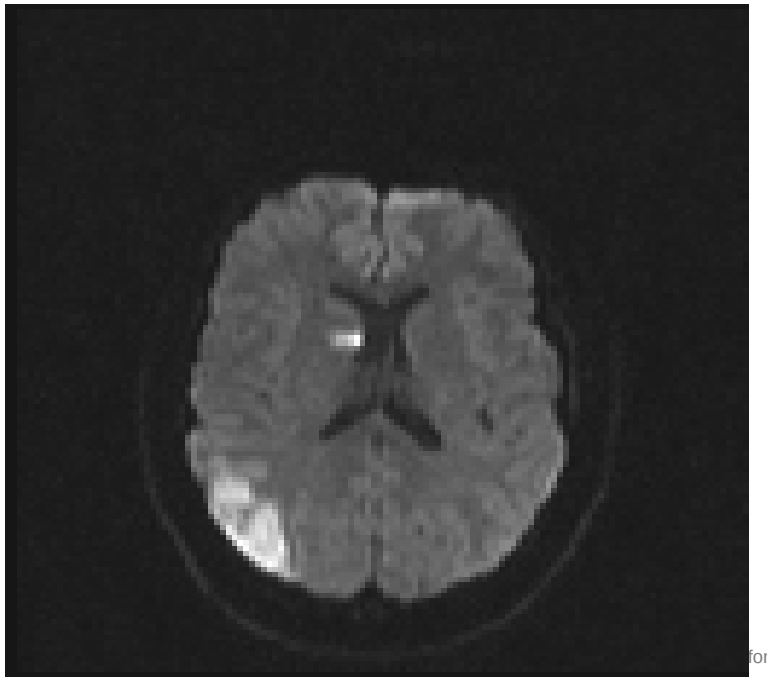




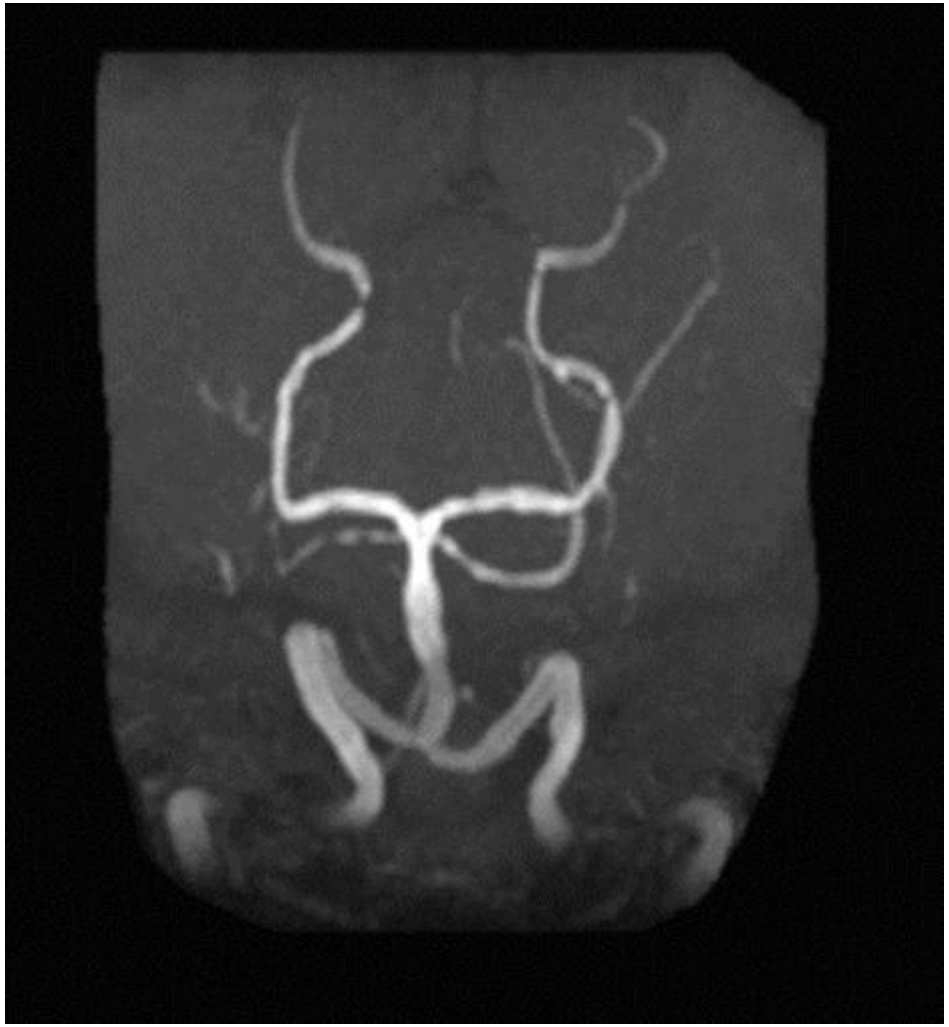








REVERSIBLE CEREBRAL VASOCONSTRICTION SYNDROME (RCVS)



REVERSIBLE CEREBRAL VASOCONSTRICTION SYNDROME

- Multiple areas of **constriction involving cerebral arteries** that resolve within days to weeks
- Present with acute onset severe HA, **"thunderclap"**, with or w/o neuro signs
- Ischemic events such as TIAs/strokes occur during the 2nd week
  - Can also see ICH, SAH, & PRES
- Can occur without identifiable cause, during pregnancy/post-partum, as a response to certain meds, or illicit drugs
- **60%** 2/2 to vasoactive substances or post-partum state

Calabrese et al. Ann Intern Med. 2007

RCVS SIGNS & SYMPTOMS

- Recurrent thunderclap HA
- HA may be diffuse or local, severe & throbbing
  - Can be associated with nausea, emesis, photophobia
- Can occur spontaneously while at rest or can be precipitated by exertion
- Ischemia can result in
  - Visual defects, hemiplegia, dysarthria/aphasia, ataxia
- Transient HTN (sometimes severe)
- Seizures during the acute period

CRITICAL ELEMENTS FOR RCVS DIAGNOSIS

- Severe, acute headache, with or without additional neurologic signs or symptoms
- No evidence for aneurysmal subarachnoid hemorrhage
- Angiography documenting multifocal segmental cerebral artery vasoconstriction
- Normal or near-normal CSF (protein<80, wbc< 10, normal glucose)
- Angiographic reversibility <12 weeks

Calabrese et al. Ann Intern Med. 2007

RCVS TRIGGERS

- Pseudoephedrine
- Ergotamine
- SSRIs
- Triptans
- Cocaine, ecstasy, marijuana, amphetamine
- Cyclophosphamide
- Tacrolimus
- IVIG
- Erythropoetin
- pseudoephedrine, ephedrine
- Nicotine patches

- Anger/sudden emotion
- Sexual activity
- Cough
- Head trauma
- Pheochromocytoma
- Hypercalcemia
- Ginseng
- Binge drinking
- Post-partum
  - With or without vasoactive substances, with or w/o eclampsia or pre-eclampsia

RCVS TREATMENT

- No randomized controlled trials; observational data are guiding us
- Stop offending drugs
- Parenteral or oral calcium channel blockers
- 4-12 weeks
- Repeat neuroimaging

50 y/o M presents to stroke clinic s/p hospitalization last month for a Left PCA ischemic stroke. No vascular risk factors. Hypercoagulability studies: negative. He has been compliant with daily ASA since his stroke.

TEE: large PFO with R-to-L shunt & associated atrial septal aneurysm.

LE doppler neg for DVT. 30-day Holter: normal sinus rhythm.

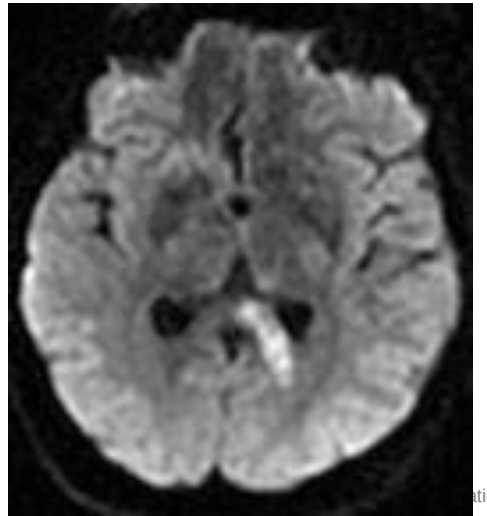
What is the next best step in management?

A. Consider referral to Cardiology for PFO closure

B. Switch to warfarin

C. Switch to clopidogrel

D. Switch to apixaban



PATENT FORAMEN OVALE (PFO) CLOSURE FOR CRYPTOGENIC STROKE

- PFO is a failure of the primum & secundum atrial septa to fuse postpartum
  - Prevalence in general pop is **20-26%**

- PFO is associated w cryptogenic stroke & considered a possible source in some
  - potentially allows for a **paradoxical embolus** originating in venous circulation to cross over into arterial circulation & reach the brain

- Percutaneous closure of PFOs in pts w cryptogenic stroke has received considerable interest to reduce the risk of recurrent stroke

3 LANDMARK PFO CLOSURE TRIALS SEPT 2017

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 14, 2017 VOL. 377 NO. 11

Patent Foramen Ovale Closure or Anticoagulation vs. Antiplatelets after Stroke

J.-L. Mas, G. Derumeaux, B. Guillon, E. Massardier, H. Hosseini, L. Mechtouff, C. Arquizan, Y. Béjot, F. Vuillier, O. Detante, C. Guidoux, S. Canaple, C. Vaduva, N. Dequatre-Ponchelle, I. Sibon, P. Garnier, A. Ferrier, S. Timsit, E. Robinet-Borgomano, D. Sablot, J.-C. Lacour, M. Zuber, P. Favrole, J.-F. Pinel, M. Apoil, P. Reiner, C. Lefebvre, P. Guérin, C. Piot, R. Rossi, J.-L. Dubois-Randé, J.-C. Eicher, N. Meneveau, J.-R. Lusson, B. Bertrand, J.-M. Schleich, F. Godart, J.-B. Thambo, L. Leborgne, P. Michel, L. Pierard, G. Turc, M. Barthelet, A. Charles-Nelson, C. Weimar, T. Moulin, J.-M. Juliard, and G. Chatellier, for the CLOSE Investigators*

ORIGINAL ARTICLE

Patent Foramen Ovale Closure or Antiplatelet Therapy for Cryptogenic Stroke

Lars Søndergaard, M.D., Scott E. Kasner, M.D., John F. Rhodes, M.D., Grethe Andersen, M.D., D.M.Sc., Helle K. Iversen, M.D., D.M.Sc., Jens E. Nielsen-Kudsk, M.D., D.M.Sc., Magnus Settergren, M.D., Ph.D., Christina Sjöstrand, M.D., Ph.D., Risto O. Roine, M.D., David Hildick-Smith, M.D., J. David Spence, M.D., and Lars Thomassen, M.D., for the Gore REDUCE Clinical Study Investigators*

ORIGINAL ARTICLE

Long-Term Outcomes of Patent Foramen Ovale Closure or Medical Therapy after Stroke

Jeffrey L. Saver, M.D., John D. Carroll, M.D., David E. Thaler, M.D., Ph.D., Richard W. Smalling, M.D., Ph.D., Lee A. MacDonald, M.D., David S. Marks, M.D., and David L. Tirschwell, M.D., for the RESPECT Investigators*

CLOSE TRIAL

MAS ET AL NEJM 2017 SEP 14; 377(11): 1011-1021

- PFO closure + antiplatelet vs antiplatelet vs anticoagulation
  - Randomized 1:1:1; 663 pts (16 – 60yr)

- recent stroke (w/in 6 mo) attributed to PFO, w an assoc. **atrial septal aneurysm** or **large interatrial shunt** (>30 microbubbles)

- Results: ø stroke 238 pts PFO closure group vs 14/235 pts antiplatelet-only group; **HR 0.03** (p<0.001)

- New-onset **Afib higher in PFO** closure group (**4.6% vs 0.9%** p=0.02)

- 5-yr risk of stroke was **4.9%** lower w PFO closure + antiplatelet than antiplatelet alone
  - **NNT 20** to prevent 1 stroke in 5 yrs

REDUCE TRIAL

SØNDERGAARD ET AL NEJM. 2017 SEP 14; 377(11): 1033-1042

- PFO closure + antiplatelet vs antiplatelet-only
  - Randomized 2:1; 664 pts (18-59 yr)

- Cryptogenic stroke w/in 6 months

  81% had moderate or large shunt (6-25,> 25 microbubbles)

- Results: Incidence of new brain infarctions (clinical + silent MRI) was significantly lower in PFO closure group
  - **5.7%** vs **11.3%**; **RR 0.51** (p<0.04)

- **Afib higher in PFO closure group** (6.6% vs 0.4%)

- **NNT 28** to prevent 1 stroke in 24 mos

RESPECT TRIAL

SAVER ET AL NEJM 2017 SEP 14; 377(11): 1022-1032

- PFO closure vs med tx (ASA, warfarin, clopidogrel, or ASA & dipyridamole)
  - Cryptogenic stroke in the previous 9 mos
  - Randomized 1:1; 980 pts (18 – 60 yr)
    - Previously reported w 2.1y f/u; Extended f/u (median 5.9y)

- Results: recurrent ischemic stroke occurred in 3.6% PFO closure group vs 5.8% in med tx grp; **HR 0.55** (p=0.046)

- **NNT 42 to prevent 1 stroke over 5 yrs**

- Greater benefit PFO closure among pts w an **atrial septal aneurysm** & w a **grade 3 shunt** (>20 microbubbles)

	CLOSE	REDUCE	RESPECT
Number patients	663	664	980
Age	16 - 60 yo	18 - 59 yo	18 – 60 yo
Mean follow up	5.3 years	3.2 years	5.9 years
Comparator	Antiplatelet / anticoagulation	Antiplatelet	Antiplatelet and warfarin
Stroke	Cryptogenic	Cryptogenic	Cryptogenic
PFO characteristics	Large shunt Atrial septal aneurysm	All (81% moderate-to-large shunt)	All (substantial shunt 48.8%, atrial septal aneurysm 35.7%)
Primary outcome	Stroke	Ischemic stroke and new brain infarction on imaging	Composite non-fatal ischemic stroke, fatal ischemic stroke, early death (45 days)
HR	0.03	0.23	0.55
NNT	20 (in 5 years)	28 (in 2 years)	42 (in 5 years)
PFO closure success (6-12m)	93%	94.5%	93.5%
Atrial fibrillation	4.6% vs 0.9%	6.6% vs 0.4%	1.2% vs 0.8% (no sig)
Procedure/device complications	5.9%	3.9%	5%

ROPE SCORE

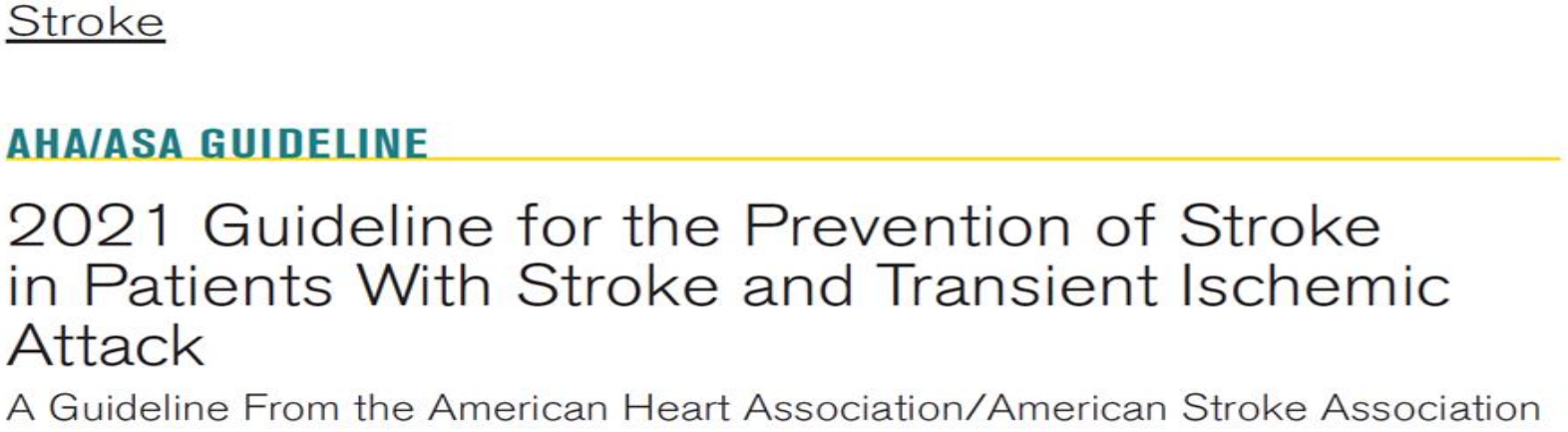
- Scale developed to estimate the likelihood that PFO is the cause of cryptogenic stroke

- 1 point for no history of hypertension
- 1 point for no history of diabetes
- 1 point for no history of stroke or TIA
- 1 point for nonsmoker
- 1 point for cortical infarct on imaging
- greater number of points for younger age, decade-step

META-ANALYSIS CLOSURE OF PFO VS MEDICAL THERAPY IN PTS WITH CRYPTOGENIC STROKE OR TIA

- 5 RCTs; 3627 pts w 3.7 yr median f/u
- Ischemic stroke recurrence less in pts w PFO closure
  - 0.53 vs 1.1 per 100 pt-yrs; **OR 0.43**; RRR 50.5%; NNT, **46.5 for 3.7 yrs**
- Outcomes better with high-risk PFO
  - 0.51 vs 1.4 per 100 pt-yrs; **OR 0.39**; RRR 61%; NNT, **30 for 3.7 yrs**
- **No difference** in outcomes in **low-risk** PFOs
- No difference in TIA, all-cause mortality, or MI
- New-onset **Afib more frequent** in PFO closure grp
  - 56% transient; 72% resolved w/in 45 days

Ntaios et al. Stroke. 2018 Feb;49(2):412-418.



- In patients with ischemic stroke or TIA in whom patent foramen ovale (PFO) closure would be contemplated**, TCD (transcranial Doppler) with embolus detection** might be reasonable to screen for right-to-left shunt.
- In patients **18 to 60 years of age** with a nonlacunar ischemic stroke of undetermined cause despite a thorough evaluation and a **PFO with high-risk anatomic features**, it is reasonable to **choose closure** with a transcatheter device and long-term antiplatelet therapy over antiplatelet therapy alone for preventing recurrent stroke.
- In patients **18 to 60 years of age** with a nonlacunar ischemic stroke of undetermined cause despite a thorough evaluation and a **PFO without high-risk anatomic features**, the benefit of closure with a transcatheter device and long-term antiplatelet therapy over antiplatelet therapy alone for preventing recurrent stroke is not well established.
- In patients 18 to 60 years of age with a nonlacunar ischemic stroke of undetermined cause despite a thorough evaluation and a PFO, **the comparative benefit of closure with a transcatheter device versus warfarin is unknown.**
- The clinical relevance of Afib related to PFO closure and overall risk of stroke requires further investigation

GENETIC CAUSES OF STROKE

Family history, hearing loss, neuropathy, diffuse white matter lesions on MR

- Fabry’s Disease
- CADASIL, CARASIL
- MELAS
- Sickle cell disease
- Homocystinuria
- Moya-moya

31 yo man had suffered from an acute pontine stroke. You notice a rash on his abdomen & lower extremities. He also has a history of kidney & heart disease. What is the treatment?

- Anti-platelet therapy
- Anti-coagulation
- Enzyme replacement
- Chronic infusion therapy

FABRY'S DISEASE

- Angiokeratoma Corporis Diffusum
- X-linked recessive storage disorder
- Alpha galactosidase A (GAL) gene on chrom 22 mutation (can't metabolize globotriaosylceramide (Gb3))
- Accumulate Gb3 in lysosomes of endothelial cells and smooth muscle cells (brain, heart, dorsal root ganglia, ANS)

- 2nd most prevalent metabolic storage disease after Gaucher's
- 1:40 to 60K males
- 1: 117K live births
- Predominantly in Caucasians

CLINICAL MANIFESTATIONS – "SPECKS"

- **S**troke
  - Small vessel ischemic strokes
  - Thrombosis due to Gb3 deposits
- **P**ain small fiber neuropathy, acute episodic crises
- **E**yes tortuous vessels, corneal dystrophy
  - 3rd or 4th decade of life
  - Risk ↑ with age
- **C**ardiac MI, cardiomyopathy, arrhythmia, valvulopathy
- **K**idney proteinuria, progressive renal failure, HTN
  - Associated cardiac and kidney disease ↑ risk of stroke
- **S**kin hyperkeratotic areas of dilated blood vessels, purple black color, swim trunk region

SPECKS – PAIN (PAIN CRISES)

- Acute, episodic, neurogenic pain crises
- May begin as early as age 4; mean age 10
- Triggers: stress, heat, fatigue, exercise
- Hands / Feet – may radiate proximally
- EMG / NCS – normal- small fiber neuropathy
- Abnormality in cold perception on QST
- Acroparesthesia
  - Often develops before cutaneous lesions
  - Chronic burning or tingling pain in extremities

FABRY'S – DIAGNOSIS

- Low or absent alpha galactosidase A enzyme level
  - Plasma, serum, leukocytes, cultured fibroblasts
- DNA analysis
  - Females may have normal enzyme levels
- Biopsy
  - Skin, kidney, conjunctiva

FABRY'S – TREATMENT

- Alpha Galactosidase A Replacement
  - Decreases pain & ↑ QOL
  - Long term safety & efficacy of enzyme replacement not studied
- Stroke prevention
  - No antithrombotic treatment shown to be safe / effective for thrombosis
- Genetic Counseling
- Annual evaluation for renal & cardiac abnormalities
- Pain Crises
    - Carbamazepine, Phenytoin, Gabapentin

MELAS

- Mitochondrial myopathy
- Encephalopathy
- Lactic Acidosis
- And
- Stroke-like episodes

MELAS – CLINICAL MANIFESTATIONS

- Ischemic Stroke (doesn't follow arterial borders), before age 40
  Stroke like episodes may reflect neuronal hyperexcitability

- Progressive Encephalopathy
- Seizures
- Deafness
- Myopathy

MELAS - INVESTIGATIONS

- Lactic acidosis: ↑ blood lactic acid & lactate to pyruvate ratio
- CSF lactate & pyruvate

- Basal Ganglia calcification
- Cerebral, cerebellar, & brainstem atrophy

- MR spectroscopy : ↑ Lactate / Creatine ratio in region of acute stroke like event
- Skeletal muscle biopsy: Ragged Red Fibers on Gomori trichrome stain

MELAS – MANAGEMENT

- Coenzyme Q 10, Idebenone
- Arginine
- Citrulline
- Sodium dichloroacetate
- Genetic Counseling
- Avoid statins
- Avoid Depakote for seizures
  - Causes severe paradoxical reaction of repeated convulsions

Scaglia F, Northrop JL. The mitochondrial myopathy encephalopathy, lactic acidosis with stroke-like episodes (MELAS) syndrome: a review of treatment options. CNS Drugs (Vol. 20, Issue 6)

SICKLE CELL DISEASE

- Autosomal recessive disorder
- Point mutation of glutamate to valine substitution at position 6 of beta globin gene
- Polymerization or aggregation of hemoglobin within RBCs
- Sickled red blood cells are stiff and angular, causing them to become stuck in small capillaries
- Cerebrovascular disease occurs in 25% of SCD
- Progressive cerebral vasculopathy

SICKLE CELL DISEASE

- Vaso-occlusive crises
  - Pain in back, chest, extremities
- Stroke
  - Ischemic stroke
    - Before age 20
    - 1st incidence peak of stroke = Age 2 to 5
  - Hemorrhagic stroke
    - Older individuals

SCD - STROKE PREVENTION

- Stroke Prevention in Sickle Cell Disease **(STOP) Trial**
- **Chronic transfusion therapy** to Hgb S < 30% total Hgb ↓ first ever stroke in high-risk patients
- 93% lower risk of stroke in treatment vs. control group
- Risk of iron overload
- Hydroxyurea

MOYA-MOYA

- Disease vs. Syndrome
- Acquired vs. Congenital

- The vasculopathy (non-atherosclerotic, non inflammatory) etiology unknown
- Pathology: intimal thickening, duplication/triplication of internal elastic lamina composed of smooth-muscle cells. Attenuation of underlying media
- Mural thrombi in stenotic areas
- Aneurysmal formation
- Leptomeningeal anastomoses

MOYA-MOYA

- Peaks of distribution:
  - ✓Under 10 years of age
  - ✓25 to 49y

Extracranial disease:

- Carotids
- Renal arteries
- Pulmonary arteries
- Coronary
- Systemic intimal thickening ~ FMD

- Vertebro-basilar system rarely involved

CLINICAL SYMPTOMS AND SIGNS

- TIA
- Ischemic Stroke – 63% (childhood)
- Intracranial hemorrhage - 22% (adults)
- Seizures (childhood)
- Headaches
- Telangiectasia
- Intellectual disability

MOYA-MOYA DISEASE

Diagnosis:

- Clinical manifestations
- Exclude other conditions (if secondary = syndrome)
- Angio (or MRA/CTA) showing:
  - ✓Stenosis of terminal ICA and
  - ✓Stenosis of proximal ACA and MCA
  - ✓Bilateral findings

Treatment:

- anti-platelet therapy, calcium channel blockers
- revascularization surgery (by-pass surgery)

STROKE IN PREGNANCY & PUERPERIUM

- Triple incidence compared to stroke in non-pregnant women of same age
- Approximately 30/100.000 deliveries
- Clinical features of stroke are not unique, except for eclampsia
- Highest risk peripartum any immediate postpartum
- The majority postpartum, half are hemorrhagic

Miller E. Maternal Stroke Associated With Pregnancy. CONTINUUM (MINNEAP MINN) 2022;28(1, NEUROLOGY OF PR E G N A N C Y) : 93–121.

STROKE IN PREGNANCY

- Risk factors for maternal stroke: older age, hypertensive disorders of pregnancy, migraine, cardiac disease, primary hypercoagulable states, smoking
- Hypercoagulable state due to pregnancy, pre-eclampsia/ eclampsia, peripartum
- Peri-partum cardiomyopathy
- Amniotic fluid embolism
- Trophoblastic embolism (choriocarcinoma)
- Reversible cerebral vasoconstriction syndrome = post-partum angiopathy

ANTITHROMBOTIC THERAPY AND T-PA DURING PREGNANCY

- Anticoagulant: LMWH or unfractionated heparin
- Warfarin is contraindicated
- ASA: safe after 12 weeks
- Clopidogrel: insufficient evidence of safety
- IV t-PA during pregnancy seems to be safe
- IA t-PA
- Direct oral anticoagulants: insufficient evidence of safety

INTRACEREBRAL HEMORRHAGE

- Incidence 4.6 / 100,000 deliveries
- Risk at puerperium RR 28
  - cerebral aneurysm
  - arterio-venous malformation
  - cavernous malformation
  - pre-eclampsia/ eclampsia
  - cocaine use
- Timing: increased peripartum, 2nd trimester reported for AV malformation

NEURORADIOLOGY IN WOMEN OF CHILDBEARING AGE

CT

- Fetus exposed to radiation scattered through the mother's body
- Conception-implantation (days 0-15) highest risk period
- Avoid iodinated contrast (class B). If used check thyroid function during first week of life
- OK to use contrast during breast-feeding

NEURORADIOLOGY IN WOMEN OF CHILDBEARING AGE

MRI

- Modality of choice during pregnancy
- OK up to 3 Tesla
- Avoid use of gadolinium (class C)
- OK to use gadolinium during lactation, 24h period of “pump and dump”

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THANK YOU FOR YOUR ATTENTION

QUESTIONS & ANSWERS