CAROTID ARTERY ATHEROSCLEROTIC DISEASE

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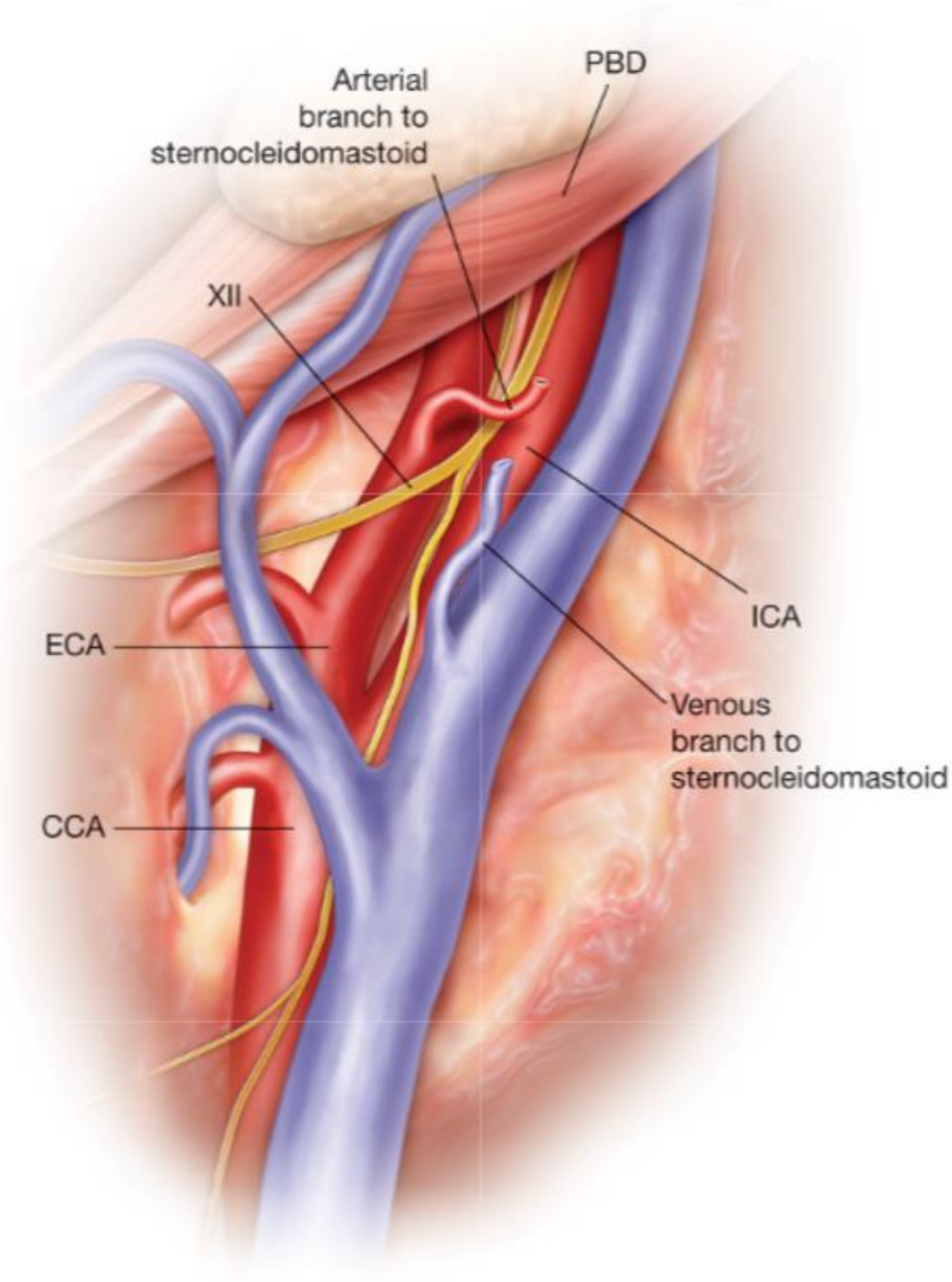
Jan 12, 2021



DISCLOSURES

- None

OUTLINE

- Background
- Investigations and Diagnosis
- Management (medical, surgical, interventional)
- Key Randomized Control Trials
- Asymptomatic Carotid Disease
- Algorithm for Carotid Disease Management

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BACKGROUND

- Cerebrovascular disease is the third-largest cause of death in Canada, second leading cause of death worldwide (9.5% of all deaths)
  - Leading cause of long-term disability in the United States
- 15-35% of all strokes are fatal or severely disabling
- 80% of strokes are ischemic in nature
  - Cardioembolic
  - Large vessel disease
  - Small vessel disease
  - Strokes related to unusual causes
  - Strokes of undetermined etiology

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- 80% of strokes are ischemic in nature
  - Cardioembolic
  - **Large vessel disease → 40% of ischemic strokes → ½ are in the extracranial segment (correctible)**
  - Small vessel disease
  - Strokes related to unusual causes
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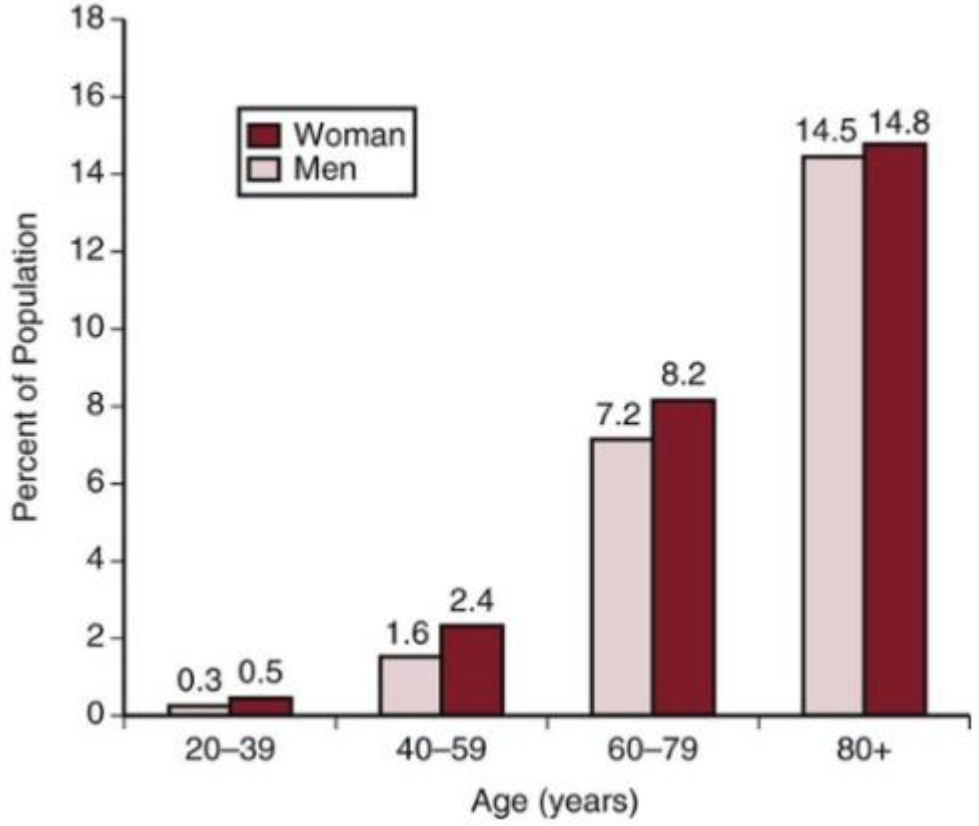
BACKGROUND

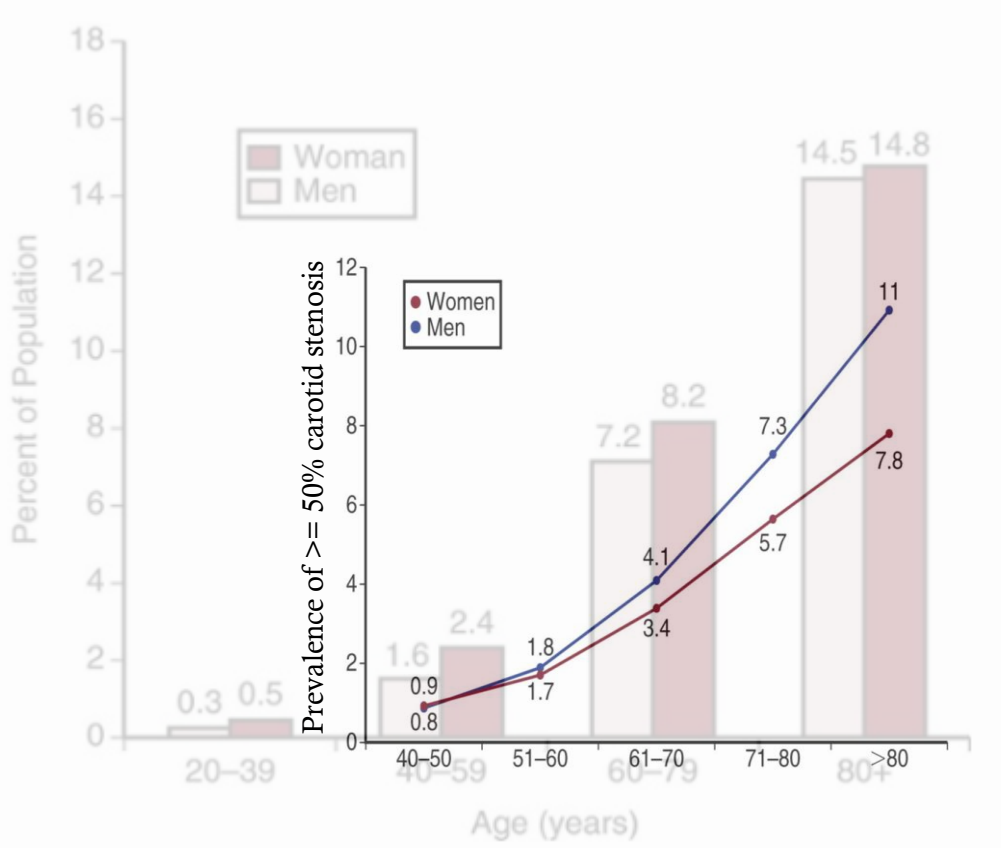


Prevalence of stroke by age and sex
National Health and Nutrition Examination Survey (2005-2008)

Risk Factors	
Age	For each decade after 55, risk of stroke 2 x
Hypertension	2 x
Family History	1.4 – 3.3 x
Smoking	2 – 4 x
Dyslipidemia	1.25 x
Diabetes	2 x
Obesity	Association
Physical activity / stress	Association
Alcohol	Association
Renal insufficiency	Association

Rutherfords Vascular Surgery, 8th Edition

BACKGROUND



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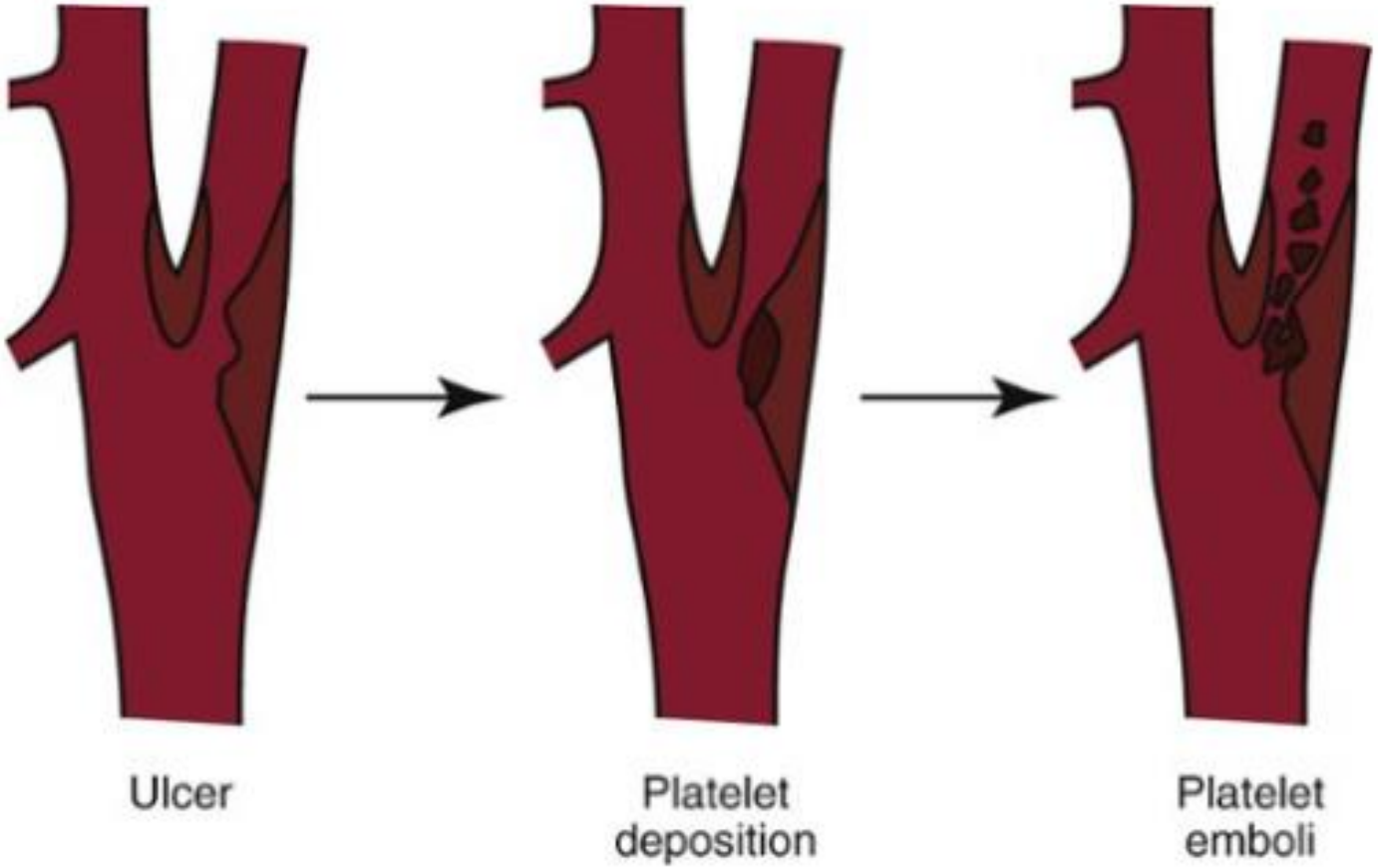
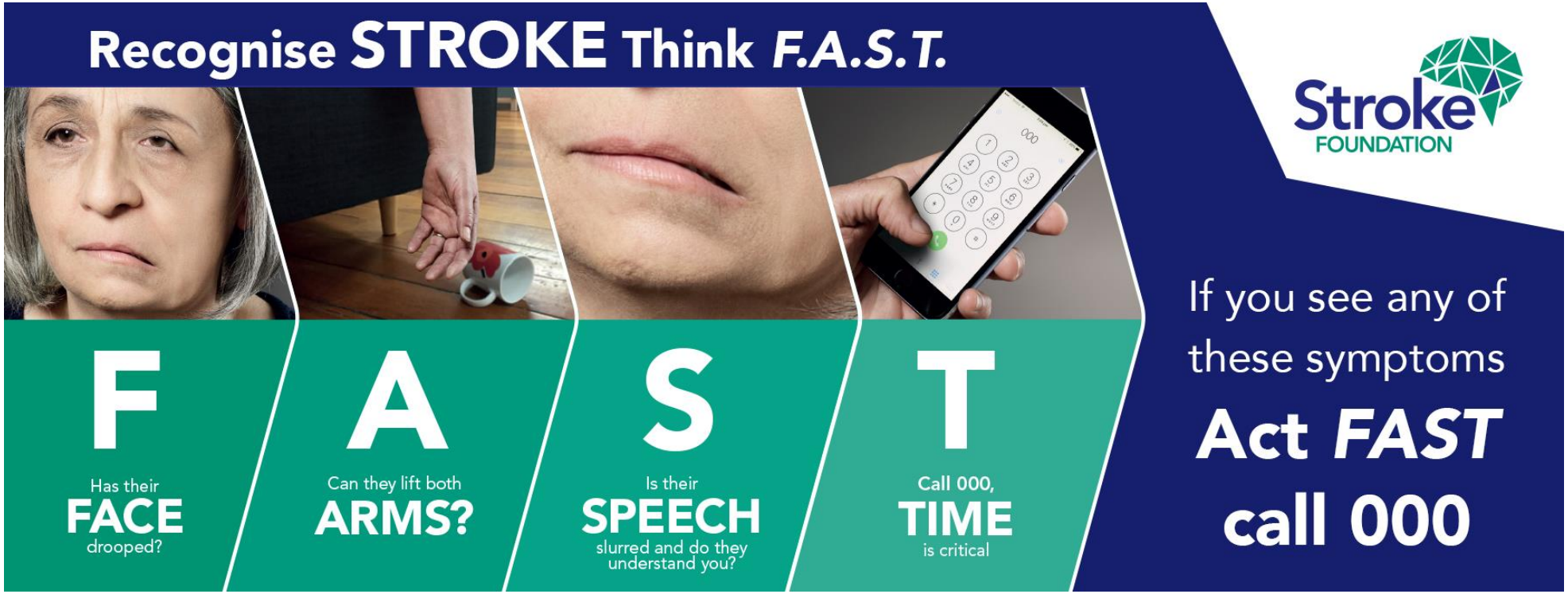


BACKGROUND

- After the first event, the risk of recurrent stroke is 20-30% within the first 3 months, with the greatest risk within the first week.

- *$ABCD^2$ score*
  - Age >= 60 years, BP >= 140/90, Clinical Features of TIA, Duration of symptoms, Diabetes

BACKGROUND – SYMPTOM PRESENTATION



BACKGROUND – SYMPTOM PRESENTATION

Patient 1:

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CT suggests 80% stenosis of right internal carotid artery

Patient 2:

75 y/o male who had slurring of speech and right-arm weakness, now improved. Ultrasound suggests bilateral carotid disease, worse on the left side (>70%)

Patient 3:

92 y/o female with loss-of-consciousness and multiple pre-syncopal episodes, CTA shows left carotid stenosis of 65%

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BACKGROUND – SYMPTOM PRESENTATION

Signs or symptoms suggestive of an extracranial carotid artery event	Signs or symptoms unlikely to be related to extracranial carotid artery event
Contralateral extremity motor or sensory impairment (transient, fluctuating, or persistent)	Lightheadedness
Monocular vision loss (ipsilateral)	Vertigo
Acute speech deficit or change	Bilateral visual disturbances
Facial droop	Headache
	Bilateral extremity motor or sensory impairment
	Ataxia

Management of transient ischemic attack or nondisabling stroke related to extracranial internal carotid artery stenosis
Varun Kapila MD, Prasad Jetty MD MSc, Vincenzo S. Basile MD BEd, Luc Dubois MD MSc
CMAJ 2019 April 15;191:E418-22. doi: 10.1503/cmaj.180735

BACKGROUND

Stroke
Investigations
Review with Neurology, +/- TPA
Referral to Vascular Surgery

INVESTIGATIONS

- Blood Work:
- Imaging:
- Cardiac:

INVESTIGATIONS

- **Blood Work:**
  - Complete Blood Count (rule out thrombocytopenia, thrombocytosis, anemia, polycythemia, sickle cell disease)
  - Renal function
  - HbA1c
  - Cholesterol and triglyceride levels
  - Other: Autoimmune screen, fasting homocysteine levels, drug screen)
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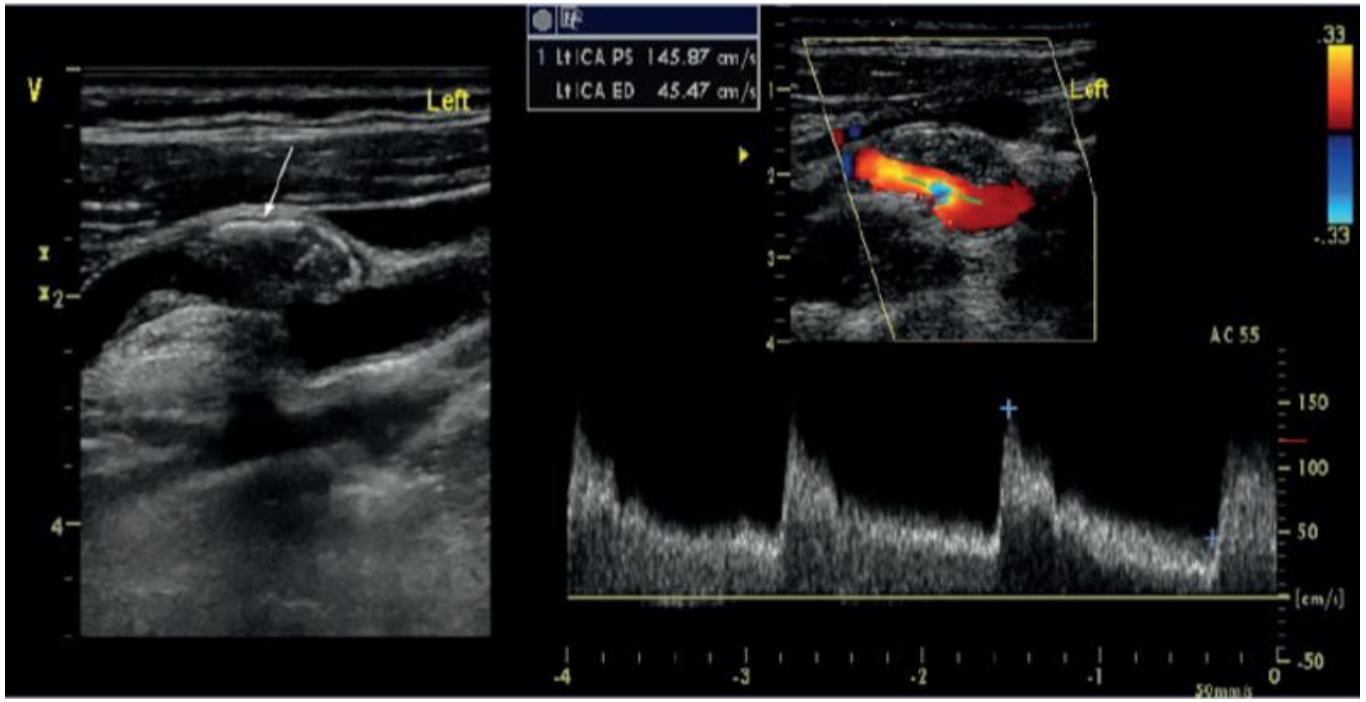
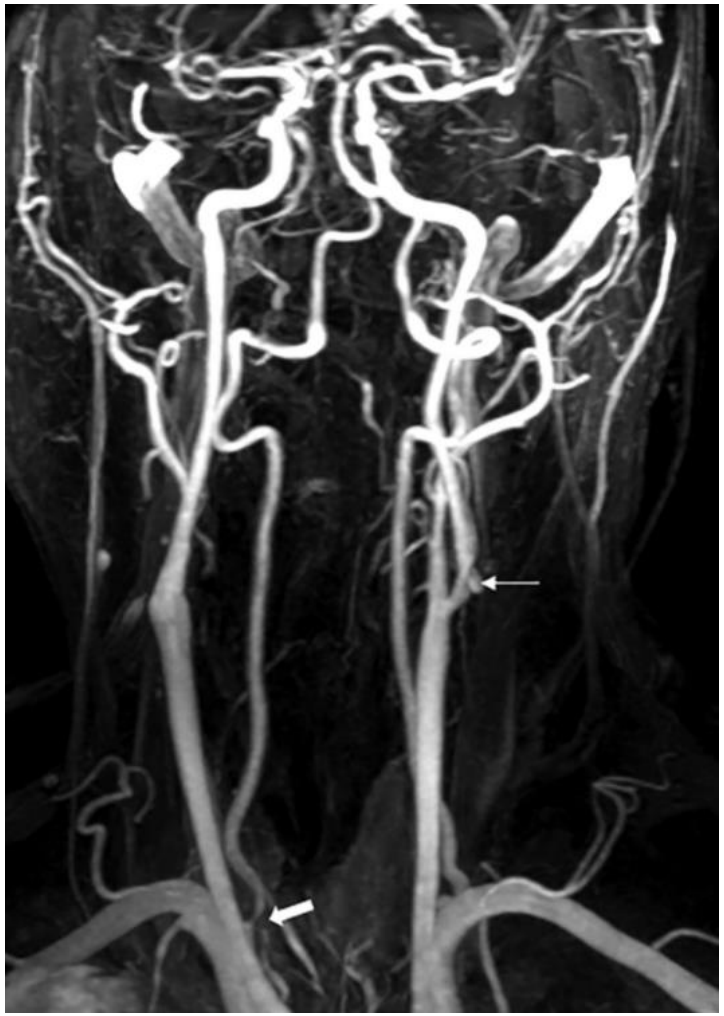
- **Imaging:**
  - CT-plain Head and CT-Angiogram from Aortic Arch to Head
  - Ultrasound duplex - Useful in patients with renal dysfunction
  - MR-Angiogram – usually ordered by Neurology. Has higher sensitivity for detecting intracranial embolization / infarcts
- Cardiac:

INVESTIGATIONS

ULTRASOUND VS CT-ANGIOGRAM





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- **Cardiac:**
  - Troponin, ECG – rule out arrhythmias / infarcts
  - Holter - outpatient

FOR ACUTE STROKES, NEUROLOGY CONSULTATION FOR THROMBOLYSIS

MANAGEMENT

Optimal Medical Therapy

Procedural Intervention

MEDICAL MANAGEMENT
OPTIMAL MEDICAL THERAPY

- Antiplatelet Therapy
- Statins
- Antihypertensive therapy

- Smoking cessation
- Diabetes control
- Avoid excessive alcohol consumption

MEDICAL MANAGEMENT
OPTIMAL MEDICAL THERAPY

- **Antiplatelet Therapy (Dual antiplatelet regimen x 21-30 days, followed by mono-therapy)**
  - All acute stroke patients not receiving Alteplase should receive 160 mg ASA, followed by 81 mg daily
  - Clopidogrel 300 mg loading dose, followed by 75 mg daily

- Evidence:
  - *CAPRIE (Lancet 1996):* Randomised, blinded trial of Clopidogrel vs ASA: slight benefit to Plavix
  - *MATCH (Lancet 2004)*: Clopidogrel vs. Clopidogrel + ASA (no difference)
  - *CHARISMA (N Engl J Med 2006):* ASA vs Clopidogrel + ASA (no difference)

  - *CHANCE (N Engl J Med 2013):* ASA vs Clopidogrel + ASA for TIA patients (11.7% mono vs 8.2% dual over 90 days)
  - *POINT (N Engl J Med 2018):* ASA vs Clopidogrel + ASA
    - (6.5% mono vs 5% dual over 90 days, but major hemorrhage 0.9% dual vs 0.4% mono)

MEDICAL MANAGEMENT
OPTIMAL MEDICAL THERAPY

- **Statin therapy:**
  - High-dose statins (Atorvastatin 80 mg daily)

- Evidence:
  - For every 1 mmol/L reduction in LDL, there is a 25% reduction in cardiovascular mortality and 15% reduction in stroke over 5 years. (Meta-Analysis of 27 randomized trials by *Mihaylova et al.* Lancet 2012)

  - *SPARCL (Stroke 2009):* 33% reduction in fatal and non-fatal strokes over 5 years
  - *Kennedy et al. (Stroke 2005):* Retrospective Western-Canadian trial - Use of statins in perioperative period of CEA reduced perioperative mortality by 75% and stroke/death by 45%
  - NO Randomized trials exist assessing statins immediately post-stroke

MEDICAL MANAGEMENT
OPTIMAL MEDICAL THERAPY

- **Antihypertensive therapy:**
  - Decrease blood pressure in hypertensive patients to 120 / 80 mm Hg, but slowly
  - Exception: During first 24 hrs, allow for hypertension up to 180 mm Hg for cerebral perfusion pressure

- Evidence:
  - Multiple meta-analyses: Treatment of hypertension reduces risk of stroke by 24%

MEDICAL MANAGEMENT
OPTIMAL MEDICAL THERAPY

- Antiplatelet Therapy
- Statins
- Antihypertensive therapy

- Smoking cessation
- Diabetes control – Aim for A1c < 7, No benefit in acute phase or tight glucose control
- Avoid excessive alcohol consumption

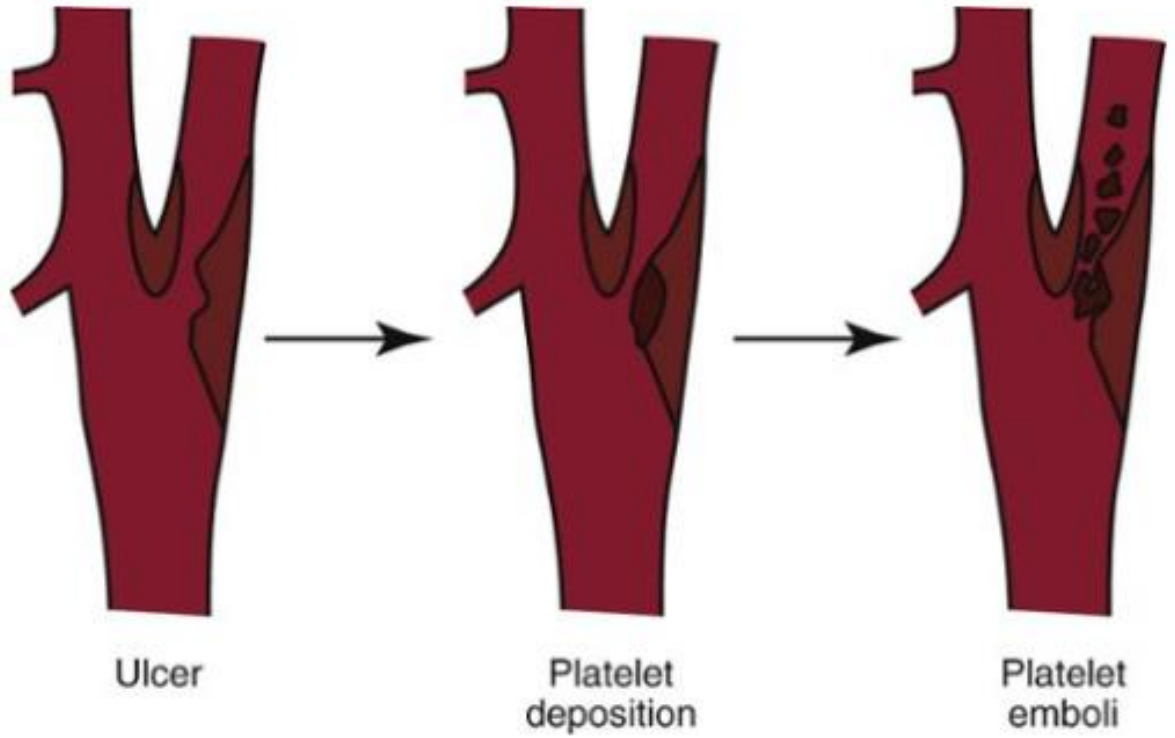
MEDICAL MANAGEMENT
OPTIMAL MEDICAL THERAPY

Symptomatic Patients

Study	Population	Stroke Rate with OMT
NASCET	649 patients with >=70% stenosis	26% (2-yr), 28% (5-yr)
NASCET	858 patients with 50-69% stenosis	15% (2-yr), 22.2% (5-yr)
ECST	1279 with 60-99% stenosis	20.6% (3-yr)

1. The North American Symptomatic Carotid Endarterectomy Trial (Stroke 1999).
2. European Carotid Surgery Trial (Lancet 1998).

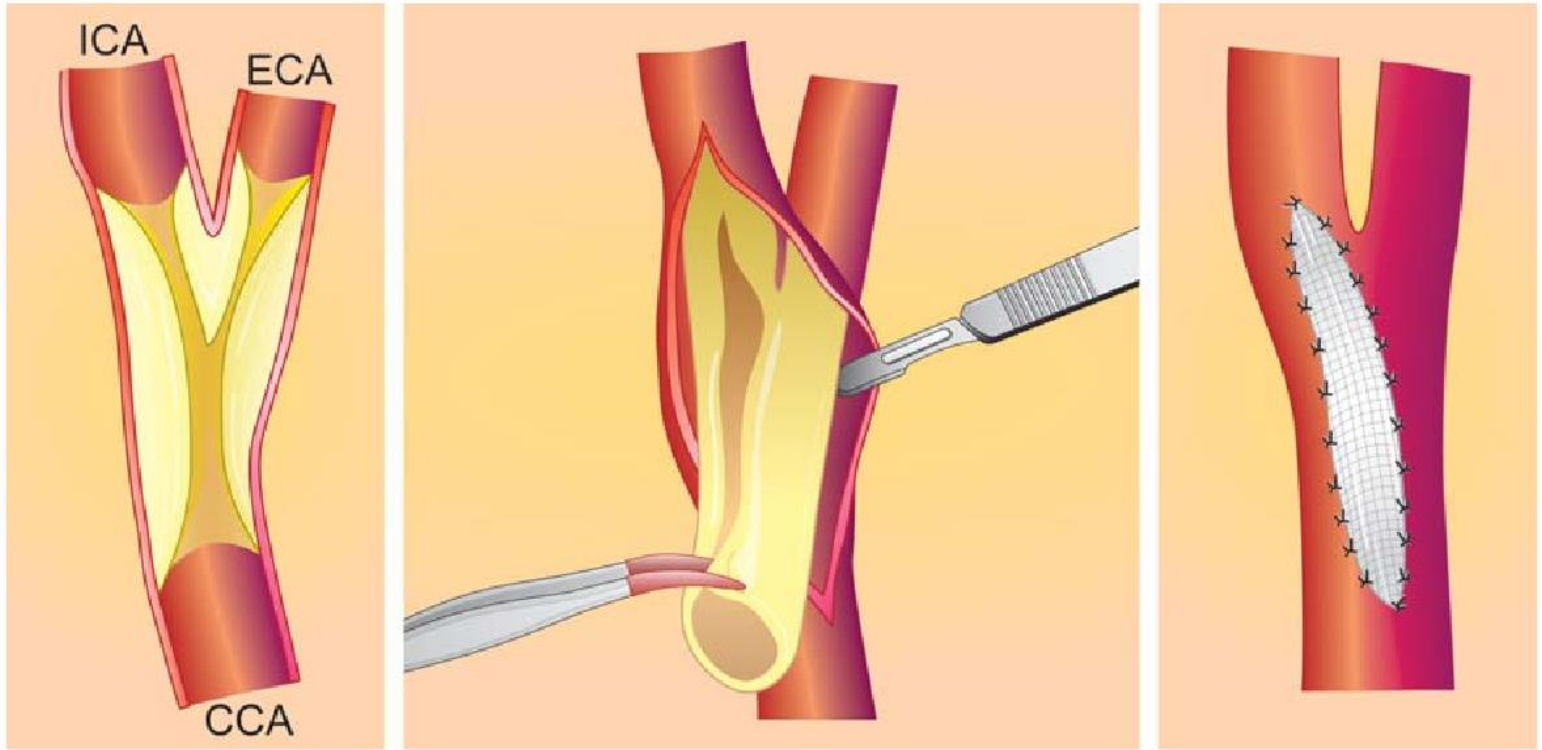
PROCEDURAL MANAGEMENT



PROCEDURAL MANAGEMENT

- Carotid Endarterectomy
- Carotid Stenting

PROCEDURAL MANAGEMENT
CAROTID ENDARTERECTOMY



PROCEDURAL MANAGEMENT
CAROTID ENDARTERECTOMY

MEDICAL MANAGEMENT
OPTIMAL MEDICAL THERAPY + CAROTID ENDARTERECTOMY

Symptomatic Patients

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ECST[2]	1279 with 60-99% stenosis	20.6% (3-yr)	6.8% (3-yr)

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PROCEDURAL MANAGEMENT
CAROTID ENDARTERECTOMY

Complications:

- **Perioperative Stroke**
- Myocardial Infarction
- Nerve Injury
  - Auricular
  - Facial nerve (VII)
  - Hypoglossal (XII)
  - Vagus (X) (Recurrent and superior laryngeal)
  - Spinal Accessory (XI)
  - Glossopharyngeal (IX)

5% in reported literature, but
Contemporary: 2-3%

PROCEDURAL MANAGEMENT
CAROTID ENDARTERECTOMY

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2.3% in CREST trial (2010)
Contemporary: Approx. 1%

PROCEDURAL MANAGEMENT
CAROTID ENDARTERECTOMY

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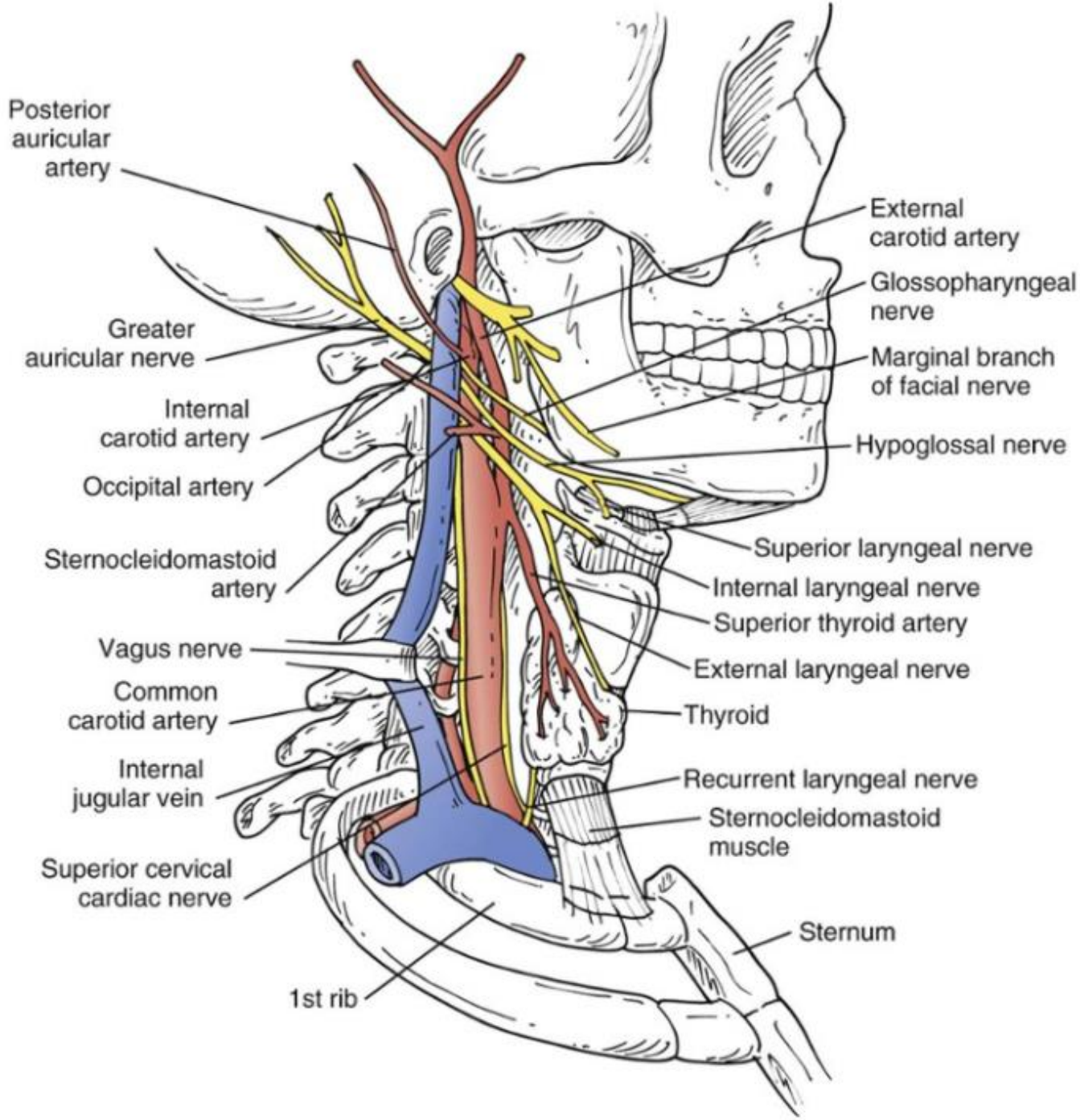

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Incidence in literature was 5% to as high as 39% in retrospective studies

Randomized Trials

ECST (European Carotid Surgery Trial): 0.5% permanent deficit

CREST (US and Canada): 4.7%

CREST QoL analysis 1-year post carotid endarterectomy: No significant impact of nerve injury

PROCEDURAL MANAGEMENT

- Carotid Endarterectomy

- Carotid Stenting

PROCEDURAL MANAGEMENT

CAROTID STENTING

PROCEDURAL MANAGEMENT

- Carotid Endarterectomy

- Carotid Stenting
  - Can be performed through percutaneous femoral access
  - Theoretically lower morbidity / mortality complications

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PROCEDURAL MANAGEMENT
CAROTID STENTING

Complications:

Carotid Revascularization Endarterectomy vs Stenting Trial (CREST)

- Perioperative Stroke
  - Higher than CEA
- Myocardial Infarction
  - 50% Less than CEA
- Nerve Injury
  - Nil

PROCEDURAL MANAGEMENT

CAROTID STENTING

Trial	Sample Size	Population	Study Details	Primary Endpoint	Results
SAPPHIRE[15,16] 2004, 2008	334 (2400 planned)	Symptomatic >50% stenosis Asymptomatic >80% stenosis (duplex) High risk	Multicenter CAS vs. CEA Noninferiority United States	30-day stroke, MI, death + 1-y ipsilateral stroke, death	1-y: 12.2% CAS vs. 20.1% CEA; *P* = .004
EVA-3S[17,18] 2006, 2008	527 (872 planned)	Symptomatic >60% stenosis (NASCET) Standard risk	Multicenter CAS vs. CEA Noninferiority Europe	30-day stroke, death 4 y: 30-day stroke, death + ipsilateral stroke	30-day: 9.6% CAS vs. 3.9% CEA; *P* = .01 4-y: 11.1% CAS vs. 6.2% CEA; *P* = .03
SPACE[19-21] 2006, 2008	1196 (>2500 planned)	Symptomatic >70% stenosis (ECST) Standard risk	Multicenter CAS vs. CEA Noninferiority Europe	30-day ipsilateral stroke, death 2 y: 30-day stroke, death + ipsilateral stroke	30-day: 6.9% CAS vs. 6.5% CEA; *P* = .09 2-y: 9.5% CAS vs. 8.8% CEA; *P* = .06
ICSS[22] 2010	1713	Symptomatic >50% stenosis (NASCET) Standard risk	Multicenter CAS vs. CEA Europe	120-day stroke, death, MI	120-day: 8.5% CAS vs. 5.2% CEA; *P* = .006
CREST[28-37] 2010	2502	Symptomatic Asymptomatic >50% stenosis (NASCET) Standard risk	Multicenter CAS vs. CEA Canada, United States	30-day stroke, MI, death + 4-y ipsilateral stroke	30-day: 5.2% CAS vs. 4.5% CEA; *P* = .38 4-y: 7.2% CAS vs. 6.8% CEA; *P* = .51 30-day stroke, death: Symptomatic: 6.0% CAS vs. 3.2% CEA; *P* = .02 Asymptomatic: 2.5% CAS vs. 1.4% CEA; *P* = .15

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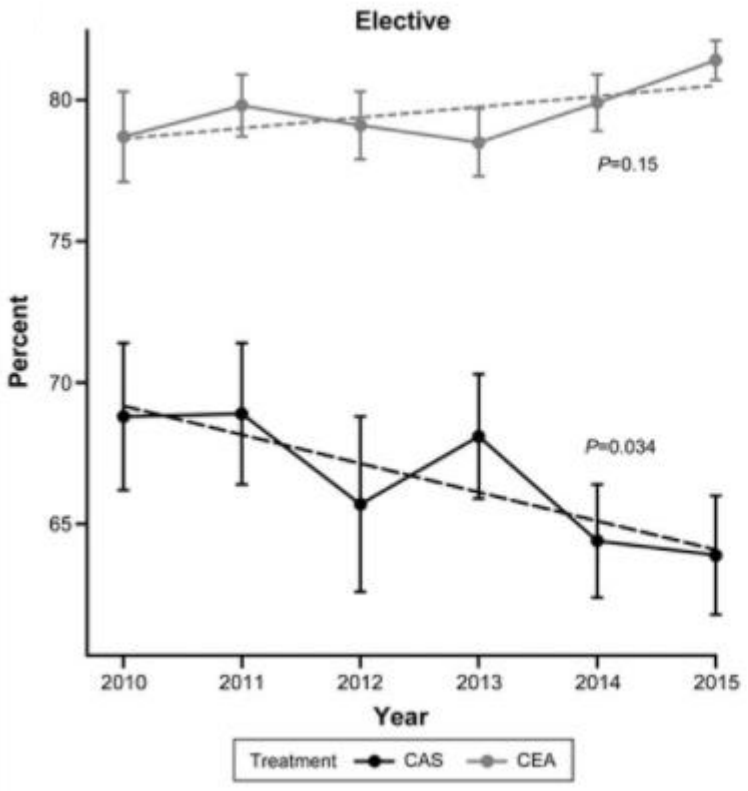
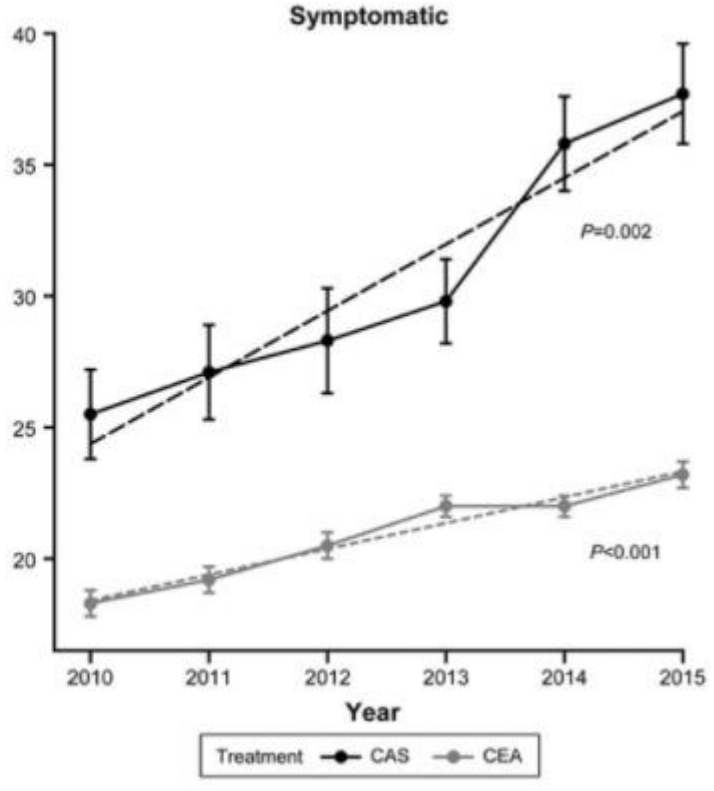
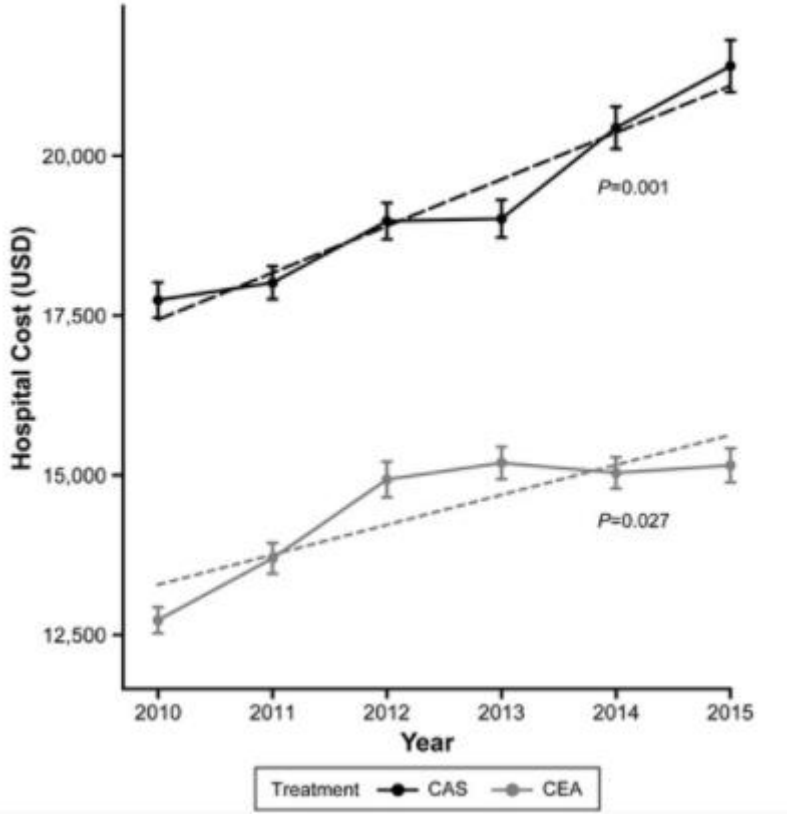
Periprocedural stroke rates are higher with stenting than with endarterectomy

PROCEDURAL MANAGEMENT
ENDARTERECTOMY VS STENTING







Nationwide Trends in Carotid Endarterectomy and Carotid Artery Stenting in the Post-CREST Era (Stroke 2019).

PROCEDURAL MANAGEMENT

ENDARTERECTOMY VS STENTING

ASYMPTOMATIC PATIENTS

- Data are clear on the benefits of endarterectomy with optimal medical therapy for symptomatic patients, but what about patients with *asymptomatic* carotid stenosis?

ASYMPTOMATIC PATIENTS

Study	Population	No. of Patients	OMT	OMT + CEA
ACAS[1]	Asymptomatic patients with carotid stenosis ≥60%	1662	11% (5 yr)	5.1% (5 yr)
ACST[2]	Asymptomatic patients with carotid stenosis ≥60%	3120	11.8% (5 yr)	6.4% (5 yr)

1. Endarterectomy for asymptomatic carotid artery stenosis (JAMA 1995).
2. Asymptomatic Carotid Surgery Trial (Stroke 2004).

ASYMPTOMATIC PATIENTS

- With improvements in OMT, stroke rate for an asymptomatic high-grade (>=70%) lesion is 2% per year.
- Carotid endarterectomy results in a 50% Relative Risk reduction, or an ABSOLUTE reduction of 1% per year
- Patients must be carefully selected before undergoing surgery (patients < 75, ideally <70, no other significant comorbidities, life expectancy > 5 years).

ASYMPTOMATIC PATIENTS

- Carotid artery stenting is NOT recommended for asymptomatic patients
  - American Heart Association, SVS, ESC, Australian, NICE guidelines

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Rates of intervention for Asymptomatic Carotid Stenosis (2015):

United States: 90%
Italy: 68.6%
Germany: 60%
UK: 16.8%
Canada: 15%
Denmark: ~0%

Attar, Talal (2016). Ohio State's 7th Contemporary Multidisciplinary Cardiovascular Conference.

SYMPTOM PRESENTATION

RECOMMENDED TREATMENT FOR CAROTID STENOSIS

Patient 1:

83 y/o female with chronic headache, loss of balance, and generalized weakness.

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Patient 2:

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Optimal Medical Management

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Optimal Medical Management

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Optimal Medical Management

ALGORITHM FOR CAROTID DISEASE MANAGEMENT

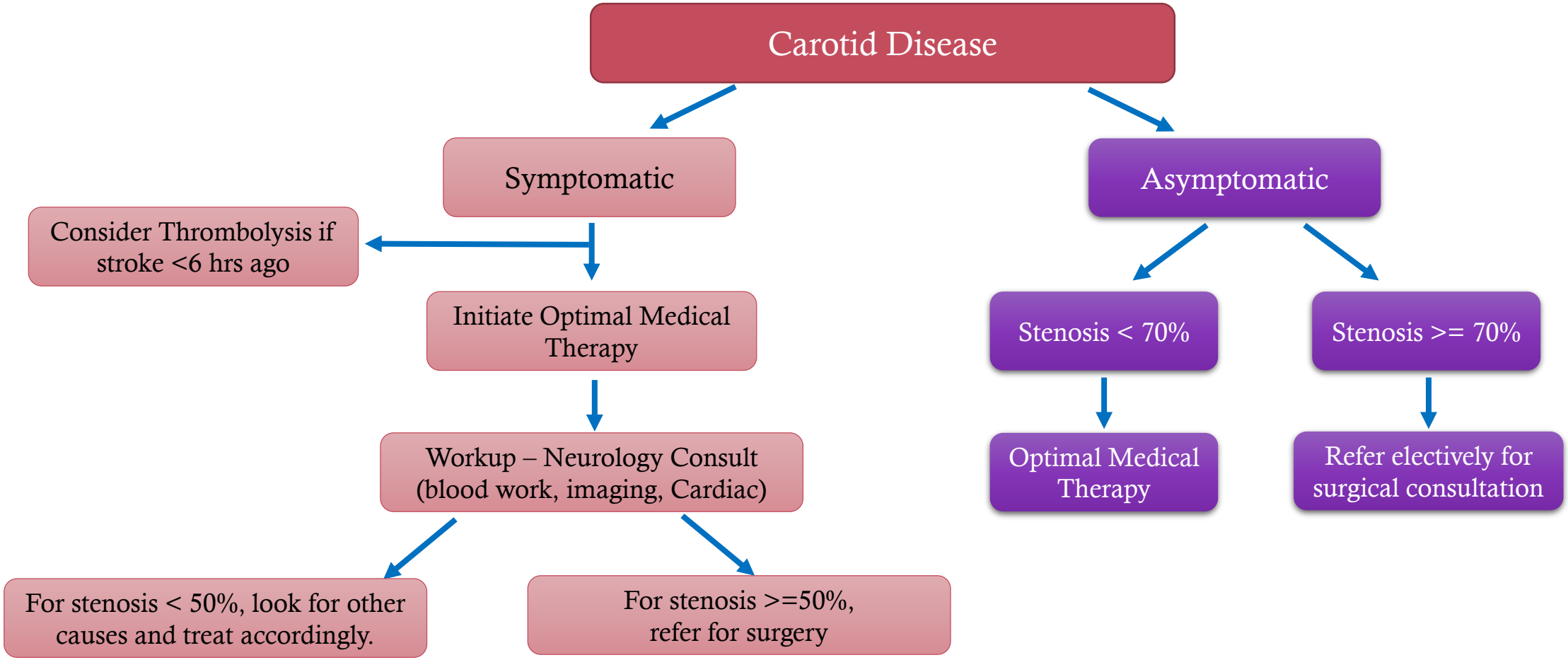
- Symptomatic carotid stenosis represents an emergency
- Patients should be treated ideally with endarterectomy within 3-5 post-stroke, and certainly within 2 weeks.

Urgent Intervention	TIME	>2 weeks
NNT to prevent 1 stroke		NNT to prevent 1 stroke
6		125

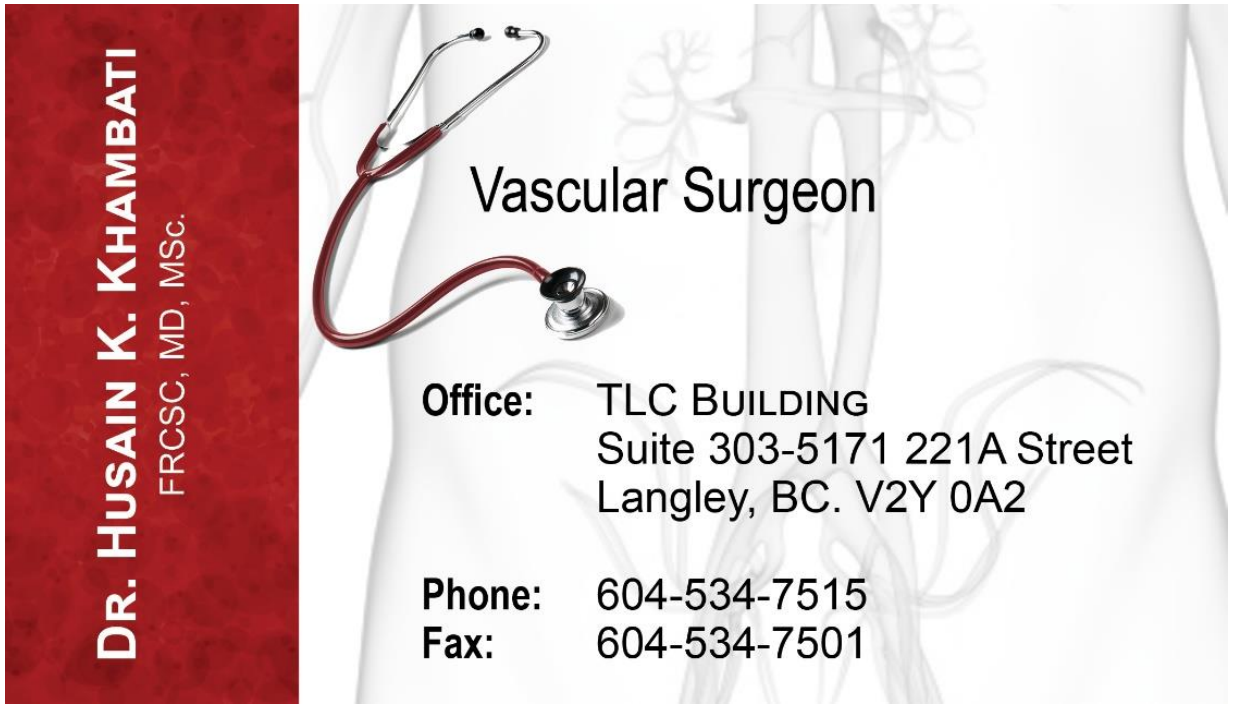
ALGORITHM FOR CAROTID DISEASE MANAGEMENT

- Asymptomatic patients should be evaluated on a case-by-case basis.

ALGORITHM FOR CAROTID DISEASE MANAGEMENT



5171
221A Street
TLC Medical Centre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Thank You