Evidence Based Management of Retinal Artery Occlusions

Edward Chu, OD, FAAO

Disclosure Statement:
Nothing to disclose
Questions to ponder today…

What clinical signs/symptoms help me identify a retinal artery occlusion (RAO)? Past RAO?

What is my responsibility to patient when I diagnose a RAO? Lab test? Imaging?

If my patient has a RAO, what is his/her risk for stroke? How urgently do I need to refer?
Retinal Artery Occlusion (RAO)

- Interrupted blood flow
  - Embolic occlusion retinal vasculature
  - Non-obstructive hypoperfusion
- Analogous to cerebral infarction
  - Thromboembolus ischemic CVA
  - Blockage blood, no O\(^2\) → brain vs retina
  - Irreversible tissue injury/death 2-3 hours
  - Neuro deficit vs vision loss
  - Overlapping systemic risk factors
Vascular supply to ON
-ICA
-Ophthalmic
-Central Retinal

Brain/Retina same arterial blood supply!
Retinal Emboli Composition

- 70 patients
- Emboli composition
  - Cholesterol 74% - migrate
  - Calcified material 10.5% - rough, stationary
  - Platelet-fibrin 15.5% - smooth, migrate
- TMVL - cholesterol
- Permanent occlusion (RAO) - Calcific

Arruga J, Sanders MD. Ophthalmologic findings in 70 patients with evidence of retinal embolism. Ophthalmology 1982; 89: 1336-1347
Cholesterol Plaques

- AKA Hollenhorst Plaques
- Refractile
- Yellow, white, copper color
- Round, rectangular
- Endothelial damage → Hemes
- TMVL
- Carotid Ultrasound
“...appearance of these bright cholesterol crystals in the retinal system are a potent warning of disaster or impending disaster in the cardiovascular system.”
Calcific Emboli

- Damaged heart valve
  - Calcific aortic stenosis
  - Mitral and aortic valve disease
- Flat and white
- Optic nerve BV
- Retinal Arterial Occlusion
- Electrocardiogram
- Echocardiogram
Fibrinoplatelet Plaque

- Dull gray/white plugs
- Mobile
- Long, smooth shape
- Carotid artery disease
- Heart valves
  - Rheumatic disease
  - Floppy mitral valve
  - Systemic Lupus
Central Retinal Artery Occlusion

• Most serious RAO
• Term, branch Oph. artery, no collaterals
• Acute, painless, monocular vision loss
• Retinal whitening/opacity
  ◦ Ischemia, giant CWS, swollen NFL
• Retinal arteriole attenuation
• Segmental blood flow (box-car)
• Cherry red spot
240 CRAOs
Main findings during initial examination

- Cherry Red Spot: 90%
- Opacity in posterior pole: 58%
- Optic Nerve Pallor: 39%
- Retinal arterial attenuation: 32%
- Optic Disk Edema: 22%
- Box-Carring: 19%

Emboli seen only 20% of cases
244 patients CRAO
VA and VF improved primarily first 7 days

74.2% present CF or worse vision

<table>
<thead>
<tr>
<th>Initial visual acuity</th>
<th>20/40 better</th>
<th>CF/worse</th>
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</thead>
<tbody>
<tr>
<td>NA-CRAO (66.9%)</td>
<td>None</td>
<td>93.2%</td>
</tr>
<tr>
<td>NA-CRAO w/ cilioretinal sparing (14.3%)</td>
<td>20%</td>
<td>60%</td>
</tr>
<tr>
<td>Transient NA-CRAO (16%)</td>
<td>37.9%</td>
<td>37.9%</td>
</tr>
<tr>
<td>Arteritic CRAO (4.5%)</td>
<td>None</td>
<td>75%</td>
</tr>
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</table>

Prognosis → Acute Phase: extent ME, layer structure/organization
Retinal thinning final (worse w/ subfoveal choroidal thinning)
Acute CRAO: Dislodge Embolus??

- Ocular massage
- A/C Paracentesis: IOP down to zero
- Breath into paper bag: Increase CO$_2$
- Thrombolysis: IV thrombolytic agent or locally via ophthalmic artery
  - Fibrinolytic agents only dissolve fibrinoplatelet embolus, not cholesterol/calcific
  - CRA blocked – little chance fibrinolytic agent reaching thrombus
Central Retinal Artery Occlusion

- Hayreh Primate Studies
  - No detectable damage CRAO ~97 min
  - After ~ 100 minutes → longer CRAO, more extensive + irreversible damage
  - 240 minutes (4 hours) → Retina dead

- “Parking Lot or Waiting Room CRAO”

- “CRAO a classic case of a disease without any treatment that has many treatments” – SS Hayreh
Arteritic CRAO

- 5% of all CRAOs
- 2/2 Giant Cell Arteritis
  - ESR, CRP, Platelets
- GCA w/ ocular involvement
  - 10 % CRAOs
- Steroid treatment
  - Fellow eye involvement within days
  - **TIME SENSITIVE!**
- **CRAO REQUIRES R/O GCA**

~21.2% GCA patients + visual loss

NO SYSTEMIC SYMPTOMS GCA

Headache, scalp tender, fever, fatigue, weight loss, jaw claudication, neck pain

CRAO requires r/o GCA even when NO SYMPTOMS


Transient CRAO

- Occlude CRA temporarily, then dislodge
- Non-Obstructive Hypoperfusion
  - Fall perfusion pressure
  - Drop blood pressure (nocturnal)
  - Surgery, Dialysis, Shock
- Rise IOP
- Vasospasm of CRA
- Carotid Artery Stenosis
Retinal Artery Occlusion
Associated Systemic and Ophthalmic Abnormalities

Sohan Singh Hayreh, MD, PhD, Patricia A. Podhajsky, BSN, M. Bridget Zimmerman, PhD

DM 2, HTN, ischemic heart disease, smoking, Stroke/TIA
all significantly higher than prevalence in matched US population

Carotid Doppler/Angiography
Ipsilateral ICA >50% stenosis
31% NA-CRAO

Plaque present
71% NA-CRAO

Abnormal echocardiogram (EKG) of an embolic source
52% of NA-CRAO
mostly calcified valve

CRAO require HEART + CAROTID evaluation

Embolic Work-up

- Carotid U/S
  - Evaluates hemodynamically significant stenosis → carotid endarterectomy?
  - Plaque may be present w/ or w/o any significant carotid stenosis
- Absence stenosis does not rule out carotid as source of embolism
Embolic Work-Up

• Heart Disease
• Electrocardiography (EKG)
  ◦ Record heart electrical activity
  ◦ Heart arrhythmias - Afib
  ◦ Weaknesses different parts of heart muscle
• Echocardiography (“Echo”)
  ◦ Heart Sonogram/Ultrasound
  ◦ Valve dysfunction
  ◦ Chamber abnormalities
European Assessment Group for Lysis in Eye (EAGLE) study

77 patients complete medical examination

**Carotid Doppler**, Echocardiography, Electrocardiography, BP
Pulse rate, urine analysis, BMI analysis, Labs

Ipsilateral significant carotid artery stenosis ~ 40%
Only 3% diagnosed pre-CRAO → **order Carotid U/S**!

Previously **undiagnosed** vascular factors 78% CRAO
Recommend comprehensive diagnostic work-up

*Callizo et al. Ophthalmology 2015; 122: 1881-1888*
3248 patients: 464 RAO, 2784 Control
19.61% patients w/ RAO suffered stroke
10.05% patients control group suffered stroke

Stroke risk highest 1st month (9.5x higher) vs controls
Most strokes first 6 months
CRAO >> BRAO stroke risk/incidence

RAO increases risk subsequent stroke
Early neuro eval, stroke prevention needed
33 consecutive acute RAO patients, MRI within 7 days

Acute ischemic stroke Dx 24.2% (8 total of 33)
5 CRAO, ipsilateral brain lesion ALL

37.5% suffered silent stroke, no neuro signs/symptoms

Acute cerebral infarctions accompany RAO
→ Recommend MRI
Risk and Risk Periods for Stroke and Acute Myocardial Infarction in Patients with Central Retinal Artery Occlusion

Sang Jun Park, MD, MSc, Nam-Kyong Choi, PhD, Bo Ram Yang, PhD, Kyu Hyung Park, MD, PhD, Joongyub Lee, MD, PhD, Sun-Young Jung, PhD, Se Joon Woo, MD, PhD

1655 Korean patients w/ CRAO

Increased risk ischemic stroke, acute MI 1st 30 days after CRAO

HIGHEST incidence FIRST WEEK

Incident Rate Ratio = 44.51

Incident CRAO → IMMEDIATE neuro evaluation preventative stroke Tx
2011: CRAO = Stroke Equivalent

- American Heart Association (AHA), American Stroke Association (ASA) definition of CNS infarction:
  “Brain, spinal cord, or retinal cell death attributable to ischemia, based on neuropathological, neuroimaging, and/or clinical evidence of permanent injury”
- CRAO = medical emergency
  ◦ IMMEDIATE referral stroke center/ER
  ◦ Establish relationship w/ 24/7 stroke center
# Ocular Arterial Occlusive Disorders and Carotid Artery Disease

Sohan Singh Hayreh, MD, PhD, M. Bridget Zimmerman, PhD

## 203 Central Retinal Artery Occlusions

<table>
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<td>74%</td>
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<td>Echocardiography (embolic)</td>
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<tr>
<td>Myocardial Infarction</td>
<td>21%</td>
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<td>TIA/Stroke before/after RAO</td>
<td>7%</td>
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TIA/Stroke absolute incidence **within 3 months** RAO

**CRAO only 1% incidence**
Retinal and Ophthalmic Artery Occlusions
Preferred Practice Pattern®
AAO Practice Pattern: RAOs

- **50 years old → r/o GCA** (BEST)
  - ESR, CRP, Platelets
- Systemic evaluation vasculitis, hypercoag state → younger patients
- **Embolic workup older patients**
  - Heart (EKG/Echo), Carotid Artery
- **RAO 2/2 embolic etiology → IMMEDIATE referral stroke center**
Life after CRAO

- Lifetime reduced ave 10 years vs healthy
- 30% RAO died after average 4.2 years
- Stroke risk 10 times higher vs general population 3.5 years
- Increased stroke risk up to 10 years

**Stroke Education**
  - DM, HTN, Hyperlipidemia

- Additional ocular sequelae
  - NV, NVI, NVA, NVG

Lorentzen SE. *Acta Oph* 1969
Hankey et al. *BMJ* 1991

Rim et al. *Stroke* 2016
Ocular neovascularization following central retinal artery occlusion: prevalence and timing of onset

Adam K. Rudkin¹, Andrew W. Lee², Celia S.

Incidence and Clinical Features of Neovascularization of the Iris following Acute Central Retinal Artery Occlusion

Young Ho Jung¹,², Seong Joon Ahn³, Jeong-Ho Hong⁴, Kyu Hyung Park⁵, Moon-Ku Han⁶, Solkyu Jung⁷, Se Joon Woo⁸

Ocular neovascularization in eyes with a central retinal artery occlusion or a branch retinal artery occlusion

10.9 - 18.2% developed neovascularization
6.4 - 15.2% developed neovascular glaucoma

Ave time Dx neo: 1-3 months (range 2-16 weeks)

Follow CRAO regular intervals 2 weeks → 4 months
Ocular Neo 2/2 CRAO?

- VEGF released 2/2 CHRONIC retinal hypoxia (CRVO, PDR, OIS)
- CRAO = ACUTE retinal hypoxia
- Ocular Ischemic Syndrome
  - Internal Carotid Artery Disease – Plaque presence >> Stenosis
  - Embolus source CRAO
- Carotid Doppler limitations
Branch Retinal Arteriole Occlusion

- 38% RAOs
- 98% temporal artery
- Embolus at vessel bifurcation
- CorrespondingVF loss
  - Improvement first 7 days
- Compared to CRAO
  - Emboli visible 65% BRAO vs 20%
  - Similar risk factors, better vision, + APD
212 BRAO, initial visual acuity > 20/40 in 74% patients
Visual acuity > 20/40, 89% eyes retain vision

BRAO < 20/40 initially, 79% improved 3 lines or more

Visual acuity better than 20/40 final visit
80-89% permanent BRAO
100% CLRAO

Am J Oph 2008; 146: 455-457
Ophthalmology 2009; 116: 1188-1194
123 consecutive BRAO patients

Retinal infarct
Ave resolution 4-6 weeks, 13% at 3 months

Optic Nerve Pallor → 65% at 3 months

Initial: OCT increased **thickening** inner layers
F/U: Destruction inner retinal layers → **thinning**
Retinal Artery Occlusion

Associated Systemic and Ophthalmic Abnormalities

Sohan Singh Hayreh, MD, PhD, 1 Patricia A. Podhajsky, BSN, 1 M. Bridget Zimmerman, PhD 2

Carotid Doppler/Angiography
Ipsilateral ICA >50% stenosis
30% BRAO

Plaque present
66% BRAO

Abnormal echocardiogram (EKG) embolic source
mostly calcified valve

42% of BRAO

BRAO/CLRAO require HEART + CAROTID evaluation

Ocular Arterial Occlusive Disorders and Carotid Artery Disease

Sohan Singh Hayreh, MD, PhD, ¹ M. Bridget Zimmerman, PhD²

127 BRAO

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TIA/Stroke absolute incidence within 3 months RAO

**BRAO – only 2 patients over 5 years**
Ocular neovascularization in eyes with a central retinal artery occlusion or a branch retinal artery occlusion

Ocular neovascularization
< 1% BRAO (ave 4.5 months)

BRAO Risk TIA/Stroke and NV SIGNIFICANTLY less vs CRAO
Cilioretinal Artery

- Normal anatomical variant
- Choroidal blood supply
  - FA: CLR artery fills during choroidal flush
- Present ~ 32% eyes
- Hook-like appearance, temporal
- 88% cilioretinal arteries supply macula
Cilioretinal Artery

Exits optic nerve separate from CRA

Derived from short posterior ciliary arteries
Cilioretinal Artery in CRAO

- Patent cilioretinal artery improves visual prognosis CRAO
- Bypass occlusion, supply macula
- Spare macula/central vision 25% CRAO
Cilioretinal Artery Occlusions

- Cilioretinal artery occluded w/ associated vision loss
- 5% RAOs
- Isolated → GIANT CELL ARTERITIS
- 3 clinical variants:
  - Isolated CLRAO (40%)
  - CLRAO + CRVO (40%)
  - CLRAO + AION (20%) – arteritic vs non-art

CRVO associated w/ CLRAO

- 1/3 transient visual blur before constant blurred vision
- Centrocecal defect most common
- Hemodynamic Block
  - Venous pressure > Arterial pressure
  - Choroidal blood supply no autoregulation
  - Lower perfusion pressure
  - FA: Oscillating blood column
CENTRAL RETINAL VEIN OCCLUSION ASSOCIATED WITH CILIORETINAL ARTERY OCCLUSION

SOHAN SINGH HAYREH, MD, PhD, DSc, FRCS, FRCOphth,*
LYNN FRATERROGO, MD,* JOST JONAS, MD†
CLRAO – Giant Cell Arteritis

- Choroidal → Posterior ciliary arteries
- Simultaneous CLRAO + AAION
- Need r/o GCA: ESR, CRP, Platelets

BRAO/CLRAO Management

- **Embolic Work-up**
  - Heart (EKG/ECG), Carotid Artery

- **R/O Giant Cell Arteritis**
  - GCA disease medium/large arteries only
    - Branch retinal arteries = arterioles
  - **CLA supplied by posterior ciliary artery**
    - need ESR/CRP/Platelets

- **Ocular Neovascularization, visual field**

- **AAO Preferred Practice Pattern**
  - Referral to Stroke Center? Triage?
Triage Stroke Risk w/ ABCD²

- **A**ge > 60 = 1 point
- **B**lood Pressure
  - Systolic > 140 and/or diastolic > 90 = 1 point
- **C**linical symptoms
  - Unilateral weakness/numbness = 2 points
  - Speech disturbance w/o weakness = 1 point
- **D**uration
  - 0 < x < 10 minutes = 0 points
  - 10 < x < 59 minutes = 1 point
  - > 60 minutes = 2 points
- **D**iabetes = 1 point
Multicenter external validation of the ABCD² score in triaging TIA patients

<table>
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<th>7-day stroke risk (95% CI)</th>
<th>90-day stroke risk (95% CI)</th>
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<tr>
<td>0-3</td>
<td>3% (0-7%)</td>
<td>4% (0-9%)</td>
</tr>
<tr>
<td>4-5</td>
<td>9% (1-17%)</td>
<td>21% (10-33%)</td>
</tr>
<tr>
<td>6-7</td>
<td>24% (6-42%)</td>
<td>43% (22-64%)</td>
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Low risk: ABCD² = 0-3; moderate risk: ABCD² = 4-5; high risk: ABCD² = 6-7.

ABCD² predicts severity recurrent events
- Disability
- Hospital stay length
- Hospital costs

CHANDRATHEVA ET AL. ABCD² Score Predicts Severity Rather Than Risk of Early Recurrent Events After TIA. Stroke. 2010; 41: 851-856
ABCD$^2$ for TIA

- Current international guidelines per
  - American Heart Association
  - American Stroke Association

**Immediate hospitalization** +
**diagnostic evaluation** TIA patients
**ABCD$^2$ score 3 or above within 24 hours** of symptom onset
RAO = Stroke Education

- Many having stroke, DO NOT KNOW they are having a stroke!
- **Signs/Symptoms**
  - Decision to call ambulance ~ 40%
    - Stroke = **SERIOUS + TREATABLE**
  - Tissue Plasminogen Activator (TPA) ~ 4%
    - Principal impediment to Tx = LATE ARRIVAL (3 hours)
- **Time sensitive!!**
Treatment (Un)Awareness

“Suppose you were having a stroke. Do you know of any medication your doctor could give you to increase your chance of recovering from stroke?”

3.6% → T-PA or “clot buster”

EDUCATION NEEDED
Stroke public awareness campaigns → NO IMPROVEMENT

STROKE EDUCATION
-SIGNS
-URGENT
-TREATABLE
“My basic and clinical studies on retinal ischemia showed that… it is not logical for the American Heart Association/ American Stroke Association to lump retinal ischemia with TIA and stroke” – SS Hayreh
RAO Management

- **Urgent R/O Giant Cell Arteritis**
  - CRAO, BRAO, CLRAO

- **Urgent Referral Stroke Center**
  - CRAO, BRAO, CLRAO

- **Embolic work-up (Heart, Carotid)**
  - CRAO, BRAO, CLRAO

  **Hayreh most important**

- **Stroke Triage (ABCD²) BRAO/CLRAO?**

- **Risk Factor Assessment**

- **Stroke Education – ALL RAOs**