Current Concepts in Glaucoma
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Is Glaucoma a Bad Disease?

Goals of Glaucoma Therapy
- Maximize the patient’s quality of life
- Patient maintains functional vision to meet the requirements of daily activities
- Glaucoma patients do not become symptomatic until late in their disease process
- Does not have to be a zero tolerance policy to visual field loss
  - We don’t stop glaucoma progression with treatment but we can slow it down
- Not every person with glaucoma goes blind (rule of 10)
- Difficult to predict the rate of glaucoma damage and how long the patient has to live
- Blinding or killing a patient to achieve a desired target pressure is not good practice

When Should We Treat?
- Does the patient have nerve damage?
  - If yes, then in most cases – TREAT
  - If no, then access risk factors to determine the benefits of treatment vs. observation
- Level of IOP
- CCT
- Age
- Race
- FOH

When to Treat Elevated IOP Without Glaucoma Damage
- NO glaucoma damage
- Elevated IOP
- Refer to OHTS
  - Greatest risk for developing glaucoma
    - IOP 26 or above
    - In conjunction with thinner CCT <555um
- OHTS lowered IOP by approximately 20% (target pressure)
  - One or two meds

No Damage, But Elevated IOP
CCT and Ocular Hypertension
Treating When There is Damage

- Strong evidence (clinical trials) that lowering IOP slows down glaucoma progression
- Generally, we are going to treat patients that exhibit glaucoma damage
- Includes patients with elevated IOP (COAG) and non-elevated IOP (NTG)
- How to determine if damage is present

Glaucoma

- Glaucoma is a disease of the ganglion cell axons
- Damage occurs at the level of the lamina cribrosa
- Selective damage to the superior and inferior poles of the optic nerve
- Relative preservation of the temporal and nasal poles

Glaucoma Discriminates

- Glaucoma often asymmetrically damages between above and below and between the two eyes
- Look for notches in the neuro-retinal rim tissue
- Occurs in 30% of glaucoma patients
- Inferior temporal pole most common site of notching
- Associated with a corresponding VF defect

ISNT Rule

- Inferior>Superior>Nasal>Temporal rim tissue
- Nasal rim tissue varies considerably because of blood vessels
- Glaucoma does not selectively damage nasal rim tissue

Modified ISNT Rule

- Ignore the nasal rim tissue
- Expected ratios: 1.5-2.0x inferior: 1.5-2.0x superior: 1.0 temporal
- Glaucoma should be suspected when the amount of inferior or superior neuro-retinal rim tissue is equal to or less than the temporal rim tissue

Disc Size Affects the ISNT Rule

- For small size nerves: >2.0x inferior: >2.0x superior: 1.0x temporal
- For medium size nerves: 2.0x inferior: 2.0x superior: 1.0x temporal
- For large size nerves: 1.5x inferior: 1.5x superior: 1.0x temporal

Does Size Really Matter?

- Is there a C/D ratio that defines glaucoma?
- Do you think this nerve has glaucoma?

A Big Cup Does Not Necessarily Mean Glaucoma

- There is no demarcation line separating a physiological cup from a glaucomatous cup
- Physiological cup size is directly related to overall disc size
- Large discs will have large physiologic cups
- Small discs will have small physiologic cups
- Physiologic disc and cup size is genetically determined
- Physiologic cup of .7 or greater occurs in 2% of normals
- A small disc with a medium size cup should be as suspicious as a large cup in a medium size disc

**How to Evaluate Disc Size**
- Use a 60 d lens at the slit lamp
- Make a thin vertical beam
- Adjust beam height
- Read disc diameter off scale on slit lamp
- Vertical disc diameter > 2.2 mm is a large disc
- Vertical disc diameter < 1.8 mm is a small disc

**Expected Physiologic Cup Size**
Based on Measured Vertical Disc Diameter
Using a 60 Diopter Lens At The Slit Lamp

<table>
<thead>
<tr>
<th>Vertical Height (mm)</th>
<th>-2std</th>
<th>-1std</th>
<th>Mean</th>
<th>+1std</th>
<th>+2std</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.6</td>
<td>1.8</td>
<td>2.0</td>
<td>2.2</td>
<td>2.4</td>
</tr>
</tbody>
</table>

| Expected C/D Ratio  | 0.0   | 0.2   | 0.4  | 0.6   | 0.8   |

**NFL Anatomy**
Patterns of Diffuse NFL Loss
Focal NFL Defects

**Cirrus™ HD-OCT**
- Optic Disc scan
- Cube scan with 6mm x 6mm area
- 200x200 (200 A-scans per B-scan; 200 B-scans)

**Does the OCT do it Better?**
**Caveat #1**
- It is difficult to create a normal data base with a structure like the optic nerve that varies significantly in regards to size, shape and number of ganglion cell axons

**Caveat #2:**
- There are structures (ie blood vessels, astrocytes and glial cells) that contribute to the measured RNFL by the OCT

**Caveat #3:**
- Your OCT is not shipped with a brain, so use yours
**Distribution of Normals**

- White represents upper 5% of normal database
- Green represents middle 90% of normal database
- Yellow represents lower 5% of normal database
- Red represents lowest 1% of normal database
- Gray not compared to the normal database

**OCT Printout**
- Thickness Map
- Deviation Map

**Quantitative Parameters**
- Thickness Profiles
- Quadrant and Sector Analysis of RNFL

**Rim Area**

- Rim area range 0.75-2.38 mm² (ave 1.31) in normative database
- We are born with different number of ganglion cell axons (700,000-1.5 million)
- No way to account for this in the database other than to average values

**Disc Area**

- Disc Area range 1.06 – 3.38 mm² (ave 1.83) in normative database
- Small - disc area < 1.63 mm²
- Medium - disc area 1.63-1.97 mm²
- Large - disc area > 1.97 mm²
- Disc area is always gray color coded
- Larger discs will have larger c/d ratios
- Larger discs generally have greater neuro rim tissue
- The current software does compare disc area size to the optic nerve parameters but not to RNFL parameters

**The Ganglion Cell Complex (ILM - IPL)**

**Should we Look Elsewhere for Glaucoma Damage Other than the Optic Nerve?**

- The ganglion cell complex (ILM - IPL)
- Ganglion cell analysis
- Measures thickness for the sum of the ganglion cell layer and inner plexiform layer (GCL + IPL layers) using data from the Macular 200 x 200 or 512 x 128 cube scan patterns

**Advantage of Ganglion Cell Analysis**

- More reproducible measurement than peripapillary RNFL
- Less physiological variation compared to peripapillary RNFL
- Less major blood vessels to create pseudo-thickness measurements
- Better symmetry between superior and inferior and between eyes than peripapillary RNFL
- Clinical Correlation is Paramount
**Squeegee Sign**
- Glaucoma initially damages the temporal side of the ganglion cell bodies in the macula
- Glaucoma asymmetrically damages between the superior and inferior ganglion cell bodies
- Squeegee Sign to the superior or inferior temporal ganglion cell bodies is the initial indication of glaucoma damage on the GCA

**Errors in Interpretation**
- Green always represents Non-Disease
- Red always represents Disease

**Red Disease Does Not Always Mean Glaucoma**
- Clinical Correlation is Key

**Does Green Always Mean Normal?**
- Symmetry is a Beautiful Thing!
- Lack of Symmetry Should Raise Suspicion!

**OCT Clinical Pearls**
- Normal data bases for optic nerve and RNFL are difficult to construct
- Blood vessels, astrocytes and glial cells can taint optic nerve and RNFL measurements
- If you simply evaluate the OCT printout in isolation, you will make interpretation errors
- Understand that GREEN does not always mean NORMAL and RED does not always mean ABNORMAL
- The doctor should always correlate the data from the OCT printout with clinical data before making management or treatment decisions in glaucoma.

**Setting Target Pressures**
- Good mental exercise to incorporate for all glaucoma and glaucoma suspect patients
- Avoids “cookbooking” glaucoma management
- Look at the individual characteristics of each patient
- Decide how aggressively or non-aggressively to treat
- Reinforces the concept that each glaucoma or glaucoma suspect patient is unique

**Setting Target Pressures**
- “Estimated IOP where the risk of future visual impairment is balanced against the side effects of treatment”
- Based on the baseline IOP readings (use the highest IOP reading)
- Based on the amount of optic nerve damage
- Based on the rate of glaucoma progression
Other Factors to Consider

- Age of the patient
- Race of the patient
- FOH of severe visual loss from glaucoma
- Status of the fellow eye
- Compliance factors

IOP

- Deemphasize that elevated IOP defines glaucoma
- Emphasize that elevated IOP is the most significant risk factor for developing glaucoma and the risk factor we can alter
- Higher the IOP the greater the risk
- Suggestion that the greater the diurnal variation of IOP, the greater the risk of developing glaucoma and progressing with glaucoma
- IOP is not a static measurement

IOP Varies More Than You Think

- Average diurnal variation for a glaucoma patient is 6 mm HG
- Mark sure you get baseline IOP readings before you start a patient on treatment
- 3 readings is the minimum
- You can never rule out an IOP spike
  - Personally I believe the highest IOP reading is more important than the average IOP reading
  - Which patient concerns you more?
    - Patient #1: IOP 24, 24, 24
    - Patient #2: IOP 24, 18, 32

Setting Target Pressures

- “Estimated IOP where the risk of future visual impairment is balanced against the side effects of treatment”
- Based on the Baseline IOP Readings (use the highest IOP reading)
- Based on the Amount of Optic Nerve Damage
- Based on the Rate of Glaucoma Progression

Quantifying Glaucoma Damage

- Optic nerve assessment
- NFL assessment
- New technology assessment
  - HRT
  - GDx
  - OCT
- Visual Field assessment

Visual Field Quantification
(Mild, Moderate, Severe)

- Mean deviation (MD)
- Number of abnormal points on the pattern deviation plots
- Decibel value of the four points just off fixation

**Mild Visual Field Defect**
- The mean deviation index (MD) is better than -5 dB
- On the pattern deviation plot, fewer than 18 (14) of the points are depressed below the 5% level and fewer than 10 (8) points are depressed below the 1% level on 30-2 (24-2)
- No point in the central 5 degrees has a sensitivity < 25 dB

**Moderate Visual Field Defect**
- The mean deviation is better than -10 dB
- On the pattern deviation plot, fewer than 36 (28) of the points are depressed below the 5% level and fewer than 20 (16) points are depressed below the 1% level on 30-2 (24-2)
- No point in the central 5 degrees has a sensitivity < 15 dB

**Severe Visual Field Defect**
- The mean deviation is worse than -10 dB
- On the pattern deviation plot, more than 36 (28) of the points are depressed below the 5% level or more than 20 (16) points are depressed below the 1% level on 30-2 (24-2)
- Any point in the central 5 degrees has a sensitivity <15
- There are points within the central 5 degrees with sensitivity <25 dB in both hemifields

**Guidelines For IOP Target Values**
- No damage - OHTS recommended 20% reduction of baseline IOP
- Mild damage - 30% reduction of baseline IOP
- Moderate damage - 30-40% reduction of baseline IOP
- Severe damage - 40-50% reduction of baseline IOP

**What’s it Going to Take?**
- 20-30% reduction - 1 or 2 meds
- 30-40% reduction - 2-3 meds +/- ALT/SLT
- 40-50% reduction - 3-4 meds +/- ALT/SLT +/- filter

**Don’t Like Math? I Generally Set 3 Target Pressures**
1. Patient with high risk ocular hypertension - elevated pressure but no glaucoma damage. Treat with 1-2 meds max
2. Patients with definite glaucoma damage, but in the mild-moderate stage of damage. Target pressure < 18 (consistent). Will use multiple meds and laser to achieve, but not filtering surgery
3. Patients with definite damage in the moderate to severe stage of damage. Target pressure < 15 (consistent). Will use multiple meds and laser to achieve and will
consider filtering surgery in select cases early and will not delay filtering surgery in cases of progression on MMT

**Glaucoma Management**
- Start with a prostaglandin
- Add beta-blocker as second line
- Change beta-blocker to Cosopt (or Combigan)
- Add Alphagan (or topical CAI) as third drug
- OR consider ALT/SLT
- Filtering surgery
- Only if the benefits outweigh the risks

**Is Cataract Surgery the New Glaucoma Surgery?**
- Cataract surgery lowers IOP 2-4 mmHG
- Clear cornea phaco lowers IOP greater than extracapsular cataract extraction
- Effect is long lasting
- 80% maintained 3 mmHG IOP lowering for 5 years

**Rhpressa**
- Aerie pharmaceuticals Rho Kinase inhibitor and norepinephrine transporter
- IOP reduction mechanism is an increase in TM outflow, decrease in aqueous production and lowering episcleral venous pressure
- .02% concentration dosed once a day
- 4 mm average diurnal IOP reduction
- Non-inferior compared to timolol bid, but only for IOP <26
- No major systemic side effects
- Conjunctival hyperemia major ocular side effect (40-60%)
- Conjunctival hemorrhages, corneal deposits and blurry vision (5-15%)
- Discontinue rate 15%

**Roclatan**
- Combination of Rhopressa and Latanoprost
- Dosed once a day
- 34% IOP reduction
- 2 mm additional IOP reduction than latanoprost alone
- Hyperemia the major side effect

**AMA0076**
- Amakem Therapeutics Rho Kinase inhibitor
- Started human clinical trials
- Less conjunctival hyperemia

Progression Rates Vary From Patient to Patient
Re-Assessment of Target Pressures
- Glaucoma progression is general slow
- Important to identify rapid progressors
- Patients are followed with various tests to judge progression
- Patient who progress at a certain target pressure need further IOP lowering
- Consider filtering surgery for patients who are rapid progressors

Cirrus Guided Progression Analysis (GPA)
- RNFL Thickness Change Maps demonstrate change in RNFL between exams. Up to 6 progression maps are compared to baseline. Areas of statistically significant change are color-coded yellow when first noted and then red when the change is sustained over consecutive visits.
- TSNIT values from baseline and current exams are plotted
- Areas of statistically significant change are color-coded yellow when first noted and then red when the change is sustained over consecutive visits
- Average RNFL thickness values are plotted for each exam
- Yellow marker denotes change from both baseline exams
- Red marker denotes change sustained over consecutive visits
- Rate and significance of change are shown in text

Cirrus GPA™ Analysis
- RNFL Summary Legend summarizes GPA analyses and indicates with a check mark if there is possible or likely loss of RNFL
- RNFL Thickness Map Progression (best for focal change)
- RNFL Thickness Profiles Progression (best for broader focal change)
- Average RNFL Thickness Progression (best for diffuse change)

Updated Guided Progression Analysis (GPA™)
Optic Nerve Head information now included
- Average cup-to-disc ratio plotted on graph with rate of change information
- RNFL/ONH summary includes item “average cup-to-disc progression”
- Printout includes an optional second page with table of values, including rim area, disc area, average & vertical cup-to-disc ratio and cup volume. Each cell of the table can be color coded if change is detected.

Glaucoma Progression Analysis