Assessing Glaucoma Risk Factors and Identifying Progression

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Disclosure

- Michael Chaglasian has the following disclosures:
  - Advisory Board: Allergan, Inc., Alcon Labs, Carl Zeiss Meditec
  - The content of this presentation is in no manner influenced by any of the aforementioned parties or companies

Agenda

- Risk Factors Overview
- Concept of Risk Assessment
- Ocular Hypertension
  - OHTS, Risk Calculator
- Ocular Perfusion Pressure
  - Low IOP and patient is progressing
- Disc Hemorrhages
  - A true Red Flag
- Corneal Hysteresis
  - Something to add to the list

Decision Making In The Management Of Glaucoma

- “To treat or not to treat?”… that is the 1st question!
- “How to treat?”… that is the next question!
- “How to modify treatment?”… that’s another good question!

Glaucoma Risk Factors Evidence Based

- Age:
  - Most commonly occurs after age 60 (risk increases with age)
  - Earlier in those with a Family History
- Race:
  - African, Hispanic, Asian
- Family history
  - First degree relatives (OR 2.9; Tielsch et al)
- Elevated Intraocular pressure
- Other ocular factors:
  - Thin central corneal thickness, narrow angles, increased cup:disc ratio, exfoliation
- Systemic factors:
  - Low diastolic pressure, hypotension,
- Genetic factors:

Risk Assessment in Clinical Practice
Assessing Glaucoma Risk Factors and Identifying Progression

**CASE AC**

- 51 year old
- Myopia, no sig. medical history
- Positive family history glaucoma
  - Father (85 yrs)
- GAT= 27 OD 25 OS

**What are the positive risk factors?**

How do you quantify them?

**What do you do now?**

**CASE AC: Risk Factors**

<table>
<thead>
<tr>
<th>Patient’s Clinical Finding</th>
<th>Risk Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>51 year old</td>
<td>Older age: yes</td>
</tr>
<tr>
<td>Myopia</td>
<td>Myopia: over 8 diopters</td>
</tr>
<tr>
<td>Medical History:</td>
<td>Hypertension:</td>
</tr>
<tr>
<td>- systemic hypertension</td>
<td>- not a RF</td>
</tr>
<tr>
<td>Positive family history</td>
<td>Positive Family History: YES</td>
</tr>
<tr>
<td>GAT= 27 OD 25 OS</td>
<td>High IOP: YES</td>
</tr>
<tr>
<td>ONH and VF</td>
<td>Varies</td>
</tr>
</tbody>
</table>

Have we fully identified this patient’s risk of developing glaucoma?
Assessing Glaucoma Risk Factors and Identifying Progression

An absolutely essential piece of information:

Central Corneal Thickness / Pachymetry:
- 565µ OD
- 565µ OS

What is your risk assessment now? Is your management plan different?

POAG Endpoints by Central Corneal Thickness and Baseline IOP (mmHg) in Observation Group* OHTS Data

<table>
<thead>
<tr>
<th>Central Corneal Thickness (microns)</th>
<th>&lt; 23.75</th>
<th>&gt; 23.75 to ≤ 25.75</th>
<th>&gt; 25.75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline IOP (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 23.75</td>
<td>17%</td>
<td>9%</td>
<td>2%</td>
</tr>
<tr>
<td>&gt; 23.75 to ≤ 25.75</td>
<td>36%</td>
<td>13%</td>
<td>6%</td>
</tr>
<tr>
<td>&gt; 25.75</td>
<td>12%</td>
<td>10%</td>
<td>7%</td>
</tr>
</tbody>
</table>

Pachymetry: 3 Outcomes

- **Thin**: < 555 µ High Risk
- **Average**: 555-588 µ No change in Risk
- **Thick**: > 588 µ Low Risk

Applied to patients with ocular hypertension

Is there anything else to do?

Risk Calculator

http://ohts.wustl.edu/risk/calculator.html

Also iPhone App

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Risk Calculator

<table>
<thead>
<tr>
<th>FACTORS</th>
<th>RIGHT EYE MEASUREMENTS</th>
<th>LEFT EYE MEASUREMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uncontrolled Intraocular Pressure (mmHg)</td>
<td>27</td>
<td>25</td>
</tr>
<tr>
<td>Central Corneal Thickness (μm)</td>
<td>595</td>
<td>565</td>
</tr>
<tr>
<td>Vertical Cup to Disc Ratio by Camera</td>
<td>0.40</td>
<td>0.30</td>
</tr>
<tr>
<td>Pattern Standard Deviation</td>
<td>2.1</td>
<td>1.6</td>
</tr>
</tbody>
</table>

The predictions derived using these methods are designed to aid, but not to replace clinical judgment.

Risk Calculator Outcomes: Guide to Patient Management

<table>
<thead>
<tr>
<th>5-Year Risk for Progression of OHTN → Glaucoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk Level</td>
</tr>
<tr>
<td>------------</td>
</tr>
<tr>
<td>Low</td>
</tr>
<tr>
<td>Moderate</td>
</tr>
<tr>
<td>High</td>
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Life Expectancy (LE)
- Risk for 50 yo is much higher
  » OHTS RC is only 5yrs;
  » LE avg. is ~28 yrs (75m/80f)
- Older Patient @ 75 yrs
  » LE is 12 yrs, not 3 yrs; Likely need to treat
  » 85 yo patient: LE is 6 yrs

Some life expectancy Risk Calculators are available online

iPhone App

Risk Calculator: Validated

Risk Calculator Limitations:
- A number of factors described as predictive in previous studies either did not add to the explanatory power of the OHTS–EGPS pooled model or were not assessed in this study. These include:
  1. Myopia
  2. Disc Hemorrhages
  3. Diabetes
  4. Race
  5. Family history of glaucoma
  6. Life Expectancy

Ocular Perfusion Pressure

Other Limitations
- A number of factors described as predictive in previous studies either did not add to the explanatory power of the OHTS–EGPS pooled model or were not assessed in this study. These include:
  1. Myopia
  2. Disc Hemorrhages
  3. Diabetes
  4. Race
  5. Family history of glaucoma
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Risk Calculator

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Pachymetry

Do Not Adjust IOP Based on CCT

Do Not Adjust IOP Based on CCT

Pachymetry: 3 Outcomes

Thin: <555 µ High Risk
Average: 555-588 µ No change in Risk
Thick: >588 µ Low Risk

Applied to patients with ocular hypertension

IOP and CCT

“Assuming that CCT can be used as a correction factor for GAT is a misinterpretation of the results of OHTS... that couldn’t be further from the truth. Adjusting IOP based on CCT is attempting to instill a degree of precision into a flawed measurement. You may actually correct in the wrong direction. The issues related to the most accurate tonometry need to include the material properties of the cornea”

» James Brandt, MD, Director, Glaucoma Services, UC Davis
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Should Pachymetry be Repeated Over Time? No

Changes in Central Corneal Thickness over Time

The Ocular Hypertension Treatment Study

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chagleian, M.</td>
<td>2014</td>
</tr>
</tbody>
</table>

However, obtain multiple (3) readings on one day.

Central Corneal Thickness: Will One Measurement Sufficient?

<table>
<thead>
<tr>
<th>Author(s)</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Wilde, L.</td>
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Is Optical/OCT pachymetry the same as Ultrasound? No

- OCT typically under measures CCT
  - range 15-55 microns
  - Corneal Edema from topical anesthetic?
  - Corneal “compression” from probe?
- As Ultrasound units were used in OHTS, it’s not appropriate to substitute an OCT based CCT measurement.

- CPT 76514:
  - Ophthalmic ultrasound, echography, diagnostic; corneal pachymetry, unilateral or bilateral.

CCT is a RF for Visual Field Loss

Central Corneal Thickness as a Risk Factor for Visual Field Loss in Patients With Preperimetric Glaucoma Optic Neuritis

<table>
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<th>Year</th>
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<tr>
<td>Weinreb, R.N.</td>
<td>2003</td>
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CCT RF for Advanced Glaucoma

Central Corneal Thickness as a Risk Factor for Advanced Glaucoma Damage

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CASE EE

IOP  22-25 mmHg OD, OS
CCT 525

Disc Photos

Visual Fields

Discussion
Case WS

- 75 yo male
- + HTN w/ multiple BP meds x 20+ yrs
  - 105/68 in office
  - 5'5", 142 lbs
- CCT= 532µ

- Initial IOP 23 mmHg
  - Now repeatedly 11-13 mmHg over 5+ years
- Current Medication:
  - PGA
- Good compliance and follow up

Guided Progression Analysis™ (GPA™)
Assessing Glaucoma Risk Factors and Identifying Progression

Stereo Photos

- Obtain Baseline Photographs
  - Stereo is preferred
  - Screen-Vu Stereo Viewer™
  - www.berezin.com
- Read, Review, and Document in record
- Repeat periodically, or when change is suspected

Case WS

- Q= What is the Explanation?
  - Progression with IOP in low teens.
- Compliance?

Other Potential Risk Factors:

- 24 Hour IOP
  - Highest IOP in Nocturnal Period (midnight-5AM)
- DOPP
  - Diastolic Ocular Perfusion Pressure

Ocular Perfusion Pressure

- The differential between arterial BP and IOP
  - Ocular perfusion is regulated to maintain constant blood flow to the optic nerve despite fluctuating blood pressure and IOP
  - The major cause of reduced blood flow is thought to be secondary to vascular dysregulation in susceptible patients, resulting from abnormal/insufficient auto-regulation.

Ocular Perfusion Pressure

- \[ \text{Ocular Perfusion Pressure (OPP)} = \text{BP} - \text{IOP} \]
  - BP is mean arterial pressure, diastolic BP, or systolic BP

OPP and Glaucoma: Hemodynamics

- SPP = SBP – IOP
- DPP = DBP – IOP  Diastolic Measure
  - easiest to use, best current evidence
- MPP = 2/3 mean arterial pressure – IOP
  - Arterial Pressure = DBP + 1/3 (SBP – DBP)
  - May best reflect perfusion physiology

Ocular Perfusion Pressure and Glaucoma

Hayreh SS. Trans Am Acad Ophthalmol 1974;78:240-54

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### Ocular Perfusion Pressure and Glaucoma

- **Higher IOP Negatively Impacts Perfusion Pressure**
- **Lower Diastolic, Systolic, or Mean Pressure Reduces Perfusion Pressure**
- **Perfusion Pressure Is a Result of A Delicate Balance Between IOP and Blood Pressure**
- **Lower Perfusion Pressure Is Associated with Increased Risk for Open Angle Glaucoma**

Hartikainen S. Trans Am Acad Ophthalmol 1979;76:249-54

### OPP and Glaucoma Progression: Population Studies

- **Baltimore Eye Survey (AA and Caucasian)**
  - 6x excess of POAG in subjects with lowest category of Ocular Perfusion Pressure (OPP)
- **Egna-Numarkt Study (Caucasian)**
  - Lower Diastolic Ocular Perfusion Pressure (DOPP) associated with marked, progressive increase in frequency of POAG
- **Barbados 4 yr Eye Study (African-Caribbean)**
  - 4-year risk of developing glaucoma increased dramatically at lower perfusion pressure
- **Proyecto Ver (Hispanic)**
  - Found lower Diastolic Perfusion Pressure (DPP) associated with increased risk of POAG

Leske et al Ophthalmology. 114 (11), November 2007

### Los Angeles Latino Eye Study

- Cross-sectional study of 6,357 Latinos, >40 years in Los Angeles, CA.
- Persons with low diastolic and systolic perfusion pressures had a higher risk of POAG.
- DOPP <50 mmHg, the prevalence of glaucoma rapidly increases linearly.


### POAG Risk Factors at year 9

**Barbados Eye Study**

- **Highest Risk**
- **Low mean PP**
- **SBP**
- **SBP (systolic blood pressure)**
- **DBP** (diastolic blood pressure)
- **BMI** (body mass index)
- **Age**
- **Gender**
- **Race**


### Studies Summary

- These large studies provide **strong evidence among different populations** for the relationship between vascular deficits and the prevalence, incidence and progression of glaucoma

- Some Limitations,
  - no direct measure of ocular blood flow
  - Varied definitions of hypertension
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Clinical Control of OPP

- Lower IOP improves OPP
- Lower systemic BP improves OPP, but do not necessarily want to raise BP:
  - Stroke #3 cause of death in US behind CVD & CA!
  - Avoid drugs that lower systemic BP beyond patient's desired systemic control.
  - Communicate with PCP

Measure blood pressure on your patients

Nocturnal Hypotension and OPP

- Low blood pressure (BP) at night, coupled with high IOP in supine position, compromise OPP.
  - Up to 50% of patients with HTN
  - Using systemic BP meds in the AM to minimize nocturnal hypotension makes sense.

- Using IOP lowering drugs that lower IOP while sleeping makes sense.
  - Avoiding IOP meds that LOWER systemic BP at night (beta blockers, alpha agonists) makes sense.

24 Hour Blood Pressure

- Holter Monitor

24 hr IOP Measure via SCL

SENSIMED Triggerfish® - Continuous IOP Monitoring

Not approved in USA

2014

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Case WS

- **DOPP**:
  - DBP of 68 mmHg @ 2PM and **IOP of 12 mmHg**
  - Gives 56 mmHg
- Nocturnal BP with Holter Monitor
  - DBP @ 2AM = 58
- Nocturnal IOP (estimate)
  - IOP of 12 mmHg @ 2PM = ?? @ 2AM ~ 18 mmHg
- Nocturnal DOPP
  - 58 - 18 = **40 mmHg**, potentially a high risk

**Is there anything else that can be done?**

**Possibly:**
- Offer Nocturnal IOP control
- Offer Improved DOPP

Add a CAI BID

Letter to PCP, explain OPP and Low BP related Risk

? Adjust BP Meds

24-hour habitual IOP Azopt vs. timolol add-on efficacy

**Summary**

- IOP Fluctuation
- Increased Nocturnal IOP
- Low Nocturnal Blood Pressure
- Low Diastolic Perfusion Pressure

Optic disc hemorrhages

- Appearance may precede NFL loss, notching, VF defect
  - Associated with **progressive VF defects in glaucoma or OHT (up to 20X greater risk)**; especially among females [Drance et al. AJO 2001]
  - More frequent in NTG than COAG or OHT
  - Also seen in PVD, RBVO, hypertensive retinopathy, NAION (< 2% of all ONH hemorrhages)

Drance/Disc hemorrhage
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Optic Disc Hemorrhage

Drance Heme and Progression

Figure 5. Example of an eye that was progressing at a rate of VFI of 0.000065 before the hemorrhage. The eye remained at -0.15/H total after the episode of hemorrhage (Group 1). The eye had no substantial change in mean VFI levels after the episode of hemorrhage compared with before hemorrhage (1.16 months vs. 3.0 months). VFI = visual field index.

CASE ML

47 yrs old
GAT = ~ 20-21 OD and OS
Asymmetric Cupping
CCT= 525 OD OS
Referred for Treatment

Baseline VFs #1

Baseline VFs #2

Photos 2 Years Later

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VF with Event Analysis

VF with Trend Analysis

Corneal Hysteresis
An Important Risk Factor to Consider

Ocular Response Analyzer
New CPT Code Coming in 2015!

Ocular Response Analyzer

Obtains the following measures:
- IOPg - Goldmann Correlated IOP
- IOPcc - Corneal Compensated IOP
- CH - Corneal Hysteresis
  - Most important for risk of glaucoma
- CRF - Corneal Resistance Factor

Ocular Response Analyzer

Applanation Signal Plot

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Definitions

Hysteresis

The phenomenon was identified, and the term coined, by Sir James Alfred Ewing in 1890. Hysteresis is a property of physical systems that do not instantly follow the forces applied to them, but react slowly, or do not return completely to their original state.

Corneal Hysteresis

Identified by David Luce, Ph.D., Corneal Hysteresis is the difference in the inward and outward pressure values obtained during the dynamic bi-directional applanation process employed in the Ocular Response Analyzer, as a result of viscous damping in the cornea.

CH: P1 - P2

The cornea and IOP measurement

Many studies have concluded that variation in corneal thickness affects with the accuracy of measured IOP. However, the over or under estimation of IOP caused by corneal interference is only valid ON AVERAGE and the relationship is not very significant.

As such, glaucoma opinion leaders caution against using CCT based IOP correction algorithms:

The problem with CCT-based IOP adjustment

_FORCE_

Pine 2x4

FORCE

Oak 2x4

Thickness is NOT resistance

Corneal Hysteresis

- Cor’ne-al ‘Hys-te*re”sis, n. [NL., fr. Luce.]
  - Identified by David Luce, Ph.D.,
  - Corneal Hysteresis is the difference in the inward and outward pressure values obtained during the dynamic bi-directional applanation process employed in the Ocular Response Analyzer, as a result of viscous damping in the cornea.

The cornea and Glaucoma

Numerous studies, such as the Ocular Hypertension Treatment Study (OHTS) have found that corneal thickness is an independent indicator of glaucoma risk.

More recent research has indicated that the Corneal Hysteresis measurement appears to be even more powerful in this regard.
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CH distribution – Normals & Glaucoma
- Glaucoma subjects have lower CH than normals, especially those who are still progressing in the disease.
- Publications support Corneal Hysteresis

Questions / Discussion

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