Corneal Hysteresis, Central Corneal Thickness, & Glaucoma
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Acknowledgement: Shandiz Tehrani, MD, PhD

How do we know patients are at risk for glaucoma progression?
Well-established risk factors
- IOP
- Age
- Ethnicity/Race
- Family history
- Central Corneal Thickness (CCT)

Possible novel risk factors
- Corneal hysteresis

Central corneal thickness basics
- Average central thickness: 540 μm
- Measured via pachymetry
- Every 10% increase in thickness, add 1.1 mmHg (Doughty & Zaman 2000, Surv Ophth)
The Ocular Hypertension Treatment Study (Gorden et al., 2002)

- Prospective study: patients with ocular htn were randomized to treatment or no treatment, watched over 5 years. Double the risk of glaucoma in un-treated group.
- First to report CCT as a risk factor.
- “Participants with a corneal thickness of 555 µm or less had a 3-fold greater risk of developing POAG compared with participants who had a corneal thickness of more than 588 µm.”
- Likely related to direct correlation with IOP measurement: thinner cornea == artificially low reading == delay intervention

Effect of age on CCT?

- Most studies conclude that it thins with age

Corneal thickness associated with race/ethnicity

| TABLE 4. Mean Central Corneal Thickness: Total Population and by Ethnic Groups |
|---------------------------------|----|----|----|----|----|
| Total Population                | Asian | Black | White | Hispanic | Other |
| Number                          | 1,665| 116  | 120  | 1,068     | 299   |
| Mean                            | 551.0| 552.8| 559.4| 569.6      | 554.8 |
| Median                          | 524.2| 531.7| 550.2| 562.7      | 539.8 |
So is corneal hysteresis...

- Study of CH vs CCT in blacks, Hispanics, and whites
- Included 807 POAG or POAG suspect eyes (abnormal disc or fam hx)
- Multivariate analysis:
  - When CCT is the outcome, CH, but not race, matters
  - When CH is the outcome, both CCT and race matter

Haseltine et al., 2012, Acta Ophthalmologica

Inheritance also important

- Another interpretation is that since CCT is highly heritable, it may be that genetic risk factors for glaucoma that are unrelated to CCT may nonetheless be co-inherited with CCT (Wang et al., 2014, J Glaucoma)
- Monozygotic vs dizygotic twin studies show monozygotic have stronger correlation for both CCT (Toh et al., 2005, IOVS) and corneal hysteresis (CH) (Carbonaro et al., 2008, Ophthalmology)
What is hysteresis?

- The difference between the pressure at which the cornea bends inward during an airjet applanation and the pressure at which it bends out again
- Measured by "ocular response analyzer"
- Normal range: 10-11.

Determined by biochemical and biomechanical properties of the cornea relating to elasticity as well as the current pressure of the eye
- It is a behavior of the cornea, not a static property
- Implies the nature of the eye's elasticity in general (i.e. extracellular matrix)
So what?
• Predicts POAG onset and progression (Susanna et al., 2018, Am J Ophthalmology)
• Prospective cohort study of glaucoma suspects, at least 18 months (287 eyes)
• Glaucoma def: repeatable (at least 3 consecutive) abnormal visual field test results
• Every 1 mmHg lower CH, 21% more chance of developing POAG.
• Mean CH in healthy eyes, mean age 49: 10.97 ± 1.59 mmHg (Mangouritsas et al., 2009, Acta Ophthalmologica)
• Mean CH in POAG, mean age 62: 8.95 ± 1.27 mmHg

How does CH relate to risk of optic neuropathy?
**Answer:** Possibly a reporter for the optic nerve structures
• Prospective case series at UCSD (Wong et al., 2019)
• 147 eyes, minimum 3-year follow-up
• Every 1 mm Hg decrease in CH leads to a 0.66 μm/year posterior displacement of the anterior lamina cribosa surface
Effect of age on CH?

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<th>Age group (years)</th>
<th>25-30</th>
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El Massry et al., 2020, International Ophthalmology
What accounts for more glaucoma: CH or CCT?

- Prospective cohort study at UCSD (Medeiros et al, 2013, Ophthalmology)
- Multivariate analyses for visual field decline
- Both CH and CCT statistically significant
- CH explained a larger proportion of the variation in slopes of VFI change than CCT (17.4% versus 5.2%, respectively)

- Prospective study at New York Eye & Ear Infirmary (Gustavo De Moraes et al, 2012, J Glaucoma)
- 153 eyes with mean follow-up 5 years
- Multivariate analysis for visual field decline
- Higher IOP, age, and CH, but not CCT, showed significance

So what’s more important: CCT vs CH

- Some evidence that CH is more important but more research is needed. Regardless, CCT is a great, readily accessible, simple measurement that should be included in all assessments of a glaucoma evaluation.
How do CH and CCT change during treatment?

- In general, lowering IOP probably increases CH.
- No medical treatments consistently show impact on CCT.
- More research is needed, especially with how to target CH.
- Maybe CH can become a part of what we target, rather than only IOP.

Conclusive pearls

- **Corneal Hysteresis**
  - New and potentially useful novel glaucoma risk factor
  - More studies will shed light on its importance in the next few years
  - May see more commercialization of CH measurement devices

- **CCT**
  - Very useful and well-established glaucoma risk factor
  - Susceptible to significant variability between measurements
  - (Shildkrot, 2004)
  - Thus, important to be trained well on obtaining accurate and precise measurements

Bibliography
Thank you!
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