

How do we know patients are at risk for glaucoma progression? <u>Well-established risk factors</u> • IOP • Age • Ethnicity/Race • Family history • **Centra Corneal Thickness (CCT)** <u>Possible novel risk factors</u>

Corneal hysteresis

2



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 \mu m 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 delayed intervention

4







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

7

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)

8

Failure to understand this ──→ delayed diagnosis ──→ racial disparity

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.



10

• 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

13



14

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 $\mu m/year$ posterior displacement of the anterior lamina cribosa surface









Age groups (years)	10-20	21-30	31-40	41-50	>50
IOPg (mean ± SD,	range, median) (mmHg)				
OD	15.6 ± 3.8 (7.8-25.7, 15.1)	14.1 ± 2.8 (7.8–22.8, 14.0)	14.1 ± 3.5 (5.7–26.6, 14.0)	14.9 ± 3.3 (7.4–23.8, 15.1)	15.4 ± 4.1 (7.5–25.4, 15.4
OS	15.3 ± 3.5 (9.1-26.9, 14.7)	13.9 ± 3.2 (3.0-23.2, 14.2)	13.5 ± 3.0 (5.9-25.9, 13.8)	14.5 ± 3.7 (7.7-25.1, 14.5)	15.3 ± 4.0 (6.9-25.2, 14.8
IOPcc (mean ± SD,	range, median) (mmHg)				
OD	15.3 ± 3.3 (8.2-24.1, 14.5)	15.3 ± 2.5 (8.4–20.3, 15.5)	15.1 ± 3.0 (8.6-24.6, 15.1)	16.0 ± 3.2 (8.6-23.4, 16.1)	16.6 ± 3.7 (8.5-27.4, 16.3
OS	15.7 ± 3.3 (7.9-25.3, 15.6)	15.6 ± 2.9 (8.1-24.5, 16.0)	15.1 ± 2.7 (7.8-24.8, 15.2)	16.1 ± 3.3 (9.5-25.7, 15.8)	16.9 ± 3.8 (8.0-25.1, 16.2
CH (mean ± SD, ra	nge, median) (mmHg)				
OD	11.2 ± 2.0 (8.0–15.8, 11.0)	10.0 ± 1.5 (5.9-14.2, 9.9)	10.1 ± 1.4 (7.2–13.8, 10.0)	9.8 ± 1.7 (6.8–14.1, 9.7)	9.7 ± 1.5 (6.3-13.2, 9.7)
OS	$10.6 \pm 2.2 \; (6.720.4, 10.7)$	$9.6\pm1.5(5.613.5,9.5)$	9.6 ± 1.4 (6.5–14.2, 9.4)	$9.5 \pm 1.6 \; (6.614.3, 9.4)$	9.3 ± 1.6 (5.0-13.1, 9.2)
FIMassov	et al., 2020, Internatio	nal Onbthalmology			



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)

19

 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

20

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, lowing 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?

22

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 (Shidkrot, 2004, J Glaucoma)...thus, important to be trained well on obtaining accurate and precise measurements

23

Bibliography

