Glaucoma Beyond IOP: Implications and Management of Progression at Low Pressure

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Progression at low IOP
- Reasons for progression at low IOP
- Treatment options
- Strategy for management

Measurement of Progression
- Clear and reproducible evidence of visual field deterioration, retinal nerve fiber layer thinning, or visible optic nerve head changes

What are potential causes of progression at low IOP?
- Is IOP really low all the time?
- Is IOP stability important?
  - Variability:
    - Long-term variability
    - Diurnal variability
    - Short-term variability

Disclosures
- No disclosures to report.

Glaucoma Clinic: Your Low IOP Patient

Normal tension glaucoma
Successfully-treated elevated IOP
Low tension glaucoma equivalent
Intermittent Angle closure

LOW IOP PATIENT
What are potential causes of progression at low IOP?

- Biomechanical Considerations
  - Central corneal thickness
  - Corneal hysteresis
  - Cerebrospinal fluid pressure
  - Normal aging
  - Vascular dysregulation
  - Systemic hypotension/hypertension
  - Obstructive sleep apnea
  - Migraine disorder

Biomechanical Considerations

- Mechanical failure and hypercompliance
  - A certain amount of increased stress or prolonged duration of stress may result in intrinsic damage to the laminar beams of the lamina cribrosa.
  - Hypercompliance may ensue, and the lamina cribrosa, having endured elevated IOP for prolonged period of time, is now deformed.
  - Burgoyne: these are changes in the macroscopic behavior of tissue that follow the onset of mechanical failure.

Biomechanical Considerations: Corneal thickness, rigidity, hysteresis

- Corneal thickness
  - A problem of inaccurate measurement?
  - Average around 540
  - Thin corneas may underestimate IOP
  - Thick corneas may overestimate IOP

Biomechanical Considerations: Corneal thickness, rigidity, hysteresis

- Measurement errors
  - Be aware of factors that can cause false readings of IOP:
    - Corneal edema (false low)
    - Soft contact lenses (false low)
    - Scleral buckle (false low)
Biomechanical Considerations: Corneal thickness, rigidity, hysteresis

- Corneal hysteresis:
  - A measure of the viscoelastic damping properties of the cornea
  - Can be estimated by analyzing the ability of the tissue to resist controlled deformation
  - Hysteresis is a physical property related to the ability of connective tissue to dampen pressure changes
  - Is the cornea a surrogate for the optic nerve head and lamina cribrosa?

Cerebrospinal fluid pressure

- Corneal hysteresis:
  - Multiple studies indicate an association between reduced CH and increased glaucoma risk
  - Zhang et al: (Accepted manuscript for Am J Ophthalmol, DOI: 10.1016/j.apo.2016.02.034): Corneal hysteresis and progressive retinal nerve fiber layer loss in glaucoma
  - Corneal hysteresis and IOP reduction:
    - IOP reduction may be less in eyes with higher hysteresis, but risk of progression may be lower, and vice-versa

Methods

- Retrospective chart analysis from Mayo Clinic’s EMR
- All patients who underwent LP
  - December 1, 1996 to December 31, 2009
- CSFP, Time and date of LP, age, sex, race, height & weight
- Subgroup of patients: IOP

Exclusion Criteria:

- All known medical diseases, surgeries, or medications known or theoretically could cause change in CSFP
  - Regardless of when LP was performed
- Anyone with more than one LP
- Patients grouped into 5 year age groups for comparison
  - Eventually, a 20-49 year age group was created as a representative sample

Results

Medical records from 33,932 subjects were reviewed

- Of these, 13,715 met all initial inclusion criteria
- After focusing on an adult-only population, N: 12,122
Fleischman, David - "Glaucoma Beyond IOP: Implications and Management of Progression at Low Pressure"

**CSFP and Age**

Relative to mean CSFP at age group 20-49 (mean 11.5 ± 2.8 mmHg) Mean CSFP declined steadily after age 50:
- 2.5% reduction at 50-54 age group (mean 11.2 ± 2.7 mmHg, p=0.001)
- 19.4% for the 85-89 group (mean 9.2 ± 3.0 mmHg, p<0.001)
- 26.9% for the 90-95 group (mean 8.4 ± 2.4 mmHg, p<0.001)

**Aging**

Every study examining axon count, or its imaging-surrogate of RNFL thickness, has determined a reduction in number or thickness with advancing age:
- Leung, et al: "Age-related changes of macular and circumpapillary RNFL measurements can be detected in normal eyes and can affect the analysis of glaucoma progression. The impact is more substantial in analyzing macular progression than circumpapillary RNFL progression." (Ophthalmology 120:2485-2492, 2013)

**Treatment Options for Progression at Low IOP**

- IOP variability
  - Prostaglandins, laser trabeculoplasty, surgery
- Biomechanical failure
  - Lower IOP target
- Thin cornea
  - Lower IOP target
- Edematous cornea, scleral buckle
  - Lower IOP target
- Reduced cerebrospinal fluid pressure
  - Lower IOP target

- Vascular dysregulation
  - Nutrition: fruits and vegetables, rich in flavonoids and anthocyanoides (antioxidants); flavanols (cocoa); omega-3-fatty acids; green tea
  - Magnesium supplementation
  - Calcium channel blockers:
    - Water-soluble: nifedipine
  - Ginkgo biloba
  - Brimonidine
- Nocturnal hypotension
  - Fludrocortisone or salt tablets
  - Avoid blood pressure medication in the evening
Treatment Options for Progression at Low IOP

- Obstructive sleep apnea
  - Polysomnography
  - Refer to primary care provider for evaluation and treatment, possibly with CPAP
- Migraine disorder
  - Aggressive treatment of migraine disease
- Uncharacteristic visual field progression
  - Re-evaluate all old and new medications and changes in patient’s health status

Treatment Strategies

- Assess severity of the disease:
  - Unless the patient has severe disease, you should have the time to acquire testing to determine progression velocity
  - Even with severe disease, set up visual field so that patient could succeed on testing (for example, 10-2 stimulus V full threshold)

- Treatment Strategies
  - After establishing progression velocity…
    - Decide, based on relevant clinical factors, which treatment option you intend to implement
    - Continue to follow closely

- General tips:
  - IOP tends to be the safest and most effective variable to adjust
  - Employ the assistance of primary care provider if recommending calcium channel blockers, blood pressure modification, herbal supplementation
  - If patient begins to progress after a period of stability, without changes in IOP, re-evaluate and re-assess patient’s medical history and medications
  - Frequent fields, OCT, photographs to assess if unconventional trials have beneficial effect. If not, Stop