Glaucoma For The " Regular" Optometrist

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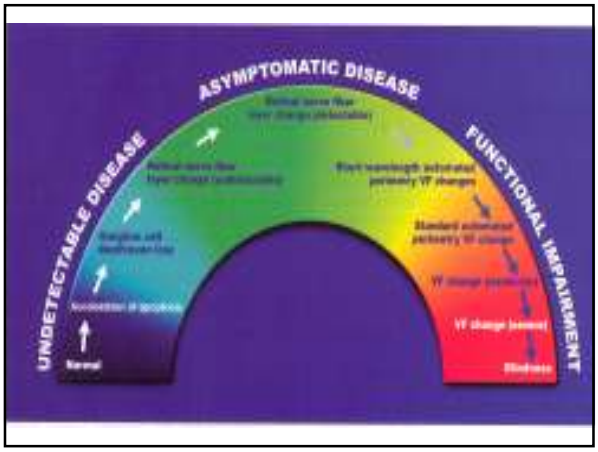
A Review Of Risk Factors

- FINDACAR
  - Family history
  - IOP
  - Nearsightedness
  - Diabetes/Vascular disease
  - Age
  - Corneal thickness
  - Asymmetry
  - Race



A risk factor analysis is critical

- For the diagnosis
- To increase your level of suspicion
- For initiating therapy
- For changing therapy

- BUT…are any of these more important than others?

Glaucoma Risk Factors

- FINDACAR

- The more risk factors one has, the more likely one is to develop glaucoma

- The more risk factors one has, the lower the IOP target should be

Reviewing The Glaucoma Studies

What do they all mean?

EMGT Conclusions

1) Reducing IOP (by 25%) prevents or slows VF defect and progression
2) For each 1mm of IOP reduction there is a 10% lower risk of VF loss
3) Study design and outcome show that these results are only due to IOP reduction (non IOP related factors showed difference between the 2 groups)
4) Tx effect was equal across age and glaucoma categories

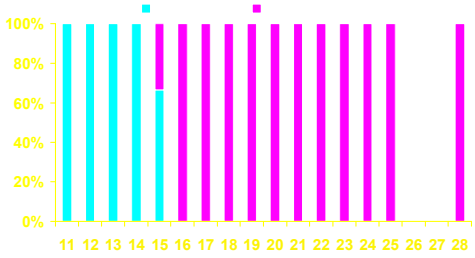
Low IOP Slows or Halts Vision Loss in Open-Angle Glaucoma

Miglior et al, AJO, 1994

Eric's spin on the EMGT

- 1-2 extra mm Hg may indeed be important- especially in advanced cases.
- For those pxs who need treatment, aggressive therapy is warranted
- It is probably better to treat early than late
- You do not necessarily need to wait until the VF defects arise before therapy is initiated
- The benefit of treatment does last throughout the lifetime of the px – just remember the risk/benefit

Aggressive IOP Lowering Needed In Advanced POAG IOP <15 mm Hg

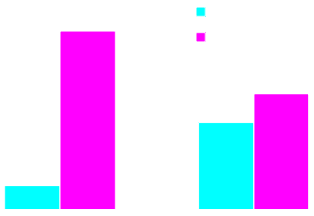


Shirakashi et al, Ophthalmologica, 1998

AGIS Results

- Pxs who achieved IOP < 18mm on 100% of f/up visits showed no VF progression (avg IOP 12.3mm)
- Pxs w/ IOP < 18mm on<50% of f/up visits showed VF progression (mean IOP 20.2mm)

Diurnal IOP Fluctuations Speed Glaucomatous Progression



Asrani et al, J Glauc, 2000

AGIS Results

- Diurnal Curve Is Real Important
  - Avg IOP of 15mm with a curve btwn 13mm – 17mm progresses less than if curve is btwn 11mm – 19mm
- The peak IOP is important
- Which tx best affect the diurnal curve?
- Also remember risk/benefit ratio

OHTS

- Goal of tx – 20% drop in IOP
  - 24mm target IOP

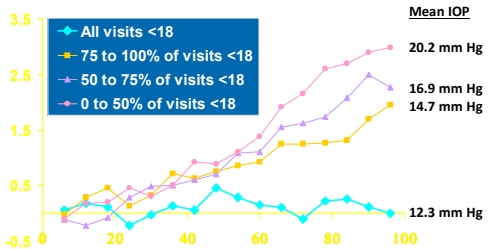
RESULTS: At 5 years

4.4% of tx group developed POAG

9.5% of no tx group developed POAG

So - lowering IOP in Oc Hx reduced the likelihood of glaucoma by 50% - RIGHT?

Consistently Low IOP Reduces Vision Loss



AGIS 7, AJO, 2000

OHTS – A Closer Look

- 90% of untreated group did not progress
- 95.6% of tx group did not progress
- It proved that ***in those individuals who are going to progress*** to POAG lowering IOP by 22.4% will delay the onset by at least 5 yrs.
- Who are " those individuals at risk"?

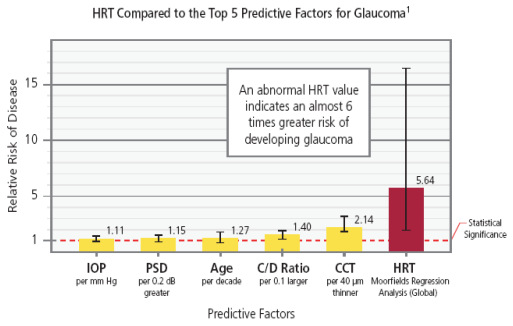
Factors to consider when setting a target IOP

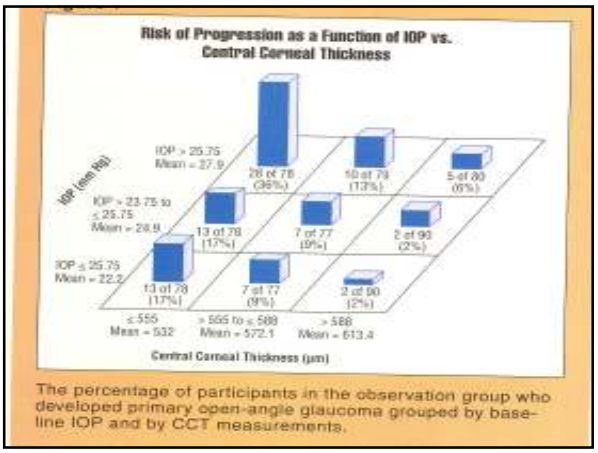
- Age
- Race
- ONH status
- VF status
- Systemic status
- Beginning IOP

OHTS – The Nitty Gritty

- The most predictive factors for conversion:
  - Older age
    - 22% increase/ decade
  - Larger horizontal and vertical C/D
    - 32% increase/0.1 larger
  - Higher baseline IOP
    - 10% increase/ mm Hg
  - Thinner corneas
    - 71% increase in risk/ 40 microns thinner

Risk Factors For Conversion





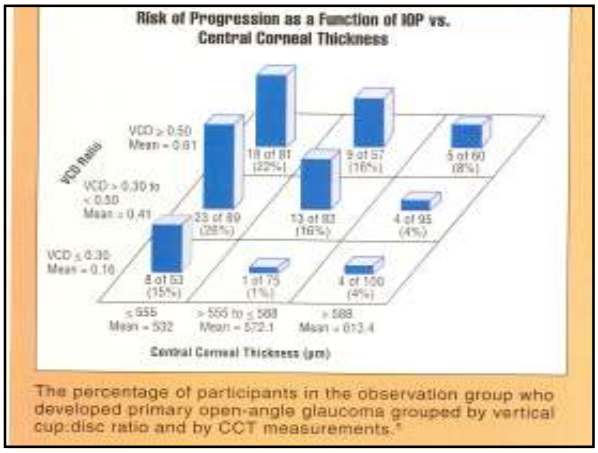
The percentage of participants in the observation group who developed primary open-angle glaucoma grouped by baseline IOP and by CCT measurements.

The pachymetry issue

- Juicy Data
  - 36% of pxs w/ IOP >25.75 AND K thickness < 555 microns developed POAG
  - 6% of pxs w/ same IOP but K thickness > 588 converted toPOAG
- Juicy Data II
  - 15% pxs w/ C/D .3/.3 and K thickness < 555 microns converted but
  - 4% of pxs w/ same disk parameters and K thickness> 588 microns converted

More Pachymetry Chatter

- African-Americans have thinner corneas
- Perhaps thin corneas translate to poor connective tissue at the disk as well
- Is there a fudge-factor for K thickness?
  - Baseline of 545 microns
  - Add or subtract 2.5mm Hg for every 50 microns deviation (Doughty and Zaman, Surv Ophthalmol, 2000).
- How should you use this data?



The percentage of participants in the observation group who developed primary open-angle glaucoma grouped by vertical cup:disc ratio and by CCT measurements.[1]

Corneal Thickness And Glaucoma The Latest Scoop

- CCT and VF loss –
  - CCT is a strong predictor for field loss in both NTG and POAG
  - CCT-adjusted IOP does not predict VF loss
    - Sullivan-Mee, Halverson, et.al. Optometry 2005;76:228-38.

Corneal Thickness and Glaucoma

- CCT and Visual Function In OHT pxs
  - OHT pxs with abnormal SWAP results had significantly thinner CCT than normals or OHT pxs with no VF defects
  - Abnormal VF – 545microns
  - OHT w/ normal VF – 572 microns
  - Normals – 557 microns
    - Medeiros, Sample, Weinreb – AJO Feb, 2003 135,No.2
- So????

CNTGS Results

- 35% untreated progressed over 3 yrs
- 7% of treated eyes progressed
- 30% IOP reduction achieved w/ drops, laser or surgery
- Showed that several VF were needed before progression was shown
- A very low IOP is beneficial

CCT And Glaucoma- More latest scoop

- RNFL thickness and CCT in OHT pxs
  - RNFL in OHT pxs with CCT < 555 was significantly thinner than in those with CCT >555.
  - RNFL of normals and OHT pxs with CCT >555 were similar
  - Points to an inherent structural predispositon to glaucomatous damage?
    - Kaushik,S, et.al, AJO May 2006, 884-890.

Predictive Factors For Progressing POAG

- Older age
- Advanced VF damage
- Smaller neuroretinal im
- Larger zone Beta
  - Martus, Jonas, et.al. AJO, June 2005
- Baseline IOP, *but not Mean IOP*
  - Martinez-Bello, et al, AJO March 2000.

CCT and Treatment Response

- OHTS group –AJO, November, 2004
- Pxs with thinner corneas responded better to PGA and beta-blockers
  - 1mm difference for beta-blockers
  - 1.5-2.5 mm difference for PGAs
  - 550 microns was tipping point
- Fan and Camras reported similar results with brimonidine (ARVO, 2004)
- Why??? And what clinical implications are there?

Risk factors for progression

- Predictive Factors for Progressive Optic Nerve Damage in Various Types of Chronic Open-Angle Glaucoma -
  - Martus, Budde, Jonas, et.al. – AJO 6/05
- POAG-
  - Older age
  - Advanced perimetric damage
  - Smaller neuroretinal rim
  - Larger Beta zone
- NTG-
  - Baseline disk hemorrhage

When deciding to treat …

- Identify…
  - Risk factors for conversion
  - Risk factors for progression
  - Risk factors for rate of progression
    - Initial peak IOP
    - Age
    - C/D ratio
    - Systemic/vascular status
  - Noscitur a sociis!

When Is The Peak IOP?

- 3,025 IOP readings on 1,072 eyes
- NTG, POAG, Pre-perimetric G, OHT
- Results:
  - Peak IOP – 7AM – 20.4%
  - Noon – 17.8%
  - 5PM - 13.9%
  - 9PM – 26.7%
    - Jonas, Budde, et al. AJO, June 2005;139:136-137

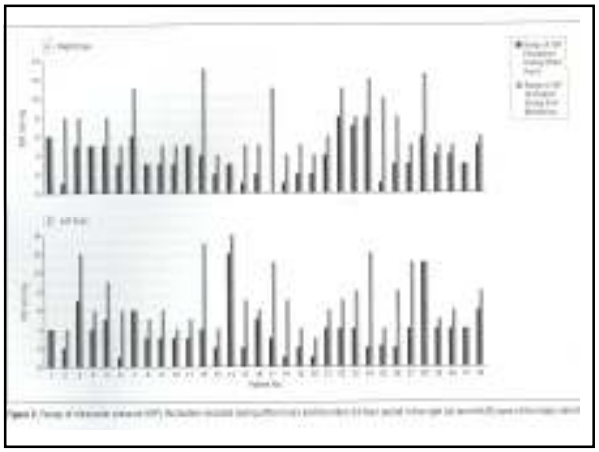
IOP and Glaucoma

- Which IOP is most important?
  - Mean IOP
  - Peak IOP
  - Trough IOP
  - IOP range
- Are we measuring it correctly?

Jonas study conclusion

- "Any single IOP measurement taken between 7AM and 9PM has a higher than 75% chance to miss the highest point of the diurnal curve."
- Stresses the need for serial tonometry.

- For pxs who showed progression of glaucoma despite IOP at acceptable range
  - 3% showed a peak IOP >21mm
  - 35% showed a range of IOP >5mm
    - Collaer, Caprioli, et.al, J Glaucoma 2005;14(3): 196-200
- Underscores the importance of serial tonometry *even in well controlled pxs*



"New" Goal of treatment in Glaucoma

- Low and *Stable* IOP
- Minimize the diurnal curve
- Prevent IOP peaks
- Maximize compliance

When should the target IOP be changed?

- VF progression (even at target IOP)
- Neuroretinal rim recession (even at target IOP)
- Parametric changes
- Long term stability – even if on multiple meds

General Rule #1

- 30% decrease as an initial target
- Target decrease from highest untreated IOP
- CNTGS, OHTS

Importance of IOP Stability

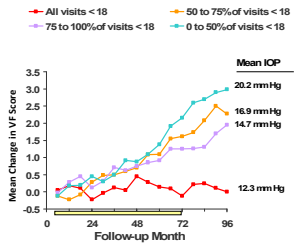
- IOP variation is a risk factor for VF loss in glaucoma
- VF protected best when pressures are consistently kept under 18 mm Hg
- Wide swings in IOP during the day or from visit to visit should be avoided
- Stabilizing IOP is vital

General Rule #2

- Mild glaucoma – decrease IOP 30%
- Moderate glaucoma – decrease IOP 40%
- Severe glaucoma – decrease IOP 50% (at least)

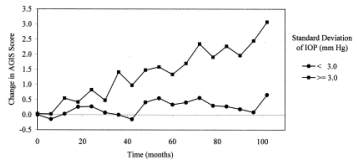
AGIS: Need to Maintain Low IOP Over Time

- ALT or surgery in uncontrolled glaucoma
- Target IOP <18 mm Hg
- 100% of visits <18 mm Hg: on average no loss in VF
- Any visits with IOP target not met: on average significant VF loss
  - 2-unit loss in VF over 7 years when target met at <75% of visits



CONCLUSION: Progression is minimized when IOP is kept consistently low (<18 mm Hg)

AGIS: Patients With Small IOP Variation Had Stable Fields



- Eyes with variation < 3 mm Hg: no average progression
- Eyes with variation ≥ 3 mm Hg: on average, significant progression

Eric's 7 Simple Rules For Treatment

1. Choose 30% IOP decrease as initial target
2. Squash the diurnal curve (Keep IOP peak <18mm)
3. Assess risk factors for progression and rate of progression
   (CT<555, IOP >26,C/D 0.5)

Treatment Paradigm Summary

- Mean IOP in study populations
  - Early treatment to lower IOP reduces and delays progression
  - NEI trials show better outcomes at lowest IOP
- IOP in individual patient
  - To preserve vision, every mm Hg matters
  - Individualized, low target IOP recommended
- New predictors of progression
  - Diurnal fluctuation and long-term variation in IOP within individual patients can cause glaucomatous damage
- Treatment goal: get IOP low, and keep it low

Heijl et al. *Arch Ophthalmol*. 2002; Kass et al. *Arch Ophthalmol*. 2002; Lichter et al. *Ophthalmology*. 2001; AGIS Investigators: 7. *Am J Ophthalmol*. 2000.

Eric's Rules cont.

4. If you are going to treat; treat aggressively
5. KISS
6. Be mindful of perfusion issues
7. Above all, do no harm

MSOffice1

Primary Medical Therapy

- **Building block approach**
- **Start with the STRONGEST FOUNDATION**
- **Efficacy Goals of Primary Therapy**
  - **Achieve lowest IOP on single agent**
  - **High response rate – every mm Hg matters**
  - **Maintain consistent long term and diurnal pressure lowering**

The Glaucoma Treatment Universe 2011

- Prostaglandins
- Alpha –agonist
- CAI
- Combo drugs
- Ginkgo , etc
- Beta-blockers
- Cardioselective beta-blockers
- ALT/SLT
- Trabeculectomy
- Nutrition issues

What if Target Pressure Is Not Reached With Even the Most Powerful Monotherapy?

- Add a second medication!

Treatment Paradigm, Part III

1. Prostaglandins alone
2. Brimonidine or beta-blocker alone
3. Prostaglandin + beta-blocker or brimonidine (unless 1 of these absolutely sucked!)
4. Consider CAI or Cosopt/Combigan if (3) is not successful

Primary Considerations in Choosing Adjunctive Therapy

- Efficacy when used with the first-line medication
  - IOP should be reduced by at least an additional 15% to a level as low as possible
  - A medication that is effective monotherapy, or when added to one medication, may not be effective when added to a different medication!
- Safety
  - Safety concerns increase with each additional medication: add the safest medication possible

Treatment paradigm, part IV

- If on 2 meds and target IOP not met…
  - 1. Consider 3rd drop (Betoptic S or CAI)
  - 2. Substitute Cosopt/Combigan for least successful drop
  - 3. Consider ALT or SLT
- What is maximum medical therapy nowadays?
- SLT/ALT and trabeculectomy should not be considered weapons of last choice or last chance

Treatment paradigm – Step 2

- Prostaglandins 1st
- If not successful – try another agent by itself: Brimonidine bid or timolol QAM or CAI BID
- If neither of these get IOP to desired level then add

Remember The Diurnal Curve!!!

- PGAs
- Trabeculectomy
- Brimonidine -*TID*
- CAI – *TID*
- What about beta-blockers?
  - BID vs QAM
  - ½% vs ¼%
  - Effect on diurnal curve

- *Systemic Adverse Effects of Beta-adrenergic Blockers: An Evidence-based Assessment (Lama, AJO Nov 2002)*
  - Many of the claimed adverse side effects of beta-blockers are not supported by clinical trials
  - Most anectodal claims
  - More patients may be eligible for beta-blockers
  - Careful medical hx and checking pulse rate and rhythm should be sufficient

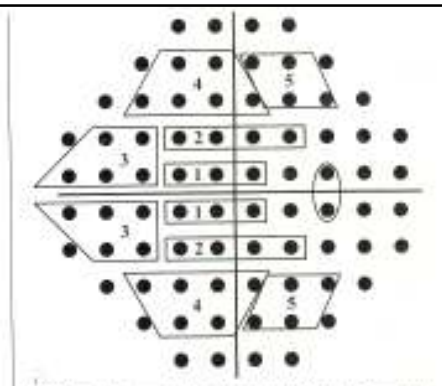


FIGURE 1. Representation of the point clusters that comprise the glaucoma hemifield test segments.

Visual Fields and Glaucoma

- Are they still cool?
- Are they considered the standard of care?
- How often?
- Do they better measure early detection or progression?

Which VF instrument is best?

- SAP, SWAP or FDT
  - FDT and SWAP similar in flagging abnormal locations
  - FDT defects were more extensive in 62%
- SWAP more specific and accurate than SAP but harder to administer
- FDT questionable in end stage glaucoma
- Use 10-2 strategy in advanced glaucoma

Are certain VF parameters more predictive for progression?

- Johnson, Sample et al. – AJO 8/2002 177-185
- Highest predictors of conversion
  - GHT "outside normal limits"
  - 2 hemifield clusters worse than 5% level
  - 4 abnormal (P<.05) locations on pattern deviation probability plot
  - Specificity increased with 2nd confirmatory VF test

What About Imaging Units?

- Are they essential?
- What do they do ?
- What do they don't do?
- Are they the standard of care?

2 Questions For The Audience:

- 1. What is your definition of glaucoma?
- 2. What is the pathology of glaucoma?
- 3. Is retinal imaging the standard of care for treating glaucoma?

RNFL and Glaucoma

- RNFL changes are early to occur in glaucoma
- Up to 50% of the retinal nerve fibers may be lost before a visual field defect is detectable
- Early detection of glaucoma by RNFL imaging and analysis leads to early treatment, improving the chance to delay or halt the disease progression

3 Phases of Glaucoma and Retina Patient Care

1. ASSESS – Risk Assessment at Initial Visit
2. DIAGNOSE – Moving past "suspect"
3. MANAGE – Track progression & monitor treatment

RNFL and Glaucoma

Glaucoma is a disease of the RNFL

- Axons of retinal ganglion cells form the retinal nerve fiber layer (RNFL)
- Glaucoma is characterized by loss of ganglion cells leading to loss of retinal nerve fibers

It's Like An Alphabet Soup!!!

- GDx
- HRT
- OCT
- RTA

- Are they all the same?
- Are they all different?
- Are there clinical studies to prove their claims?

ASSESS: The New OHTS Results

CLINICAL SCIENCES

Baseline Topographic Optic Disc Measurements Are Associated With the Development of Primary Open-Angle Glaucoma

The Confocal Scanning Laser Ophthalmoscopy Ancillary Study to the Ocular Hypertension Treatment Study

Linda M. Zangwill, PhD; Robert N. Weinreb, MD; Julia A. Beiser, MS; Charles C. Berry, PhD; George A. Cioffi, MD; Anne L. Coleman, MD, PhD; Gary Trick, PhD; Jeffrey M. Liebmann, MD; James D. Brandt, MD; Jody R. Piltz-Seymour, MD; Keri A. Dirkes, MPH; Suzanne Vega, MPH; Michael A. Kass, MD; Mae O. Gordon, PhD; for the Confocal Scanning Laser Ophthalmoscopy Ancillary Study to the Ocular Hypertension Treatment Study Group

Archives of Ophthalmology, September 2005