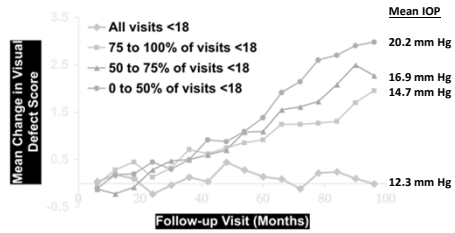


60 Minute Glaucoma Update

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Consistently Low IOP Reduces Vision Loss



AGIS 7, AJO, 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

However – Realini, Ophthal 2011

IOP DOES NOT FOLLOW A REPEATABLE PATTERN

Diurnal IOP performed on one day inadequately reflects diurnal IOP variability short term

Between visit agreement of IOP change was uniformly poor

No repeatable IOP pattern was discerned

There is a difference in diurnal IOP patterns from each visit¹

Time	Right Eye			Left Eye		
	Visit 1	Visit 2	Difference	Visit 1	Visit 2	Difference
0800	16.7±2.7	15.9±4.1	0.8	17.2±3.1	16.3±3.9	0.9
1000	16.8±2.7	15.3±3.4	1.5*	17.6±3.2	15.9±3.7	1.7*
1200	16.7±3.2	15.4±3.1	1.3*	17.0±3.1	16.1±3.4	0.9
1400	15.7±3.2	14.5±3.2	1.2	16.2±3.6	15.0±3.1	1.3
1600	16.0±3.0	15.1±3.3	0.9	16.2±3.2	15.4±3.4	0.8
1800	16.2±2.9	15.3±3.1	0.9	16.7±3.4	15.7±3.4	1.0
2000	15.9±3.0	14.9±2.9	1.1	16.5±3.1	15.1±2.9	1.4*

*P<0.05.

Reference:
1. Realini T, Wisneki RN, Wisneki S. Short-term repeatability of diurnal intraocular pressure patterns in glaucomatous individuals. Ophthalmology. 2011;119(1):47-51.

24 Hour IOP Control

How Important Is It?

How Can It Be Measured?

How Can Diurnal Spikes Be Best Controlled?

How IOP is Usually Measured

Typically a **single observation**

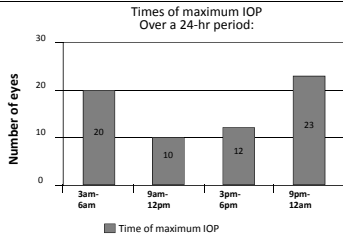
During **office hours**

A moment in time or representative of the entire day?

Are we missing spikes, peak, or elevated IOPs at other times of day?

7

Peak IOP Outside Office Hours for 2/3 of Eyes



Nakakura S, et al. *J Glaucoma* 2007; 16(2): 201-204.

8

IOP is Higher at Night

PURPOSE: To characterize the 24 hr pattern of IOP in untreated patients

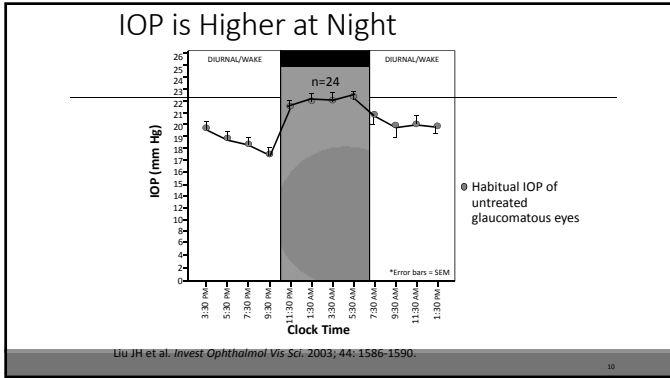
METHODS:

24 untreated patients with newly diagnosed glaucomatous optic discs and/or abnormal visual fields

24 hr IOP values obtained with a pneumotonometer at 2 hr intervals, in the sitting and supine position during the diurnal/wake period and in the supine position during the nocturnal/sleep period

Liu JH et al. *Invest Ophthalmol Vis Sci*. 2003; 44: 1586-1590.

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Observations

- Reducing IOP reduces risk of progression¹⁻⁵
- Peak IOPs often occur outside normal office hours⁶⁻⁹
- IOP during office hours does not provide a complete picture of diurnal and nocturnal IOP⁶⁻⁹
- What does this mean about your choice of medical therapy?

1. Hsieh A, et al. Arch Ophthalmol. 2002; 120(10): 1268-1279.

2. Akai M, et al. Arch Ophthalmol. 2002; 120(10): 701-713.

3. AGIS Investigators. Am J Ophthalmol. 2000; 130(4): 429-440.

4. Lottor W, et al. Ophthalmology. 2001; 108: 1943-1953.

5. CVIS Study Group. Invest Ophthalmol Vis Sci. 1994; 35(7): 257-267.

6. Nakamura S, et al. J Glaucoma. 2007; 16(2): 201-204.

7. Mwanza S, et al. Arch Ophthalmol. 2005; 123: 320-324.

8. Hughes E, et al. J Glaucoma. 2003; 12: 232-236.

9. Liu JH et al. Invest Ophthalmol Vis Sci. 2003; 44: 1586-1590.

Further 24 Hour IOP Data

- Nocturnal IOP 2-4mm Hg higher in G pxs than in normals
- Both have higher supine and nocturnal IOP
- Less of a trough at night
- More significant because BP rises at night

Sets up the perfect storm

Glaucoma Therapy and Nocturnal IOP

Beta-blockers – no nocturnal effect

Alphagan P – No nocturnal effect

CAI – 70% effect at night

PGA – 50% effect at night

CCT increases at night, but hysteresis doesn't

Diurnal IOP

So clinically...

- The rationale behind checking IOP at same time of day is not sound

Confirming IOP change by multiple measurements over time is more accurate and less likely to be affected by diurnal variability

Diurnal IOP

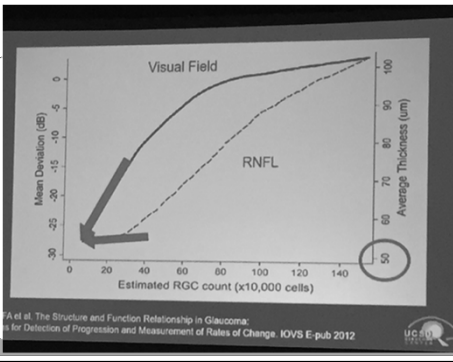
• So clinically...

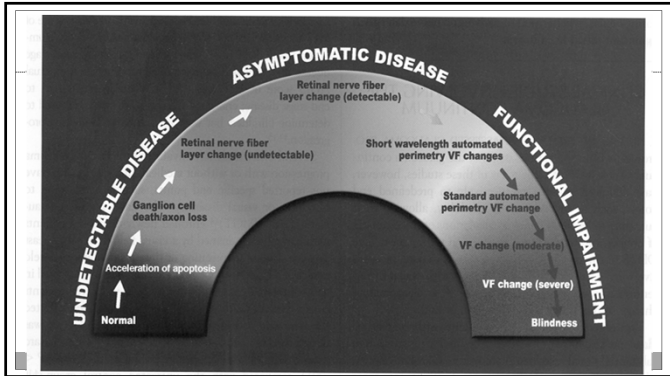
- The rationale behind checking IOP at same time of day is not sound

• Confirming IOP change by multiple measurements over time is more accurate and less likely to be affected by diurnal variability

Glaucoma Damage

- Occurs in a curvilinear/logarithmic plot as opposed to a linear fashion
- The further the disease has progressed the more rapid the RGC loss is
- Early glaucoma rate of RGC loss is 1.5%dB change/yr
- Late stage rate translates to 10%dB change/yr





Rate Of Progression

- RGC loss in normals -0.5% /yr
- RGC loss in Glaucoma - 3.5% / yr
- RGC loss in treated G - 1.5%/yr

Rate of Progression for Various Glaucomas

- NTG- 56% progression at 6 yrs
- POAG -74% progression rate (6 yrs)
- PXG - 93 % - progression rate at 6 yrs
- Pxs older than 68 progressed much faster compared to younger pxs

Progression according to CIGTS

- Seen in 56.7% in 6 years
 - Biggest risk factors
 - Inadequate IOP control
 - Disk hemorrhage
- Proving once again that if you diagnose a px with POAG REALLY treat them!

Speaking of NTG...

- Do we know anything new about it?
- Brand new 8 year data
- Over half progressed
- Thinner corneas and those with disk hemes more likely to progress
- Progression defined as either disk or VF changes

More New NTG stuff

- Peak IOP in progression group - 17.6mm Hg
- Peak IOP in non-progressors - 15.8mm Hg
- Mean IOP in both groups - ~13.1
- So consistently low IOP is crucial
- Squash the spikes, set a **LOOOW** IOP
- Age of pxs didn't matter

Treatment Considerations in NTG

- Avoid beta-blockers
- Keep Diurnal Curve Tight!!
- Choose a Low Target and Identify The Peak

**Neuroprotection –
Does it actually exist?**

- Well, does it?

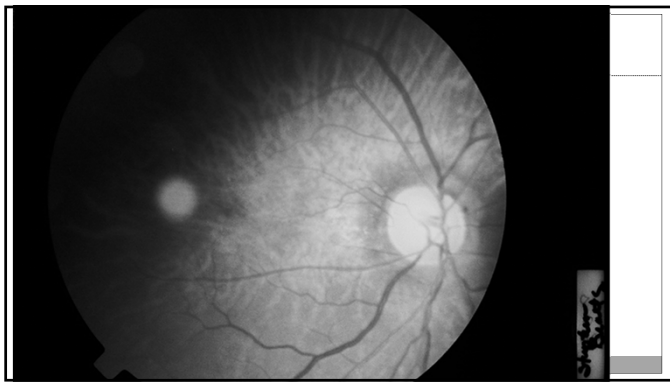
**Effect of Brimonidine on retinal vascular autoregulation..(Feke,
Bex et al, AJO 7/14)**

- NTG study
- 50% of pxs in study exhibited poor autoregulation (vascular dysregulation)
- Treated with Brimonidine 0.15% for 8 weeks
- 14/17 returned to normal autoregulation
- Mean IOP was 1.2mm lower
- No alteration in visual function

Brimonidine and the LoGTS

- Brimonidine was superior at preserving VF over a 3 year period as compared to Timolol ½%
- Yet Timolol reduced IOP by 1.5 more mm.
- So?>?>?... Does neuroprotection exist?

Peripapillary Atrophy in Glaucoma



Relationship between Beta zone PPA and POAG

- Sullivan-Mee, Pensyl et al – AJO 6/15
- Eyes with zone beta have decreased juxtapapillary choroidal volume
- Eyes with POAG have worse choroidal volume than those with OHT or normals- IF A ZONE BETA IS PRESENT!!!
- If no zone beta the choroidal volume then the choroidal volume was not different between the 3 groups
- Sooo...

Relationship between Zone Beta PPA and POAG

- Beta zones MAY be a biomarker for decreased choroidal volume
- Decreased choroidal volume MAY be a biomarker for vascular compromise
- POAG pxs with vascular compromise tend to develop VF loss at a greater rate
- SOOO...??? Clinically???
- OCTA will provide us with more evidence of this

Disk hemorrhages and Rate of Progression (Medeiros et al)

- Cohort of the DIGS
- Pxs followed for 8 years for VF progression (using the VFI)
- 20% had disk hemorrhage
- Eyes with disk heme had more than double the rate of VF loss
- Eyes w/ more than 1 disk heme showed an even higher rate of VF progression
- Persons with disk heme in general had a more severe glaucoma

Compliance, adherence and side effects of therapy

- Compliance decreases the more bottles Rx'd
- Robin – Each extra bottle used decreased compliance by 1/3
- The more topical meds used the more ocular side effects occur
- OSD in G pxs (way) higher than initially thought
- 60% of G pxs use ocular lubricants

What are the biggest barriers to proper compliance?

- 1. Forgetfulness
- 2. Ability to put drops in
- 3. Unaware of the importance of the drops
- Cost was not in the top 5!!!

Tricks To Increase Compliance

- Improved and increased Dr/Px Communication
- Improve px education as to what Glaucoma is
- Discussion on consequences of untreated glaucoma
- Be a partner with your patients
- Medication review at EVERY VISIT
- More frequent visits??

What Does This Mean To Doctors?

- Rethink Maximum Medical Therapy
- SLT Earlier
- Doctors must do more to stress adherence and look for side effects

Glaucoma Effect on Quality Of Life

- Way Higher than previously thought
- Glare Complaints in >50%
- Peripheral Vision Complaints >22%
 - Inf field defects are more bothersome to pxs
- 30 of 471 drivers stopped driving at 54 months due to increased mean VF defects or drop in VA
- What does this mean to us?

By The Way...

- Traditional White-on-white SAP predicted change in Quality Of Life better than FDT perimetry (AJO 1/15)

The Structure vs Function Dilemma

- Structural damage leads to functional damage
- Do they always correlate though?

- If they don't why???

Elasil, Wang et al , (AJO, May 2014)

- Conclusion – “In POAG substantial RNFL thinning or structural loss appears to be necessary before functional visual field defects become detectable.”
- Study showed that there are tipping points on RNFL thickness after which VF defects appear
 - AVG mean RNFL thickness 89 microns BUT>>>
 - Superior RNFL tipping point was 100 microns
 - Inferior RNFL tipping point was 73 microns

Clinically Important???

- What is the significance of this data?
- Does this give greater import for 1 test over another?

Speaking of Structure vs Function..

- Banegas SA, et al. – J Glaucoma May 2015
- Compared VF, OCT and Stereo Photographs for their ability to pick up progression
- 68% of progressive cases identified by OCT were initially classified as G suspects
- 61% of progressive cases identified by VF were initially classified as POAG

Conclusion

- “Progressing Eyes detected by OCT had a higher mean RNFL thickness (>83 microns) and higher mean VFI than progressing eyes detected by VF or stereophotos.”
- Soooo....
 - OCT is more likely to detect progression in pre-perimetric disease
 - VF and Photos better at detecting progression in more advanced stages of the disease

- This gives further credence that ALL 3 of the tests have value INDEPENDENT of each other!!

VF Progression in POAG

- 1 more time!
- The percentage of pxs showing substantial VF IMPROVEMENT over 5 years was basically THE SAME as those who showed VF loss over a 5 year period.
- Musch, Gillespie, et al AJO, July 2014)
- After 5 years though the risk of VF progression increases and improvement decreases
- Low and stable IOP is the key

So Now What?

- Aggressively reducing IOP in these pxs slowed down rate of progression
- At least 4 VF tests were needed to assess progression
- Substantially lowering IOP in these pxs is recommended

IOP 20mmHg, CCT 500μ

Glaucoma Risk Estimator						
Age	RIGHT EYE MEASUREMENTS			LEFT EYE MEASUREMENTS		
	1 st	2 nd	3 rd	1 st	2 nd	3 rd
70						
Untreated Intraocular Pressure (mm Hg)	20	20	20	20	20	20
Central Corneal Thickness (microns)	500	500	500	500	500	500
Vertical Cup to Disc Ratio by Contour	0.55			0.55		
Pattern Standard Deviation						
<input type="radio"/> Humphrey <input type="radio"/> Octopus loss variance	1.0	1.0		1.0	1.0	

Glaucoma risk is 20.7%

Ocular Hypertension Threshold to Treat Calculator

- Similar to the Glaucoma Risk Calculator
- Helps Dr decide at which maximum IOP px should require treatment
- Uses different dynamics to help Dr make treatment decision

• <http://oil.wilmer.jhu.edu/threshold>

Threshold To Treat calculator

- Age
- Pattern Standard Deviation (0.5-4.0)
- Central Corneal thickness
- Vertical cup-to-disk
- Threshold for 5 year risk of progression

- Provides you with Estimated Threshold To Begin Treatment
 - The IOP at which you should be concerned

Statin Use and POAG

- Stein et al, Ophthal 2012:119
- Risk of OAG decreased 0.3% for every month of statin use
- Pxs had 8% lower risk of developing POAG if on statin for 2 years as opposed to those who received no statin
- Risk of progression from G suspect to POAG decreased 0.4% for every month of statin usage
- 9% lower rate of conversion over 2 years as compared to those who did not use statins
- No difference in surgical rates

So Clinically...

- Is hyperlipidemia bad???

- Is it countered by the use of statins???

Katz – J Glaucoma Sept 2012

- Compared SLT to PGA
- Followed for 1 year
- SLT was 360 degrees ; 1 tx
- Add'l meds or tx could be used if target IOP not met

PGA vs SLT as primary therapy

- IOP drop
 - 4.3 mm if SLT only
 - 3.9mm if SLT combined to PGA
 - 6.2mm if SLT combined with other G meds!
- Previous studies showed 6-8mm drop w/ SLT
- Higher IOP pre-procedure; better response to laser

Results

- | | |
|--|---|
| <ul style="list-style-type: none">• SLT group• Baseline IOP – 24.5• Median IOP post-tx<ul style="list-style-type: none">◦ 18.2• 25.8% reduction
• 11% required add'l SLT | <ul style="list-style-type: none">• PGA group• Baseline IOP – 24.7• Median post-tx IOP<ul style="list-style-type: none">◦ 17.7• 28.3% reduction
• 27% required add'l meds |
|--|---|

So if SLT is so great why isnt it used more?

- Doctor bias in training
- Pxs associate laser with surgery
- Confusion with AMD and DR treatment

- Reimbursement issues???

New SLT vs PGA study

- Eyes either got PGA or SLT as initial therapy

- Similar IOP drop -27%- out to 1 year

- 0 serious complications in SLT group

- What does SLT do to blunt 24 hr curve?
- Does SLT improve compliance?

Final Thoughts on SLT

- Gonioscopy is key to procedure
- No side effects
- Improves compliance
- Failure is often due to inadequate therapy
- Movement moving to 360 degree therapy
- Is it really as good as a drop?

- What do y'all think?
