Detecting Visual Field Progression in Glaucoma

Danica J. Marrelli, OD, FAAO, AAO Diplomate
University of Houston College of Optometry

Disclosure

• I have received speaking and/or consulting fees from:
  – Carl Zeiss Meditec**
  – Aerie Pharmaceuticals, Inc.
  – Allergan
  – Bausch & Lomb
  – Novartis

Glaucoma

• A chronic, progressive disease of retinal ganglion cells that results in characteristic optic nerve and retinal nerve fiber layer changes and corresponding visual field loss
Glaucoma Progression

"Once the diagnosis of glaucoma has been made, the MOST IMPORTANT remaining question is whether the disease is stable and the therapy/compliance are sufficient, or whether the disease is progressive and the therapy in relation to the life expectancy has to be intensified."

Progression of Glaucoma, World Glaucoma Association, 2011 Kugler Publications

Progression of Glaucoma

"Although most glaucoma patients will show some evidence of progression if followed long enough, the rate of deterioration can be highly variable among them. While most patients progress slowly, others have aggressive disease with fast deterioration which can eventually result in blindness or substantial impairment unless appropriate interventions take place."

Detection of visual field progression in glaucoma with standard achromatic perimetry: A review and practical implications

Korey Yuuki Hikosaka, Yutaka Nishizawa, Akimasa Ishikawa, Joseph C. Ciulla

Fig. 1. Schematic demonstrating potential sources of progression with regard to visual function in the individual with glaucoma over time. Serially progressive glaucoma is the most likely to result in visual disability compared to many other disease. Serial deterioration is more likely to affect visual disability compared to their intervention.
WGA Consensus Statements on Structure & Function

• Both ON structure and function should be evaluated for detection of progression
• Currently, no specific test can be regarded as the perfect standard for determination of progression
• Progression detected by functional means will not always be corroborated using structural tests, and vice-versa

WGA Consensus Statements

• The use of standard automated perimetry as the sole method for detection of change may result in failure to detect or underestimation of progression in eyes with early glaucoma damage.
• Progressive structural changes are often but not always predictive of future development of or progression of functional deficits in glaucoma.

FUNCTION

• Previously believed that only advanced glaucoma impacts patient’s ability to function. More recent studies have demonstrated that early glaucomatous VF loss has an impact on the patient’s ability to function
  – Activity limitation
  – General health, lifestyle, emotion
Trends in Use of Ancillary Glaucoma Tests for Patients with Open-Angle Glaucoma from 2001 to 2009

Joshua D. Sain, MD, MS, Nishi Takkar, MA, Alejandra M. LeFevre, BS, Bu Nan, PhD, Paul R. Leber, MD

Results: For patients with OAG, the odds of undergoing VF testing decreased by 36% from 2001 to 2006, by 10% from 2006 to 2008, and by 6% from 2008 to 2009. By comparison, the odds of having ODI increased by 100% from 2001 to 2003, by 24% from 2003 to 2006, and by 14% from 2001 to 2006. Probabilities of undergoing FP were relatively low (13%–15%) for both provider types and remained stable across the decade. For patients cared for exclusively by optometrists, the probability of VF testing decreased from 66% in 2001 to 64% in 2008. Among those seen exclusively by ophthalmologists, the probability of VF testing decreased from 83% in 2001 to 81% in 2008. The probability of having ODI increased by 46% over the decade for patients of optometrists and from 30% in 2001 to 46% in 2008 for patients of ophthalmologists. By 2008, patients with OAG receiving care exclusively by optometrists had a higher probability of undergoing ODI than VF testing.

Conclusions: From 2001 to 2009, ODI increased dramatically whereas VF testing declined considerably. Because ODI has not been shown to be as effective as detecting OAG or disease progression compared with VF testing, increased reliance on ODI technology, in lieu of VF testing, may be detrimental to patient care.

Ophthalmology Volume 119, Number 4, April 2012
WGA Consensus Statements

• A statistically significant change in structure and/or function is not always clinically relevant.
• Life expectancy should be considered when evaluating the clinical relevance of a structural and/or functional change in glaucoma.
• Structural and/or functional testing should be conducted throughout the duration of the disease.
  — Detection of progression is more difficult in eyes with advanced disease

When Should We Suspect Progression?

• Rates of blindness in POAG are relatively low
  — @ 20 years
    • 1965-1980: 25.8% blind in one eye
    • 1981-2000 13.5% blind in one eye


Risk Factors for Progression

• Clinical risk factor assessment in glaucoma serves two roles:
  1. Prognostic information
  2. A basis for disease management
• Risk factor assessment should take into account
  1. The strength of the risk factor
  2. The practicality & potential harm of reducing that risk factor
Risk Factors for Progression

- Higher mean IOP
  - Higher IOP fluctuations
- Thinner CCT in patients with higher baseline IOP
- Presence of pseudoexfoliation
- Presence of disc hemorrhage
- Older age
- Lower ocular perfusion pressure
- Advanced visual field at presentation
- Family history of glaucoma (1st degree relative)

IDENTIFYING VISUAL FIELD PROGRESSION

- Much more difficult than detecting loss
- Background of dynamic “noise”
- No algorithm uniformly agreed upon for detecting change
- Three main changes:
  - Deepening of defect
  - Enlargement of defect
  - New defect

IDENTIFYING PROGRESSION

- Long-term fluctuation
  - The single biggest problem in determining progression
  - Deeper defects: more long term fluctuation
  - More advanced glaucoma: more long term fluctuation, more fatigue
IDENTIFYING PROGRESSION

Progression of VF
Functional Progression - WGA

- Standard white-on-white automated perimetry (SAP) covering at least 24° is preferred
- Decisions on progression should NOT be made by comparing only the most recent VF with the one before.
- Suspected progression should be confirmed with repeat testing.

Frequency of VF Exams

- Baseline Data – first 2 years
  - At least 2 reliable VF within the first 6 months
    - 3 within first 6 months when there is a high likelihood of visual disability
  - At least 2 further VF within the next 18 months
  - VF testing should be repeated sooner than scheduled if possible progression is identified
  - SIX VF within the first 2 years allows the clinician to identify rapid progression
Frequency of VF Exams

• Follow-up data (after first 2 years)
  – Frequency of testing should be based on the risk of clinically significant progression (based on extent of damage, life expectancy)
  – In low- and moderate-risk patients, VF should be at least once per year
    • Sooner if possible progression seen on VF –OR- on other clinically relevant observations
  – In high risk patients, subsequent VF should be at least 2 per year

VF Progression: EA vs TA

• Event analysis (EA): change from baseline greater than a predefined threshold based on test-retest variability according to the level of damage
• Trend analysis (TA): rate of change over time; significance is determined by both the magnitude of change and the variability of the measurement
Event Analysis


VF Progression: EA vs TA

• In general, event analysis is used for follow-up when fewer VF are available
  – When suspected progression is identified, at least TWO further tests should confirm that
• In general, trend analysis (rate) is used later in the follow up (later than 2 years)

Functional Progression - WGA

“Use available software support. Subjective judgment of VF printouts is unreliable and agreement among clinicians is poor.”
GUIDED PROGRESSION ANALYSIS (GPA)

- Humphrey Field Analyzer
  - Based on results of GLAUCOMA patients from mild to advanced disease
  - Patients took 12 different visual field tests within a 4 week period
  - Developed a model for what is “expected” test-test variation for patients with glaucoma

GPA

- Uses 2 baseline exams (any strategy)
  - Follow up tests must be SITA-Standard or SITA-Fast (all same strategy)
- Symbols used on Follow Up Tests
  - Open Triangles
  - Half Triangles
- Messages
  - Possible Progression
  - Likely Progression
- Rate of Progression

Elements of GPA 1-Page Summary Report

- Baseline Tests
- VFI (Trend Analysis)
- Today’s VF (Event Analysis)
The VFI Regression Plot
- VFI plotted against age
- Extrapolates rate of change up to 5 years

The VFI Bar
- Historical and projected VFI loss

Sample: Progression Detected
Sample: High LTF, No progression
Sometimes the messages are contradictory
RATE OF PROGRESSION: \(-1.4 \pm 0.7\) %/YEAR (95% CONFIDENCE)
SLOPE SIGNIFICANT AT P < 0.05
Functional Progression - WGA
• Do not rely on VF reliability indices
• Stick with the same test throughout the follow-up period
• In advanced glaucoma, there may be a benefit to testing using a 10-2 strategy in a minority of patients.

Pearls for VF Progression – Event Analysis
• About 5% chance that a single point will fall outside the expected change on a single test
  – Much less likely that same point will do the same in a subsequent test
  – If point is in same region of VF as existing defect – much more likely to be “real” change
  – Point in central 10 degrees exceeding expected change is much more likely to be “real” change

Alternatives to GPA
• Non-parametric Analysis (MD, VFI, PSD)
  – 3 baseline VF
  – Suspected progression:
    • 1 field with MD worse than lowest MD of baseline tests
  – Possible progression:
    • 2 consecutive fields with MD worse than lowest MD of baseline tests
  – Likely progression:
    • 3 consecutive fields with MD worse than lowest MD of baseline tests
<table>
<thead>
<tr>
<th>GPA</th>
<th>Suspected Progression</th>
<th>Possible Progression</th>
<th>Likely Progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;/= 3</td>
<td>△</td>
<td>△</td>
<td>△</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NPA</th>
<th>&gt;/= 3 consecutive fields with MD worse than lowest of 3 baseline VF</th>
<th>&gt;/= 3 consecutive fields with MD worse than lowest of 3 baseline VF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-Up 1: No Suspected Progression</td>
<td>Follow-Up 2: Suspected Progression</td>
<td>Follow-Up 3: Possible Progression</td>
</tr>
<tr>
<td>Baseline</td>
<td>Follow-Up 1: No Suspected Progression</td>
<td>Follow-Up 2: Suspected Progression</td>
</tr>
<tr>
<td>GPA</td>
<td>GPA</td>
<td>GPA</td>
</tr>
<tr>
<td>GPA</td>
<td>GPA</td>
<td>GPA</td>
</tr>
</tbody>
</table>

NPA can also be applied to PSD (for MD up to ~ -10dB) and/or to VFI
Alternatives to GPA

- Deepening of existing scotoma at 2+ points by 10+dB
- Expansion of 2+ points adjacent to baseline scotoma by 10+dB
- New scotoma
  - 2 or more adjacent points with p<1% on PD probability plot
- Change of 1 point in central 10° of 10+dB in a previously normal location

Example
Drawbacks of GPA

• Cannot be used in advanced glaucoma
• Trend analysis may not be able to detect progression in patients with smaller paracentral scotomas (often limited to a single point)
Trend Analysis

- Need a minimum of 6-8 tests for valuable slope
- Cut-off value of 1dB/yr is probably a reasonable, clinically relevant cutoff value
- Greatly influenced by outliers – WATCH FOR OUTLIERS

Excluding non-representative exams
There’s Progression! What Now?

- Think there is progression? VERIFY!
- Know there is progression?
  - Did glaucoma cause the progression?
- Glaucoma caused the progression
  - Consider a change in treatment

Think There’s Progression? Verify!

- Structural tests: Confirm with additional test
- Visual field: Confirm with at least two additional tests

• FAILURE TO CONFIRM PROGRESSION is evidence of stability!

There’s Progression: Is it Glaucoma?

- Structure:
  - Other causes of structural changes? Esp important in polarimetry
- Function:
  - Optical explanation LESS LIKELY
    • Equal damage to total and pattern deviation plots
    • Individual test locations with normal sensitivity
    • Increased PSD
    • Absence of media opacities (Duh!)
  - Optical explanation MORE LIKELY
    • No increase in PSD, in cases where MD is better than -10dB
Glaucoma Caused the Progression: Now What?

• Factors to Consider:
  – Compliance
  – Glaucoma Stage
  – Rate of progression/ time to “event”
  – Location of scotoma
  – Life expectancy of patient
  – Patient preference
  – Potential impact of next therapeutic step

New Baseline!!

• Every time a target IOP is adjusted or there is a significant change in the therapy, the tests need to be re-baselined
  – Last 2 tests that determined/confirmed progression can be the new baseline exams
  – Frequency of testing needs to increase again

Thoughts on Treatment

• ASSESS COMPLIANCE!!!!
  – Poor compliance:
    • Important conversation regarding compliance
    • Emphasize importance of compliance
    • May or may not need to lower target IOP
    • Consider laser trabeculoplasty or surgery
  – Good compliance:
    • Lower target IOP
    • Added medication
    • Laser trabeculoplasty or surgery
Thank you for your attention!

Questions?
Email me:
Dmarrelli@uh.edu