

Computerized Assessment of Visual Field Progression

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Everyday clinicians who care for patients with glaucoma make disease management decisions based on visual field testing. The detection of glaucomatous progression is crucial to important decisions: Is the IOP low enough? Is it time to initiate treatment? Should the patient have surgery? There is hope that computerized analyses of visual fields will improve our ability to recognize progression to guide these decisions. This "Peer Review" column addresses recent work on computerized visual field analysis methods. Is help on the way?

—Barbara Smit, MD, PhD, section editor

THE PROBLEM WITH GLAUCOMATOUS PROGRESSION

Although much work has been done in the development of new technologies to detect and measure the progression of glaucoma, standard "white-on-white" automated visual field testing remains the best-studied way to assess glaucomatous progression. One might assume that progression assessment using standard visual field testing would be fairly straightforward. Data are numeric, and untreated glaucoma worsens on average by at least 1 to 2 db per year, which is well within the sensitivity range of these tests. However, many factors confound accurate progression analysis using the data typically generated. Visual field tests are inherently variable, particularly in the locations of the field that are abnormal. Media opacity development, such as cataract, can affect the results. Most importantly, distraction, inattentiveness, or other factors involving the patient's participation make visual field tests unreliable. As a result, even among expert analyses of visual field series, there are high levels of disagreement as to whether or not glaucoma is progressing in a particular patient. For example, Viswanathan et al found that, even with a reliable series of standard visual fields analyzed by different expert clinicians, correlation kappa levels were only .32, not a high level of agreement.¹

In light of these difficulties, computer-assisted analysis programs have been developed with the intent of improving progression assessment. It is to be hoped that these programs can correct the "noise" and the distraction of variability in visual field data. This in turn can reveal changes within the data that indicate true progression, which would otherwise be difficult for a skilled human analyzer to detect. Several different approaches of computer-assisted analysis have been designed over the years, including some specifically for use in large multicenter studies of glaucoma, but only a few have been incorporated into widespread clinical use. Two major approaches to evaluating the progression of visual field defects have been employed. Event-based change analysis asks the question, "Has existing glaucoma progressed?" by comparing a visual field result to a prior or baseline visual field. Trend-based analysis looks for the rate of change in the visual field over time.

EVENT-BASED CHANGE ANALYSIS AND GLAUCOMA PROGRESSION ANALYSIS SOFTWARE

Glaucoma Progression Analysis (GPA) was the first event-based change analysis software to be put into widespread clinical use. GPA was designed to be used with Humphrey field analyzers (Carl Zeiss Meditec, Inc., Dublin, CA). Research using GPA can likely be extrapolated, with some caveats, to other event-based analysis tools. GPA identifies significant pointwise progression based on statistical probabilities using at least three sequential visual fields. Nouri-Mahdavi et al compared the performance of GPA, the Advanced Glaucoma Intervention Study (AGIS) method for identifying progression, and point-wise linear regression in predicting visual field progression. They found that GPA detected true clinical progression slightly more often than the other two methods, with a false positive prediction between 1% and 3%.² When GPA was compared with

evidence of clinical progression using expert opinion as the reference standard, Arnalich-Montiel et al³ found that there was high correlation of progression detection (kappa index of 0.87 ± 0.06) where two consecutive visual fields showed progression out of a series of five.

Sensitivity and specificity were 93% and 95%, respectively, in that case. When three fields were needed to show progression, the correlation was not as strong.

Suffice it to say, these and additional research articles show that, in comparison to expert analyses and other research-based progression analysis tools, GPA shows comparable results. Other new research with practical clinical applications involves how GPA interacts with more traditional methods. In a recent analysis by Tanna et al,⁴ five glaucoma experts evaluated a set of visual fields for progression. Agreement was not enhanced by the addition of GPA to subjective analysis of the same series of visual fields, both among and within each participant's analyses. Similarly, Lester et al⁵ found that, with three different experts, using GPA printouts actually led to less inter-observer agreement regarding progression than with the standard Humphrey field analyzer overview printouts with the same series of visual fields. In these studies, computerized assessment did not lead to improved agreement among experts as to whether progression was occurring.

TREND-BASED PROGRESSION TOOLS

It has been suggested that, in clinical practice, global trend-based analyses for progression are more practical and may be more specific to detect glaucoma progression, although they may be less sensitive in comparison to event-based analysis. The standard global indices of mean deviation and pattern standard deviation have been used for many years and, in general, have been found to be less sensitive than event-based analysis in detecting progression.⁶

Newer, more sophisticated trend-based analyses are now available. Visual Field Index (VFI) is a global index that assigns a number between 1% and 100% based on an aggregate percentage of visual, function with 100% being a perfect age-adjusted visual field. Central visual field points are more heavily weighted, and the percentage of visual field loss is calculated based on pattern or total deviations depending on the depth of loss. When a minimum of five examinations are completed over 3 years, the VFI values of all of the examinations are plotted as a function of patient's age to help make judgments about the clinical significance of the velocity of progression.

In one of the original research projects on VFI, Bengtsson Heijl found that the progression rates calculated by VFI were much less affected by cataract development and cataract surgery than the traditional mean deviation index

or the pattern standard deviation.⁷ In comparison to expert opinion about progression, Ang et al found that VFI analysis was quite specific at kappa values of .93 but not very sensitive at only .45, which was similar to the same fields analyzed with GPA.⁸ VFI also does not appear to be immune to artifacts solely due to the severity of disease. Rates of progression calculated by VFI appear to decrease as the glaucoma becomes more severe, independent from expert judgment of the velocity of clinical progression.⁹

COMPARISONS: WHICH IS BETTER AND WHEN?

This information raises the interesting question: which method, event-based or trend-based, is better to detect progression in specific situations? Several recent research projects have compared GPA and VFI analysis to give more guidance on clinical use. Of particular interest is whether, with a given set of visual fields, one method is more specific or sensitive than the other to detect progression. It is also thought that, as the visual field becomes more severely abnormal, trend-based analysis becomes more sensitive to detect change.¹⁰ This is why the VFI analysis in particular was constructed to weigh the central points of the visual field more heavily in its progression-detection algorithm.

In a direct comparison of methods, Casas-Llera et al found that GPA analysis indicated probable clinical progression in 26 of 90 eyes, whereas VFI indicated progression in 12 of 90. No patients were found to have progression by VFI that were found stable by GPA. In this series, VFI was found to be much more accurate in determining the rate of progression when compared with the mean deviation index.¹¹ In contrast, Lester et al found no statistically significant difference in the detection of progression in a series of visual fields analyzed by nine different experts using the Humphrey visual field analyzer overview printouts, GPA, or GPA2 printouts, which include the GPA plus the VFI analysis.¹² In a long-term retrospective study involving an average of 10 visual field tests per patient, Giraud et al found a similar indication of progression when comparing GPA and VFI, but GPA failed to detect progression in later-stage disease, while progression was detected by VFI.¹⁰

In general, the results of these comparative studies appear to show that event-based analyses are more likely to detect progression earlier and are more sensitive. Trend-based analyses take longer to detect progression but do so with higher specificity, and they become more useful as the disease becomes more severe. The advantages and disadvantages of the two approaches complement each other and, as such, can be used together to guide the assessment of visual fields clinically.

PRACTICAL RECOMMENDATIONS AND THE FUTURE

From a current review of the peer-reviewed literature on the subject, some general conclusions can be drawn in terms of the practical application of computer-assisted progression assessment of standard visual fields. First of all, any analysis relies on good data. The old adage “garbage in, garbage out” applies to visual field progression analysis in particular. Eliminating poor fields from baseline as well as “outliers” in a series of visual fields is important no matter what type of progression analysis is used. In addition, establishing a new set of baseline fields after significant relevant events, such as glaucoma surgery, or a long absence from obtaining fields with significant change from previous fields should be considered.

For most progression analysis, experts agree that at least four to five field tests in a series are the minimum required to identify progression, with more being needed for trend-based analysis. Chauhan et al¹³ have shown that, for reasonable certainty to detect an overall change in the mean deviation index of 4 dB over 2 years (with trend-based analysis, a reasonable rate to expect with untreated or progressive glaucoma), at least three examinations per year would be required in a patient with average visual field variability. Obviously, this is more often than what is standard clinical practice for most patients with moderate glaucoma, and it is expected that, with event-based analysis, the number of fields needed would probably be less.

Using a combination of methods at the time of a single analysis in a series, such as with the GPA with the current HVF software packages, is probably helpful to most clinicians, with the caveats that have been described about sensitivity and specificity. Having the age of the patient as part of the regression analysis of the VFI is especially useful in making treatment decisions, as it places the velocity of glaucomatous progression in context for each patient.

Some newer hybrid types of analysis such as the Progressor (Medisoft, Leeds, United Kingdom) or the EyeSuite polar analysis (Haag-Streit USA, Inc., Mason, OH) combine both types of analysis into a single graphical presentation of trend- and/or event-based analysis using linear regression at each point of the visual field. This is a method that has been used in research for some time but now has a graphical interface that can be used fairly easily clinically with these analytical tools. Different combinations or “clusters” of adjacent worsening points of the field are determined to be significant or not based on location and the amount of progression. In theory, this type of analysis appears to improve the specificity of a strictly event-based analysis and probably is more sensitive to identify progression than a strictly global trend index. In the study by Viswanathan et al, reanalysis of the same series of fields using the Progressor program

increased the agreement median kappa between experts from .32 to .59, which appears to be much better than with similar studies using GPA in the same fashion.¹

CONCLUSION

Computer software programs to assist in the clinical detection of glaucomatous visual field progression and the determination of the rate of progression will no doubt continue to improve and become easier to use. As electronic medical records within the practice of ophthalmology become more ubiquitous, these computer-based analyses will become more convenient, with information easily organized on a computer screen rather than on a paper printout. Physicians' current options have some drawbacks, which must be kept in mind when making clinical decisions. They provide more information than simple inspection of sequential fields and, one hopes, will improve the ability to identify clinically relevant progression in patients with glaucoma. □

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