

Target IOP for Advanced Glaucoma

Does everyone need an IOP of 12.3 mm Hg? Why would we even ask?

BY ROBERT D. FECHTNER, MD

Figure 1 shows a patient's substantial loss of the superior neuroretinal rim with a corresponding, dense, inferior visual field defect. How low should her IOP be? Because IOP reduction is the mainstay of glaucoma treatment, we set the target IOP range for each patient based on a number of factors. All the major, recent, large clinical trials support that glaucomatous damage is IOP-related at all levels of pressure (although there may be other factors that contribute to the damage). As a result, we set a target and lower the patient's IOP. Simply put, target IOP is that pressure range at which we believe we can minimize the pressure-related component of glaucomatous damage.

AGIS AND IOP

The evidence (as demonstrated in the Ocular Hypertension Treatment Study [OHTS], Early Manifest Glaucoma Trial [EMGT], and Advanced Glaucoma Intervention Study [AGIS]) is compelling that lowering IOP prevents or delays the onset or progression of glaucoma.^{1,2}

"All the major, recent, large clinical trials support that glaucomatous damage is IOP-related at all levels of pressure."

AGIS enrolled 591 patients between 1988 and 1992. Seven hundred eighty-nine eyes total were identified as needing surgery after insufficient IOP control with medical therapy. Investigators randomized enrolled eyes to one of two surgical treatment sequences starting with either laser trabeculoplasty or trabeculectomy. The measures for comparison were visual acuity (ETDRS), IOP (Goldmann applanation), and visual field (Humphrey program 24-2; Carl Zeiss Meditec, Inc., Dublin, CA). Among the several reported results were an interaction between race and treatment (AGIS 4),³ visual function improvement after cataract surgery (AGIS 6),⁴ more cataracts after trabeculectomy (AGIS 8),⁵ and race-

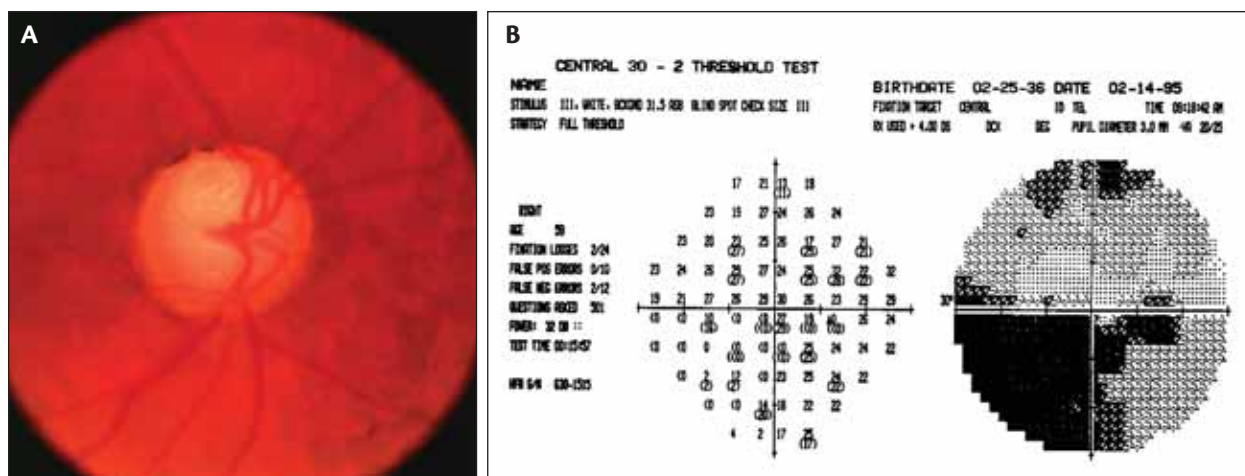


Figure 1. This patient has lost a substantial portion of the superior neuroretinal rim (A) and has a dense inferior visual field defect (B).

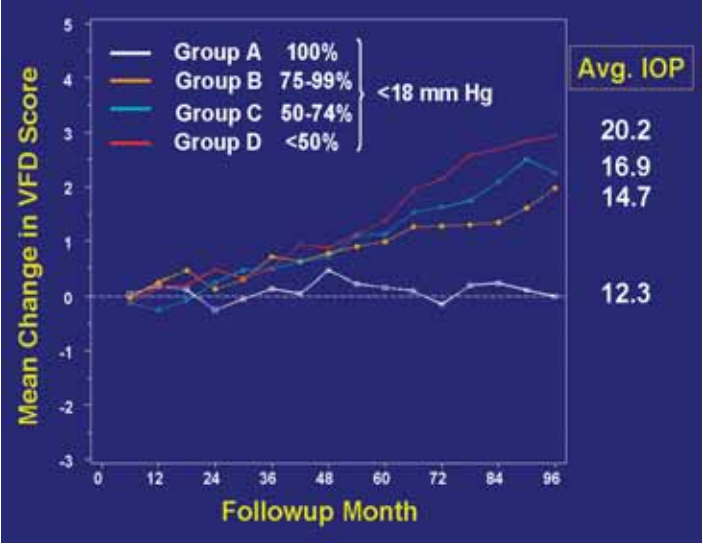


Figure 2. The Associative Analysis of AGIS 7.

dependent differences in the course of advanced glaucoma (AGIS 9).⁶ None of these reports has generated much excitement in ophthalmologists, however.

The publication from AGIS that has been widely discussed recently is the AGIS 7 report. In it, the investigators analyzed the relationship between IOP control and visual field loss over the first 6 years of follow-up.⁷ It is important to understand that the study eyes were assigned to a sequence of surgeries (argon laser trabeculoplasty-trabeculectomy-trabeculectomy or trabeculectomy-argon laser trabeculoplasty-trabeculectomy) supplemented with medical treatment to achieve a target IOP of below 18 mm Hg. In other words, this is a study of the effect of surgery supplemented with medication to achieve a target IOP of less than 18 mm Hg. Subjects' initial presurgery IOP averaged 25 mm Hg. At 1 year, the mean IOPs were 16 mm Hg in the trabeculectomy-first group and 17 mm Hg in the laser-first group. No further comment will be made in this discussion on differences between treatment sequences. The AGIS 7 analysis combined both treatment arms.

Although the study design of AGIS is clearly described in publications, the AGIS 7 report has been interpreted as providing evidence that glaucoma patients should have an IOP of 12.3 mm Hg. Do the results really support this conclusion, however?

ASSOCIATIVE ANALYSIS

The Associative Analysis performed as a part of AGIS 7 might be thought of as a surrogate measure for consistent IOP control. The target IOP for this study was less than 18 mm Hg. Investigators assigned subjects to one of four

groups based on the percentage of visits at which their IOP was at target: 100% (group A), 75% to <100% (group B), 50% to 74% (group C), and 0 to <50% (group D). The analysis included 586 eyes followed for at least 6 years of patients who had missed no more than two 6-month visits (Figure 2).

In the Associative Analysis, group A (always at or below target) had mean changes from baseline visual field scores close to zero (14.4% had 4 or more visual field units of worsening at 7 years, while 8.8% had 4 or more units of improvement). The mean IOP for group A was 12.3 mm Hg. Mean visual field scores worsened in the other groups.

TARGET IOP IN STUDIES

The large glaucoma trials have not been consistent in the target IOPs they have used to guide treatment (Table 1). In none was the target IOP set in the low teens. Realistically, we now hope for a 25% to 30% IOP reduction with medical treatment. We can achieve lower IOPs with surgery. Looking at the mean IOP reductions in the treated subjects of the large glaucoma trials, we can see that, even with surgery (Collaborative Initial Glaucoma Treatment Study [CIGTS]), a 48% reduction in IOP gave a mean IOP of 14 mm Hg. Moreover, the field loss in the surgery group was similar to that in the medication group, which achieved a 37% IOP reduction (Table 2).

It might well be that most patients with advanced glaucoma would benefit from an IOP of around 12 mm Hg, but this target is not easily achieved, even with surgery.

TABLE 1. GLAUCOMA TRIALS AND TARGET IOP

Study	Target IOP
OHTS ¹	20% reduction or 18 mm Hg
EMGT ²	No target laser trabeculoplasty + betaxolol
AGIS	<18 mm Hg
CIGTS	Formula (35% to 50% reduction)

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2. Heijl A, Leske MC, Bengtsson B, et al; Early Manifest Glaucoma Trial Group. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. *Arch Ophthalmol*. 2002;120:10:1268-1279.

TABLE 2. GLAUCOMA TRIALS AND IOP REDUCTION

Study	Baseline IOP (mm Hg)	Treated IOP (mm Hg)	IOP Reduction
OHTS	24.9	19.3	22.4%
EMGT	20.6	15.5	25%
AGIS	23.7 to 24.8	15.1 to 16.7	30% to 37%
CIGTS (Surgery)	27	14	48%
CIGTS (Medicine)	27	17	37%

Surgical intervention can result in profound complications, and there are additional costs as well as risks.

DO THE AGIS 7 RESULTS APPLY TO ALL PATIENTS?

The results from the AGIS 7 report have been used to support the argument that the target IOP for all patients should be approximately 12 mm Hg. It is important to realize the limitation of this analysis and to place the results in a broader context. AGIS is specific to patients with primary open-angle glaucoma, and its findings may not be applicable to patients with other forms of glaucoma or with ocular hypertension. The AGIS patients all underwent surgery—either laser, incisional, or both, possibly with adjunctive medical therapy. We do not know clearly whether these results are applicable to patients undergoing medical therapy alone.

DOES EVERYONE WITH ADVANCED GLAUCOMA NEED AN IOP OF 12 MM Hg?

Probably not, unless this target IOP is achievable without complications, and all treatment has complications. AGIS had a target IOP of less than 18 mm Hg, not 12.3 mm Hg. Similarly, OHTS did not require an IOP reduction to below 18 mm Hg. The EMGT did not have a target IOP, but subjects received additional treatment when their IOPs exceeded 25 mm Hg.

Although we can calculate estimates of risk associated with the level of IOP or with the extent of IOP reduction, no studies have demonstrated the level of IOP reduction that provides maximal benefit. At present, we tend to set lower target IOPs when the disease is more advanced. Medical therapy remains the initial treatment for most US patients. The available evidence supports the practice of aiming for low normal IOP—as long as complications are avoided. Surgery and antifibrotic agents can achieve low IOPs, but the complications of such surgery are well known. As in so many areas of

medicine, the physician and patient must weigh the risks and benefits of therapy.

We do not yet have the ability to identify which patients are at greatest risk and might benefit most from aggressive treatment. Studies such as OHTS and EMGT have collected information that could be useful for constructing models of risk and risk calculators.^{8,9}

The data from the AGIS study also provide part of the foundation for this effort.

Does everyone with glaucoma need an IOP of 12 mm Hg? The consistent control of IOP may be very important, and the IOP of AGIS group A was always below 18 mm Hg. Nevertheless, an IOP of 12.3 mm Hg is not easily achieved and involves risks as well as costs. We should treat aggressively those patients who are most likely to develop visual disability, but we need tools to assess the individual risk of progression. □

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