The Evolution of Target Pressure

This concept is evolving as the databases of large clinical trials are analyzed.

BY PAUL F. PALMBERG, MD, PHD

Imagine this. At some time in the future, you are sitting in your office and evaluating a new patient with open-angle glaucoma. On the screen of the electronic medical record system are displayed for each eye the presenting IOP; the automated visual field; spectral domain optical coherence tomography scans of the retinal nerve fiber layer, disc, and macular ganglion complex; the central corneal thickness; the patient's age and race; and your observations about other relevant findings (eg, pseudoexfoliation, disc hemorrhage). You click on the icon for "risk versus treated IOP" and view the computed values. The initial IOP is 26 mm Hg, mean deviation (MD) -5 dB, etc. The risk of a 3-dB MD progression in 5 years is 62% without treatment, 46% at an IOP of 21 mm Hg, 15% at an IOP of 17 mm Hg, and 5% at an IOP of 13 mm Hg.

You show this to the patient, who agrees with you on a goal to lower the IOP by at least 35% to 17 mm Hg. You then recommend a prostaglandin analogue eye drop to be used daily, with which there is a 50% chance that the goal will be reached with that treatment alone. You explain that, in reserve if needed, are other medications, laser treatment, and surgery. You will be monitoring the patient for changes in the optic nerve's tissue and function, and you both will be able to see if stability is maintained or if an advancement of treatment is indicated. The risk of blindness is very low if the patient keeps appointments and uses the treatment. The target pressure concept could thus inform your decisions as well as educate—and, one hopes, motivate—the patient.

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Actually, much of the data needed for the presented scenario exist in the databases of the landmark clinical trials, and data from the Ocular Hypertension Treatment Study (OHTS) are already being used for ocular hypertensives. It surely would be handy if electronic medical record systems would provide such a risk assessment. One hopes that the databases are merged and analyzed for that purpose!

How did this all come about?

THE 1960s

Going back to the 1960s, the target pressure concept appears to have emerged first in the observations of Paul Chandler[1,2] and Morton Grant.[3] Chandler shared

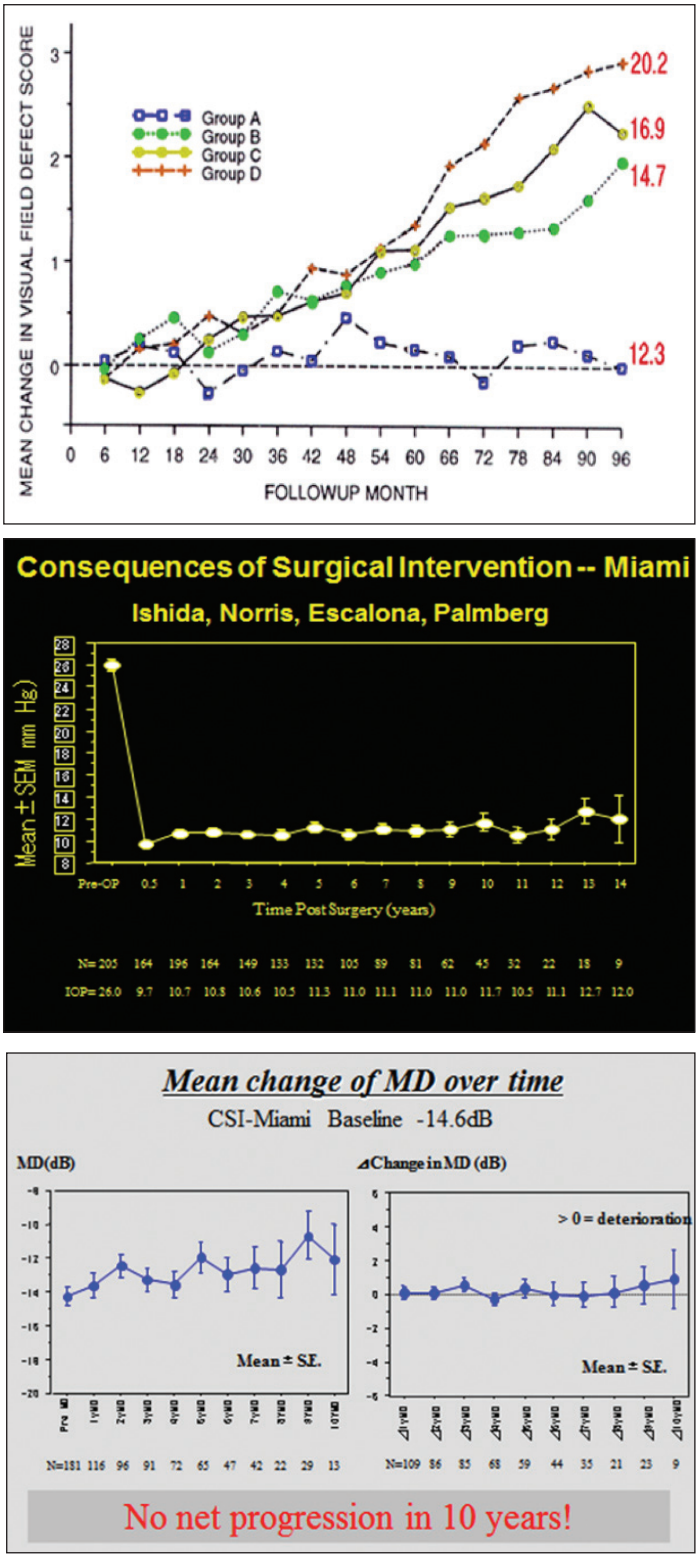

Figure 1. The visual field outcomes in the AGIS and in the Consequences of Surgical Intervention-Miami Study. (Data adapted from AGIS investigators[4] and Ishida et al.[5])

his experience and advice on how to achieve visual field stability as follows:

- "Eyes with advanced cupping … require pressures below the average of the population."
- "Eyes with limited cupping, confined to one pole of the disc, appear to withstand tension better."
- "Eyes with a normal disc appear to withstand pressure well … over many years."
- "The appearance of the disc may serve as an important guide to the management of glaucoma."

The data upon which Chandler's advice was based were meager, however, and it took another 40 years and several clinical trials to provide solid evidence confirming his observations.

ADVANCED PRIMARY OPEN-ANGLE GLAUCOMA

The report from the Advanced Glaucoma Intervention Study (AGIS) that analyzed the relationship between IOP during follow-up and visual field outcome showed that eyes with advanced damage (average MD, -10.5 dB) had no average progression in 8 years of follow-up at pressures consistently reduced to less than 18 mm Hg.[4] It is easily misunderstood that one could aim for 17 mm Hg and achieve this goal. Indeed, the average IOP of those achieving consistently low pressures was 12 mm Hg. Those with less consistently reduced IOPs and a mean IOP in the midteens suffered progression of about 2.5 dB MD, and those with a mean IOP of 20 mm Hg suffered progression of about 3.5 dB on average. Another way to think about it would be to say that, at 12 mm Hg, the risk of a 3-dB MD progression was 13% (and, in 13%, the field appeared better, some of that "noise" and some real, with no net change). In the midteens, however, the risk was about 30%, and at 20 mm Hg, the risk was about 70%. Our study of primary antimetabolite filtering surgery achieved visual field stability (no average change for the whole group of 105 eyes) in cases of advanced damage at an IOP averaging 11 mm Hg[5] (Figures 1 and 2).

EARLY PRIMARY OPEN-ANGLE GLAUCOMA

In subjects recruited at diagnosis in a mass screening (average MD, -5 dB), the Early

Manifest Glaucoma Trial (EMGT) demonstrated that 72% of eyes with primary open-angle glaucoma randomized to no treatment experienced disease progression in 6 years versus 50% randomized to a standard (and in retrospect suboptimal) treatment.[6] In the Collaborative Initial Glaucoma Treatment Study (CIGTS), in similar patients, there was no average visual field progression in 7 years due to insistence upon achieving an aggressive target pressure, requiring about a 30% IOP reduction in mild cases and progressively greater reduction for more advanced cases.[7] Thus, a reduction from an average of 26 to 17.6 mm Hg in the medical group and to 14 mm Hg in the surgical arm resulted in no net visual field progression in each group.

A TWIST FROM NEW CIGTS DATA

A recently published reassessment of the CIGTS database complicates the story.[8] Some 15% of subjects in the medical and surgical arms of the CIGTS experienced glaucomatous progression from baseline in 7 years. This seemed odd, because there was no net visual field progression in either group. The apparent discrepancy is now explained in that an equal percentage of subjects appeared to improve. I thought then, as a member of the monitoring committee, that repeated testing was only collecting noise. I was wrong. The reanalysis found a positive correlation between those appearing to improve and the IOP, with low peak IOPs correlating with improvement. Other identified factors were sex (women do better) and cardiovascular disease (less chance of improvement). The average recovery was about 10% of the field loss in patients with peak IOPs of 17 mm Hg or less, with the percentage of subjects improving over worsening being best for those with a peak IOP of 13 mm Hg.

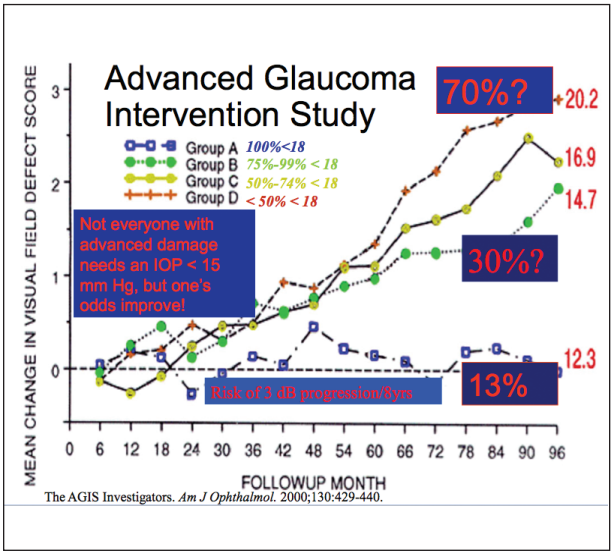

Figure 2. The average change in visual field score over 8 years of follow-up in a post-hoc analysis. The groups were based upon the percentage of visual fields with all semi-annual IOPs under 18 mm Hg, being 100%, 75% to 99%, 50% to 74%, and less than 50%. The visual field change units are AGIS units, peculiar to the study, and correspond to approximately 1.25 dB of MD per AGIS unit. The average IOPs during follow-up are also given for each group as well as an estimate of the chance that the visual field of a subject in each group has progressed by 3 dB of MD. (Data adapted from AGIS investigators.[4])

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IMPLICATION FOR PRACTICE

The new results from CIGTS suggest that, when there are very safe ways of achieving low normal IOPs, it would be desirable to employ them. Some visual field recovery would be a benefit beyond the stability achieved by reaching pressures in the midnormal range in such cases. ■

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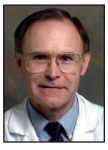

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