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TARGET AUDIENCE

This educational activity is intended for general ophthalmologists, glaucoma specialists, and resident ophthalmologists.

LEARNING OBJECTIVES

- Name the randomized clinical trials that confirm that lowering intraocular pressure in early glaucoma slows progression of the disease.
- List three benefits and two limitations of using a risk calculator in deciding whether to treat patients with ocular hypertension.
- Discuss the limitations of applying data from RCTs to individual patients.
- List three factors that come into play when setting a target intraocular pressure.

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RCTs: KEYS TO EVIDENCE-BASED MANAGEMENT

SPECIAL FEATURE

Randomized Clinical Trials: Keys to Evidence-based Management of Glaucoma

Anne L. Coleman, MD, PhD

Over the past decade, several large, prospective, multicenter clinical trials have investigated specific scientific questions in the treatment of glaucoma and ocular hypertension. My goal in this paper is to review briefly the study design and main outcomes of six of these large clinical trials. In each case, I give an overview of what was learned about the effects of treatment on glaucoma or ocular hypertension.

Advanced Glaucoma Intervention Study¹⁻¹²

The Advanced Glaucoma Intervention Study (AGIS) asked which of two surgical sequences was more effective in treating open-angle glaucoma. Patients in the study had ongoing visual loss that could not be controlled by maximally effective and tolerated medication. Patients were considered eligible for AGIS if they met pre-specified criteria for deterioration. These included changes in visual acuity, visual field, intraocular pressure (IOP), and optic disk rim deterioration.

These criteria were also used to measure the decrease in vision following allocated treatment, which was a surgical sequence of either trabeculectomy followed by argon laser trabeculoplasty and a second trabeculectomy (TAT) vs argon laser trabeculoplasty followed by trabeculectomy and then a second trabeculectomy (ATT).

Findings included:

- Patients assigned to TAT had a greater mean decrease in IOP.
- There was a greater rate of failure of the first intervention in patients assigned to ATT.
- Fewer black patients assigned to ATT had visual field loss compared to TAT.
- Fewer white patients assigned to TAT had visual field loss.
- Having a trabeculectomy first increased the risk of cataract in both blacks and whites.
- Prognostic factors included older age and male gender in the ATT sequence, and diabetes in the TAT sequence (Table 1). (Optic nerve and visual field characteristics were excluded as risk factors because they were study endpoints. Prognostic factors are traits or conditions associated with an elevated risk of disease progression.)

Collaborative Normal-Tension Glaucoma Study¹³⁻¹⁵

The goal of the Collaborative Normal-Tension Glaucoma Study (CNTGS) was to compare treatment vs no treatment in patients with normal-tension glaucoma. The goal of treatment was to lower IOP by 30%. Inclusion criteria were unilateral or bilateral glaucoma with optic disk abnormalities and visual field defects characteristic of glaucoma.

Normal tension was defined as a maximum IOP less than 24 mmHg with a mean pressure of 20 mmHg or less from 10 separate IOP

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STATEMENT OF NEED AND PROGRAM DESCRIPTION

Recent months and years have seen significant advances in our understanding of glaucoma. Much has been learned, not only about damage mechanisms and pathogenesis, but also about diagnosis and management. Treatment options—both medical and surgical—continue to expand. This program will review this new knowledge with an emphasis on incorporating recent insights into day-to-day practice.

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measurements. Treatment could include medication or surgery, either of which could be augmented to reach the desired goal of a 30% IOP reduction. (Beta-blockers and adrenergic agonists could not be used because of the potential for systemic crossover.)

Findings included:

- Fewer eyes in the intervention group progressed compared to the observation-only group (12% vs 35%); and those that did progress in the treated group progressed later ($P < .0001$ using survival analysis with 8 years of followup).
- The risk of cataracts development was greater in the intervention group ($P = .001$).
- The one prognostic factor (excluding optic nerve and visual field characteristics) was a history of migraine (hazard ratio = 2.58; 95% confidence interval [CI] = 1.32-5.07) (Table 1). ("Hazard ratios" are estimates of the relative risk of a disease or outcome in individuals with a trait compared to individuals without that trait.)

Collaborative Initial Glaucoma Treatment Study¹⁶⁻¹⁸

The goal of the Collaborative Initial Glaucoma Treatment Study (CIGTS) was to compare surgical vs medical treatment for patients newly diagnosed with glaucoma. Patients were included only if they had had no previous surgical treatment for their glaucoma and less than 14 days of medical treatment. Patients also had to have some evidence of damage as evidenced by specific combinations of increased IOP and visual field or optic disk deterioration.

Findings included:

- No difference in progression (visual field change) between treatment groups at 4 years.
- Visual acuity loss initially appeared to be greater in surgery group, but this may have been confounded by increased incidence of cataract in this group; at 4 years there was no difference in visual acuity loss between groups.

- Prognostic factors (not including optic nerve or visual field characteristics) were older age, ancestry, and diabetes (Table 1).

Ocular Hypertension Treatment Study¹⁹⁻²²

The Ocular Hypertension Treatment Study (OHTS) compared the effect of either a stepped regimen of medication or careful observation on the onset of visual field loss and/or optic nerve damage in persons with ocular hypertension who were at risk for developing primary open-angle glaucoma (POAG). Patients with elevated IOP (defined as between 24 and 32 mmHg in the study eye and between 21 and 32 mmHg in the fellow eye) and normal Humphrey visual fields and optic disks were randomly assigned to either an active treatment group or to an observation group.

Treatment consisted of topical ocular hypotensive therapy, the goal of which was to reduce IOP by 20% or to reach an IOP of 18 mmHg or less. Patients in the observation group did not use any medication until there was evidence of glaucomatous visual field or optic disk change.

Findings included:

- IOP reduction was greater in the intervention group than the observational group (22.5% vs 4.0%).
- The probability of progression in the treated group was less than in the observational group (4.4% vs 9.5%; hazard ratio = 0.40, CI = 0.27-0.59).
- Risk factors (excluding optic nerve or visual field characteristics) were older age, higher baseline IOP, and thinner central corneal pachymetry. Diabetes was protective (Table 1).

Early Manifest Glaucoma Trial²³⁻²⁵

The goal of the Early Manifest Glaucoma Trial (EMGT) was to compare the effect of immediate medical therapy to lower IOP vs no treatment or delayed treatment for patients with newly diagnosed open-angle glaucoma. As in the CIGTS, study participants had not been previously diagnosed with or treated

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for glaucoma and showed some early visual field deterioration at entry. Treatment included topical beta-blocker medication with argon laser trabeculoplasty scheduled 1 week later. The comparison group either was not treated or was treated only following progression of visual field loss or optic disk changes. The primary outcome was progression of visual loss as shown by

- Prognostic factors (excluding optic nerve or visual field characteristics) were older age, number of eligible eyes (hazard ratio = 1.88; CI = 1.35-2.63), baseline IOP of 21 mmHg or greater (hazard ratio = 1.77; CI = 1.29-2.43), thinner central corneal pachymetry, low systolic blood pressure, and pseudoexfoliation (Table 1).

TABLE 1 Risk and prognostic factors (hazard ratios with 95% confidence intervals) for development or progression of open-angle glaucoma

	OHTS (5 yrs follow up) N = 1,493	EGPS (5 yrs follow up) N = 1081	CNTGS (5 yrs follow up) N = 230	AGIS (6 yrs follow up) N = 591	EMGT (11 yrs follow up) N = 255	CIGTS (4 yrs follow up) N = 607
	Risk Factors			Prognostic Factors		
Age (per decade)	1.29 (1.09-1.53)	1.40 (1.14-1.73)	-	-	-	-
Age (per older year)	-	-	-	-	-	1.04 (1.02-1.05)
Age (per 5 years)	-	-	-	1.28 (1.10-1.49)	-	-
Age ≥68 yrs	-	-	-	-	1.51 (1.11-2.07)	-
Ancestry	n.s.	-	n.s.	n.s.	-	1.50 (1.08-2.07)
Gender male	n.s.	n.s.	n.s.	2.23 (1.54-3.23) ATT	n.s.	n.s.
OAG family history	n.s.	n.s.	n.s.	-	n.s.	n.s.
IOP (per mmHg)	1.10 (1.04-1.17)	1.18 (1.06-1.31)	n.s.	n.s.	-	-
CCT (per 40 μm thinner)	1.92 (1.60-2.30)	1.40 (1.14-1.72)	-	-	1.25 (1.01-1.55)	-
SBP (≤125 mmHg)	-	-	-	-	1.42 (1.04-1.94)	-
Diabetes	0.38	n.s.	n.s.	1.87 (1.18-2.97) TAT	n.s.	1.59 (1.07-2.38)
Migraine	-	-	2.58 (1.32-5.07)	-	-	-
PEX	-	n.s.	-	-	2.12 (1.30-3.46)	-

OHTS: Ocular Hypertension Treatment Study
 CNTGS: Collaborative Normal-Tension Glaucoma Study
 EMGT: Early Manifest Glaucoma Trial
 OAG: open-angle glaucoma
 CCT: central cornea thickness
 PEX: pseudoexfoliation syndrome

EGPS: European Glaucoma Prevention Study
 AGIS: Advanced Glaucoma Intervention Study
 CIGTS: Collaborative Initial Glaucoma Treatment Study
 IOP: intra-ocular pressure
 SBP: systolic blood pressure

n.s. not statistically significant

Humphrey visual field deterioration or optic disk changes.

Findings included:

- The treated group had less frequent and later progression (visual field and optic nerve disk change) than the observational group (at 6 years, hazard ratio = 0.50, CI = 0.35-0.71).

European Glaucoma Prevention Study²⁶⁻²⁷

The European Glaucoma Prevention Study (EGPS) compared topical medication to placebo as treatment to prevent or delay onset of POAG in individuals with ocular hypertension. Patients with elevated IOP (greater than 21 up to 29 mmHg in

Core Concepts

- Forming a foundation for evidenced-based treatment in glaucoma, large, multicenter, randomized clinical trials have investigated the effects of treating glaucoma and ocular hypertension.
- The Advanced Glaucoma Intervention Study (AGIS) asked which of two surgical sequences was more effective in treating open-angle glaucoma.
- The goal of the Collaborative Normal-Tension Glaucoma Study (CNTGS) was to compare treatment vs no treatment in patients with normal-tension glaucoma and found less and slower progression in the treated group.
- The Ocular Hypertension Treatment Study (OHTS) looked at the ability of treatment to delay the conversion of ocular hypertension to POAG.
- The Early Manifest Glaucoma Trial (EMGT) found that immediate treatment of POAG reduced vision loss compared to no treatment or delayed treatment.
- The European Glaucoma Prevention Study (EGPS) compared topical medication (dorzolamide) to placebo as treatment to prevent or delay onset of POAG and found that the treated group had less frequent and later progression.

at least one eye) and normal visual fields and optic disks were randomly assigned to either 2% dorzolamide three times a day or to placebo also applied three times a day. Findings included:

- There was no difference in the cumulative probability of reaching a study endpoint (worsening of either visual field or optic nerve) between dorzolamide and placebo study groups (hazard ratio = 0.86; CI = 0.58-1.26).
- No difference was found in the cumulative probability of reaching a study endpoint or safety endpoint (IOP of

35 mmHg) between dorzolamide and the placebo study groups (hazard ratio = 0.73; CI = 0.51-1.06).

- Using the last observation carried forward, there was a reduction in IOP in both groups with a larger reduction in the dorzolamide group (17.9%) compared with placebo group (13.7%).
- Risk factors (not including optic nerve or visual field characteristics) were older age, higher baseline IOP, and thinner central corneal pachymetry (Table 1). ●

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Risk Assessment in the Treatment of Ocular Hypertension and Glaucoma Patients

Steven L. Mansberger, MD, MPH

Risk assessment, a well-accepted tool in a variety of medical fields, can help ophthalmologists identify which ocular hypertensive patients are most at risk to develop glaucoma and, in patients with glaucoma, how likely their disease is to progress. Predictive factors for conversion from ocular hypertension to glaucoma, as identified by the Ocular Hypertension Treatment Study (OHTS) and the European Glaucoma Prevention Study (EGPS), include older age and African descent, higher intraocular pressure (IOP), certain features of optic nerve anatomy, and thinness of the cornea. The Early Manifest Glaucoma Trial (EMGT) reported similar results in predicting glaucoma progression. In this article I will discuss the pros and cons of risk assessment as it applies to clinical practice.

Why Use Risk Assessment?

Elevated IOP, a common condition affecting 8% of Americans over age 40, is considered the leading risk factor for development of open-angle glaucoma.¹ The challenge ophthalmologists face is to determine which of their patients is most likely to develop glaucoma from ocular hypertension and, based on patients' personal and ocular characteristics, how vigorously they should treat them.

The Ocular Hypertension Treatment Study (OHTS) and European Glaucoma Prevention Study (EGPS) addressed these questions and arrived at baseline factors that can predict the onset of primary open-angle glaucoma (POAG) in ocular hypertensive patients.² By considering these factors, clinicians can identify patients at moderate to high risk for developing glaucoma and which patients will most likely benefit from early treatment.

Risk Calculators

The decision whether or not to treat an ocular hypertensive patient is complex without a risk calculator. The newest OHTS multivariate regression contains five variables that are predictive of developing glaucoma from ocular hypertension: age, central corneal thickness (CCT), IOP, pattern standard deviation (PSD), and vertical cup/disk ratio by contour (C/D).^{3,4} Even if one simplifies the continuous variables of age, corneal thickness, IOP, and PSD into highest, middle, and lowest thirds and uses just nine different C/D ratio ranges (0.0-0.8), 729 different results are possible for ocular hypertensive patients. This large number of combinations is difficult for clinicians to decipher when deciding whether to treat a particular ocular hypertensive patient.

At Devers Eye Institute we surveyed ophthalmologists' ability to predict the risk of glaucoma in ocular hypertensive patients.⁵ Ophthalmologists had the benefit of an oral review and written handouts summarizing the OHTS results. We found that ophthalmologists tended to underestimate patient risk when compared to the actual risk found by the risk calculator. Within the group there was a wide range of predictions, sometimes differing from the actual risk by 40% (Figure 1). In general, this study shows that eyecare providers may frequently over- or undertreat their ocular hypertensive patients because of the difficulty in assessing risk.

Integrating Evidence-based Medicine

Evidence-based medicine (EBM) uses current best evidence from scientific and medical research to make decisions about

Core Concepts

- Two studies—OHTS and EGPS—arrived at five variables predictive of developing glaucoma from ocular hypertension.
- Because of the difficulty in assessing glaucoma risk, eyecare providers frequently over- or undertreat their ocular hypertensive patients.
- Risk calculators encourage patient-centered rather than population-centered treatment and may help patient compliance.
- A risk calculator provides a mean risk based on patients with similar characteristics.

the care of individual patients. This decision-making approach involves formulating questions relevant to the care of particular patients, searching the scientific and medical literature, identifying and evaluating relevant research results, and applying the findings to patients.⁶ EBM integrates best practice approaches with clinical experience. The results of randomized controlled trials can be complex; risk assessment may help to simplify them.

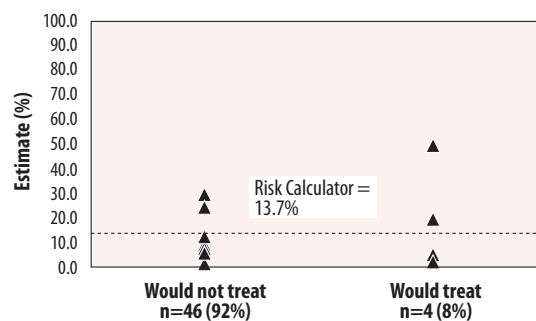


FIGURE 1 In a study performed at the Devers Eye Institute, ophthalmologists' assessment of patient risk was compared to an analysis of the same patient made by a risk calculator. Although there was a wide range of responses, physicians tended to believe that the patients' risk levels were lower than the risk level determined by the calculator.

Benefits to Patients

The OHTS risk calculator provides clinicians an individualized estimate of a patient's susceptibility to developing glaucoma in 5 years; thus, risk calculators

encourage patient-centered rather than population-based treatment. Patients are more likely to adhere to therapy if they have a definite expectation of risk, rather than something vague, such as “higher” or “lower” risk. Thus, risk calculation can strengthen the physician-patient relationship and enhance compliance.

Risk calculators may simultaneously save money and decrease blindness. An economic analysis has shown that not all patients require treatment of ocular hypertension, just those at higher risk.⁷

Risk Assessment for Glaucoma Progression

The Early Manifest Glaucoma Trial (EMGT) randomized patients with early glaucoma either to argon laser trabeculoplasty plus the beta blocker betaxolol (n = 129) or to monitoring without immediate treatment (n = 126).⁸ These 255 patients were identified during a community glaucoma screening. After 6 years of follow up, the rate of progression was 45% in the treated group vs 62% in the untreated group.

Scientists found treatment reduced IOP approximately 25% and decreased the risk of worsening glaucoma by 50%.⁹ The study identified elevated IOP, exfoliation, bilateral disease, worse mean standard deviation with perimetry, and older age as baseline risk factors for glaucoma progression. Central corneal thickness (CCT) was not found to be an absolute risk factor, but during follow up, the presence of disk hemorrhages was found to increase the risk of progression.

The EMGT recently published the predictors of long-term progression (mean 8 years) in patients with early glaucoma.¹⁰ Their results are similar to those reported earlier, but now show an increased risk of glaucomatous progression with thin CCT and decreased perfusion pressure. An interesting finding is that statistical interaction between CCT and IOP occurred, with CCT only a risk factor in those with an IOP greater than 21 mmHg. Overall, interpretation of these results is more difficult than in the OHTS study. Also, the EMGT study has a smaller sample size. Therefore, a risk assessment equation may be less precise and difficult to understand. The authors have not released an equation.

Caveats of Risk Calculators

A 1995 study suggested that in a critical care setting, clinicians may not change their

treatment based on use of a risk calculator.¹¹ Authors concluded that the doctors studied were unwilling to apply results from the calculator due to “inertia” and “lack of incentives.” Presumably, implementation of risk assessment could differ between a critical care setting and an ophthalmologist’s office. But the point remains that simply providing a risk assessment tool does not guarantee that clinicians will adopt it.

Risk assessment and calculation have several other limitations. Risk calculators are based on the best available information; thus, their use should be restricted to patients who fit the inclusion criteria of the study. For example, with regards to a risk calculator based on the OHTS, ophthalmologists should not assume that eyes with secondary causes of ocular hypertension, such as pseudoexfoliation or pigmentary dispersion syndrome, will have similar risk factors to the OHTS study population. Clinicians need to understand that a risk calculator provides a mean risk based on a group of patients with similar characteristics.

Conclusion

Predicting the development of glaucoma from ocular hypertension is fundamental to the decision whether or not to treat. Risk calculators can simplify management of ocular hypertension and glaucoma patients and help in the provision of evidence-based treatment. Eyecare providers should recognize, however, that risk assessment is evolving and requires refinement. Therefore, they should consider the result of a risk calculator as supplemental information when deciding whether or not to treat. ●

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overly sensitive, GPA may alert physicians to patients who need more careful monitoring or more aggressive therapy.

Recent imaging modalities—such as the HRT3 (Heidelberg Engineering), GDx™ (Carl Zeiss Meditec), and optical coherence tomography (OCT)—provide semi-quantitative measures of optic nerve morphology. This provides the potential to add objective optic nerve therapeutic targets to glaucoma management strategies. At this point, however, there are limited published reports on the change analysis software used with these imaging devices. Disk assessment over time still requires disks to be documented by either photography or imaging.

Fundamental to the process of setting therapeutic targets is that the clinician must be willing to continually adjust goals when there is progression. The therapeutic target may be dynamic and responsive to the patient’s disease and general health. Fortunately, most glaucoma patients do not reach the stage of functional impairment in their lifetimes. The physician’s job is to predict which patients are headed that way and treat those patients aggressively, leaving the majority with less stringent targets.¹⁻⁵ ●

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Applying RCT Results to Individual Patients and Patient Groups

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Wouldn't it be nice if disease followed our treatment guidelines? If it did, we could simply watch our ocular hypertension (OHT) patients. When a fraction of them inevitably developed early visual field loss, we would treat them using the Collaborative Initial Glaucoma Treatment Study's (CIGTS) target intraocular pressure (IOP) values. For patients with severe disease, we would target an IOP less than 18 mmHg at all times (with an average IOP of 12 mmHg). On paper, these interventions should stop disease progression in its tracks.

RCT Limitations

Unfortunately, clinical care of glaucoma patients is more complicated. Not only do many patients in clinical practice behave differently from those enrolled in the randomized clinical trials (RCTs), but outcomes are highly variable. In addition, there are important questions that RCTs have not answered:

- What happens to glaucoma patients after longer periods of time, say 10 to 15 years? Current RCTs report outcomes that are relatively short-term compared to most of our patients' life expectancies. We need longer follow up from current RCTs, and long-term information from other large cohorts of patients under care.
- Preservation of patients' quality of life is the most important goal in glaucoma care. Yet, although the CIGTS and Early Manifest Glaucoma Trial (EMGT) provide some cross-sectional information about quality of life, they do not consider the relative importance of reported symptoms.^{1,2} Nor have these or other RCTs studied how glaucoma progression influences quality of life.

Quality of Life

Indeed, there is no accepted scientific method for evaluating the impact of glaucoma on quality of life; we know, for example, when visual field loss starts to affect patients' ability to perform daily activities.³⁻⁵ Visual fields are surrogate measures of the patient's ability to function, but patients with early visual field loss may not have any significant impairment in quality of life. And the impact of advanced glaucoma on patients' quality of life is highly variable. Some patients with advanced field loss in both eyes are very happy because their daily activities are unaffected. Others are devastated because they can't drive a car.

Treatment Factors

Is the rate of visual deterioration constant in glaucoma, or does it accelerate with advancing disease? Current RCTs did not measure rate of progression, which is a critical measure for predicting long-term outcomes and for guiding clinical interventions (eg, increasing treatment if progression is noted).

Life expectancy should be a key factor in tailoring treatment strategy. Disease progression is usually slow in glaucoma (approximately 0.5-0.6 dB per year), but treatment should be more aggressive in younger patients and those with advanced disease. For elderly patients with incipient glaucoma in only one eye, without high IOP or pseudoexfoliation, it may be perfectly acceptable to simply observe and let an indolent glaucoma take its course. Efforts to diagnose early glaucoma in elderly individuals are probably unnecessary.

There are many unanswered questions that need further exploration. The consensus opinion derived from recent RCTs is that we should target for an IOP of 18 mmHg in patients with early glaucomatous field loss, 15mmHg in moderate glaucoma, and 12 mmHg where there is advanced loss. While sensible, this is not necessarily the best possible strategy for

Core Concepts

- RCTs provide useful information for clinical practice, but there are important clinical care questions they leave unanswered.
- RCTs don't shed light on longer-term outcomes (ie, more than a decade), the impact of glaucoma on quality of life, or the rate at which the disease progresses.
- Treatment should be more aggressive for younger glaucoma patients and those with advanced disease.
- Glaucoma treatment should be individualized to patients' needs and preferences.

every patient. Glaucoma care needs an individualized approach and sound clinical judgment. ●

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Setting Therapeutic Targets

Helen V. Danesh-Meyer, MBChB, MD, FRANZCO

For glaucoma patients, the ultimate goal of therapy is preservation of functional vision and quality of life. This goal implies stabilizing the patient's glaucoma with treatment that the patient can tolerate. Therapeutic targets provide the clinician with a framework within which to formulate specific treatment objectives.

Three clinical parameters are used to monitor glaucoma: intraocular pressure (IOP), visual field testing, and optic nerve assessment, and none of these has universally applicable target endpoints. Clinicians use data from visual field and optic nerve assessments to set the target IOP, which is a risk factor for progression.¹⁻⁵ Therapeutic targets must be individualized and can only be set after a comprehensive assessment of the patient. This includes a detailed ophthalmological assessment, evaluation of the medical history, and an understanding of the patient's social circumstances.

Setting the Target

The first step is to assess the degree of injury, which is typically determined by optic nerve assessment and reliable visual field testing (Table 1). The next step is to review factors that may influence the patient's rate of progression, including patient history. (It helps greatly to have previous disk photographs, visual fields, or IOP records.) Information that suggests rapid change may warrant a different set of therapeutic targets than data suggesting a gradual or even questionable change over long periods of time. The role of IOP is well recognized in progression, with higher IOP associated with more rapid visual field loss and optic nerve damage. Other important risk factors are listed in Table 2.

The third step involves the integrating of the above analyses with an understanding

of the patient's general health and social circumstances. For example, a frail, elderly patient with limited life expectancy may not need an aggressive therapeutic target, especially if there is minimal damage. Alternatively, features suggesting a very aggressive glaucoma may result in a different set of therapeutic targets—such as a lower target IOP and/or a lesser degree of progression before moving to surgery.⁵

TABLE 1 Features Suggestive of Significant Damage

Optic Nerve Features
Neuro-retinal rim thinning with loss greater than predicted by the ISNT rule
Focal notching
Retinal nerve fiber layer hemorrhage
Optic nerve pseudo-pit
Visual Field Features
Bilateral visual field loss
Visual field loss inferiorly and superiorly
Paracentral defects encroaching on fixation
Dense visual field loss inferiorly

TABLE 2 Factors Associated with Greater Risk of Glaucoma Progression

Race
Age
Pseudoexfoliation
Pigment dispersion
Cardiovascular disease
Lower ocular systolic perfusion pressure
Thinner corneal thickness in patients with higher baseline IOP
Lower systolic pressure in patients with lower baseline IOP

Selecting the Target Range

The most studied therapeutic target is a lower IOP, the “target” pressure or range. The target is a range of IOPs that is thought to significantly slow progressive injury to the optic nerve.¹⁻³ To set a clinically meaningful target, the clinician must have good insight into the patient's baseline IOP. This requires

Core Concepts

- Therapeutic targets can only be set after a comprehensive patient assessment.
- Setting the target requires input from three sources: ophthalmic assessment, medical history, and analysis of the patient's social circumstances.
- Patients with more aggressive or more advanced disease need more aggressive targets.
- Clinicians must be willing to continually adjust therapeutic goals when there is progression.

multiple IOP measurements and may include a diurnal IOP curve. The target IOP set should be sufficiently low that, even with the expected IOP oscillations, the pressure will remain within a safe range.

The amount of IOP reduction recommended varies with the level of disease. A target range of 25% to 50% below baseline or absolute values below 24 mmHg may be desirable in ocular hypertension, while levels below 12 mmHg may be appropriate for advanced glaucoma. The World Glaucoma Association's Consensus Series publication *Intraocular Pressure* provides a detailed discussion of IOP targets (Table 3).² It is now believed that there is not one “normal” IOP, and hence “normalizing the IOP” to a target (eg, 21 mmHg or below) is no longer appropriate strategy.

TABLE 3 Factors to Consider in Determining Target

Amount of glaucoma damage
IOP at which damage has occurred
Life expectancy of the patient
Status of the fellow eye
Family history of severe glaucoma

Assessment of Clinical Progress

Visual field testing and optic nerve assessment are part of the process for assessing the success of the therapeutic target. Both visual field interpretation and optic nerve assessment have their challenges, however. The normal variability of visual field testing means that multiple visual fields may be required to confirm deterioration. A measure of visual field progression may be obtained with Glaucoma Progression Analysis (GPA). Although criticized as

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