

PREFERRED PRACTICE PATTERN®



**Primary
Open-Angle
Glaucoma**

**Prepared by the American Academy of
Ophthalmology Glaucoma Panel**

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This document should be cited as:
American Academy of Ophthalmology
Glaucoma Panel. Preferred Practice Pattern®
Guidelines. Primary Open-Angle Glaucoma.
San Francisco, CA: American Academy of
Ophthalmology; 2010. Available at:
www.aao.org/ppp.

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FINANCIAL DISCLOSURES

The panel and committee members have disclosed the following financial relationships occurring from January 2009 to September 2010:

David F. Chang, MD: Advanced Medical Optics – Consultant/Advisor; Alcon Laboratories, Inc. – Consultant/Advisor; Allergan, Inc. – Lecture fees; Calhoun Vision, Inc. – Consultant/Advisor, Equity owner; Eyemaginations, Inc. – Consultant/Advisor, Patent/Royalty; Ista Pharmaceuticals – Consultant/Advisor, Grant support; LensAR – Consultant/Advisor; Hoya – Consultant/Advisor; Peak Surgical – Consultant/Advisor; Revital Vision – Equity owner; SLACK, Inc. – Patent/Royalty; Transcend Medical – Consultant/Advisor; Visiogen, Inc. – Consultant/Advisor, Equity owner

Emily Y. Chew, MD: No financial relationships to disclose.

Robert S. Feder, MD: No financial relationships to disclose.

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Steven J. Gedde, MD: Lumenis, Inc. – Lecture fees

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Lisa F. Rosenberg, MD: No financial relationships to disclose.

R. Michael Siatkowski, MD: National Eye Institute – Grant support

Rohit Varma, MD, MPH: Alcon Laboratories, Inc. – Consultant/Advisor, Lecture fees; Allergan, Inc. – Consultant/Advisor, Grant support; Aquesys – Consultant/Advisor, Equity owner, Grant support; Bausch & Lomb Surgical – Consultant/Advisor; Genentech, Inc. – Consultant/Advisor, Grant support; Merck & Co., Inc. – Consultant/Advisor; National Eye Institute – Grant support; Optovue – Grant support; Pfizer, Inc. – Consultant/Advisor, Lecture fees, Grant support; Replenish, Inc. – Consultant/Advisor, Equity owner, Grant support



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INTRODUCTION

The Preferred Practice Pattern® (PPP) guidelines have been written on the basis of three principles.

- ◆ Each PPP should be clinically relevant and specific enough to provide useful information to practitioners.
- ◆ Each recommendation that is made should be given an explicit rating that shows its importance to the care process.
- ◆ Each recommendation should also be given an explicit rating that shows the strength of evidence that supports the recommendation and reflects the best evidence available.

In the process of revising this document, a literature search of the Cochrane Library and PubMed was conducted on December 3, 2008 and April 28, 2009 on the subject of primary open-angle glaucoma (POAG) for the years 2004 to the date of the search. In addition, the evidence synthesis¹ prepared by the British National Collaborating Centre for Acute Care for the National Institute for Health and Clinical Excellence clinical guideline on Glaucoma: diagnosis and management of chronic open-angle glaucoma and ocular hypertension clinical guideline was reviewed.² Details of the literature search are available at www.aaio.org/ppp. The results were reviewed by the Glaucoma Panel and used to prepare the recommendations, which they rated in two ways. The panel first rated each recommendation according to its importance to the care process. This “importance to the care process” rating represents care that the panel thought would improve the quality of the patient’s care in a meaningful way. The ratings of importance are divided into three levels.

- ◆ Level A, defined as most important
- ◆ Level B, defined as moderately important
- ◆ Level C, defined as relevant but not critical

The panel also rated each recommendation on the strength of evidence in the available literature to support the recommendation made. The “ratings of strength of evidence” also are divided into three levels.

- ◆ Level I includes evidence obtained from at least one properly conducted, well-designed, randomized, controlled trial. It could include meta-analyses of randomized controlled trials.
- ◆ Level II includes evidence obtained from the following:
 - ◆ Well-designed controlled trials without randomization
 - ◆ Well-designed cohort or case-control analytic studies, preferably from more than one center
 - ◆ Multiple-time series with or without the intervention
- ◆ Level III includes evidence obtained from one of the following:
 - ◆ Descriptive studies
 - ◆ Case reports
 - ◆ Reports of expert committees/organizations (e.g., PPP panel consensus with peer review)

Evidence is that which supports the value of the recommendation as it relates to the quality of care. The committee believes that it is important to make available the strength of the evidence underlying the recommendation. In this way, readers can appreciate the degree of importance the committee attached to each recommendation, and they can understand what type of evidence supports the recommendation.

The ratings of importance and the ratings of strength of evidence are given in bracketed superscripts after each recommendation. For instance, “[A:II]” indicates a recommendation with high importance to clinical care [A], supported by sufficiently rigorous published evidence, though not by a randomized controlled trial [II].

The sections entitled “Orientation” and “Background” do not include recommendations; rather they are designed to educate and provide summary background information and rationale for the recommendations that are presented in the Care Process section. A summary of the major

recommendations for care is included in Appendix 2. Appendix 3 has an algorithm for the management of POAG. Appendix 4 contains the International Statistical Classification of Diseases and Related Health Problems (ICD) codes for the disease entities that the PPP covers.



ORIENTATION

DISEASE DEFINITION

Primary open-angle glaucoma is a progressive, chronic optic neuropathy in adults in which intraocular pressure (IOP) and other currently unknown factors contribute to damage and in which, in the absence of other identifiable causes, there is a characteristic acquired atrophy of the optic nerve and loss of retinal ganglion cells and their axons. This condition is associated with an anterior chamber angle that is open by gonioscopic appearance.

CLINICAL FINDINGS CHARACTERISTIC OF PRIMARY OPEN-ANGLE GLAUCOMA

Primary open-angle glaucoma is a chronic ocular disease process that is progressive, generally bilateral, but often asymmetric. It is associated with the following characteristics.

- ◆ Evidence of optic nerve damage from either, or both, of the following:
 - ◆ *Optic disc or retinal nerve fiber layer structural abnormalities*
 - Diffuse thinning, focal narrowing, or notching of the optic disc rim, especially at the inferior or superior poles
 - Documented, progressive thinning of the neuroretinal rim with an associated increase in cupping of the optic disc
 - Diffuse or localized abnormalities of the peripapillary retinal nerve fiber layer, especially at the inferior or superior poles
 - Disc rim or peripapillary retinal nerve fiber layer hemorrhages
 - Optic disc neural rim asymmetry of the two eyes consistent with loss of neural tissue
 - ◆ *Reliable and reproducible visual field abnormality* considered a valid representation of the subject's functional status
 - Visual field damage consistent with retinal nerve fiber layer damage (e.g., nasal step, arcuate field defect, or paracentral depression in clusters of test sites)³
 - Visual field loss in one hemifield that is different from the other hemifield, i.e., across the horizontal midline (in early/moderate cases)
 - Absence of other known explanations
- ◆ Adult onset
- ◆ Open anterior chamber angles
- ◆ Absence of other known explanations (i.e., secondary glaucoma) for progressive glaucomatous optic nerve change (e.g., pigment dispersion, pseudoexfoliation [exfoliation syndrome], uveitis, trauma, and corticosteroid use)

Primary open-angle glaucoma represents a spectrum of disease in adults in which the susceptibility of the optic nerve to damage varies among patients. While many POAG patients present with elevated IOP, a substantial minority with otherwise characteristic POAG may not have elevated IOP measurements.⁴ The vast majority of patients with POAG have disc changes or disc and visual field changes,⁵ but there are rare cases where there may be early visual field changes before there are detectable changes to the optic nerve.

The severity of glaucoma damage can be estimated using the following:

- ◆ Mild: optic nerve abnormalities consistent with glaucoma as detailed above and a normal visual field as tested with standard automated perimetry

- ◆ **Moderate:** optic nerve abnormalities consistent with glaucoma as detailed above, and visual field abnormalities in one hemifield that are not within 5 degrees of fixation as tested with standard automated perimetry
- ◆ **Severe:** optic nerve abnormalities consistent with glaucoma as detailed above, and visual field abnormalities in both hemifields and/or loss within 5 degrees of fixation in at least one hemifield as tested with standard automated perimetry

PATIENT POPULATION

The patient population consists of adults 18 or older with POAG.

ACTIVITY

Identification and management of a patient with POAG.

PURPOSE

To identify and treat POAG and to preserve visual function while minimizing adverse effects of therapy, thereby enhancing the patient's health and quality of life.

GOALS

- ◆ Document the status of optic nerve structure and function on presentation
- ◆ Estimate an IOP below which further optic nerve damage is unlikely to occur (see discussion of target pressure in the Care Process section)
- ◆ Attempt to maintain IOP at or below this target level by initiating appropriate therapeutic intervention(s)
- ◆ Monitor the structure and function of the optic nerve for further damage and adjust the target IOP to a lower level if deterioration occurs
- ◆ Minimize the side effects of treatment and their impact on the patient's vision, general health, and quality of life
- ◆ Educate and involve the patient and appropriate family members/caregivers in the management of the disease



BACKGROUND

EPIDEMIOLOGY

Primary open-angle glaucoma is a significant public health problem. It is estimated that 45 million people in the world have open-angle glaucoma (OAG).⁶ Glaucoma (both open-angle and angle-closure) is the second leading cause of blindness worldwide, with approximately 8.4 million people blind from glaucoma.⁶ Overall in 2004, the prevalence of POAG for adults 40 and older in the United States was estimated to be about 2%.⁷ Open-angle glaucoma affects an estimated 2.2 million people in the United States, and that number is likely to increase to 3.3 million in 2020 as the population ages. However, large differences exist in the prevalence of glaucoma among different ethnic groups (see Table 1 and Figure 1). Overall, there appears to be a threefold higher prevalence of OAG in African Americans relative to non-Hispanic Whites in the United States.^{7,8} It is also the leading cause of blindness in African Americans.⁸ Further, the prevalence of OAG is even higher in Afro-Caribbeans relative to African Americans. Recent evidence on Hispanics/Latinos suggests that they have high prevalence rates of OAG that are comparable to African Americans.⁹ There are no data on the prevalence of OAG in Asians in the United States.

TABLE 1 THE PREVALENCE OF DEFINITE OPEN-ANGLE GLAUCOMA AS REPORTED IN OTHER STUDIES

Study	Racial/Ethnic Group	Age-Specific Prevalence					
		Age Groups (yrs)					
		40–49	50–59	60–69	70–79	80+	Total
Baltimore Eye Study ¹	African American	1.27	4.15	6.19	8.88	12.87	4.97
Barbados Eye Study ²	Afro-Caribbean	1.4	4.1	6.7	14.8	23.2	6.8
LALES	Latino	1.32	2.92	7.36	14.72	21.76	4.74
Proyecto VER ³	Latino	0.50	0.59	1.73	5.66	12.63	1.97
Baltimore Eye Study ¹	NHW	0.18	0.32	1.53	3.33	1.94	1.44
Blue Mountains Eye Study ⁴	NHW	0.4*		1.3	4.7	11.4	3.0
Visual Impairment Project ⁵	NHW	0.5	1.5	4.5	8.6	9.9	3.4
Beaver Dam Eye Study ⁶	NHW						2.1
Roscommon ⁷	NHW	0.72		1.76	3.2	3.05	1.88

LALES = Los Angeles Latino Eye Study; NHW = non-Hispanic White

* The study combined ages 40–59 into one group.

NOTE: The studies reporting prevalence used different definitions of disease; therefore, caution should be exercised when comparing these studies.

SOURCE: Adapted with permission from Varma R, Ying-Lai M, Francis B, et al, Los Angeles Latino Eye Study Group. Prevalence of open-angle glaucoma and ocular hypertension in Latinos: the Los Angeles Latino Eye Study. *Ophthalmology* 2004;111:1445.

1. Tielsch JM, Sommer A, Katz J, et al. Racial variations in the prevalence of primary open-angle glaucoma. The Baltimore Eye Survey. *JAMA* 1991;266:369-74.
2. Leske MC, Connell AM, Schachat AP, Hyman L. The Barbados Eye Study. Prevalence of open angle glaucoma. *Arch Ophthalmol* 1994;112:821-9.
3. Quigley HA, West S, Rodriguez J, et al. The prevalence of glaucoma in a population-based study of Hispanic subjects: Proyecto VER. *Arch Ophthalmol* 2001;119:1819-26.
4. Mitchell P, Smith W, Attebo K, Healey PR. Prevalence of open-angle glaucoma in Australia. The Blue Mountains Eye Study. *Ophthalmology* 1996;103:1661-9.
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7. Coffey M, Reidy A, Wormald R, et al. Prevalence of glaucoma in the west of Ireland. *Br J Ophthalmol* 1993;77:17-21.

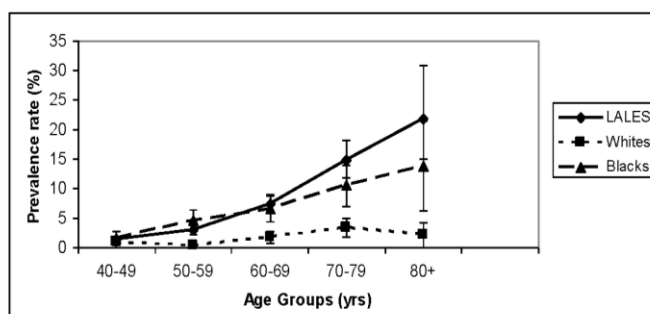


FIGURE 1. Comparison of age-specific prevalence of open-angle glaucoma in Latinos (Los Angeles Latino Eye Study), African Americans/Blacks and non-Hispanic Whites (the Baltimore Eye Study)¹

* The data shown from LALES is from a different study.

SOURCE: Adapted with permission from Varma R, Ying-Lai M, Francis B, et al, Los Angeles Latino Eye Study Group. Prevalence of open-angle glaucoma and ocular hypertension in Latinos: the Los Angeles Latino Eye Study. *Ophthalmology* 2004;111:1446.

1. Tielsch JM, Sommer A, Katz J, et al. Racial variations in the prevalence of primary open-angle glaucoma. The Baltimore Eye Survey. *JAMA* 1991;266:369-74.

RISK FACTORS

The findings of epidemiological investigations and clinical trials provide a framework for assessing the risk factors associated with POAG. The important risk factors associated with POAG are as follows:

- ◆ Intraocular pressure level
- ◆ Older age
- ◆ Family history of glaucoma
- ◆ African ancestry or Latino/Hispanic ethnicity
- ◆ Thinner central cornea¹⁰
- ◆ Low ocular perfusion pressures^{11,12}
- ◆ Type 2 diabetes mellitus¹³⁻¹⁵
- ◆ Myopia^{12,16-18}
- ◆ Genetic mutations¹⁹

Intraocular Pressure

Several population-based studies have demonstrated that the prevalence of POAG^{4,20-26} increases as the level of IOP increases (see Figures 2 and 3). These studies provide strong evidence that IOP plays an important role in the neuropathy of POAG. Furthermore, studies have demonstrated that reduction in the level of IOP lessens the risk of visual field progression in OAG (see Table 2).²⁷⁻³² In addition, treated eyes that have a greater IOP fluctuation may be at increased risk of progression, although this has not been shown consistently.³³⁻³⁷

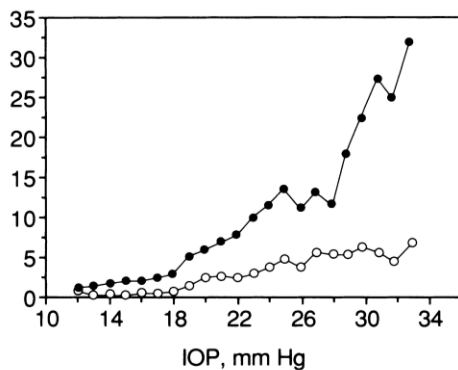


FIGURE 2. Prevalence of Primary Open-Angle Glaucoma in Relation to Screening Intraocular Pressure
African American subjects, n = 4,674 eyes (closed circles);
Caucasian American subjects, n = 5,700 eyes (open circles).

SOURCE: Sommer AE, Tielsch JM, Katz J, et al. Relationship between intraocular pressure and primary open angle glaucoma among white and black Americans. *Arch Ophthalmol* 1991;109:1092. Copyright 1991. Reprinted with permission from the American Medical Association. All rights reserved.

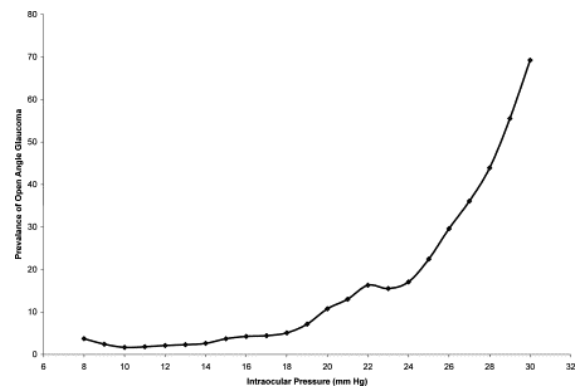


FIGURE 3. The relationship between prevalence of open-angle glaucoma and intraocular pressure (measured using Goldmann applanation tonometry) in Latinos (n=5970) in the Los Angeles Latino Eye Study.

SOURCE: Adapted with permission from Francis B, Varma R, Chopra V, et al, Los Angeles Latino Eye Study Group. Intraocular pressure, central corneal thickness, and prevalence of open-angle glaucoma: the Los Angeles Latino Eye Study. *Am J Ophthalmol* 2008;146:743.

TABLE 2 RANDOMIZED CLINICAL TRIALS WITH PUBLISHED RESULTS

Name	Study Design	No. of Patients	Follow-up Duration (years)	Finding
Scottish Glaucoma Trial ^{1,2}	Newly diagnosed POAG: medical therapy vs. trabeculectomy	116	4.6 (mean)	Trabeculectomy lowered IOP (-58%) more than medicine (-42%); medical therapy group had more deterioration in visual fields than trabeculectomy group.
Moorfields Primary Treatment Trial ³	Newly diagnosed POAG: medical therapy vs. laser trabeculoplasty vs. trabeculectomy	168	5+	Trabeculectomy lowered IOP the most (-60%); laser trabeculoplasty (-38%) and medical therapy groups (-49%) had more deterioration in visual fields than trabeculectomy group.
Collaborative Normal-Tension Glaucoma Study ⁴	POAG in eyes with normal IOP: rate of progression, effect of IOP reduction on progression rate	230	5+	Lowering IOP (-37%) retarded the progression rate of visual field loss compared with untreated eyes (-1%).
Early Manifest Glaucoma Trial ^{5,6,7}	Newly diagnosed POAG: medical therapy and laser trabeculoplasty vs. no treatment	255	8 (median)	Lowering IOP with medical therapy and trabeculoplasty (-25%) slowed progression of optic disc and visual field damage.
Collaborative Initial Glaucoma Treatment Study ⁸	Newly diagnosed POAG: medicine vs. trabeculectomy	607	5+	Lowering IOP with initial filtering as surgery (-46%) was as effective as medical therapy (-38%) to inhibit progression of visual field damage, though the amount of reduction was slightly greater after surgery.
Advanced Glaucoma Intervention Study (AGIS) ^{9,10}	POAG after medical therapy failure with no previous surgery: laser trabeculoplasty vs. trabeculectomy	591	10–13	Surgical outcome varied by race; patients with African ancestry did better with laser trabeculoplasty as first surgery (-30% IOP), while in the longer term (4+ years) Caucasian American patients did better with trabeculectomy as first surgery (-48% IOP). Lowest IOP group during follow-up after surgical interventions (-47%) prevented further visual field deterioration in advanced glaucoma patients.

IOP = intraocular pressure; POAG = primary open-angle glaucoma

1. Jay JL, Allan D. The benefit of early trabeculectomy versus conventional management in primary open angle glaucoma relative to severity of disease. *Eye* 1989;3:528-35.
2. Jay JL, Murray SB. Early trabeculectomy versus conventional management in primary open angle glaucoma. *Br J Ophthalmol* 1988;72:881-9.
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4. Collaborative Normal-Tension Study Group. Comparison of glaucomatous progression between untreated patients with normal-tension glaucoma and patients with therapeutically reduced intraocular pressures. *Am J Ophthalmol* 1998;126:487-97.
5. 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;120:1268-79.
6. Leske MC, Heijl A, Hussein M, et al, Early Manifest Glaucoma Trial Group. Factors for glaucoma progression and the effect of treatment. The Early Manifest Glaucoma Trial. *Arch Ophthalmol* 2003;121:48-56.
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9. The AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS): 7. The relationship between control of intraocular pressure and visual field deterioration. *Am J Ophthalmol* 2000;130:429-40.
10. The AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS): 13. Comparison of treatment outcomes within race. Ten-year results. *Ophthalmology* 2004;111:651-64.

In spite of the relationship between the level of IOP and POAG, there is great interindividual variation in the susceptibility of the optic nerve to IOP-related damage. Population-based studies indicate that a variable proportion of patients with IOP greater than 21 mmHg (Northern Italy [13%],³⁸ Los Angeles [18%],⁹ Arizona [20%],²³ Blue Mountains [25%],²¹ Melbourne [39%],³⁹ Baltimore [45%],⁴⁰ Rotterdam [61%],⁴ Barbados [71%]¹²) have glaucomatous optic nerve damage.²⁰ This suggests that an IOP level of greater than 21 mmHg is an arbitrarily defined level and highlights the poor value of utilizing a specific IOP cutoff as a measure for screening and diagnosing POAG.

Age

Older age is another important risk factor for the presence of POAG.^{21-23,39,40} A number of epidemiological studies demonstrate that the prevalence of glaucoma increases dramatically with age, particularly among individuals of Latino/Hispanic and African descent (see Table 1, Figures 1 and 4). African Americans 73 to 74 years old and 75 and older had a prevalence of 5.7% and 23.2%, respectively. Similarly, the prevalence of OAG was 3.4% for white individuals 73 and 74 years old and 9.4% for those 75 and older.⁴¹

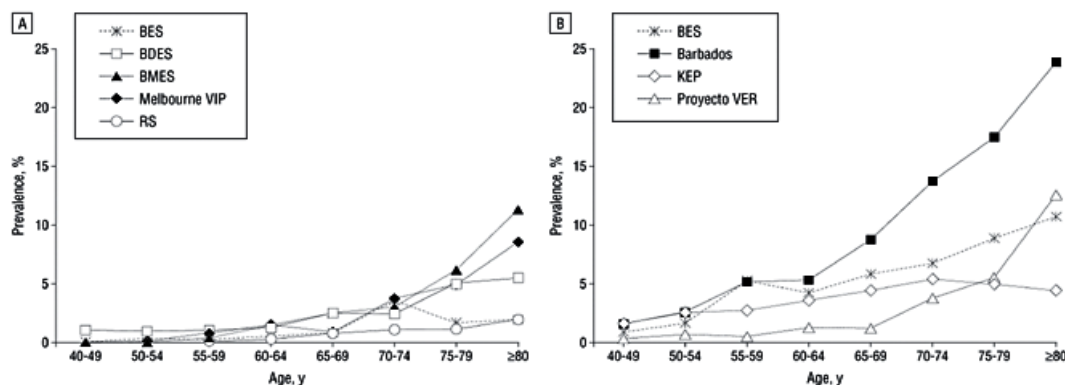


FIGURE 4. Prevalence of glaucoma in white (A) and black and Hispanic (B) subjects. BES indicates Baltimore Eye Survey,¹ Baltimore, Md; BDES, Beaver Dam Eye Study,² Beaver Dam, Wis; BMES, Blue Mountains Eye Study,³ Sydney, New South Wales; Melbourne VIP, Melbourne Visual Impairment Project,⁴ Melbourne, Victoria; RS, Rotterdam Study,⁵ Rotterdam, the Netherlands; Barbados, Barbados Eye Study,⁶ Barbados, West Indies; KEP, Kongwa Eye Project,⁷ Tanzania; and Proyecto VER, Vision Evaluation Research,⁸ Nogales and Tucson, Ariz.

SOURCE: Friedman DS, Wolfs RC, O'Colmain BJ, et al. Prevalence of open-angle glaucoma among adults in the United States. *Arch Ophthalmol* 2004;122:535. Copyright 2004. Reprinted with permission from the American Medical Association. All rights reserved.

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Family History

Family history is a risk factor for glaucoma. In the Rotterdam Eye Study, where all siblings of glaucoma cases and controls were examined, the odds of having POAG was 9.2-fold higher for individuals who have a first-degree relative (sibling or parent) with medically confirmed POAG.⁴² Other studies in which family members were not physically examined depend on patient reports of the status of family members, and these are known to be subject to several biases. Nonetheless, they support the concept that first degree relatives of those with OAG are at greater risk. For example, in the Baltimore Eye Survey and the Los Angeles Latino Eye Study (LALES), for individuals with POAG the odds were twice as high (1.92 and 2.85, respectively) of reporting a first-degree relative (parent, child, or sibling) with glaucoma compared with individuals who did not have glaucoma. However, the odds increased to over three times as high if they reported that they had a sibling with glaucoma (LALES 3.47,⁴³ Baltimore 3.7⁴⁴). Interestingly, the odds rose to fivefold higher if there were two or more siblings who were reported to have a history of glaucoma.

Race or Ethnicity

For POAG, ethnicity is an important risk factor (see Figures 1 and 4). The prevalence of POAG is higher in individuals of West African, Afro-Caribbean, or Latino/Hispanic origin than of other groups.^{9,22,23,40,45,46} The prevalence is three times higher in African Americans and Hispanics of Mexican ancestry compared with non-Hispanic Whites.^{9,40} Blindness from glaucoma is at least six times more prevalent in African Americans than in Caucasian Americans.⁸

Central Corneal Thickness

Because applanation tonometry measurements are derived from resistance to corneal indentation and corneal stiffness, differences in central corneal thickness (CCT) may introduce artifacts in IOP measurement.^{10,29,47-53} The mean CCT in healthy human eyes varies by race/ethnicity. The average CCT measured ultrasonically in Caucasian Americans is 556 μm , in Latinos it is 546 μm ⁵⁴ and in African Americans it is 534 μm .⁵² If IOP is underestimated in those with thinner CCT, the relationship between IOP level and OAG damage may be underestimated, since the IOP is actually higher than measured. Conversely, if IOP is overestimated in those with a nonedematous thicker CCT, the relationship between IOP level and OAG damage may be overestimated, since the IOP is actually lower than measured. Although several tables and figures have been published, no standard nomogram correcting applanation IOP measurements for CCT has yet been fully validated.^{55,56}

A thinner central cornea has been reported as an independent risk factor (independent of IOP) associated with POAG,⁵⁷ though not in all studies. In LALES, the risk of having OAG was higher in persons with thinner CCT compared with those with normal or thicker CCT even after adjusting the IOP (see Figure 5).⁵⁸ Studies show that differences in corneal biomechanics across individuals may have a greater impact on IOP measurement errors than CCT.^{59,60}

Low Ocular Perfusion Pressure

Ocular perfusion pressure is the difference between blood pressure (at systole or diastole) and the IOP. It has been hypothesized that low ocular perfusion pressures lead to alterations in blood flow at the optic nerve head and contribute to progressive glaucomatous optic nerve damage. Population-based studies in African Americans, Hispanics, and non-Hispanic Whites have provided evidence that low diastolic perfusion pressure (<50 mmHg) is associated with a higher prevalence of POAG.^{11,23,61,62} In addition, in the Early Manifest Glaucoma Treatment Study, low systolic perfusion pressure (≤ 125 mmHg) was associated with a higher risk of glaucoma progression (relative risk of 1.42) over an 8-year period.³⁶

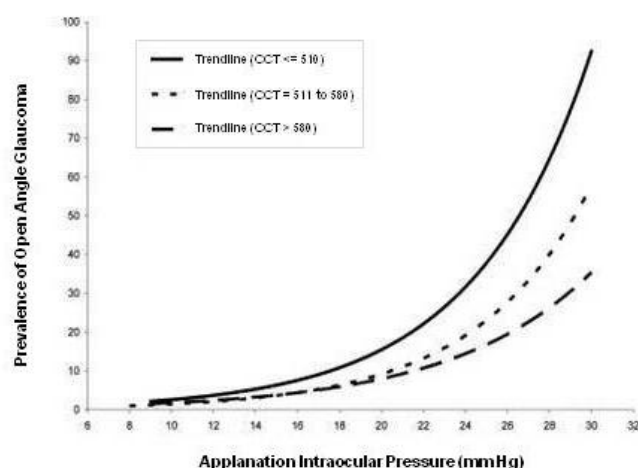


FIGURE 5. The relationship between the prevalence of open-angle glaucoma and applanation intraocular pressure stratified by central corneal thickness (CCT) in micrometers in the Latinos (n=5970) in the Los Angeles Latino Eye Study.

SOURCE: Adapted with permission from Francis B, Varma R, Chopra V, et al, Los Angeles Latino Eye Study Group. Intraocular pressure, central corneal thickness, and prevalence of open-angle glaucoma: the Los Angeles Latino Eye Study. *Am J Ophthalmol* 2008;146:743.

Type 2 Diabetes Mellitus

While there are some conflicting data on the association between type 2 diabetes mellitus (type 2 DM) and POAG,^{13-15,63-69} there is increasing evidence from population-based studies suggesting that type 2 DM is an important risk factor for POAG.^{13-15,65,67} Population-based assessments of Hispanics (in Los Angeles, California),¹⁴ non-Hispanic Whites (in Beaver Dam, Wisconsin and Blue Mountains, Australia),^{13,67} and a large cohort enrolled in the Nurses' Health Study⁶⁵ have shown that persons with type 2 DM are more likely (40% higher odds in Hispanics, twofold higher odds in non-Hispanic Whites) to have POAG. Further, in the LALES,¹⁴ longer duration of type 2 DM was associated with a higher risk of having POAG. One explanation for this observation is that microvascular changes in the optic nerve may contribute to the greater susceptibility of optic nerve damage in persons with type 2 DM.⁶⁶

Myopia

Large cross-sectional epidemiologic studies in Afro-Caribbeans, Hispanics, non-Hispanic Whites, Chinese, Asian Indians, and Japanese suggest that persons with myopia have a higher prevalence of OAG than those without myopia.^{12,16-18,70-73} More recently, data from the LALES have provided evidence of an independent relationship between longer axial length (axial myopia) and a higher prevalence of OAG.⁷⁴ The underlying hypothesis is that individuals with axial myopia have weaker scleral support at the optic nerve, and this contributes to a greater susceptibility of the optic nerve to glaucomatous damage.

Genetic Factors

The first gene to be linked to POAG was the myocilin gene (*MYOC*) on chromosome 1.⁷⁵ In one study, 3% to 4% of cases with POAG were found to have mutations in the myocilin gene.¹⁹ Several chromosomal regions have now been linked to POAG and additional genes identified.^{76,77} However, a majority of the cases with POAG do not have an identified genetic abnormality, suggesting that glaucomatous optic nerve damage may be multifactorial in its development, with different genes modifying the impact of various factors such as age, IOP, and blood flow.

Other Factors

In addition, migraine headache and peripheral vasospasm have been identified as risk factors for glaucomatous optic nerve damage.⁷⁸⁻⁸⁰ The association between POAG and factors such as concurrent cardiovascular disease and systemic hypertension has not been demonstrated consistently.^{12,16,61,62,81-85}



POPULATION SCREENING FOR GLAUCOMA

Population-based screening for glaucoma is currently not cost-effective.⁸⁶ Screening may be more useful and cost-effective when it is targeted at populations at high risk for glaucoma, such as older adults,⁷ those with a family history of glaucoma,^{42,44,87-89} and African Americans and Hispanics.⁷ Screening for glaucoma could be included in general screening for eye disease, especially among older populations. Once screening technologies improve, screening may be indicated for a wider population. In 2009, the U.S. Agency for Healthcare Research and Quality Effective Health Care Program funded a review of the comparative effectiveness of screening for glaucoma. These results, when available, will assist in identifying which screening methods should be used.

It is important to consider methods for screening the general population for POAG, because patients are asymptomatic until late in the disease process. It is possible to treat patients with POAG and to either slow or prevent the progression of visual field loss. Even mild visual field loss decreases health-related quality of life.^{90,91} There are three main approaches to screening patients for POAG—measuring the IOP, assessing the optic nerve head and retinal nerve fiber layer, and evaluating the visual field. The IOP, appearance of the optic nerve, and status of visual function provide complementary clues, but to evaluate all in a single session would be impractical in population-based screening programs.⁹²

Measuring IOP is not an effective method for screening populations for glaucoma. Using an IOP above 21 mmHg, the sensitivity for the diagnosis of POAG by tonometry was 47.1% and the specificity was 92.4% in one population survey.⁹³ Population-based studies suggest that half of all individuals with POAG have IOP levels consistently below 22 mmHg, the usual screening cutoff.^{4,21} Furthermore, half of all individuals with POAG have IOP below 22 mmHg at a single screening.²⁰ Additionally, most individuals with elevated pressures at a screening measurement do not have, and may never develop, optic nerve damage, although risk increases with higher IOP.^{20,21} Studies show that approximately 1 of every 10 to 15 individuals with elevated IOP at screening can have demonstrable optic nerve damage, and half of these (1 in 20 to 30 individuals) may not previously have been diagnosed with glaucoma.^{20,21,94,95}

A second method of screening for glaucoma is to assess the optic nerve head and retinal nerve fiber layer. Current approaches to do this are technology dependent; they require examination expertise and, therefore, do not have ideal screening characteristics. While some authors report high sensitivity and specificity for subjective optic disc examination, others have found poor agreement and high interobserver variation.⁹⁶⁻⁹⁸

A third method of screening for glaucoma is to evaluate the visual field. Visual field testing has been used in mass screening but at unknown rates of sensitivity and specificity.⁹⁹ Perimetry based on frequency doubling technology shows promise as a screening tool to detect moderate glaucomatous damage. In a clinic-based population, frequency doubling technology correctly identified 91% of eyes with an abnormal Glaucoma Hemifield Test and 94% of glaucoma suspects with normal visual fields on Humphrey Field Analyzer (Carl Zeiss Meditec, Inc., Dublin, CA) threshold testing.¹⁰⁰ Test time with this technique was about 1 minute per eye. When used in a population-based glaucoma screening in Japan, the frequency doubling technology alone showed a positive predictive value ranging between 32.6% and 45.1% based on 14,814 subjects, while the negative predictive value was estimated at 98.7% based on a subset of 4141 subjects.¹⁰¹

In January 2002, the Centers for Medicare and Medicaid Services initiated coverage for glaucoma examinations by eye care professionals in the office for beneficiaries with diabetes mellitus, those with a family history of glaucoma, African Americans 50 or older, and Hispanic Americans 65 or older. While this is referred to as a screening benefit or examination, it is not applicable to examination of individuals in the community at random.

In 2005, the National Committee for Quality Assurance introduced a new quality measure for health plans that offer Medicare Advantage coverage in recognition of the importance of identifying patients with glaucoma and the difficulties of screening. The measure is based on a comprehensive eye examination conducted in the previous 2 years for older adults. The intent of the quality measure is to allow purchasers and consumers to compare the performance of managed health plans reliably.



CARE PROCESS

PATIENT OUTCOME CRITERIA

- ◆ Preservation of visual function
- ◆ Maintenance of quality of life

DIAGNOSIS

The comprehensive initial glaucoma evaluation (history and physical examination) includes all components of the comprehensive adult medical eye evaluation¹⁰² in addition to, and with special attention to, those factors that specifically bear upon the diagnosis, course, and treatment of POAG. The examination may require more than one visit. For instance, an individual might be suspected of having glaucoma on one visit but may return for further evaluation to confirm the diagnosis, including additional IOP measurements, gonioscopy, CCT determination, visual field assessment, and optic nerve head and retinal nerve fiber layer evaluation and documentation.

Evaluation of Visual Function

Self-reported functional status or difficulty with vision can be assessed either by patient complaints or by using specific questionnaires, including the National Eye Institute - Visual Function Questionnaire-25.^{90,103-109} [A:III] Patients with glaucoma may have sufficient visual field loss to impair night driving, near vision, and outdoor mobility.^{91,110-112}

Ophthalmic Evaluation

In completing the elements in the comprehensive adult medical eye evaluation,¹⁰² the ophthalmic evaluation specifically focuses on the following elements:

- ◆ History^[A:III]
- ◆ Visual acuity measurement^[A:III]
- ◆ Pupil examination^[B:II]
- ◆ Anterior segment examination^[A:III]
- ◆ Intraocular pressure measurement^[A:I]
- ◆ Gonioscopy^[A:III]
- ◆ Optic nerve head and retinal nerve fiber layer examination^[A:III]
- ◆ Fundus examination^[A:III]

History

- ◆ Ocular,^[A:III] family,^{4,42,44} [A:II] and systemic history (e.g., asthma).^[A:III] The severity and outcome of glaucoma in family members, including history of visual loss from glaucoma, should be obtained during initial evaluation.^{42,44} [B:III]

- ◆ Review of pertinent records,^[A:III] with particular reference to the past IOP levels, status of the optic nerve, and visual field.^[A:III]
- ◆ Current ocular and systemic medications (e.g., corticosteroids) and known local or systemic intolerance to ocular or systemic medications.^[A:III]
- ◆ Ocular surgery.^[A:III]

A history of LASIK or photorefractive keratectomy is associated with a falsely low IOP measurement due to thinning of the cornea.¹¹³ Cataract surgery may also lower the IOP compared with the presurgical baseline.¹¹⁴ A history of prior glaucoma laser or incisional surgical procedures should be elicited.

Visual acuity measurement

Visual acuity with current correction (the power of the present correction recorded) at distance and, when appropriate, at near should be measured.^[A:III] Refraction may be indicated to obtain the best-corrected visual acuity.

Pupil examination

The pupils are examined for reactivity and an afferent pupillary defect.^{115-117 [B:II]}

Anterior segment examination

A slit-lamp biomicroscopic examination of the anterior segment can provide evidence of physical findings associated with narrow angles, such as shallow peripheral anterior chamber depth and crowded anterior chamber angle anatomy,^{118,119} corneal pathology, or a secondary mechanism for elevated IOP such as pseudoexfoliation (exfoliation syndrome), pigment dispersion with Krukenberg spindle and/or iris transillumination defects, iris and angle neovascularization, or inflammation.^[A:III]

Intraocular pressure measurement

Intraocular pressure is measured in each eye, preferably by Goldmann applanation tonometry, before gonioscopy or dilation of the pupil.^{5,27,30-32,120-128 [A:III]} Recording time of day of IOP measurements may be helpful to assess diurnal variation. Unrecognized fluctuations in IOP may lead to progression of POAG.¹²⁹⁻¹³² Therefore, additional measurements may be indicated, either at different hours of the day on the same day or on different days.

Gonioscopy

The diagnosis of POAG requires careful evaluation of the anterior chamber angle to exclude angle closure or secondary causes of IOP elevation, such as angle recession, pigment dispersion, peripheral anterior synechiae, angle neovascularization, and inflammatory precipitates.^{133 [A:III]} (See www.gonioscopy.org and Selected Reference Texts section for discussion of the techniques of gonioscopy.)

Optic nerve head and retinal nerve fiber layer examination

Examination of the optic nerve head and retinal nerve fiber layer provides valuable structural information about glaucomatous optic nerve damage.¹³⁴⁻¹³⁶ Visible structural alterations of the optic nerve head or retinal nerve fiber layer and development of peripapillary choroidal atrophy frequently occur before visual field defects can be detected.^{135,137-144} Careful study of the optic disc neural rim for small hemorrhages is important, since these hemorrhages often precede visual field loss and further optic nerve damage in patients with glaucoma.^{27,28,30,36,145-149} In the Ocular Hypertension Treatment Study, the incidence of POAG in eyes with disc hemorrhage was 13.6% compared with 5.2% in eyes without disc hemorrhage over 8 years.¹⁴⁶ In the Early Manifest Glaucoma Trial, 13% of patients had disc hemorrhages at baseline examination, and hemorrhages were associated with progression.³⁰

The preferred technique for optic nerve head and retinal nerve fiber layer evaluation involves magnified stereoscopic visualization (as with the slit-lamp biomicroscope), preferably through a

dilated pupil.^[A:III] In some cases, direct ophthalmoscopy complements magnified stereoscopic visualization, providing additional information of optic nerve detail due to the greater magnification of the direct ophthalmoscope. Red-free illumination of the posterior pole by stereo-biomicroscopy with an indirect lens at the slit lamp, the direct ophthalmoscope, or with digital red-free photography may aid in evaluating the retinal nerve fiber layer.¹⁵⁰

Fundus examination

Examination of the fundus, through a dilated pupil whenever feasible, includes a search for other abnormalities that may account for optic nerve changes and/or visual field defects (e.g., optic nerve pallor, disc drusen, optic nerve pits, disc edema from central nervous system disease, macular degeneration, retinovascular occlusion, and other retinal disease).^[A:III]

Supplemental Ophthalmic Testing

Supplemental ophthalmic testing includes the following components:

- ◆ Central corneal thickness measurement^[A:II]
- ◆ Visual field evaluation^[A:III]
- ◆ Optic nerve head and retinal nerve fiber layer analysis^[A:II]

Central corneal thickness measurement

Measurement of CCT aids the interpretation of IOP readings and helps to stratify patient risk for ocular damage.^{29,53,57,151} ^[A:II] An overestimation of the real IOP may occur in eyes with corneas that are thicker than average, while an underestimation of the real IOP tends to occur in eyes with corneas that are thinner than average. Several studies have sought to quantify the relationship between measured IOP level and CCT, but there is no generally accepted correction formula. There is a controversy over whether CCT represents a risk factor for glaucoma due to its effect on IOP measurement or whether CCT is a risk factor itself, unrelated to IOP.^{50,152,153} While it is clear that thinner CCT is a risk factor for the development of POAG, studies of progression have had variable findings. Some studies have found an association while others have not (see Table 3).

Visual field evaluation

Automated static threshold perimetry is the preferred technique for evaluating the visual field.¹⁵⁴ ^[A:III] The frequency doubling technology (FDT) method with the central 20-degree test program (C-20) and short-wavelength automated perimetry (SWAP) with the central 24-degree test program (24-2) are two of several alternative testing methods to screen for a defect before conducting more definitive threshold testing.¹⁵⁴ Visual field testing based on SWAP¹⁵⁵ and FDT¹⁵⁶ may detect defects or progression of defects earlier than conventional white-on-white perimetry in some patients.¹⁵⁷ Careful manual combined kinetic and static threshold testing (e.g., Goldmann visual fields) is an acceptable alternative when patients cannot perform automated perimetry reliably or if it is not available.^[A:III] Repeat, confirmatory visual field examinations may be required for test results that are unreliable or show a new glaucomatous defect before changing management.^{27,124} ^[A:III] It is best to use a consistent examination strategy for visual field testing.

TABLE 3 SUMMARY OF RESULTS FOR CENTRAL CORNEAL THICKNESS AS A RISK FACTOR FOR PROGRESSION OF GLAUCOMA

Study	No. of Patients	Level of Evidence	Risk	Comments
Early Manifest Glaucoma Trial ¹	255	I	+	Thin CCT is a risk factor for progression of glaucoma (in those with baseline IOP ≥ 21 mmHg)
Kim ²	88	II	+	Thin CCT is associated with visual field progression in glaucoma
Chauhan ³	54	II	-	CCT did not predict visual field or optic disc progression
Jonas ⁴	454	II	-	CCT is not associated with progression of visual field damage
Jonas ⁵	390	II	-	CCT is not associated with optic disc hemorrhages
Congdon ⁶	230	II	-	CCT is not associated with glaucoma progression (though corneal hysteresis was)
Stewart ⁷	310	III	+/-	CCT is associated with progression on univariate analysis but is not associated on multivariate analysis

CCT = central corneal thickness

SOURCE: Adapted with permission from Dueker D, Singh K, Lin SC, et al. Corneal thickness measurement in the management of primary open-angle glaucoma: a report by the American Academy of Ophthalmology. *Ophthalmology* 2007;114:1784.

1. Leske MC, Heijl A, Hyman L, et al. Early Manifest Glaucoma Trial Group. Predictors of long-term progression in the Early Manifest Glaucoma Trial. *Ophthalmology* 2007;114:1965-72.
2. Kim JW, Chen PP. Central corneal pachymetry and visual field progression in patients with open-angle glaucoma. *Ophthalmology* 2004;111:2126-32.
3. Chauhan BC, Hutchison DM, LeBlanc RP, et al. Central corneal thickness and progression of the visual field and optic disc in glaucoma. *Br J Ophthalmol* 2005;89:1008-12.
4. Jonas JB, Stroux A, Velten I, et al. Central corneal thickness correlated with glaucoma damage and rate of progression. *Invest Ophthalmol Vis Sci* 2005;46:1269-74.
5. Jonas JB, Stroux A, Oberacher-Velten IM, et al. Central corneal thickness and development of glaucomatous optic disk hemorrhages. *Am J Ophthalmol* 2005;140:1139-41.
6. Congdon NG, Broman AT, Bandeen-Roche K, et al. Central corneal thickness and corneal hysteresis associated with glaucoma damage. *Am J Ophthalmol* 2006;141:868-75.
7. Stewart WC, Day DG, Jenkins JN, et al. Mean intraocular pressure and progression based on corneal thickness in primary open-angle glaucoma. *J Ocul Pharmacol Ther* 2006;22:26-33.

Optic nerve head and retinal nerve fiber layer analysis

The appearance of the optic nerve should be documented.^{136,158 [A:II]} Color stereophotography is an accepted method for documenting optic nerve head appearance. Computer-based image analysis of the optic nerve head and retinal nerve fiber layer is an alternative for documentation of the optic nerve. As improvements in these instruments continue, the capacity for them to help the clinician diagnose glaucoma and identify progressive nerve damage becomes more reliable.¹⁵⁹⁻¹⁶¹ Stereoscopic disc photographs and computerized images of the nerve are distinctly different methods for optic nerve documentation and analysis.¹⁶² Each is complementary with regard to the information they provide the clinician who must manage the patient. In the absence of these technologies, a nonstereoscopic photograph or a drawing of the optic nerve head should be recorded, but these are less desirable alternatives to stereophotography or computer-based imaging.^{163 [A:III]} In patients with advanced glaucomatous optic neuropathy, there is limited benefit of using stereophotography to identify progressive optic nerve change.^{164,165}

There are three types of computer-based imaging devices currently available for glaucoma: confocal scanning laser ophthalmoscopy, optical coherence tomography, and scanning laser polarimetry. In a systematic review, the versions of these devices that were studied were similar in their ability to distinguish glaucoma from controls.^{136,166} When examined for the ability of these devices to detect glaucoma progression, studies have shown a relative lack of concordance between the structural (the imaging devices) and functional (visual field) tests.^{167,168} Taken together, computer-based imaging devices for glaucoma provide useful, quantitative information for the clinician when analyzed in

conjunction with other relevant clinical parameters. As device technology evolves (e.g., higher resolution spectral domain optical coherence tomography), the diagnostic performance is expected to improve accordingly.

MANAGEMENT

Goals

The goals of managing patients with POAG are to achieve the following:

- ◆ Controlled IOP in the target range
- ◆ Stable optic nerve/retinal nerve fiber layer status
- ◆ Stable visual fields

Because elevated IOP is a treatable cause of POAG damage, one can expect to reduce the risk of disease progression in many patients by lowering the IOP by means of medication, laser therapy, or incisional glaucoma surgery. Results from randomized controlled trials (summarized in Table 2) and other studies reinforce this expectation and provide evidence that the more the IOP is lowered, the more likely is it to slow the rate of progression of POAG.^{5,27-32,36,120,122,123,126,169-180}

Management is a challenge for the patient and the doctor, because POAG is a chronic, often asymptomatic, condition that may require frequent use of multiple and expensive medications¹⁸¹ that may cause side effects or may require laser or incisional surgery. The effects of treatment, the patient's quality of life, and the patient's life expectancy are important to consider when choosing therapy. The diagnosis, severity of the disease, prognosis and management plan, and likelihood of long-term therapy should be discussed with the patient.^[A:III] Substantial field loss in glaucoma is associated with a decrease in quality of life measures.^{90,91,182}

Target Intraocular Pressure for Patients with POAG

The goal of glaucoma treatment is to maintain the IOP in a range at which a patient is likely to remain stable or at which worsening of glaucoma will be slow enough that the risk of additional intervention is not justified.^{183,184} The estimated upper limit of this range is considered the "target pressure." The initial target pressure is an estimate and a means toward the ultimate goal of protecting the patient's vision. The target pressure should be individualized and may need adjustment during the course of the disease.^[A:III]

When initiating therapy, the ophthalmologist assumes that the measured pretreatment pressure range contributed to optic nerve damage and is likely to cause additional damage in the future. Lowering the pretreatment IOP by 25% or more has been shown to inhibit progression of POAG.^{27,30-32,123,125 [A:II]} It is reasonable to select an initial target pressure at least 25% lower than pretreatment levels. Choosing an even lower target IOP can be justified if there is more severe optic nerve damage, if the damage is progressing rapidly, or if other risk factors such as family history, age, or disc hemorrhages are present (see Risk Factors for Progression). Choosing a less aggressive target IOP may be reasonable if the risks of aggressive treatment outweigh the benefits (e.g., if a patient does not tolerate medical therapy well and surgical intervention would be difficult or if the patient's life expectancy is short). In a study of newly diagnosed patients with moderate to advanced glaucoma, a subset of patients randomized to initial lowering of IOP by surgery did better than those assigned to medical treatment over an 8-year period, and this could be due to the lower mean posttreatment IOP in the surgery group.¹⁸⁵

The adequacy and validity of the target pressure are periodically reassessed by comparing optic nerve status (by optic disc appearance, quantitative assessments of the disc and nerve fiber layer, and visual field tests) with previous examinations. If progression occurs at the target pressure, undetected IOP fluctuations and adherence to therapy can be re-evaluated before adjusting the target IOP. However, target pressure is an estimate, and all treatment decisions must be individualized according to the needs of the patient.

Therapeutic Choices

The IOP can be lowered by medical treatment, laser therapy, or incisional glaucoma surgery (alone or in combination). The choice of initial therapy depends on numerous considerations, and discussion of treatment with the patient should include the relative risks and benefits of the three options.^[A:III]

Medical treatment

Unless contraindicated, medical therapy is presently the most common initial intervention to lower IOP. There are many drugs available for initial therapy, and medication choice may be influenced by potential cost, side effects, and dosing schedules (see Table 4 for an overview of options available). Patient adherence to therapy is enhanced by using eyedrops with the fewest side effects as infrequently as necessary to achieve the target IOP. If target IOP is not achieved by one medication, then additional separate medications, combination therapies, or switching of treatments may be considered to reach the target IOP.

Prostaglandin analogs and beta-blockers are the most frequently used initial eye drops for lowering IOP in patients with glaucoma.^{186,187} Prostaglandin analogs are the most effective drugs at lowering IOP and can be considered as initial medical therapy unless other considerations such as cost, side effects, intolerance, or patient refusal preclude this.^{188,189 [A:I]} Other agents in addition to prostaglandin analogs and beta-blockers include alpha₂ adrenergic agonists, parasymphomimetics, and topical and oral carbonic anhydrase inhibitors.^{190,191}

The ophthalmologist should consider the balance between side effects and effectiveness in choosing a regimen of maximal effectiveness and tolerance to achieve the desired IOP reduction for each patient.^{192-195 [A:III]} Frequent dosing and side effects (such as depression, exercise intolerance, and impotence with topical beta-blockers) may affect adherence to therapy.^{193,196}

To determine the effectiveness of topical therapy, it is necessary to distinguish between the therapeutic impact of an agent on IOP and ordinary background fluctuations of IOP. It may be useful to begin by treating only one eye and comparing the relative change of the IOP in the two eyes at follow-up visits.¹³¹ However, because the two eyes of an individual may not respond equally to the same medication, and because of the possibility of asymmetric spontaneous fluctuations and the potential for contralateral effect of monocular topical medications,¹⁹⁷ it is acceptable to compare the effect in one eye relative to multiple baseline measurements.¹⁹⁸ Additional studies are needed to compare directly monocular and binocular drug trials to find out whether a monocular trial is better at determining a nonresponder than a binocular trial. If a drug fails to reduce IOP sufficiently despite good adherence to therapy, it can be replaced with an alternate agent until effective medical treatment is established. If a single medication is effective in lowering IOP but the target pressure is not reached, combination therapy¹⁹⁹ or switching to an alternative therapy may be appropriate.

The patient and ophthalmologist together decide on a practical and feasible regimen to follow in terms of dosing, cost, and adherence in the context of the patient's age and preferences.¹⁵⁸ The ophthalmologist should assess the patient who is being treated with glaucoma medication for local ocular and systemic side effects; toxicity, including interactions with other medications; and potential life-threatening adverse reactions.^{200 [A:III]} To reduce systemic absorption, patients should be educated about eyelid closure or nasolacrimal duct occlusion when applying topical medications (see Related Academy Materials section for public information brochures).²⁰¹

TABLE 4 GLAUCOMA MEDICATIONS

Drug Classification	Methods of Action	IOP Reduction*	Side Effects	Contraindications
Prostaglandin analogs	Increase uveoscleral and/or trabecular outflow	25%–33%	<ul style="list-style-type: none"> - Cystoid macular edema - Conjunctival injection - Increased eyelash growth - Periocular hyperpigmentation - Iris color change - Uveitis - Possible herpes virus activation 	<ul style="list-style-type: none"> - Macular edema - History of herpetic keratitis
Beta-adrenergic antagonists (beta-blockers)	Decrease aqueous production	20%–25%	<ul style="list-style-type: none"> - Corneal toxicity - Allergic reactions - CHF (classic teaching, although cardiologists use beta-blockers as first line treatment in CHF) - Bronchospasm (seen with nonselective) - Bradycardia - Depression - Impotence 	<ul style="list-style-type: none"> - Chronic obstructive pulmonary disease (nonselective) - Asthma (nonselective) - CHF (check with cardiologist) - Bradycardia - Hypotension - Greater than first degree heart block
Alpha-adrenergic agonists	Nonselective: improve aqueous outflow Selective: decrease aqueous production; decrease episcleral venous pressure or increase uveoscleral outflow	20%–25%	<ul style="list-style-type: none"> - Conjunctival injection - Allergic reactions - Fatigue - Somnolence - Headache 	<ul style="list-style-type: none"> - Monoamine oxidase inhibitor therapy - Infants and children younger than 2 years
Parasympathomimetic agents	Increase trabecular outflow	20%–25%	<ul style="list-style-type: none"> - Increased myopia - Eye or brow ache/pain - Decreased vision - Cataract - Periocular contact dermatitis - Corneal toxicity - Paradoxical angle closure 	<ul style="list-style-type: none"> - Neovascular, uveitic, or malignant glaucoma - Need to regularly assess fundus
Carbonic anhydrase inhibitors (mainly with systemic use)	Decrease aqueous production	15%–20%	With topical route: <ul style="list-style-type: none"> - Metallic taste - Allergic dermatitis/conjunctivitis - Corneal edema With oral route: <ul style="list-style-type: none"> - Stevens-Johnson syndrome - Malaise, anorexia, depression - Serum electrolyte imbalance - Renal calculi - Blood dyscrasias (aplastic anemia, thrombocytopenia) - Metallic taste 	<ul style="list-style-type: none"> - Sulfonamide allergy - Kidney stones - Aplastic anemia - Thrombocytopenia - Sickle cell disease

CHF = congestive heart failure; IOP = intraocular pressure

* Data from the European Glaucoma Society. Terminology and Guidelines for Glaucoma. 3rd ed. Savona, Italy:Editrice Dogma S.r.l.; 2008:127. Available at: www.eugs.org/eng/EGS_guidelines.asp. Accessed May 28, 2010.

SOURCE: Adapted with permission from the American Academy of Ophthalmology Practicing Ophthalmologists Curriculum (POC) Panel Chairs and Vice Chairs. MOC Exam Study Kit. Core ophthalmic knowledge. Core topics for glaucoma: Medical management of glaucoma. Available to Academy members only at: <http://one.aao.org/CE/MOC/MOCStudyResources.aspx>. Accessed May 28, 2010.

Adequate treatment of glaucoma requires a high level of adherence to therapy. Frequently this is not achieved; studies indicate relatively poor adherence to therapy.^{192,202-204} Even with instruction, free medication, once-daily administration, use of a dosing aid, and electronic monitoring of adherence, nearly 45% of patients in one study took fewer than 75% of their prescribed doses.²⁰⁴ Instilling eyedrops correctly is difficult for patients, and their ability to do so may worsen as glaucoma progresses.^{205,206} Repeated instruction and counseling in proper techniques for using medication as

well as a clearly written medication regimen and follow-up telephone calls may improve adherence to therapy.^{204,207,208} At each examination, medication dosage and frequency of use should be recorded.^[A:III] Reviewing the time medication was taken may be useful. Adherence to the therapeutic regimen and recommendations for therapeutic alternatives or diagnostic procedures should be discussed.^[A:III] Cost may be a factor in adherence, especially when multiple medications are used.²⁰⁸ Patient education and informed participation in treatment decisions may improve adherence²⁰⁸ and overall effectiveness of glaucoma management.

Laser trabeculoplasty

Laser trabeculoplasty can be considered as initial therapy in selected patients^{122,209 [A:I]} or an alternative for patients who cannot or will not use medications reliably due to cost, memory problems, difficulty with instillation, or intolerance to the medication. Laser trabeculoplasty lowers IOP by improving aqueous outflow and can be performed using argon, diode, and frequency-doubled YAG lasers.

Argon and diode laser trabeculoplasty

Studies using continuous-wave argon laser with a wavelength spectrum that peaks at 488 nm (argon laser trabeculoplasty [ALT]) found that treatment increases aqueous outflow and provides a clinically significant reduction of IOP in more than 75% of initial treatments of previously unoperated eyes (see Table 5).^{122,123} Since these initial studies, more compact solid-state diode lasers have mostly replaced the original argon laser with equal IOP lowering efficacy.

TABLE 5 RANDOMIZED CLINICAL TRIALS OF LASER TRABECULOPLASTY WITH PUBLISHED RESULTS

Name	Study Design	No. of Patients	Follow-up Duration (years)	Finding
Glaucoma Laser Trial (GLT) ^{1,2}	Newly diagnosed POAG: medical therapy vs laser trabeculoplasty	271	2.5–5.5	Initial laser trabeculoplasty lowered IOP more (-9 mmHg) than initial treatment with topical timolol maleate (-7 mmHg) over 2 years; initial laser trabeculoplasty was at least as effective in preserving visual field and optic disc status over 5.5 years.
Glaucoma Laser Trial Follow-up Study ²	Participants in the GLT	203	6–9	Longer follow-up reinforced the earlier findings that initial laser trabeculoplasty lowered IOP more (-1.2 mmHg) than initial treatment with topical timolol maleate and was at least as effective in preserving visual field and optic disc status.
Moorfields Primary Treatment Trial ³	Newly diagnosed POAG: medical therapy vs. laser trabeculoplasty vs. trabeculectomy	168	5+	Trabeculectomy lowered IOP the most (-60%); laser trabeculoplasty (-38%) and medical therapy groups (-49%) had more deterioration in visual fields than trabeculectomy group.
Early Manifest Glaucoma Trial ^{4,5,6}	Newly diagnosed POAG: medical therapy and laser trabeculoplasty vs. no treatment	255	4–10	Lowering IOP with medical therapy and trabeculoplasty (-25%) slowed progression of optic disc and visual field damage.
Advanced Glaucoma Intervention Study (AGIS) ^{7,8}	POAG after medical therapy failure with no previous surgery: laser trabeculoplasty vs. trabeculectomy	591	10–13	Surgical outcome varied by race; patients with African ancestry did better with trabeculoplasty as first surgery (-30% IOP), while in the longer term (4+ years) Caucasian American patients did better with trabeculectomy as first surgery (-48% IOP). Lowest IOP group during follow-up after surgical interventions (-47%) protected against further visual field deterioration in advanced glaucoma patients.

IOP = intraocular pressure; POAG = primary open-angle glaucoma

1. Glaucoma Laser Trial Research Group. The Glaucoma Laser Trial (GLT). 2. Results of argon laser trabeculoplasty versus topical medicines. *Ophthalmology* 1990;97:1403-13.
2. Glaucoma Laser Trial Research Group. The Glaucoma Laser Trial (GLT) and Glaucoma Laser Trial Follow-up Study: 7. Results. *Am J Ophthalmol* 1995;120:718-31.
3. Migdal C, Gregory W, Hitchings R. Long term functional outcome after early surgery compared with laser and medicine in open-angle glaucoma. *Ophthalmology* 1994;101:1651-7.
4. 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;120:1268-79.
5. Leske MC, Heijl A, Hussein M, et al, Early Manifest Glaucoma Trial Group. Factors for glaucoma progression and the effect of treatment: the Early Manifest Glaucoma Trial. *Arch Ophthalmol* 2003;121:48-56.
6. Leske MC, Heijl A, Hyman L, et al, Early Manifest Glaucoma Trial Group. Predictors of long-term progression in the Early Manifest Glaucoma Trial. *Ophthalmology* 2007;114:1965-72.
7. AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS): 7. The relationship between control of intraocular pressure and visual field deterioration. *Am J Ophthalmol* 2000;130:429-40.
8. AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS): 13. Comparison of treatment outcomes within race: 10-year results. *Ophthalmology* 2004;111:651-64.

For patients initially treated with ALT, the amount of medical treatment required for glaucoma control is reduced.^{121,122} Results from long-term studies of patients receiving maximum medical therapy who subsequently had laser and incisional surgery indicate that 30% to more than 50% of eyes require additional surgical treatment within 5 years after ALT.^{123,210-213} For eyes that have failed to maintain a previously adequate response, repeat ALT has a low long-term rate of success, with failure occurring in nearly 90% of these eyes by 2 years.²¹⁴⁻²¹⁸ After previous applications to the full circumference of the anterior chamber angle, repeat ALT has a lower success rate than initial therapy^{216,217} in eyes that have not had a reduction in IOP for at least a year following the first laser surgery.²¹⁷ Compared with initial laser trabeculoplasty, there is an increased risk of problems and complications such as IOP spikes after repeat laser trabeculoplasty.^{214,215,218,219}

Selective laser trabeculoplasty

The introduction of selective laser trabeculoplasty (SLT) is most likely responsible for the increase in use of laser trabeculoplasty in 2001 after a previous decline.²²⁰ Selective laser trabeculoplasty uses a Q-switched, frequency doubled, 532 nm Nd:YAG laser that delivers less energy and is purported to be selectively absorbed by pigmented cells in the trabecular meshwork.²²¹ These attributes appear purportedly to produce less thermal damage to the trabecular meshwork compared with ALT.²²² However, several prospective and retrospective studies indicate that SLT appears comparable to but not better than ALT in lowering IOP.²²³⁻²³⁰ Selective laser trabeculoplasty also appears to be comparable in efficacy to medical therapy with prostaglandin analogs,^{209,231} although in one prospective study, SLT was only comparable to latanoprost when 360 degrees of the trabecular meshwork was treated.²³¹ In this study, latanoprost had a better IOP-lowering effect compared with 90 and 180 degrees of treatment.

It has been claimed that SLT has greater success than ALT with repeated treatments, but no controlled, randomized clinical trial has shown that this is true. Only one study with a significant sample size has studied the results of SLT repeated after prior SLT treatment. This was a retrospective study of repeat 360 degree SLT after prior successful 360-degree SLT.²³² In the postoperative period, repeat SLT treatment lowered IOP, but the effect was less than that with initial SLT treatment at 1 to 3 months and 5 to 8 months. These results suggest that repeat SLT may be less efficacious compared with primary treatment, but further studies are needed to clarify this issue. The safety profile of SLT appears to be good, with mild anterior chamber inflammation after treatment and less ocular discomfort compared with ALT.²²⁶ Intraocular pressure spikes have been noted after SLT in 4.5% to 27% of eyes in various studies.^{224,231,233}

Perioperative care in laser trabeculoplasty

The ophthalmologist who performs the laser surgery has the following responsibilities:^{234,235 [A:III]}

- ◆ To obtain informed consent from the patient or the patient's surrogate decision maker after discussing the risks, benefits, and expected outcomes of surgery^[A:III]
- ◆ To ensure that the perioperative evaluation confirms the need for surgery^[A:III]

- ◆ To perform at least one IOP check within 30 minutes to 2 hours of surgery²³⁶ [A:I]
 - ◆ To perform a follow-up examination within 6 weeks of surgery or sooner if there is concern about IOP-related damage to the optic nerve during this time^{210,237-239} [A:III]
- Medications that are not being used chronically may be used perioperatively to avert temporary IOP elevations, particularly in those patients with severe disease.^{236,240,241}

Incisional glaucoma surgery

Trabeculectomy

Filtering surgery is effective in lowering IOP; it is generally indicated when medicine or laser therapy is insufficient to control disease and can be considered in selected cases as initial therapy.^{185,242} [A:I]

Filtering surgery provides an alternative path for the escape of aqueous humor, and it often reduces IOP and the need for medical treatment. Estimates of success rates over time range from 31% to 56% in different populations.²⁴³⁻²⁴⁵ The failure rate of filtering surgery, without the use of adjunctive antifibrotic medications, alone or combined with medical therapy in a previously unoperated eye in the Advanced Glaucoma Intervention Study¹²³ reached approximately 30% in African American patients and 20% in Caucasian American patients over a 10-year period.¹²³ While long-term control is often achieved, many patients may require further therapy or a reoperation, which carries a higher failure rate.^{123,246-249} Furthermore, filtering surgery increases the likelihood that phakic eyes may undergo cataract surgery.^{125,250,251} In eyes that have undergone previous cataract surgery involving the conjunctiva, the success rate of initial glaucoma surgery is reduced.¹⁷⁰

Antifibrotic agents may be used intraoperatively and postoperatively to reduce the subconjunctival scarring after filtration surgery that can result in failure of the operation. The use of intraoperative mitomycin-C reduces the risk of surgical failure both in eyes at high risk of surgical failure^{252,253} and in eyes that have not undergone previous surgery.²⁵³⁻²⁵⁶ Some studies have demonstrated a benefit of intraoperative 5-fluorouracil^{257,258} and others have not.²⁵⁹ The use of postoperative injections of 5-fluorouracil also reduces the likelihood of surgical failure in both high-risk eyes^{170,260-262} and eyes that have not undergone previous surgery.²⁶²⁻²⁶⁴

The use of an antifibrotic agent carries with it an increased likelihood of bleb-related complications such as hypotony,²⁶⁵⁻²⁶⁷ hypotony maculopathy,²⁶⁵ late-onset bleb leak,^{262,268} and late-onset infection^{269,270} that must be weighed against the benefits when deciding whether or not to use these agents. These complications may be even more common in primary filtering surgery of phakic patients.²⁷¹⁻²⁷³

Aqueous shunts

All aqueous shunts (also known as tube shunts, glaucoma drainage devices, and setons) consist of a tube that diverts aqueous humor to an end plate located in the equatorial region of the eye. The primary resistance to flow through these devices occurs across the fibrous capsule that develops around the end plate. Aqueous shunts differ in their design with respect to the size, shape, and material from which the end plate is made. They may be further subdivided into valved and nonvalved shunts, depending on whether or not a valve mechanism is present to limit flow through the shunt if the IOP becomes too low. Examples of nonvalved implants are the Baerveldt glaucoma implant (Abbott Medical Optics, Santa Ana, CA) and the Molteno implant (Molteno Ophthalmic Ltd., Dunedin, New Zealand). Examples of the valved implants are the Ahmed glaucoma valve (New World Medical, Inc., Rancho Cucamonga, CA) and the Krupin implant (Eagle Vision, Inc., Memphis, TN).

Aqueous shunts have traditionally been used to manage medically uncontrolled glaucoma when trabeculectomy has failed to control IOP or is deemed unlikely to succeed. This includes eyes with neovascular glaucoma, uveitic glaucoma, extensive conjunctival scarring from previous ocular surgery or cicatrizing diseases of the conjunctiva, and congenital glaucoma in which angle surgery has failed. However, the indications for using aqueous shunts have been broadening, and these devices are being increasingly utilized in the surgical management of glaucoma. Medicare data show a steady rise in the number of shunts placed from 1995 to 2004, while there has been a

concurrent decline in the number of trabeculectomies performed.²⁷⁴ Recent surveys of the American Glaucoma Society membership have also demonstrated a progressive increase in the number of surgeons using tube shunts.^{275,276}

A systematic review concluded that aqueous shunts are comparable with trabeculectomy for IOP control and duration of benefit, that larger end-plate surface area provides better IOP control, and that there appears to be no advantage to the use of antifibrotic agents or systemic corticosteroids as adjuncts to aqueous shunt procedures.^{277,278} The need for comparative studies and long-term follow-up was identified by the authors.

Several studies have compared aqueous shunts with trabeculectomy. A retrospective study evaluating surgical results in matched patient groups reported similar IOP reduction with the single-plate Molteno implant and trabeculectomy with 5-fluorouracil.²⁷⁹ However, another retrospective case-control study observed a higher 5-year success rate after trabeculectomy with mitomycin-C than with Ahmed glaucoma valve implantation.²⁸⁰ A randomized clinical trial in Sri Lanka comparing the Ahmed implant and trabeculectomy in patients with primary open-angle and angle-closure glaucoma found comparable IOP reduction and success rates with a mean follow-up of 31 months.²⁸¹ The Tube Versus Trabeculectomy (TVT) Study is a multicenter, prospective, randomized clinical trial that compared the safety and efficacy of tube-shunt surgery using the 350-mm² Baerveldt glaucoma implant and trabeculectomy with mitomycin-C in patients with previous cataract extraction and/or failed trabeculectomy. Tube-shunt surgery had a higher success rate than trabeculectomy (85% vs. 69%) after 3 years of follow-up as defined by loss of vision, and/or IOP less than or equal to 5 mmHg or greater than or equal to 21 mmHg.²⁸² Both surgical procedures were associated with similar IOP reduction and use of supplemental medical therapy at 3 years. Postoperative complications occurred more frequently after trabeculectomy compared with tube-shunt surgery, but the rate of serious complications associated with vision loss and/or reoperation to manage the complication was similar with both procedures.

Aqueous shunts are associated with intraoperative and postoperative complications that are similar to those that occur with trabeculectomy. In addition, they have unique complications related to implantation of a foreign body. Erosion of the tube may occur through the conjunctiva, and this typically develops a few millimeters behind the limbus following anterior chamber insertion. Diplopia may result from extraocular muscle fibrosis or a mass effect of the bleb overlying the end plate. Tube-cornea touch can lead to progressive endothelial cell loss and persistent corneal edema. The risk of postoperative infection appears to be less with aqueous shunts than after trabeculectomy with an antifibrotic agent.

Combined surgeries

Patients with POAG who have a visually significant cataract have a range of options to consider. If IOP control is at target on one or few medications, cataract surgery alone may be adequate, with the additional benefit that it may lower IOP slightly. If IOP is markedly uncontrolled on several medications after laser trabeculoplasty and the patient has a moderate cataract, then glaucoma surgery may be indicated initially, with the plan to perform cataract surgery once IOP is adequately controlled. In between these two extremes, the decision of which procedure(s) to perform first or whether to combine cataract and glaucoma surgery is determined by the ophthalmologist and patient after discussion of the risks and benefits of each course of action.

Cataract surgery with IOL implantation alone results in a modest reduction in IOP of less than 2 mmHg on average.¹¹⁴ Generally, combined cataract and glaucoma surgery is not as effective as glaucoma surgery alone in lowering IOP,^{114,283} so patients who require filtration surgery who also have mild cataract may be better served by filtration surgery alone and cataract surgery later.^[B:III] The use of mitomycin-C, but not 5-fluorouracil, results in lower IOP in combined procedures.^{114,253,283} A systematic review published in 2002 found moderate quality evidence that separating the cataract and glaucoma incisions results in lower IOP than a one-site combined procedure, but the differences in outcomes were small.²⁸³ Subsequent publications have found no difference between the two approaches.²⁸⁴⁻²⁸⁶

Potential benefits of a combined procedure (cataract extraction with IOL implantation and trabeculectomy) are protection against the IOP rise that may complicate cataract surgery alone and

the possibility of achieving long-term glaucoma control with a single operation. Therefore, an ophthalmologist may reasonably choose to perform a combined surgery due to these perceived advantages to an individual patient. Despite these presumed advantages, the evidence to date does not support routinely combining cataract and glaucoma surgery for all patients, because IOP outcomes with two-stage surgery are likely similar.¹¹⁴ Additionally, combined procedures are technically more complex. Ultimately, however, the decision of which surgical route to pursue is best left to the treating ophthalmologist and the individual patient.

Other types of glaucoma surgery can also be combined with cataract surgery, such as implantation of glaucoma drainage devices and endocyclophotocoagulation (see discussion in next section). Combined cataract and glaucoma drainage device surgery can also improve vision while providing IOP control.²⁸⁷⁻²⁸⁹

Other glaucoma surgeries

Nonpenetrating glaucoma surgery is an alternative to trabeculectomy. The precise role of nonpenetrating surgery in the surgical management of glaucoma remains to be determined. The two main types of nonpenetrating glaucoma surgery are viscocanalostomy and nonpenetrating deep sclerectomy. The rationale for nonpenetrating glaucoma surgery is that by avoiding a continuous passageway from the anterior chamber to the subconjunctival space, the incidence of complications such as bleb-related problems and hypotony can be reduced. The nonpenetrating procedures have a higher degree of surgical difficulty compared with trabeculectomy and require special instrumentation. Randomized clinical trials comparing viscocanalostomy with trabeculectomy generally suggest greater IOP reduction with trabeculectomy, but more complications with viscocanalostomy.²⁹⁰⁻²⁹⁸

One randomized clinical trial found that trabeculectomy was more effective than nonpenetrating deep sclerectomy at lowering IOP,²⁹⁹ and several others found that the two surgeries were equally effective.³⁰⁰⁻³⁰³

Other glaucoma surgical procedures currently under evaluation³⁰⁴ are canaloplasty with a tensioning suture³⁰⁵ (Prolene [Ethicon Inc., Somerville, NJ]), ab interno trabeculotomy using the Trabectome (NeoMedix, Tustin, CA),^{306,307} trabecular meshwork bypass stent,³⁰⁸ and the Ex-PRESS mini glaucoma shunt (Alcon Laboratories, Inc., Ft. Worth, TX).

Perioperative care in incisional glaucoma surgery

The ophthalmologist who performs incisional glaucoma surgery has the following responsibilities:^{234,235 [A:III]}

- ◆ Obtain informed consent from the patient or the patient's surrogate decision maker after discussing the risks, benefits, and expected outcomes of surgery.^{309 [A:III]}
- ◆ Ensure that the preoperative evaluation accurately documents the findings and indications for surgery.^[A:III]
- ◆ Prescribe topical corticosteroids in the postoperative period.^{310,311 [A:II]}
- ◆ Perform a follow-up evaluation on the first postoperative day (12 to 36 hours after surgery) and at least once during the first 1 to 2 weeks to evaluate visual acuity, IOP, and status of the anterior segment.^{312-317 [A:II]}
- ◆ In the absence of complications, perform additional postoperative visits during a 6-week period to evaluate visual acuity, IOP, and status of the anterior segment.^{312-317 [A:III]}
- ◆ Schedule more frequent follow-up visits, as necessary, for patients with postoperative complications such as a flat or shallow anterior chamber or evidence of early bleb failure, increased inflammation, or Tenon's encapsulated bleb formation.^{312-317 [A:III]}
- ◆ Undertake additional treatments as necessary, including injection of antifibrotic agents, repair of bleb leaks, bleb massage, suture lysis, bleb needling, or other surgical revisions of the bleb or surgical procedures to correct a flat anterior chamber to maximize the chances for a successful long-term result.^{318-320 [A:III]}

- ◆ Explain that filtration surgery places the eye at risk for endophthalmitis for the duration of the patient's life, and that if the patient has symptoms of pain and decreased vision and the signs of redness and discharge, he or she should notify the ophthalmologist immediately^{321 [A:III]}

Cyclodestructive surgery

Cyclodestructive procedures reduce the rate of aqueous production. There are several ways to reduce ciliary body function, such as cyclocryotherapy, transscleral and noncontact Nd:YAG laser, and transscleral and noncontact endodiode laser cyclophotocoagulation.^{322,323} Cyclodestructive procedures have traditionally been used for refractory glaucomas, and success rates have been reported in the range of 34% to 94%.³²³ They have been associated with a subsequent decrease of visual acuity^{324,325} and, rarely, cases of sympathetic ophthalmia.^{326,327} Disadvantages of cyclodestructive procedures include postoperative inflammation, IOP spike, and the frequent need for repeat treatment weeks or months later.³²⁸ Compared with cyclocryotherapy, laser cyclophotocoagulation causes less postoperative pain and inflammation. Therefore, cyclocryotherapy is now rarely used. Laser cyclodestructive procedures have advantages over filtration surgery that include technical ease and reduced postoperative care.

In 2005, 47% of all Medicare cyclophotocoagulation procedures were performed endoscopically; in 2006, 58%; and in 2007, 65%.³²⁹ Endoscopic cyclophotocoagulation (ECP) consists of a solid-state 810-nm laser, a video camera, aiming beam, and a xenon light source housed together in a fiberoptic cable³²³ that can be introduced inside the eye for direct visualization and treatment of the ciliary processes. Theoretically, this allows better titration of laser treatment. The efficacy of ECP appears to be good, with IOP reduction reported in the range of 34% to 57%.³³⁰⁻³³² It appears that treating 270 to 360 degrees of the ciliary body is necessary to achieve significant IOP lowering.^{330,332} Fibrin exudates, hyphema, cystoid macular edema, vision loss, hypotony, choroidal detachment,³³⁰ and phthisis³³³ have been noted after ECP in eyes with advanced glaucoma, but more recent studies involving eyes with less advanced glaucomatous damage seem to report fewer of these complications.³³¹

Endoscopic cyclophotocoagulation^{330,331,334} may be combined with cataract surgery or tube-shunt surgery. One randomized trial comparing cataract surgery combined with either ECP or trabeculectomy suggested that IOP lowering efficacy is similar for both,³³⁵ and another study comparing ECP with the Ahmed drainage implant also showed comparable efficacy in IOP lowering, although the rate of complication with the latter surgery was higher.³³⁶

Other therapeutic considerations

Among patients there is a growing interest in complementary and alternative medicinal approaches to the treatment of glaucoma. There is a lack of scientific evidence that herbal medicines or nutritional supplements are beneficial in treating glaucoma.^{337,338} One study based on patient questionnaires found an association between higher intake of certain fruits and vegetables (green collards, kale, and carrots) and reduced risk of glaucoma.³³⁹ The American Academy of Ophthalmology Complementary Therapy Task Force found no scientific evidence of increased benefit or diminished risk with the use of marijuana to treat glaucoma compared with conventional medications.³⁴⁰

Follow-up Evaluation

Guidelines for follow-up of patients with POAG are summarized in Table 6. These recommendations apply to ongoing glaucoma management and not to visits for other purposes. Follow-up evaluation includes examination as well as optic nerve head and visual field assessment as indicated.

TABLE 6 RECOMMENDED GUIDELINES FOR FOLLOW-UP GLAUCOMA STATUS EVALUATIONS WITH OPTIC NERVE AND VISUAL FIELD ASSESSMENT^[B:III] *

Target IOP Achieved	Progression of Damage	Duration of Control (months)	Approximate Follow-up Interval (months)**
Yes	No	≤6	6
Yes	No	>6	12
Yes	Yes	NA	1–2
No	Yes	NA	1–2
No	No	NA	3–6

IOP = intraocular pressure; NA = not applicable

* Evaluations consist of clinical examination of the patient, including optic nerve head assessment (with periodic color stereophotography or computerized imaging of the optic nerve and retinal nerve fiber layer structure) and visual field assessment.

** Patients with more advanced damage or greater lifetime risk from POAG may require more frequent evaluations. These intervals are the maximum recommended time between evaluations.

History

The following interval history can be elicited at POAG follow-up visits:

- ◆ Interval ocular history^[A:III]
- ◆ Interval systemic medical history^[B:III]
- ◆ Side effects of ocular medications^[A:III]
- ◆ Frequency and time of last IOP-lowering medications and review of use of medications^[B:III]

Ophthalmic examination

The following components of the ophthalmic examination should be performed at POAG follow-up visits:

- ◆ Visual acuity measurement^[A:III]
- ◆ Slit-lamp biomicroscopy^[A:III]
- ◆ Intraocular pressure measurement^[A:I]

Based on the understanding of the effect of CCT on IOP measurements,^{5,29,341} measurement of CCT should be repeated after any event (e.g., refractive surgery³⁴²) that may alter CCT.^[A:II]

Gonioscopy

Gonioscopy is indicated when there is a suspicion of an angle-closure component, anterior chamber shallowing or anterior chamber angle abnormalities, or if there is an unexplained change in IOP.^[A:III] Gonioscopy may also be performed periodically (e.g., 1 to 5 years).^[A:III]

Optic nerve head and visual field evaluation^[A:III]

Optic nerve head evaluation and documentation by imaging, photography, or drawing^{139,163,343,344} and visual field evaluation³⁴⁵⁻³⁴⁸ should be performed at the recommended intervals listed in Table 6.

Within each of the recommended intervals, factors that determine frequency of evaluations include the severity of damage (mild, moderate, severe, with more frequent evaluations for more severe disease), the rate of progression, the extent to which the IOP exceeds the target pressure, and the number and significance of other risk factors for damage to the optic nerve.^[A:III] In certain cases, follow-up visual field testing may be required more frequently than the recommended intervals (e.g., a second test to establish a baseline for future comparisons, to clarify a suspicious test result, or to overcome an apparent testing artifact). For example, a patient with glaucomatous damage who has shown long-term stability can be followed every 6 to 12 months, depending on how severe the damage is, while a patient with evidence of glaucomatous progression may receive a change in care plan with more frequent follow-up.

Risk Factors for Progression

The risk factors for progression in eyes already diagnosed with OAG are related to the level of IOP and factors independent of IOP:

- ◆ Intraocular pressure: Several multicenter randomized clinical trials have investigated the relationship between IOP and risk of glaucomatous progression. Higher baseline IOP,³⁰ higher mean IOP during follow-up,^{32,349} and higher yearly average IOP³⁵⁰ were associated with greater progression of glaucoma as measured by visual field or optic nerve changes. Greater IOP fluctuation in some, but not all studies, has also been shown to be related to visual field progression, but this strongly correlated with absolute IOP level and may not be an independent risk factor.^{33-37,185}
- ◆ Beta-zone peripapillary atrophy: Either the baseline presence^{351,352} or the size^{137,353} of peripapillary atrophy adjacent to the optic nerve (beta zone) has been related to visual field or optic nerve progression in several large prospective and retrospective studies.
- ◆ Older age^{30,36,185,349,353,354}
- ◆ Disc hemorrhage: Either presence of a disc hemorrhage^{351,353} or percentage of visits with disc hemorrhage^{30,36} have been associated with progression of visual field defect or optic nerve damage. The association has been reported in both normal-tension and in high-pressure glaucoma.
- ◆ Larger cup-to-disc ratio or small optic nerve rim area^{352,355}
- ◆ Thinner central cornea: Strong evidence exists for thinner central cornea as a risk factor for progression from ocular hypertension to POAG, but evidence is mixed for thinner central cornea as a risk factor for progression in glaucoma.^{53,57,60,341,356-361}

Damage in one eye is associated with an increased risk of future damage in the other eye.^{36,362,363} A retrospective study in eyes with OAG and severe visual field damage in one eye showed a risk of progression in the other eye (Kaplan Meier estimate of visual field progression = 12.1%).³⁶⁴ Risk factors for progression were larger initial cup-to-disc ratio and lower calculated ocular perfusion pressure. In a separate retrospective study, progression in visual field damage between eyes showed a significant correlation.³⁶³ In a large retrospective study of eyes with normal-tension glaucoma and unilateral visual field damage, the risk factors for progression in the normal eye were greater visual field damage in the eye with glaucoma and smaller neuroretinal rim area.³⁶⁵

Adjustment of Therapy

The indications for adjusting therapy are as follows:^[A:III]

- ◆ Target IOP is not achieved and the benefits of a change in therapy outweigh the risks for the patient
- ◆ A patient has progressive optic nerve damage despite achieving the target IOP
- ◆ The patient is intolerant of the prescribed medical regimen
- ◆ The patient does not adhere to the prescribed medical regimen because of cost or other issues
- ◆ Contraindications to individual medicines develop
- ◆ Stable optic nerve status and low IOP occurs for a prolonged period in a patient on glaucoma medications. Under these circumstances, a carefully monitored attempt to reduce the medical regimen may be appropriate.

Downward adjustment of target pressure can be made in the face of progressive optic disc or visual field change.^{366-370 [A:III]}

Upward adjustment of target pressure can be considered if the patient has been stable and if the patient either requires (because of side effects) or desires less medication. A follow-up visit in 2 to 8 weeks may help to assess the response and side effects from washout of the old medication or onset of maximum effect of the new medication.

PROVIDER AND SETTING

The performance of certain diagnostic procedures (e.g., tonometry, pachymetry, perimetry, optic disc imaging, and photography) may be delegated to appropriately trained and supervised personnel.

However, the interpretation of results and medical and surgical management of the disease require the medical training, clinical judgment, and experience of the ophthalmologist.

Most diagnostic and therapeutic procedures can be safely undertaken on an outpatient basis. In some instances, however, hospitalization may be required. This includes, for example, patients who have special medical or social needs.

PHYSICIAN QUALITY REPORTING INITIATIVE

The Physician Quality Reporting Initiative program, initially launched by the Centers for Medicare and Medicaid Services in July 2007, encourages quality improvement through the use of clinical performance measures on a variety of clinical conditions. There are two measures in the 2010 Physician Quality Reporting Initiative program for POAG.³⁷¹ One measure is reduction of IOP by at least 15% from the preintervention level or documentation of a plan of care if treatment has not been successful in reducing IOP by at least 15%. The second measure is an optic nerve head evaluation within 12 months.³⁷¹

COUNSELING/REFERRAL

It is important to educate and engage patients in the management of their condition. Patients should be educated about the disease process, the rationale and goals of intervention, the status of their condition, and the relative benefits and risks of alternative interventions so that they can participate meaningfully in developing an appropriate plan of action.^[A:III] Patients should be encouraged to alert their ophthalmologists to physical or emotional changes that occur when taking glaucoma medications.^[A:III] The diagnosis of glaucoma can itself lead to negative psychological effects and to fear of blindness.³⁷²⁻³⁷⁶

Numerous studies have been performed to characterize the psychological profile of the glaucoma patient, and some have shown the prevalence of anxiety to be higher in this population.^{372,375,377} It has been much harder to demonstrate a consistent presence of depression in glaucoma patients; numerous studies have been unable to do so^{106,372,378,379} and only a minority do.^{375,376}

Glaucoma affects the patient's visual and health-related quality of life in many ways^{91,380}; this includes employment issues (e.g., fear of loss of job and insurance from diminished ability to read and drive), social issues (e.g., fear of negative impact on relationships and sexuality), and loss of independence and activities that require good visual acuity (e.g., sports and other hobbies). The ophthalmologist should be sensitive to these problems and provide support and encouragement.^[A:III] Some patients may find peer-support groups or counseling helpful.

Patients considering keratorefractive surgery should be informed about the possible impact laser vision correction has on reducing contrast sensitivity, altering visual field testing results, and decreasing the accuracy of IOP measurements.^[A:III] During the conduct of LASIK the IOP will briefly increase from the effect of the suction ring to make the eye rigid during creation of the superficial flap. This effect may cause additional damage in patients whose optic nerves already have advanced damage.³⁸¹ Therefore, LASIK may be relatively contraindicated in such individuals, but photorefractive keratectomy may be possible. In addition, postoperative fluid may develop in the corneal flap-stromal interface and lead to temporary underestimation of the applanation IOP in patients treated aggressively with topical corticosteroids to resolve interface inflammation, who may actually have an undetected, corticosteroid-induced elevation of IOP.³⁸² Conversely, corticosteroid-induced IOP elevation may cause interface fluid that mimics interface inflammation and leads to IOP underestimation.^{383,384} Patients with glaucomatous optic neuropathy considering implantation of a multifocal intraocular lens should be informed of the risk of reduced contrast sensitivity.³⁸⁵ ^[A:III] It is important to establish preoperative and baseline documentation of optic nerve head status and visual field to facilitate subsequent glaucoma management.

If the diagnosis or management of POAG is in question or if the condition is refractory to treatment, consultation with or referral to an ophthalmologist with special training or experience in managing glaucoma should be considered. Patients with substantial visual impairment or blindness can be referred for and encouraged to use appropriate vision rehabilitation and social services.³⁸⁶ ^[A:III] More information on vision rehabilitation, including materials for patients, is available at www.aao.org/smartsight.



APPENDIX 1. QUALITY OF OPHTHALMIC CARE CORE CRITERIA

*Providing quality care
is the physician's foremost ethical obligation, and is
the basis of public trust in physicians.*

AMA Board of Trustees, 1986

Quality ophthalmic care is provided in a manner and with the skill that is consistent with the best interests of the patient. The discussion that follows characterizes the core elements of such care.

The ophthalmologist is first and foremost a physician. As such, the ophthalmologist demonstrates compassion and concern for the individual, and utilizes the science and art of medicine to help alleviate patient fear and suffering. The ophthalmologist strives to develop and maintain clinical skills at the highest feasible level, consistent with the needs of patients, through training and continuing education. The ophthalmologist evaluates those skills and medical knowledge in relation to the needs of the patient and responds accordingly. The ophthalmologist also ensures that needy patients receive necessary care directly or through referral to appropriate persons and facilities that will provide such care, and he or she supports activities that promote health and prevent disease and disability.

The ophthalmologist recognizes that disease places patients in a disadvantaged, dependent state. The ophthalmologist respects the dignity and integrity of his or her patients, and does not exploit their vulnerability.

Quality ophthalmic care has the following optimal attributes, among others.

- ◆ The essence of quality care is a meaningful partnership relationship between patient and physician. The ophthalmologist strives to communicate effectively with his or her patients, listening carefully to their needs and concerns. In turn, the ophthalmologist educates his or her patients about the nature and prognosis of their condition and about proper and appropriate therapeutic modalities. This is to ensure their meaningful participation (appropriate to their unique physical, intellectual and emotional state) in decisions affecting their management and care, to improve their motivation and compliance with the agreed plan of treatment, and to help alleviate their fears and concerns.
- ◆ The ophthalmologist uses his or her best judgment in choosing and timing appropriate diagnostic and therapeutic modalities as well as the frequency of evaluation and follow-up, with due regard to the urgency and nature of the patient's condition and unique needs and desires.
- ◆ The ophthalmologist carries out only those procedures for which he or she is adequately trained, experienced and competent, or, when necessary, is assisted by someone who is, depending on the urgency of the problem and availability and accessibility of alternative providers.
- ◆ Patients are assured access to, and continuity of, needed and appropriate ophthalmic care, which can be described as follows.
 - ◆ The ophthalmologist treats patients with due regard to timeliness, appropriateness, and his or her own ability to provide such care.
 - ◆ The operating ophthalmologist makes adequate provision for appropriate pre- and postoperative patient care.
 - ◆ When the ophthalmologist is unavailable for his or her patient, he or she provides appropriate alternate ophthalmic care, with adequate mechanisms for informing patients of the existence of such care and procedures for obtaining it.
 - ◆ The ophthalmologist refers patients to other ophthalmologists and eye care providers based on the timeliness and appropriateness of such referral, the patient's needs, the competence and qualifications of the person to whom the referral is made, and access and availability.
 - ◆ The ophthalmologist seeks appropriate consultation with due regard to the nature of the ocular or other medical or surgical problem. Consultants are suggested for their skill, competence, and accessibility.

They receive as complete and accurate an accounting of the problem as necessary to provide efficient and effective advice or intervention, and in turn respond in an adequate and timely manner.

- ♦ The ophthalmologist maintains complete and accurate medical records.
- ♦ On appropriate request, the ophthalmologist provides a full and accurate rendering of the patient's records in his or her possession.
- ♦ The ophthalmologist reviews the results of consultations and laboratory tests in a timely and effective manner and takes appropriate actions.
- ♦ The ophthalmologist and those who assist in providing care identify themselves and their profession.
- ♦ For patients whose conditions fail to respond to treatment and for whom further treatment is unavailable, the ophthalmologist provides proper professional support, counseling, rehabilitative and social services, and referral as appropriate and accessible.
- ♦ Prior to therapeutic or invasive diagnostic procedures, the ophthalmologist becomes appropriately conversant with the patient's condition by collecting pertinent historical information and performing relevant preoperative examinations. Additionally, he or she enables the patient to reach a fully informed decision by providing an accurate and truthful explanation of the diagnosis; the nature, purpose, risks, benefits, and probability of success of the proposed treatment and of alternative treatment; and the risks and benefits of no treatment.
- ♦ The ophthalmologist adopts new technology (e.g., drugs, devices, surgical techniques) in judicious fashion, appropriate to the cost and potential benefit relative to existing alternatives and to its demonstrated safety and efficacy.
- ♦ The ophthalmologist enhances the quality of care he or she provides by periodically reviewing and assessing his or her personal performance in relation to established standards, and by revising or altering his or her practices and techniques appropriately.
- ♦ The ophthalmologist improves ophthalmic care by communicating to colleagues, through appropriate professional channels, knowledge gained through clinical research and practice. This includes alerting colleagues of instances of unusual or unexpected rates of complications and problems related to new drugs, devices or procedures.
- ♦ The ophthalmologist provides care in suitably staffed and equipped facilities adequate to deal with potential ocular and systemic complications requiring immediate attention.
- ♦ The ophthalmologist also provides ophthalmic care in a manner that is cost effective without unacceptably compromising accepted standards of quality.

Reviewed by: Council
Approved by: Board of Trustees
October 12, 1988

2nd Printing: January 1991
3rd Printing: August 2001
4th Printing: July 2005



APPENDIX 2. MAJOR RECOMMENDATIONS FOR CARE

DIAGNOSIS

The comprehensive initial glaucoma evaluation (history and physical examination) includes all components of the comprehensive adult medical eye evaluation¹⁰² in addition to, and with special attention to, those factors that specifically bear upon the diagnosis, course, and treatment of POAG.

Evaluation of Visual Function

Self-reported functional status or difficulty with vision can be assessed either by patient complaints or by using specific questionnaires, including the National Eye Institute - Visual Function Questionnaire-25.^{90,103-109} [A:III]

Ophthalmic Evaluation

History

- ◆ Ocular,^[A:III] family,^{4,42,44} [A:II] and systemic history (e.g., asthma).^[A:III] The severity and outcome of glaucoma in family members, including history of visual loss from glaucoma, should be obtained during initial evaluation.^{42,44} [B:III]
- ◆ Review of pertinent records,^[A:III] with particular reference to the past IOP levels, status of the optic nerve, and visual field.^[A:III]
- ◆ Current ocular and systemic medications (e.g., corticosteroids) and known local or systemic intolerance to ocular or systemic medications.^[A:III]
- ◆ Ocular surgery.^[A:III]

Visual acuity measurement

Visual acuity with current correction (the power of the present correction recorded) at distance and, when appropriate, at near should be measured.^[A:III] Refraction may be indicated to obtain the best-corrected visual acuity.

Pupil examination

The pupils are examined for reactivity and an afferent pupillary defect.¹¹⁵⁻¹¹⁷ [B:II]

Anterior segment examination

A slit-lamp biomicroscopic examination of the anterior segment can provide evidence of physical findings associated with narrow angles, such as shallow peripheral anterior chamber depth and crowded anterior chamber angle anatomy,^{118,119} corneal pathology, or a secondary mechanism for elevated IOP such as pseudoexfoliation (exfoliation syndrome), pigment dispersion with Krukenberg spindle and/or iris transillumination defects, iris and angle neovascularization, or inflammation.^[A:III]

Intraocular pressure measurement

Intraocular pressure is measured in each eye, preferably by Goldmann applanation tonometry, before gonioscopy or dilation of the pupil.^{5,27,30-32,120-128} [A:I] Recording time of day of IOP measurements may be helpful to assess diurnal variation. Unrecognized fluctuations in IOP may lead to progression of POAG.¹²⁹⁻¹³² Therefore, additional measurements may be indicated, either at different hours of the day on the same day or on different days.

Gonioscopy

The diagnosis of POAG requires careful evaluation of the anterior chamber angle to exclude angle closure or secondary causes of IOP elevation, such as angle recession, pigment dispersion, peripheral anterior synechiae, angle neovascularization, and inflammatory precipitates.^{133 [A:III]}

Optic nerve head and retinal nerve fiber layer examination

The preferred technique for optic nerve head and retinal nerve fiber layer evaluation involves magnified stereoscopic visualization (as with the slit-lamp biomicroscope), preferably through a dilated pupil.^[A:III]

Fundus examination

Examination of the fundus, through a dilated pupil whenever feasible, includes a search for other abnormalities that may account for optic nerve changes and/or visual field defects (e.g., optic nerve pallor, disc drusen, optic nerve pits, disc edema from central nervous system disease, macular degeneration, retinovascular occlusion, and other retinal disease).^[A:III]

Supplemental Ophthalmic Testing

Central corneal thickness measurement

Measurement of CCT aids the interpretation of IOP readings and helps to stratify patient risk for ocular damage.^{29,53,57,151 [A:I]}

Visual field evaluation

Automated static threshold perimetry is the preferred technique for evaluating the visual field.^{154 [A:III]} Careful manual combined kinetic and static threshold testing (e.g., Goldmann visual fields) is an acceptable alternative when patients cannot perform automated perimetry reliably or if it is not available.^[A:III] Repeat, confirmatory visual field examinations may be required for test results that are unreliable or show a new glaucomatous defect before changing management.^{27,124 [A:III]}

Optic nerve head and retinal nerve fiber layer analysis

The appearance of the optic nerve should be documented.^{136,158 [A:II]} Color stereophotography is an accepted method for documenting optic nerve head appearance. Computer-based image analysis of the optic nerve head and retinal nerve fiber layer is an alternative for documentation of the optic nerve. In the absence of these technologies, a nonstereoscopic photograph or a drawing of the optic nerve head should be recorded, but these are less desirable alternatives to stereophotography or computer-based imaging.^{163 [A:III]}

Management recommendations are described in the main body of the text.

Follow-up Evaluation

Guidelines for follow-up of patients with POAG are summarized in Table 6. These recommendations apply to ongoing glaucoma management and not to visits for other purposes. Follow-up evaluation includes examination as well as optic nerve head and visual field assessment as indicated.

TABLE 6 RECOMMENDED GUIDELINES FOR FOLLOW-UP GLAUCOMA STATUS EVALUATIONS WITH OPTIC NERVE AND VISUAL FIELD ASSESSMENT^[B:III] *

Target IOP Achieved	Progression of Damage	Duration of Control (months)	Approximate Follow-up Interval (months)**
Yes	No	≤6	6
Yes	No	>6	12
Yes	Yes	NA	1–2
No	Yes	NA	1–2
No	No	NA	3–6

IOP = intraocular pressure; NA = not applicable

* Evaluations consist of clinical examination of the patient, including optic nerve head assessment (with periodic color stereophotography or computerized imaging of the optic nerve and retinal nerve fiber layer structure) and visual field assessment.

** Patients with more advanced damage or greater lifetime risk from POAG may require more frequent evaluations. These intervals are the maximum recommended time between evaluations.

History

- ◆ Interval ocular history^[A:III]
- ◆ Interval systemic medical history^[B:III]
- ◆ Side effects of ocular medications^[A:III]
- ◆ Frequency and time of last IOP-lowering medications and review of use of medications^[B:III]

Ophthalmic examination

- ◆ Visual acuity measurement^[A:III]
- ◆ Slit-lamp biomicroscopy^[A:III]
- ◆ Intraocular pressure measurement^[A:I]

Based on the understanding of the effect of CCT on IOP measurements,^{5,29,341} measurement of CCT should be repeated after any event (e.g., refractive surgery³⁴²) that may alter CCT.^[A:III]

Gonioscopy

Gonioscopy is indicated when there is a suspicion of an angle-closure component, anterior chamber shallowing or anterior chamber angle abnormalities, or if there is an unexplained change in IOP.^[A:III] Gonioscopy may also be performed periodically (e.g., 1 to 5 years).^[A:III]

Optic nerve head and visual field evaluation^[A:III]

Optic nerve head evaluation and documentation by imaging, photography, or drawing^{139,163,343,344} and visual field evaluation³⁴⁵⁻³⁴⁸ should be performed at the recommended intervals listed in Table 6.

Within each of the recommended intervals, factors that determine frequency of evaluations include the severity of damage (mild, moderate, severe, with more frequent evaluations for more severe disease), the rate of progression, the extent to which the IOP exceeds the target pressure, and the number and significance of other risk factors for damage to the optic nerve.^[A:III]

COUNSELING/REFERRAL

Patients should be educated about the disease process, the rationale and goals of intervention, the status of their condition, and the relative benefits and risks of alternative interventions so that they can participate meaningfully in developing an appropriate plan of action.^[A:III] Patients should be encouraged to alert their ophthalmologists to physical or emotional changes that occur when taking glaucoma medications.^[A:III]

Glaucoma affects the patient's visual and health-related quality of life in many ways^{91,380}; this includes employment issues (e.g., fear of loss of job and insurance from diminished ability to read

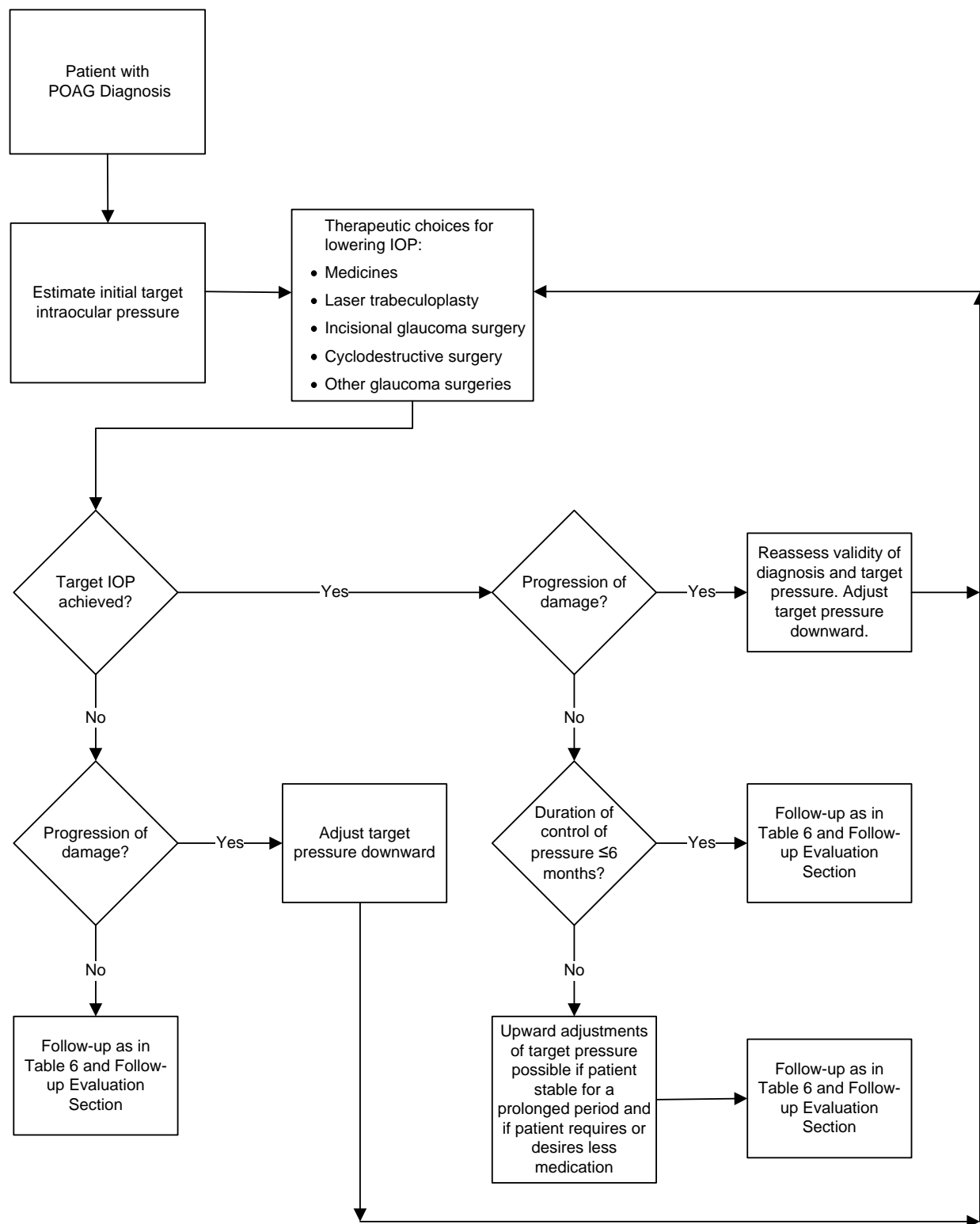
and drive), social issues (e.g., fear of negative impact on relationships and sexuality), and loss of independence and activities that require good visual acuity (e.g., sports and other hobbies). The ophthalmologist should be sensitive to these problems and provide support and encouragement.^[A:III] Some patients may find peer-support groups or counseling helpful.

Patients considering keratorefractive surgery should be informed about the possible impact laser vision correction has on reducing contrast sensitivity, altering visual field testing results, and decreasing the accuracy of IOP measurements.^[A:III] Patients with glaucomatous optic neuropathy considering implantation of a multifocal intraocular lens should be informed of the risk of reduced contrast sensitivity.^{385 [A:III]}

Patients with substantial visual impairment or blindness can be referred for and encouraged to use appropriate vision rehabilitation and social services.^{386 [A:III]} More information on vision rehabilitation, including materials for patients, is available at www.aao.org/smartsight.



APPENDIX 3. TREATMENT ALGORITHM FOR PATIENTS WITH PRIMARY OPEN-ANGLE GLAUCOMA





APPENDIX 4. INTERNATIONAL STATISTICAL CLASSIFICATION OF DISEASES AND RELATED HEALTH PROBLEMS (ICD) CODES

The POAG PPP covers the entity of open-angle glaucoma (ICD-9 #365.10) and related entities with the following ICD-9 classifications:

- ◆ Primary open-angle glaucoma (365.11)
- ◆ Low-tension glaucoma (365.12)
- ◆ Residual stage of open-angle glaucoma (365.15)
- ◆ Glaucomatous atrophy of the optic disc (377.14)



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