Primary open-angle glaucoma

Revised: 08 Jun 2013
Last Updated: 31 Jan 2013
Copyright Elsevier BV. All rights reserved.

Key points

- Primary open-angle glaucoma (POAG) is an idiopathic disorder in which the resistance to outflow through the trabecular meshwork gradually increases and the intraocular pressure (IOP) rises, causing irreversible damage to the optic nerve
- POAG is the second most common cause of vision loss in the U.S.
- Usually asymptomatic until advanced visual field loss has occurred; less than 50% of those with glaucoma are aware of their disease
- Early diagnosis and referral of patients with suspected chronic glaucoma are essential to prevent ongoing damage to the optic nerve and further loss of visual field
- IOP reduction, by medical or surgical means, has been demonstrated to delay or prevent disease progression at both the early and late stages of the disease
- Acute primary glaucoma requires immediate referral to an ophthalmologist; chronic primary glaucoma requires routine referral

Background

Description

- Glaucoma comprises a group of eye diseases that constitute the second most common cause of vision loss in the U.S.
- The common feature of all forms of glaucoma is damage to the optic nerve. Raised IOP is the only modifiable risk factor
- In 20% to 30% of cases, optic neuropathy and corresponding visual field loss develop despite an IOP that remains in the normal range (10-21 mm Hg) in a condition known as normal-tension or low-tension glaucoma. Conversely, individuals with a raised IOP may present no evidence of optic neuropathy
- In glaucoma, early diagnosis and effective treatment to reduce IOP provide the best means of preventing damage to sight, as any visual loss that takes place cannot be reversed
- POAG, the most common form of glaucoma, is an idiopathic disorder in which the resistance to outflow through the trabecular meshwork gradually increases and the IOP rises, causing damage to the optic nerve
- The anterior chamber drainage angle is anatomically open
- Secondary glaucoma develops from the presence of some other ocular or systemic condition and is less common than POAG
Aqueous humor is secreted by the ciliary body and flows anteriorly into the anterior chamber. Normal outflow occurs through the trabecular meshwork and, to a lesser extent, via the uveoscleral route.

The precise mechanism by which raised IOP damages the optic nerve is not known. It is believed that an abnormally high fluid pressure on the optic nerve head may cause death of nerve axons, possibly through an ischemic process.

Optic neuropathy is associated with characteristic features of structural damage to the optic nerve and development of corresponding visual field defects.

'Cupping' is the classical clinical finding in an optic nerve head that has been damaged by raised IOP. The diagnosis of glaucoma is made when the typical appearances of the optic disc are accompanied by corresponding visual field loss, initially affecting the peripheral fields.

The terms primary congenital glaucoma and primary infantile glaucoma tend to be used interchangeably. Strictly defined, congenital glaucoma that manifests soon after birth is called neonatal glaucoma, while infantile glaucoma includes cases that develop in the first 3 years of life. Congenital glaucoma that develops from the age of 4 years is termed juvenile glaucoma.

Chronic glaucoma is usually slow to progress and asymptomatic until advanced visual field loss has occurred.

If POAG is present in one eye, the 5-year risk of developing the condition in the other eye is increased five-fold in comparison to patients who have no evidence of POAG in either eye.

Approximately 20% of cases of chronic glaucoma are secondary to some other ocular or systemic condition, including neovascularization, trauma, and uveitis.

In ocular hypertension, IOP is raised but there is no discernible damage to the optic nerve head and no visual field restriction; 20% of people with ocular hypertension, however, develop visual field defects within 5 years.

**Epidemiology**

**Incidence**

- A wide range of estimates exists for the incidence and prevalence of POAG, possibly due to differences in the age range and ethnic origin of populations studied.
- Annual incidence rate of POAG in a predominantly white population in the U.S. has been conservatively estimated at 14.5/100,000. Rates increased with age from 1.6/100,000 in the fourth decade of life to 94.3/100,000 in the eighth decade.
- Primary infantile glaucoma is the most common form of glaucoma in infancy, with an incidence of approximately 5 to 10/100,000 live births in the western world and a higher incidence in areas where consanguineous marriage is common.

**Prevalence**

- Estimates of the overall prevalence of POAG range from 1,400/100,000 in a non-Hispanic white cohort in the U.S. to 6,800/100,000 in a predominantly African-Caribbean population study in Barbados.
In various studies, the prevalence for those aged 40 through 49 years has been reported as 200 to 500/100,000 in non-Hispanic white persons, 500 to 1,300/100,000 in Hispanics, and 1,300 to 1,400/100,000 in black persons.

For those aged 80 years or older, rates are 1,900 to 9,900/100,000 in non-Hispanic white persons, 12,600 to 21,800/100,000 in Hispanics, and 12,900 to 23,200/100,000 in black persons.

U.S. research has found age-adjusted prevalence rates for POAG to be four to five times higher in black persons as compared with non-Hispanic white persons.

### Demographics

**Age:**

- Increasing incidence and prevalence of glaucoma with increasing age
- Rare in patients younger than 40 years

**Gender:**

- No gender difference for POAG
- Primary infantile glaucoma affects more boys than girls in a ratio of 3:2

**Race:**

- In the U.S., POAG is more prevalent in black and Hispanic populations and may occur at an earlier age than in white persons
- Normal-tension glaucoma is more common in Japanese Americans

### Genetics

- Family history is a predisposing factor but the exact mode of inheritance remains unclear
- No single Mendelian mode of inheritance has been described
- First-degree relatives of individuals with POAG have an eight-fold increased risk of developing the condition as compared to the general population
- A genetic contribution to the etiology of POAG is suspected, possibly involving the interaction of multiple genes and environmental factors
- It is considered that a small proportion of POAG is attributable to single gene defects. Chromosomal locations have been mapped of several genes that can independently cause the disease. Mutations of the myocilin gene have been shown to occur in a subset of families with a high incidence of juvenile- and adult-onset POAG

### Causes and risk factors

#### Causes

Common causes:
• Cause is not known
• In normal-tension glaucoma, the optic nerve appears to be unduly sensitive and thus more prone to damage, although other factors such as abnormal blood flow have also been implicated. By definition, the IOP is normal and the anterior chamber angle is open

Rare causes:

• Primary congenital glaucoma in the first month of life (neonatal glaucoma) or up to the first 3 years of life (infantile glaucoma) is probably the result of developmental abnormality of the trabecular meshwork (trabeculodysgenesis). In 10% of cases, there is a familial link, usually demonstrating an autosomal recessive pattern of inheritance
• Glaucoma that develops from the age of 4 years (juvenile glaucoma) is sometimes inherited in an autosomal dominant fashion

Secondary glaucoma:

• Eye conditions including trauma, tumors, and intraocular inflammation such as chronic uveitis and iritis, in which synechiae (adhesions) can obstruct the flow of aqueous humor
• Certain forms of eye surgery, including cataract surgery
• Use of topical, systemic, inhaled, or periocular steroids may cause an increase in IOP. The rise is dose-dependent, and patients with a family history of the condition or who already have a raised IOP have an increased risk of variability in steroid responsiveness
• Neovascular glaucoma is a unique form that occurs when new vessels proliferate on the iris and anterior chamber angle. Invasion of the anterior chamber by a fibrovascular membrane initially obstructs aqueous outflow in an open-angle form and later contracts to produce synechial angle-closure glaucoma
• Diabetic retinopathy and central retinal vein occlusion are by far the most common conditions that predispose to the development of ocular neovascularization. Other causes are uveitis, long-standing retinal detachment, and intraocular tumors
• Behçet syndrome, a multisystem vasculitis characterized by recurrent oral and genital ulcers and ocular inflammation, is associated with both open- and closed-angle glaucoma
• In pigment dispersion syndrome, abnormal anatomy of the iris leads to mechanical friction against lens zonules causing release of iris pigment, which is deposited in the trabecular meshwork reducing aqueous humor outflow
• In pseudoexfoliation syndrome, abnormal fibrillar protein is produced within the anterior chamber and deposited in the trabecular meshwork, reducing aqueous humor outflow. This is a systemic condition with only ocular manifestations. Pseudoexfoliative material is found in multiple organs without consequence
• Secondary infantile and childhood glaucomas can be caused by inherited syndromes including Rieger syndrome, Lowe syndrome, neurofibromatosis, Peter anomaly, Sturge-Weber syndrome, and dislocated lens due to Marfan syndrome
• Other secondary causes include aniridia, retinopathy of prematurity, congenital rubella, aphakia, trauma, retinoblastoma, and any form of corticosteroids use

Risk factors
• Advancing age
• Family history of glaucoma
• Ethnicity: black, Hispanic, and Japanese-American persons
• Raised IOP, although most patients with a slightly raised IOP will not develop glaucoma
• Severe myopia
• Other medical conditions including migraine, systemic hypertension, ischemic heart disease, and peripheral vasospasm may increase risk of developing glaucoma, but the evidence is not conclusive

Screening

Summary approach

There is insufficient evidence to recommend screening young adults for glaucoma.

Population at risk

• More frequent monitoring is indicated for individuals in high risk groups:
  o Those with a family history of glaucoma
  o Older persons
  o Black, Hispanic, or Japanese-American persons
  o Persons with high myopia

Screening modalities

• Most cases of high IOP, glaucomatous optic discs, and visual field defects in adults are discovered by an optometrist during routine eye examination
• Routine eye exams are recommended every 2 to 4 years from age 40 and every 1 to 2 years from age 65
• For those at high risk, eye exams are recommended every 3 to 5 years from age 20, every 2 to 4 years from age 30, and every 1 to 2 years from age 65
• Examination should include measurement of IOP and assessments of the optic disc, retinal nerve fiber layer, and visual function
• Optometrists should refer patients to their primary care provider for secondary referral to an ophthalmologist

Primary prevention

Not applicable.

Diagnosis

Summary approach
• Diagnosis is confirmed by evidence of glaucomatous optic disc or visual field loss
• IOP may be normal or elevated

Clinical presentation

Symptoms

• Usually asymptomatic until advanced visual field loss is present
• Visual acuity may be reduced in advanced disease
• Symptomatic visual field defects can be seen in advanced disease
• Tunnel vision may develop at terminal stage as peripheral vision is lost
• Usually bilateral, although vision loss may initially affect one eye only
• Secondary glaucoma may present symptoms that are linked to the underlying cause

Congenital and secondary infantile glaucoma:

• Buphthalmos (enlargement of the eye)
• Tearing
• Blepharospasm (excessive blinking and forced lid closure)
• Photophobia
• Corneal edema and clouding

Other historical information

• Likelihood of glaucoma is increased in black and Hispanic patients
• Use of topical, systemic, or periocular steroids may cause an increase in IOP
• There is some evidence that chronic glaucoma may be more common in type 2 diabetes mellitus, but this may result from increased reporting in vision screening of diabetics
• Some studies have linked migraine, systemic hypertension, hypotension, ischemic heart disease, and peripheral vasospasm to an increased risk of developing glaucoma

Signs

• Raised IOP
• Visual field defect, usually detectable only on perimetric testing. Characteristic pattern of arcuate scotoma, followed by tunnel vision at terminal stage
• Visual field defects may be too localized to detect on confrontational fields unless very advanced disease is present
• Glaucomatous optic neuropathy: increased cup-to-disc ratio, asymmetric disc cupping (if disease is more advanced in one eye), focal notching of optic disc rim, and optic disc hemorrhages
• Relative afferent pupillary defect (Marcus-Gunn pupil) if glaucomatous optic neuropathy is asymmetric
• Secondary glaucoma may present signs that are linked to the underlying cause
• Reduced visual acuity in advanced disease
- Patients in the final stage of neovascular glaucoma experience severely reduced visual acuity and corneal edema

Congenital and secondary causes of infantile glaucoma:

- Myopia, astigmatism, and subluxation of the lens may develop
- Conjunctivitis, blepharitis, and cellulitis are less common

Other physical examination factors

- Snellen chart visual acuity should be recorded with distance lenses and, if less than 20/20, should be retested through a pinhole aperture
- Relative afferent pupillary defect may indicate asymmetric optic nerve disease secondary to glaucomatous optic neuropathy
- Optic disc should appear pink and healthy when visualized with a direct ophthalmoscope. Evidence of cupping or pallor may indicate glaucomatous damage

Diagnostic testing

- Snellen visual acuity test: visual acuity is not affected until late in the disease, but acuity should be recorded for a baseline
- An ophthalmoscope is the most helpful tool available to the non-specialist physician for the diagnosis of glaucoma
- The appearance of the optic disc should be recorded by photograph or drawing at initial assessment to allow future comparison
- Slit lamp examination provides a stereoscopic view of the optic disc under high magnification and excellent illumination. The anterior segment structures can also be examined and a preliminary assessment made of the degree of openness of the anterior chamber
- Tonometry and optic disc examination are the most useful tests in establishing glaucoma. Tonometry is usually performed by an ophthalmologist or optometrist
- Gonioscopy allows either direct or indirect visualization of the anterior chamber angle
- Pachymetry measures central corneal thickness and is usually performed by a specialist. Thin corneas have been shown to be a risk factor for open-angle glaucoma
- Automated visual field testing is usually performed by an optometrist or ophthalmologist. Physician may receive the results of such tests included in consultations
- Confocal scanning laser ophthalmoscopy, optical coherence tomography, and scanning laser polarimetry are helpful in the diagnosis, evaluation, and follow-up of glaucoma but for specialist use only
- For the assessment of childhood glaucoma, examination under anesthesia is used to evaluate IOP, corneal diameter, and axial length and to perform retinoscopy and visualization of the drainage angle of the eye by gonioscopy

Snellen visual acuity testing
Slit lamp examination
Tonometry
Gonioscopy
Optic disc examination
Pachymetry
Automated visual field testing

Differential diagnosis

- POAG must be differentiated from closed-angle glaucoma and other optic neuropathies
- Nonglaucomatous optic neuropathies often result in pallor of the optic nerve head but rarely demonstrate enlargement of the optic disc cup

Chronic primary closed-angle glaucoma
Optic neuritis
Ischemic optic neuropathy
Leber hereditary optic neuropathy
Toxic optic neuropathy
Traumatic optic neuropathy
Congenital pit of the optic disc

Consultation

- Immediate referral if signs of acute angle-closure glaucoma are present: red, painful eye with partially dilated, fixed pupil associated with reduced vision; headache; and a firm eye on palpation
- Final diagnosis or exclusion of POAG is within the scope of eye specialists. In most states in the U.S., optometrists can prescribe antiglaucoma drops; chronic glaucoma may be referred to either an optometrist or an ophthalmologist
- Patients with a raised IOP (22 mm Hg or higher), with or without abnormal optic disc head appearance or visual field abnormality, should be referred soon for ophthalmologic assessment. All individuals with optic nerve changes suggestive of glaucoma should be referred for evaluation, even if IOP is not raised
- Patients with a relative afferent pupillary defect with or without visual field defects should be referred for ophthalmologic assessment
- Patients who have asymmetric optic nerves (the physiologic cup within the optic nerve head of one eye being a different size than the cup in the other eye) should be referred for a glaucoma evaluation even if the IOP is normal
- Provide the ophthalmologist with information on previous ocular history, significant past medical history, and concurrent medication and allergies

Treatment

Summary approach

- The goal of treatment is to enhance the patient's health and quality of life by preserving visual function without causing unwelcome effects
- IOP is the only risk factor that has proved amenable to treatment. IOP reduction has been demonstrated to delay or prevent disease progression both at the early and late stages of the disease, protecting the optic nerve and preserving the visual field.
- A target IOP range should be established for each patient based on a risk assessment and set at the level below which further optic nerve damage is unlikely to occur.
- Most commonly, the initial goal of treatment is to reduce IOP by 20% to 40%, although in some cases where there is evidence of severe optic nerve damage or other risk factors, a reduction of more than 40% may be targeted.
- The greater the pre-existing damage due to glaucoma, the lower the target IOP should be, and the target should be reset to a lower level if further deterioration occurs.

**Medical treatment**

- Therapy for most patients with a new diagnosis of glaucoma commences with a single-drop treatment and the setting of a target IOP level.
- Monotherapy is preferred due to increased compliance, but different classes of ophthalmic treatments may be substituted or combined up to a point of maximal tolerated medical therapy.
- In practice, a combined approach to treatment of chronic glaucoma may be more effective in lowering the IOP and preventing glaucomatous progression than monotherapy because of a synergistic effect between therapeutic approaches.

**First-line therapies:**

- Prostaglandin analog or β-blocker ophthalmic formulations, unless there are specific contraindications in the individual patient.
- Nonselective β-blockers include timolol, levobunolol (available in preservative-free formulation), and carteolol. The selective β-1 blocker, betaxolol, has fewer respiratory adverse effects and is favored for elderly patients.

**Second-line therapies, or first-line therapies for patients in whom β-blockers are contraindicated:**

- Ophthalmic α-agonists such as brimonidine or apraclonidine may be used short-term.
- Ophthalmic carbonic anhydrase inhibitors such as dorzolamide (available in combination with timolol) and brinzolamide.

**Third-line therapies for patients who are intolerant of other ophthalmic treatments:**

- Oral carbonic anhydrase inhibitors, such as acetazolamide or methazolamide. Long-term use should be avoided because of risk of systemic adverse effects.
- Ophthalmic pilocarpine is available in 1% to 6% formulations (also available in preservative-free preparations).

**Surgical treatment**
• If target IOP is not achievable with maximal tolerated medical therapy, trabeculoplasty or trabeculectomy must be considered. Drainage shunts may be required in refractory cases
• Laser trabeculoplasty has been shown in various studies to provide a 20% to 30% reduction in IOP
• Incisional surgical procedures are generally the most effective in lowering IOP but are only considered when benefits outweigh the risks of complications

Laser surgery:

• Argon laser trabeculoplasty may be used as an adjunct to medical therapy or incisional surgery and is performed in the office
• Selective laser trabeculoplasty is similar to argon laser trabeculoplasty but uses a neodymium:yttrium-aluminum-garnet (Nd:YAG) laser
• Contact laser cyclophotocoagulation (CPC) uses an argon laser with a contact probe applied at the limbus to ablate the ciliary body and decrease aqueous production. Often used as a last resort after medication and incisional surgery have failed

Incisional surgical therapies:

• Trabeculectomy is the gold standard glaucoma filtration surgery. Should be considered when target IOP is not reached with medical or laser therapy. Should be considered if glaucomatous progression occurs despite reaching previous IOP target level
• Treatment with antimetabolites such as 5-fluorouracil (5-FU) or mitomycin C (MMC) can decrease scarring following trabeculectomy and increase long-term success
• Drainage implants and tube shunts are being used more frequently in cases of resistant glaucoma. Such devices channel aqueous from the anterior chamber through a long tube to an equatorial plate that acts as a base for a bleb to form
• Several drainage devices with varying design details are available. Implants have been associated with around 50% failure rate at 5 years. Excessive fibrosis around the bleb appears to be a major cause of long-term failure in glaucoma drainage devices
• Endocyclophotocoagulation is similar to contact CPC but instead uses a probe that combines an argon laser with a fiberoptic scope to directly visualize and ablate the ciliary body. Usually performed at the time of cataract extraction

Other forms of glaucoma

Normal-tension glaucoma:

• Limited available evidence for a beneficial effect of medical or surgical treatment is weak but suggests that lowering IOP using standard glaucoma treatments might help patients whose field loss is progressing despite normal IOP

Infantile glaucoma:

• Treatment is predominantly surgical, with medical treatment playing a limited role
- Goniotomy (used when there is a clear cornea) and trabeculotomy (used when the cornea is cloudy) are the most common procedures with a success rate up to 80% to 90%
- Trabeculectomy is when initial surgery has failed to control IOP; drainage devices are used in refractory cases
- Following surgery, a rehabilitation program can enhance pediatric patients' vision-related skills and abilities

Secondary open-angle glaucoma:

- Treatment depends on the underlying cause
- Infection or inflammation should be treated appropriately
- Panretinal photocoagulation is first-line therapy in neovascular glaucoma. Once the anterior chamber is closed by synechiae and the IOP is uncontrollably elevated, filtration surgery should be considered
- A tumor or cataract that is obstructing fluid drainage may require surgical treatment
- Raised IOP following cataract surgery is treated with glaucoma ophthalmic agents and, if unsuccessful, glaucoma filtration surgery
- Drainage implant surgery may be indicated in refractory cases

Medications

Prostaglandin analogs
β-blockers (ophthalmic)
α-adrenergic agonists
Carbonic anhydrase inhibitors (ophthalmic)
Carbonic anhydrase inhibitors (oral)
Pilocarpine

Non-drug treatments

Argon laser trabeculoplasty
Selective laser trabeculoplasty
Trabeculectomy
Drainage implants and tube shunts

Special circumstances

Very elderly, unwell patients may not undergo significant glaucomatous progression in their lifetime and may suffer considerable adverse effects from medical treatment. In consultation with the patient, it may be preferable to monitor the condition without treatment.

Comorbidities

Coexisting disease:
Coexisting bronchial asthma, severe COPD, overt heart failure, and heart block will preclude the use of topical β-blockers because of systemic absorption of the drug.

Arthritis or a previous stroke may result in poor compliance if patients have difficulty administering drop therapies.

Coexisting medication:

- Patients who are prescribed treatment with both an oral and topical β-adrenergic blocking agent should be observed for potential additive effects of β-blockade, both systemic and intraocular.
- Use of α-agonist drugs, such as brimonidine or apraclonidine, is contraindicated with concurrent MAOI use.
- Concurrent topical or oral steroid use may increase IOP and make control more difficult.

Special patient groups:

- Therapy regimens for very elderly, unwell, or incapacitated patients should be made as simple as possible to limit adverse effects and improve compliance.
- Once-a-day treatment regimens or surgical options may be more appropriate in elderly patients who rely on others to administer drops or where compliance is a problem.
- Younger patients, those with more severe disease, or those with greater risk factors for glaucomatous damage should be treated more aggressively, with lower target IOP levels.

Patient satisfaction/lifestyle priorities

Bilateral visual field loss secondary to glaucoma may affect the patient's legal ability to hold a commercial or personal driver license.

**Follow-up**

- Follow-up is essential to monitor IOP and assess compliance, progression of optic neuropathy and visual field loss.
- Frequency of follow-up is dependent on the stability of the disease.
- Target IOP should be reset to a lower level if further deterioration occurs.

Plan for review

- When treatment is commenced or changed, review is usually 6 to 8 weeks later.
- If the IOP level has responded well to topical treatment and the visual field and optic disc appearance are stable, follow-up may be every 3 to 4 months.
- Visual field and optic disc analysis should be performed at least yearly in glaucoma patients who have normalized pressures to optimize the detection of glaucomatous progression.

Ocular hypertension:
• Although there is agreement that patients with ocular hypertension require regular follow-up, the value of treating these patients to lower their IOP is uncertain, as only a subset will ultimately develop visual field abnormalities or glaucomatous optic neuropathy
• Ophthalmic preparations that are indicated for POAG may also be used for treating ocular hypertension

Prognosis

• Optic nerve damage that has already taken place at the time of diagnosis is irreversible
• Early diagnosis and effective medical and/or surgical treatment to reduce IOP provide the best means of preventing further damage to sight
• Some glaucoma patients with normalized pressure will continue to lose visual field, and the pressure may have to be reduced even further by altering medical treatment or proceeding to surgery
• The majority of patients with ocular hypertension may never develop glaucoma

Factors affecting prognosis:

• Prognosis depends on the extent of glaucomatous damage at presentation, level of the presenting IOP, age of the patient, and IOP level after medical or surgical treatment
• Elderly patients with moderate glaucomatous damage at presentation and slow progression because of suboptimal IOP control may not notice any decreased visual function over their lifetime
• In younger patients and black patients, glaucoma may progress more quickly and be more difficult to control
• In childhood glaucoma, permanent visual loss may arise as a result of amblyopia, which can develop in addition to and secondary to optic neuropathy. Consequently, amblyopia must be treated aggressively
• Risk of conversion from ocular hypertension to glaucoma is increased by older age, larger vertical or horizontal cup-disc ratio, higher IOP, greater visual field pattern standard deviation, and thinner central corneal measurement

Deterioration:

• Laser trabeculoplasty is generally reserved for cases of POAG that have not responded adequately to topical medical treatment
• Surgical trabeculectomy is considered when target IOP is not reached with medical or laser therapy
• Drainage implant surgery is used in selected cases of resistant primary and secondary glaucoma

Complications

• Uncontrolled glaucoma leads to progressive visual field loss and loss of sight
• Glaucomatous damage is irreversible
Patient education

- Drivers with bilateral glaucomatous visual field loss should be informed of their responsibility to notify the relevant driver license authorities of their condition so that eligibility to drive may be assessed. Depending upon regulations, the physician may be required to inform the state if a patient is not capable of driving safely.
- Family members and affected individuals should be advised of the need for periodic ophthalmologic examinations.

Online information for patients

- Glaucoma Research Foundation: [What is glaucoma?](#)
- Mayo Clinic: [Glaucoma](#)
- National Eye Institute: [Facts about glaucoma](#)

Resources

Summary of evidence

Evidence

The use of topical β-blockers in the surgical management of POAG is associated with significantly greater disease control than observation alone as the primary treatment.

- An RCT compared laser trabeculoplasty plus topical betaxolol hydrochloride versus no initial treatment in 255 patients with newly detected POAG or pseudoexfoliation glaucoma, previously untreated. After 6 years, there was a significant reduction in the number of people in the laser trabeculoplasty (plus topical betaxolol hydrochloride) group with progression of glaucoma compared with control (58/129 or 45% vs 78/126 or 62%, respectively (P = .007), and the average time to progression was longer in the treated group. [5] Level of evidence: 2

Comparisons between surgical and laser treatments have found that both therapies are effective. However, some studies suggest that surgical trabeculectomy is superior to other therapies.

- A systematic review with 19 studies, only 5 RCTs, involving 2,137 patients with OAG comparing laser trabeculoplasty with medical therapy (primarily topical β-blockers or pilocarpine), surgery, and no treatment. At 6 months, laser trabeculoplasty increased risk of uncontrolled IOP compared to trabeculectomy, although quality of studies interfered with data interpretation at 2 years. [6] Level of evidence: 2
- A systematic review of four trials, 888 patients, compared medical and surgical treatments for POAG. Three of the trials compared trabeculectomy with pilocarpine or a β-blocker. Risk for visual loss was similar in patients with mild glaucoma, but surgery was superior in those with severe disease. Risk for post-operative development of cataract was higher in patients undergoing surgery. [7] Level of evidence: 1
There is limited evidence that latanoprost is superior to timolol in reducing IOP in patients with POAG.

- An RCT of 267 patients compared treatment with timolol 0.5% twice daily versus latanoprost 0.005% in the morning versus latanoprost 0.005% in the evening. It found that latanoprost applied once daily in the evening was superior to timolol in reducing IOP. [1] Level of evidence: 2
- A second RCT of 268 patients compared treatment with latanoprost 0.005% once daily versus timolol 0.5% twice daily. This study found that there was a significantly greater decrease in IOP with latanoprost, which was also relatively well tolerated, compared with timolol. [2] Level of evidence: 2

There is limited evidence that brimonidine is an effective alternative to topical β-blockers as a medical therapy for POAG.

- Combined data from an RCT involving 926 patients concluded that brimonidine showed similar efficacy to timolol and had a relatively low rate of ocular allergy. [8] Level of evidence: 3
- An RCT treated 206 adults with either brimonidine 0.2% or betaxolol 0.25% for a 3-month period. Brimonidine was well tolerated and clinically and statistically more effective than betaxolol 0.25% at lowering IOP during both peak (P = .004) and trough (P < .001) IOP measurements in patients with OAG and ocular hypertension. [9] Level of evidence: 3

The combination of dorzolamide-timolol is as effective as latanoprost.

- A prospective, randomized, crossover comparison study of 53 patients, 39 with POAG and 14 with ocular hypertension, showed that after 6 months of therapy, the dorzolamide-timolol fixed combination is as effective as latanoprost in lowering IOP. [4] Level of evidence: 3

There is limited evidence that topical dorzolamide is an effective alternative to topical β-blocker therapies in the medical treatment of POAG.

- An RCT of 523 patients compared topical treatment with dorzolamide 2% three times a day versus timolol 0.5% twice daily versus betaxolol 0.5% twice daily in patients with OAG or ocular hypertension. Patients were followed up for 1 year. Results confirmed treatment with dorzolamide was as effective as betaxolol at lowering IOP. None of the significant adverse effects found with oral carbonic anhydrase inhibitors were found to occur with topical dorzolamide. [10] Level of evidence: 2

Bimatoprost in combination with timolol may prove more effective in patients refractory to treatment with latanoprost in combination with timolol.

- A prospective, multicenter, randomized, double-masked, cross-over clinical trial of 89 patients with OAG was conducted comparing bimatoprost plus timolol with travoprost
plus timolol. After 3 months, the mean IOP had decreased significantly in the bimatoprost plus timolol group (14.7 mm Hg [95% CI, 14.3 to 15.3 mm Hg] compared with the travoprost plus timolol group (15.4 mm Hg [95% CI, 15.0 to 15.9 mm Hg]; \( P = .0041 \)). [3] Level of evidence: 2

There is some evidence that surgical trabeculectomy is effective as an initial therapy for POAG.

- An RCT of 116 patients with POAG compared surgical trabeculectomy (followed by medical treatment when indicated) versus medical treatment (followed by trabeculectomy when medical treatment did not work). This study found that initial trabeculectomy significantly reduced both IOP and visual field loss compared with medical treatment, although there was no significant difference in visual acuity with either treatment. [11] Level of evidence: 1

- A large, multicenter trial involving 607 people newly diagnosed with POAG, pigmentary glaucoma, or pseudoxefoliation glaucoma compared surgical trabeculectomy (with or without 5-FU) versus medical treatment as initial treatments. It found no significant difference between groups in visual field loss after 5 years, and progression of visual field loss was similar with both treatments. Loss of visual acuity was greater in the surgical group at 5 years, but the significance of this difference was not reported. Both treatments reduced IOP, but the reduction was significantly greater in those patients treated with surgical trabeculectomy. [12] Level of evidence: 1

The use of adjunctive medications increases the success rate for surgical interventions.

- A systematic review of 9 trials of questionable methodology including 614 patients treated with trabeculectomy, randomly selected to receive postoperative 5-FU versus placebo or no injections, found that the use of higher dose postoperative 5-FU reduces the risk of surgical failure in eyes that have undergone no previous surgery and in eyes at high risk of failure. [13] Level of evidence: 2

- A systematic review of 11 trials including 698 patients treated with trabeculectomy with or without intraoperative MMC found that treated patient had a reduced risk of trabeculectomy failure in eyes that had previously failed surgery (RR = 0.32; 95% CI 0.20-0.53) and in patients new to surgery (RR = 0.29, 95% CI 0.16-0.53). [14] Level of evidence: 1

MMC and 5-FU are not significantly different when used as adjuncts to trabeculectomy.

- An RCT compared the long-term (longer than 12 months) use of intraoperative MMC versus 5-FU as adjunctive treatments used with primary trabeculectomy in 103 patients (115 eyes). There was no significant difference in complication rate, surgical failure, or reduction in IOP. Injections of 5-FU given postoperatively were beneficial but had complications such as reduced wound healing, globe perforation, and corneal epithelial defects. [15] Level of evidence: 2
Although poor methodology and few randomized trials allow for no evidence of superiority of any particular shunt over the others, there is limited evidence that the Baerveldt tube is equal to, and Ex-PRESS shunt superior to, trabeculectomy at maintaining target IOP.

- An RCT compared the 350-mm Baerveldt tube shunt versus trabeculectomy with MMC in 212 patients. Patients were required to have had a previous trabeculectomy and/or cataract extraction with intraocular lens implantation in addition to being on maximum medical therapy. There was no significant difference in mean IOP at 1 year. [16] Level of evidence: 1
- An RCT evaluated complications of the 350-mm Baerveldt tube shunt versus trabeculectomy with MMC in 212 patients. Patients were required to have had a previous trabeculectomy and/or cataract extraction with intraocular lens implantation in addition to being on maximum medical therapy. While no significant difference was found when comparing intraoperative complications, postoperative complications were greater in the trabeculectomy group than in the tube group [17] Level of evidence: 1
- An RCT compared the Ex-PRESS glaucoma mini-shunt with trabeculectomy in 78 patients (80 eyes) with POAG, pigmentary glaucoma, or pseudoexfoliation glaucoma. The Ex-PRESS shunt was found to be significantly better at maintaining the target IOP (4-15 mm Hg) at 1 year. Complication rates were not significantly different. [18] Level of evidence: 3
- A meta-analysis review of 15 trials with a total of 1,153 participants comparing various implant shunts found the small number of randomized trials and poor methodology could not provide evidence of superiority of one shunt over another. [19] Level of evidence: 2

References

Evidence references

CrossRef


Schuman JS. Clinical experience with brimonidine 0.2% and timolol 0.5% in glaucoma and ocular hypertension. Surv Ophthalmol. 1996;41:S27-37

Serle JB; Brimonidine Study Group III. A comparison of the safety and efficacy of twice daily brimonidine 0.2% versus betaxolol 0.25% in subjects with elevated intraocular pressure. Surv Ophthalmol. 1996;41:S39-47


Feiner L, Piltz-Seymour JR; Collaborative Initial Glaucoma Treatment Study. Collaborative Initial Glaucoma Treatment Study: a summary of results to date. Curr Opin Ophthalmol. 2003;14:106-11


The American Academy of Ophthalmology has produced the following:

The American Optometric Association has produced the following:

The U.S. Preventive Services Task Force has produced the following:

The National Institute for Health and Clinical Excellence (UK) has produced the following:

Further reading
- Weinreb RN, Khaw PT. Primary open-angle glaucoma. Lancet. 2004;363:1711-20


Hatt SR, Wormald R, Burr J. Screening for prevention of optic nerve damage due to chronic open angle glaucoma. Cochrane Database Syst Rev. 2006:CD006129


Codes

ICD-9 code

Type of glaucoma (primary code)

- 360.42 Blind hypertensive eye, absolute glaucoma
- 365.01 Open-angle with borderline findings, low risk
- 365.05 Open-angle with borderline findings, high risk
- 365.11 Primary open-angle glaucoma
- 365.12 Low-tension open-angle glaucoma
- 365.13 Pigmentary open-angle glaucoma
- 365.2 Primary angle-closure glaucoma
- 365.31 Corticosteroid-induced glaucoma, glaucomatous stage
- 365.4 Glaucoma associated with congenital anomalies dystrophies and systemic syndromes
- 365.5 Glaucoma associated with disorders of the lens
- 365.52 Pseudoexfoliation glaucoma
- 365.6 Glaucoma associated with other ocular disorder
- 365.61 Glaucoma associated with pupillary block
- 365.62 Glaucoma associated with ocular inflammations
- 365.63 Glaucoma associated with vascular disorders
- 365.64 Glaucoma associated with tumors or cysts
- 365.65 Glaucoma associated with ocular trauma
- 365.81 Hypersecretion glaucoma
- 365.9 Unspecified glaucoma

Stage of glaucoma (secondary code)
• 365.71 Mild stage glaucoma (defined as optic nerve abnormalities consistent with glaucoma but no visual field abnormalities on any white on white visual field test, or abnormalities present only on short-wave length doubling perimetry)

• 365.72 Moderate stage glaucoma (optic nerve abnormalities consistent with glaucoma and glaucomatous visual field abnormalities in one hemifield and not within 5 degrees of fixation)

• 365.73 Severe stage glaucoma, advanced stage glaucoma, end stage glaucoma (optic nerve abnormalities consistent with glaucoma and glaucomatous visual field abnormalities in both hemifields and/or loss within 5 degrees of fixation in at least one hemifield)

• 365.74 Indeterminate stage glaucoma (visual fields not performed yet, patient incapable of visual field testing, or unreliable/uninterpretable visual field testing)

FAQ

• **How do you treat chronic glaucoma?** Treatment of choice is medical (usually with eyedrops) followed by surgical intervention if medical therapy fails. Referral to an ophthalmologist is required

• **How long does chronic glaucoma need to be treated?** Probably for life

• **Which patients with ocular hypertension should be treated?** Current evidence suggests that those patients with an increased risk of conversion from ocular hypertension to glaucoma should be treated. The recognized risk factors are older age, larger vertical or horizontal cup-disc ratio, higher IOP, greater visual field pattern standard deviation, and, in particular, thinner central corneal measurement

**Current contributors**

Polly Henderson, MD, Chief, Glaucoma Service, Drexel University College of Medicine, Philadelphia, Pennsylvania

Myron Yanoff, MD, Professor and Chair, Department of Ophthalmology, Drexel University College of Medicine, and Adjunct Professor of Ophthalmology, University of Pennsylvania, Philadelphia, Pennsylvania

Carlton R. Fenzl, MD, Jamaica Hospital Medical Center/NYMC, Jamaica, New York