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The Medical and Surgical Management of Pseudoexfoliation Glaucoma

Manishi A. Desai, MD and **Richard K. Lee, MD, PhD**

Pseudoexfoliation (PXF) glaucoma is classically diagnosed by slit lamp visualization of white powdery deposits (PXF material) in a bull's eye configuration on the lens capsule. PXF glaucoma is the most common form of open-angle worldwide with an identifiable etiology.[1] The presence of PXF material is associated with an increased risk of developing glaucoma, but can be present in the eye without associated glaucoma. This disorder also has an association with narrow angles secondary to zonular weakness, increased rate and risk of cataract formation, and increased risk of complications during cataract extraction associated with zonular dehiscence. PXF glaucoma's primary manifestations and morbidity are ocular. However, PXF is a systemic condition with PXF material present throughout the body. The presence of PXF material has been weakly associated with cardiovascular and cerebrovascular morbidity and sensorineural hearing loss.[2–10] Unlike PXF and glaucoma, a direct cause-effect relationship remains to be clearly established between the presence of PXF material and the aforementioned systemic associations.

PXF syndrome was first described by Lindbergh in the year 1917, followed by Vogt, and initially termed "glaucoma capsulare." The classic white flaky dandrufflike material was initially thought to originate from the lens capsule.[11] Immunohistologic and electron microscopy studies suggest the PXF material deposited on the lens capsule and throughout the anterior segment of the eye (ie, the angle, corneal endothelium, etc.) is a product of abnormal extracellular matrix material metabolism.[1] PXF is distinct from true exfoliation syndrome observed in glass blowers, where a schisis of the anterior lens capsule occurs. Recent molecular and genetic studies have revealed clues as to the molecular pathogenesis of PXF material formation and the association of PXF with the extracellular matrix and cellular metabolism.[12,13]

This paper reviews current concepts in the medical and surgical management of PXF glaucoma.

What is the Population at Risk of PXF Glaucoma?

PXF is present worldwide despite its high prevalence in Scandinavian countries, where this disease has been best characterized. The condition is observed in the South African Bantu and in Japan.[14–17] The prevalence in the general population does vary from country to country depending on race and age.[14–25] The prevalence is as high as approximately 20% in Finland and over 25% in Iceland, but only ~ 5% in parts of Denmark.[18–22] Interestingly, the incidence in an Arizona Navajo population is as high as 38%.[23,24] The reasons for the prevalence variation are not entirely clear, but the incidence also varies regionally within a country. For example, in Norway, the incidence in 3 adjacent towns ranged from 10.2%, 19.6%, to 21.0%.[26] Within Crete, the prevalence in persons older than 40 years ranged from 1.5% to 27%.[27]

As noted earlier, the prevalence of PXF also varies with age. Similar to primary open-angle glaucoma, the prevalence increases with age.[17,21,25,28–30] In Finland, the incidence rose from 10% for persons aged 60 to 69 years old to 33% in persons 80 to 89 years old.[21] Increased incidence with age was also found in populations in Norway, Japan, Australian aborigines, and in the United States.[17,25,28–30]

With regards to sex, the prevalence of PXF has varied. Though a number of studies have indicated greater prevalence in women than men,[31–33] this bias has been thought to be secondary to increased lifespan. A number of studies have not demonstrated any sex predilection.[20,28,34–41]

Clinical Findings in PXF

The presence of PXF material in the eye is often a subtle observation and is not as evident as classically described or often photographed. Significant differences in clinical presentation between patients and asymmetry of clinical findings and glaucomatous disease between 2 eyes of a patient is common. Careful examination with the slit lamp is essential for diagnosis or for at least raising suspicion of the diagnosis in the setting of subtle or early findings. Not uncommonly, the clinical findings are only evident in 1 eye, even though this is a systemic disorder. Many studies have demonstrated either predominately unilateral or bilateral involvement depending on the patient demographics.[31] In general, patients with bilateral involvement tend to be older.[28,29,32] The probability of developing PXF in the fellow eye in 192 patients initially with unilateral PXF was 24% at 10 years and 29% in 15 years.[42] Other studies have estimated the probability of developing PXF in the unaffected eye ranging from 6.8% to 30% to 40% over a 5-year period.[35,43–46] Conjunctival biopsy of the fellow eye in unilateral PXF is often positive for pseudoexfoliative matter.[47,48] This suggests that despite clinical asymmetry, invariably there is bilateral involvement that may not be clinically evident except over time.

Lens

The most classic finding in PXF is the appearance of flakes of PXF material on the anterior lens capsule. The material is often observed in 3 distinct zones with a central zone of material deposition. The clear intermediate zone is secondary to iris excursion rubbing the PXF material off of the lens capsule. A peripheral zone of material is seen outside of this intermediate zone. The central zone can be absent in 20% of cases of PXF,[49] and the peripheral granular zone, though present, can only be observed with dilation. The clinician needs to carefully examine the lens capsule under a dim light in the nondilated eye to allow dilation to attempt visualization of PXF material. Most importantly, the lens capsule should be carefully reexamined after dilation with a bright slight lamp beam to increase contrast between the lens capsule and the PXF material to visualize even subtle, fine dusting of PXF material on the lens capsule that would be difficult to observe through the nondilated pupil.

In addition to these changes observed on the lens capsule, the incidence of cataract formation is increased in patients with PXF.[40,49–59] A higher percentage of nuclear opacities has been observed in PXF eyes and the affected eye of individuals with uniocular PXF often demonstrate the more advanced cataract.[54,57,58] The occurrence of cataract may simply be a consequence of the increased age of individuals with PXF as no causal link has been established.

Zonules and Ciliary Body

The pseudoexfoliative matter is found abundantly on the ciliary processes and zonules. In individuals with unilateral involvement, PXF material was found on ciliary process, zonules, or both in the fellow eye in 77% of examined eyes.[60] The PXF matter indirectly or directly is believed to lead to zonular fragility. One hypothesis is that proteolytic enzymes within the PXF material directly induce zonular damage. Another hypothesis suggests that zonular weakness arises from accumulation of PXF material at the origin of the zonules on preequatorial regions of the lens. The accumulation of this PXF material disrupts zonular architecture and leads to zonular instability and weakness. The zonular weakness translates to phacodonesis, which, when severe enough, can be observed during careful slit examination. This evaluation for

zonular weakness is particularly important before cataract extraction.[61–63] More likely is the possibility that zonular weakness is owing to intrinsic differences between normal and PXF zonules because PXF zonules are composed of modified forms of zonular fibers. The recent identification of an extracellular matrix-associated protein with increased risk of developing PXF glaucoma suggests the same associated cause for PXF glaucoma may be responsible for PXF zonulopathy.[12]

The zonulopathy can also lead to anterior displacement of the lens, that is, a phacomorphic narrowing, with intermittent pupillary block. This may be elicited from the history with the individual complaining of episodes of pain, blurry foggy vision. Clinical evidence may be present either by directly visualizing an iris bombé configuration, a narrow angle during gonioscopy, or posterior synechiae and/or a Vossius ring on the lens capsule. We recently encountered a case of pupillary block glaucoma with a very narrow anterior chamber (compared with the other eye) and iris bombé in a patient with a history of PXF glaucoma. A peripheral laser iridotomy promptly decreased the intraocular pressure (IOP) and relieved the iris bombé and deepened the anterior chamber to some degree. However, only upon dilation with visualization of a Vossius ring on the lens capsule and a subsequently even deeper central anterior chamber was it obvious that the lens had been attached to the iris at the pupil leading not only to pupillary block, but also a shallow central anterior chamber. PXF-associated lens zonular laxity led to a phacomorphic component of pupillary block angle closure associated with posterior synechia formation at the pupillary border.

Angle

PXF has been associated with a number of findings related not only to the appearance of the angle, but also to the depth of the angle. Flakes of PXF material are often visible in the angle inferiorly. Pigmentation in the angle is also often increased but irregular.[49–52,62,64–76] Additional pigmentation is observed along Schwalbe line, termed a “Sampaolesi’s line.”[72,73,77] This finding is not exclusive to PXF, but can be seen in pigment dispersion syndrome and chronic inflammation.[65] Increased pigmentation in the angle has been correlated with increased IOP.[78,79] This suggests that pigmentation might provide a clinical gauge as to the severity of glaucomatous disease.

The angle can often be narrow or occludable in cases of PXF.[28,75,80–84] The prevalence of occludable angles varies depending on the study, but range from 9% to 18%. In a small meta-analysis, the occurrence of angle closure was observed to be 2.2%.[82] Acute angle closure has been reported in a patient with PXF that was attributed to increased iridolenticular adhesions secondary to presence of PXF material.[85] More recently, angle closure in a PXF patient associated with evidence of pupillary block observed by ultrasound biomicroscopy was reported.[81] Given these findings, gonioscopy should be performed routinely in individuals with PXF to monitor the angle for consideration of a prophylactic laser peripheral iridotomy or early cataract surgery.

Iris

Flecks of white PXF material and pigment can be observed deposited on the anterior and posterior surface of the iris.[86] The pupil margin is characterized by transillumination defects resulting from atrophic and/or fibrotic changes in the iris sphincter muscle, possibly the cause of poor dilation in PXF eyes. The pupillary margin of the iris is also affected with subsequent loss of the pupillary ruff. These changes collectively result in what is described as a “moth eaten” pupil margin.[87,88] The pathogenesis of these clinical observations is not entirely clear, but may be secondary to mechanical factors associated with the pseudoexfoliative matter on the anterior lens capsule (ie, friction between iris pigment epithelium and PXF matter on lens capsule). This is demonstrated by the dispersion of pigment seen clinically after dilation.

Occasionally, mottling of the iris pupillary margin offers the first suggestion that PXF is present. Finally, angiographic studies have demonstrated hypoperfusion, peripupillary leakage, and even neovascularization in some studies. Certainly, vascular changes may also play a causal role with regard to the findings noted in the iris of PXF patients.[89,90]

Anterior Chamber

PXF syndrome has been associated with a disrupted blood-aqueous barrier. Testing with a flare meter demonstrated markedly increased flare in comparison with primary open angle glaucoma.[91–94] This increased intraocular inflammation has consequences postoperatively after cataract extraction, which are discussed later in this review.

Corneal Findings

Patients can demonstrate decreased endothelial cell density manifesting as guttata; the etiology, however, is not clear.[47,48,95–98] This may be secondary to intermittent periods of elevated IOP associated with glaucoma and possible cumulative damage to the endothelium. Aside from this endotheliopathy, flakelike PXF material and pigment can be observed dispersed on the endothelium. The pigment is believed to arise from disruption of iris pigment epithelium secondary to frictional interaction with PXF material on the lens capsule.[86] The pigment can be distributed diffusely or in spindle configuration analogous to that seen in pigment dispersion syndrome because of the convection current patterns of aqueous flow.

Association With Glaucoma

In individuals with the presence of PXF material, a significantly higher prevalence of ocular hypertension and glaucoma is observed in PXF eyes compared with normal eyes. In 1 series of 100 consecutive subjects with PXF, glaucoma was detected in 7% and ocular hypertension in 15% of patients.[32] Ocular hypertension with and without glaucomatous damage was observed in 22.7% of PXF subjects versus only 1.2% in patients without PXF[99]; similar results were observed in a Norwegian study[100] with 30% and 4.8%, respectively. Somewhat higher incidence figures were found in other populations.[56,59,74,101]

In association with the higher prevalence of ocular hypertension and/or glaucoma, PXF confers a significantly higher risk of developing glaucoma in comparison with the general population. The cumulative risk of developing glaucoma has been suggested to be approximately 5.3% and 15.4% at 5 and 10 years, respectively.[44] This can translate to a 10-fold risk compared with the general population. More recently, the Early Manifest Glaucoma Treatment Study (EMGT) demonstrated that ocular hypertension (24 to 32 mm Hg) in eyes with PXF was found to have a hazard ratio of 2.12 with regard to glaucoma progression.[102] Other studies have demonstrated also heightened risk for glaucoma in PXF patients.[44,103] Patients with PXF who were untreated progressed more quickly than treated individuals. The risk of progression was calculated to be 2-fold higher in individuals with PXF.[102,104] In a retrospective community-based study, 44% of 314 subjects over a 15-year period eventually were placed on treatment for progression to glaucoma (on the basis of visual field defect or optic nerve head appearance) or ocular hypertension.[42]

PXF glaucoma is thought to arise secondary to congestion of the trabecular meshwork by PXF material. PXF glaucoma is the most common form of secondary open angle glaucoma.[1,31] Less commonly, as noted previously, the mechanism of glaucoma is a consequence of angle closure associated with zonular laxity. In general, PXF-associated glaucoma has a more aggressive course compared with primary open angle glaucoma. The mean IOP is also higher in affected PXF glaucoma individuals compared with primary open angle glaucoma patients with IOPs that also fluctuate more widely. Those individuals who have glaucoma at the time of diagnosis

often not only have higher pressures, but also have more severe optic nerve damage.[1,29,31,40,45,68,99,104–107] One hypothesis is that the optic nerve in PXF also has an underlying intrinsic increased susceptibility, possibly owing to altered extracellular matrix in the nerve head associated with decreased structural integrity.

Management of PXF Glaucoma and Cataract

PXF glaucoma is a more difficult glaucoma to treat than primary open angle glaucoma and has a higher incidence of progression. PXF is also more likely to be recalcitrant to medical management and require surgical treatment. In 1 study, the proportion of PXF patients undergoing trabeculectomy was as high as 87.8%.[108] Regardless of its aggressive and often refractory course, medical or laser treatment is usually recommended as first line therapy.

Medical Management of PXF Glaucoma

A prospective randomized clinical trial comparing travaprost, latanoprost, and dorzolamide-timolol fixed combination in individuals with PXF showed IOP lowering ranged from 8 to 11 mm Hg.[109] Another study found a prostaglandin agonist in general to be efficacious in reducing IOP and diurnal variation in a prospective nonrandomized multicenter study.[110] In reviewing the literature, initial medical management was generally effective in reducing IOP in PXF with most agents used today.[109–114] We prefer the use of a prostaglandin agonist for initial medical treatment because of its high efficacy for lowering IOP and longer duration of action, which may be helpful in blunting PXF glaucoma-associated pressure spikes.

Of note, in the past, the preferred therapy included treatment with pilocarpine. Pilocarpine was used because it was believed to reduce iris excursion and decreased dispersion of PXF material and pigment. We do not recommend the use of pilocarpine as initial line medical therapy and recommend care when using pilocarpine, as pilocarpine can cause posterior synechiae with associated angle closure glaucoma and exacerbate the formation of cataract. Pilocarpine also can induce anterior rotation of the lens and exacerbate preexisting anterior subluxation secondary to zonulopathy with risk of pupillary block. Careful examination will dictate choice in medication, but first-line treatment with a prostaglandin analog is our preference.

Surgical Management of PXF Glaucoma

If medical treatment is not sufficient to manage PXF glaucoma, the subsequent interventions are surgical (nonincisional and incisional): typically comprising of laser trabeculoplasty (LTP), trabeculectomy, and/or implantation of a glaucoma drainage device (GDD). As mentioned previously, gonioscopy should be performed to evaluate the angle, especially in those cases where damage is progressive and high IOPs or intermittent periods of high IOP are observed. The angle can be narrow or may have progressive narrowing not only as result of a maturing cataract, but also from zonular laxity with secondary anterior lens movement. In such cases, a mixed mechanism for the development and progression of glaucoma may be present, and the individual may benefit from laser iridotomy or early cataract extraction.

LTP is a reasonable next step in PXF glaucoma management after maximal medically tolerated therapy before resorting to incisional surgery. Laser treatment, however, can also be offered as a first line therapy to individuals. PXF is particularly amenable to LTP because of the increased pigmentation of the trabecular meshwork for absorption of argon laser energy. Selective LTP seems to work similarly well for PXF glaucoma. A number of studies have demonstrated that LTP (argon LTP or selective LTP) is effective in reducing IOP.[114–125] However, the effect of LTP is not permanent,[121,125] although it is hopeful that selective LTP may be more repeatable for the treatment of glaucoma than argon LTP.

The clinician should be aware of postlaser IOP spikes.[122] IOP should be noted before laser treatment and be reevaluated an hour after treatment. Because of the disrupted blood-aqueous barrier and iris vessel leak noted previously in this article, the clinician should also be cautioned about increased inflammation after laser treatment. Treatment with steroids after LTP is controversial given that heightened inflammation may play a mechanistic role in postlaser IOP lowering with cytokine release. However, LTP patients should be administered IOP-lowering medication prophylactically (ie, iopidine) before laser treatment to minimize IOP spikes. The clinician may also elect to treat only 180 degrees to decrease inflammation and decrease the probability of an acute IOP elevation.

After treatment with LTP, the subsequent step necessary to control IOP or treat progression clinically (either noted by increased cupping of the optic nerve or progression of visual field deficits) is typically surgery.

Multiple studies evaluating surgical outcomes with trabeculectomy were not statistically different in individuals with PXF as compared with primary open angle glaucoma. The outcomes also do not seem to differ whether trabeculectomy was performed in phakic or pseudophakic eyes. The outcomes were also unaffected by the antifibrotic used (either 5-fluorouracil and or mitomycin C). In addition, no surgical complications were unique to PXF patients.[126–136] Similar results were noted in patients with combined trabeculectomy with phacoemuslification.[137,138] Because of associated increased inflammation in PXF eyes, we more aggressively treat trabeculectomy with steroids for a longer period of time to decrease the risk of bleb failure.

With regard to GDD in eyes with PXF glaucoma, there have been fewer studies. The recent Tube Versus Trabeculectomy Study enrolled a relatively small number of PXF subjects who had previous ocular surgery. Similar to other studies, no surgical complications unique to PXF were observed in the Tube Versus Trabeculectomy Study.[139,140]

The surgery of choice depends significantly on the individual's prior history. If the patient has had prior ocular surgery involving the conjunctiva with areas of conjunctival scarring superiorly, a GDD is preferred. If the individual has undergone a trabeculectomy in the fellow eye that has failed, a GDD may also be preferred. Otherwise, the primary surgical option of choice can be either trabeculectomy with an adjunctive antifibrotic agent or a GDD. We have placed a large number of primary GDDs in PXF eyes with good results. Similar to trabeculectomy, the surgeon needs to be cautious of postoperative inflammation in PXF eyes, especially when the tube opens several weeks later in nonvalved GDDs. The period of tube opening is highly inflammatory for reasons that are unclear, and this inflammation can be greater in PXF eyes compared with that observed in patients with primary open angle glaucoma in our experience.

PXF and Cataract Surgery

The evaluation of the PXF glaucoma patient for cataract surgery needs to take into consideration the control of the IOP and degree of glaucoma in addition to PXF-associated cataract surgery risks. The presence of PXF material poses unique challenges for cataract surgery including corneal endotheliopathy, poor mydriasis, zonular instability and lens subluxation, increased risk for vitreous loss, heightened postoperative inflammation, postoperative IOP elevation, and late intraocular lens implant decentration and prolapse into the posterior segment. Some surgeons have reported an increased rate of complications during extracapsular cataract extraction via phacoemulsification[141,142] in PXF eyes, whereas others have reported no difference.[143–145] PXF cataract surgery patient selection, differences in lens density and lens mobility, differences in pupil diameter, and differences in other PXF-

associated issues may have biased these results among different surgeons with different criteria for recommending cataract surgery in different patient populations.

The increased risks associated with PXF cataract surgery can be managed or at a minimum anticipated with a thorough preoperative evaluation. From the patient history, the clinician can elicit a history of trauma that may suggest a higher risk for zonular instability and/or lens subluxation with vitreous loss in association with PXF zonulopathy. The patient history can also be informative regarding use of tamulosin and anticoagulants that may require additional care with regard to surgery in light of potential iris manipulation or unanticipated conversion to extracapsular cataract surgery. The slit examination should include careful evaluation of the degree of corneal endotheliopathy, preoperative dilation, degree of cataract, and phacodonesis. A complete evaluation can aid in proper informed consent of the increased risks associated with cataract surgery and preoperative and intraoperative planning [with anticipatory equipment such as iris hooks and capsular tension rings (CTRs) at the ready, and possibly having a vitreoretinal surgeon available for vitrectomy and pars plana lensectomy].

Several key factors are important for maximizing good surgical outcomes. A small pupil not only makes for a small and difficult capsulorhexis and increases the risk of iris prolapse through the keratome incision, but also increases surgical risk owing to poor visualization of the cataract for phacoemulsification. Adequate pupillary dilation is very important before initiating a capsulorhexis or phacoemulsification. If adequate dilation cannot be achieved with dilating eye drops preoperatively, intraoperative techniques should be considered. The surgeon can stretch the pupil with instruments (eg, using 2 Kuglen hooks or a 3-prong or 4-prong Beehler pupil expander), use iris hooks, or pupil expansion rings to maintain pupil size throughout the cataract surgery. We have not found intraoperative lidocaine to be as effective for pupillary dilation in PXF eyes compared with normal eyes, probably secondary to changes within the iris vessels and stroma associated with PXF that cause an intrinsic defect with dilation. Given the presence of endotheliopathy, the surgeon should also be generous when using their viscoelastic agent of choice to protect the corneal endothelium.

After achieving adequate pupil dilation either pharmacologically or mechanically, the surgeon can further reduce stress on the capsular bag by creating a larger diameter capsulorhexis. Adequate pupil dilation also facilitates creation of a larger capsulorhexis. A larger capsular opening makes subsequent steps (grooving, cracking, etc.) much easier and minimizes the risk of capsular bag damage. Capsular phimosis (postoperative capsular bag contraction) can place additional zonular stress over time and increase the risk of late lens dislocation.[146–148] The creation of a large capsular opening minimizes capsular contraction and zonular stress after implantation of an intraocular lens.

In removing the nucleus, a preferred technique is one that minimizes stress on PXF weakened zonules. One can use chopping techniques or prolapse the lens nucleus out of the capsular bag during phacoemulsification or consider traditional extracapsular surgery and prolapse the entire lens out of the capsular bag and then out of a large corneal incision. By prolapsing the nucleus out of the capsular bag, the cataract surgeon can avoid placing any stress on the capsular bag. Our preference is to partially prolapse the lens out of the capsule bag (ie, have the lens tilted out of the capsular bag) and perform a modified phacochop technique in the iris plane to remove the cataractous lens using phacoemulsification. Should phacodonesis or zonular dialysis be noted at any time, a CTR can be inserted to stabilize the capsular bag and minimize further zonular loss. However, care needs to be taken with the insertion of a CTR, as early CTR placement can incarcerate lens cortex and make subsequent cortical removal difficult and stressful on the capsular bag. In addition, CTRs should only be inserted into an intact capsular bag because it can prolapse through a capsular rent into the vitreous cavity and require a vitrectomy for removal. Capsular tension hooks can also be helpful in stabilizing a floppy

capsule by holding on to the capsular bag while fixated to the iris or other anterior segment structures. If, however, greater than 4-clock hours of zonular dialysis are observed, options include conversion to traditional extracapsular cataract extraction with placement of a sulcus and/or anterior chamber intraocular lens implant. Another option is to suture a CTR segment to the sclera to stabilize the capsular bag.[149]

Finally, when choosing an intraocular implant, a 3-piece intraocular lens implant should be considered in all patients with PXF. The 3-piece lens plays a dual role by acting as a pseudo-CTR and reducing zonular stress with the haptics providing tension to place the capsular bag on stretch. Moreover, if there is only 1 to 2-clock hours of dialysis, the 3-piece lens may be sufficient to stabilize the capsular bag (ie, a form of poor man's CTR) if the haptics are placed along the axis of zonular weakness or dehiscence.

In addition to intraoperative concerns, PXF postcataract surgery eyes have postoperative issues to consider. PXF is associated with iris vascular leak and a compromised blood-aqueous barrier. PXF patients have more postoperative inflammation and a higher risk of postoperative pressure spikes. PXF cataract patients often need to be treated more aggressively with postoperative steroids and perhaps for a longer duration. Another concern noted previously is capsular phimosis. If observed, the capsular contraction can be treated using a neodymium-doped yttrium aluminum garnet laser by placing relaxing incisions in the anterior lens capsule at the 4 cardinal positions.[148]

In summary, an extensive discussion with the PXF cataract patient preoperatively regarding the increased risk of complications associated with PXF during cataract extraction is important for informed consent and meeting patient expectations. PXF cataract patients should be also be informed of the possible need for additional surgery at the time of cataract extraction or postoperatively if there are PXF-associated surgical complications. The patient should also be made aware of potential late decentration of the intraocular lens implant years after surgery, especially if trauma is involved. Most importantly, the cataract surgeon needs to be prepared for the possibility of intraoperative complications secondary to PXF-associated changes in the eye to maximize surgical outcomes and observe PXF cataract patients more closely and carefully in the postoperative period.

Conclusions

PXF syndrome is among the more common causes of glaucoma and is the most common form of secondary open angle glaucoma. The disorder is systemic, but at this time only ocular morbidity has been firmly established. The diagnosis of PXF requires careful slit lamp examination in both eyes as ocular signs are often asymmetric and subtle. Individuals observed to have PXF material in the eye need to be screened and followed as glaucoma suspects if they do not already have glaucoma at the time of examination given the increased risk for ocular hypertension and glaucoma associated with PXF material in the eye. Initial management is medical, but frequently surgical intervention is necessary because PXF glaucoma is more aggressive than primary open angle glaucoma. Cataract extraction in the setting of PXF requires careful surgical evaluation and communication with the patient regarding increased surgical risks. Preparing for and managing the intraoperative surgical risks and possible postoperative issues associated with PXF pathology increases successful outcomes.

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References

1. Allingham, R. Shield's Textbook of Glaucoma: Pseudoexfoliation Syndrome. Philadelphia: Lippincott Williams & Wilkins; 2005.
2. Mitchell P, Wang JJ, Smith W. Association of pseudoexfoliation syndrome with increased vascular risk. Am J Ophthalmol 1997;124:685–687. [PubMed: 9372724]
3. Ringvold A, Blika S, Sandvik L. Pseudo-exfoliation and mortality. Acta Ophthalmol Scand 1997;75:255–256. [PubMed: 9253968]
4. Shrum KR, Hattenhauer MG, Hodge D. Cardiovascular and cerebrovascular mortality associated with ocular pseudoexfoliation. Am J Ophthalmol 2000;129:83–86. [PubMed: 10653417]
5. Citirik M, Acaroglu G, Batman C, et al. A possible link between the pseudoexfoliation syndrome and coronary artery disease. Eye 2007;21:11–15. [PubMed: 16557288]
6. Schumacher S, Schlotzer-Schrehardt U, Martus P, et al. Pseudoexfoliation syndrome and aneurysms of the abdominal aorta. Lancet 2001;357:359–360. [PubMed: 11211000]
7. Hietanen J, Soisalon-Soininen S, Kivela T, et al. Evaluation of the clinical association between exfoliation syndrome and abdominal aortic aneurysm. Acta Ophthalmol Scand 2002;80:617–619. [PubMed: 12485282]
8. Detorakis ET, Chrysochoou F, Paliobei V, et al. Evaluation of the acoustic function in pseudoexfoliation syndrome and exfoliation glaucoma: audiometric and tympanometric findings. Eur J Ophthalmol 2008;18:71–76. [PubMed: 18203088]
9. Yazdani S, Tousi A, Pakravan M, et al. Sensorineural hearing loss in pseudoexfoliation syndrome. Ophthalmology 2008;115:425–429. [PubMed: 18187196]
10. Turacli ME, Ozdemir FA, Tekeli O, et al. Sensorineural hearing loss in pseudoexfoliation. Can J Ophthalmol 2007;42:56–59. [PubMed: 17361242]
11. Tarkkanen A, Kivela T, John G. Lindberg and the discovery of exfoliation syndrome. Acta Ophthalmol Scand 2002;80:151–154. [PubMed: 11952480]
12. Thorleifsson G, Magnusson KP, Sulem P, et al. Common sequence variants in the LOXL1 gene confer susceptibility to exfoliation glaucoma. Science 2007;317:1397–1400. [PubMed: 17690259]
13. Lee RK. The molecular pathophysiology of pseudoexfoliation glaucoma. Curr Opin Ophthalmol 2008;19:95–101. [PubMed: 18301281]
14. Bartholomew RS. Pseudo-capsular exfoliation in the Bantu of South Africa. I. Early or pre-granular clinical stage. Br J Ophthalmol 1971;55:693–699. [PubMed: 5124845]
15. Bartholomew RS. Pseudocapsular exfoliation in the Bantu of South Africa. II. Occurrence and prevalence. Br J Ophthalmol 1973;57(1):41–45. [PubMed: 4705496]
16. Miyazaki M, Kubota T, Kubo M, et al. The prevalence of pseudoexfoliation syndrome in a Japanese population: the Hisayama study. J Glaucoma 2005;14:482–484. [PubMed: 16276281]
17. Iizuka S, Nakae R, Motokura M. Incidence of pseudoexfoliation syndrome. 2001:926.
18. Forsius H. Prevalence of pseudoexfoliation of the lens in Finns, Lapps, Icelanders, Eskimos, and Russians. Trans Ophthalmol Soc UK 1979;99:296–298. [PubMed: 298430]
19. Forsius H. Exfoliation syndrome in various ethnic populations. Acta Ophthalmol Suppl 1988;184:71–85. [PubMed: 2853925]
20. Sveinsson K. The frequency of senile exfoliation in Iceland. Fibrillopathy or pseudoexfoliation. Acta Ophthalmol (Copenh) 1974;52:596–602. [PubMed: 4479477]
21. Krause U. Frequency of capsular glaucoma in central Finland. Acta Ophthalmol (Copenh) 1973;51:235–240. [PubMed: 4801581]
22. Krause U, Alanko HI, Karna J, et al. Prevalence of exfoliation syndrome in Finland. Acta Ophthalmol Suppl 1988;184:120–122. [PubMed: 2853908]
23. Faulkner HW. Pseudo-exfoliation of the lens among the Navajo Indians. Am J Ophthalmol 1971;72:206–207. [PubMed: 5571208]
24. Friederich R. Eye disease in the Navajo Indians. Ann Ophthalmol 1982;14:38–40. [PubMed: 7125439]
25. Taylor HR, Hollows FC, Moran D. Pseudoexfoliation of the lens in Australian Aborigines. Br J Ophthalmol 1977;61:473–475. [PubMed: 889760]

26. Ringvold A, Blika S, Elsas T, et al. The prevalence of pseudoexfoliation in three separate municipalities of Middle-Norway. A preliminary report. Acta Ophthalmol Suppl 1987;182:17–20. [PubMed: 2837055]
27. Kozobolis VP, Papatzanaki M, Vlachonikolis IG, et al. Epidemiology of pseudoexfoliation in the island of Crete (Greece). Acta Ophthalmol Scand 1997;75:726–729. [PubMed: 9527341]
28. Tarkkanen A. Pseudoexfoliation of the lens capsule. A clinical study of 418 patients with special reference to glaucoma, cataract, and changes of the vitreous. Acta Ophthalmol Suppl 1962;(suppl 71):1–98. [PubMed: 13993343]
29. Hiller R, Sperduto RD, Krueger DE. Pseudoexfoliation, intraocular pressure, and senile lens changes in a population-based survey. Arch Ophthalmol 1982;100:1080–1082. [PubMed: 7092647]
30. Aasved H. Mass screening for fibrillopathia epitheliocapsularis, so-called senile exfoliation or pseudoexfoliation of the anterior lens capsule. Acta Ophthalmol (Copenh) 1971;49:334–343. [PubMed: 5109796]
31. Ritch R. Exfoliation Syndrome. Clinical Entities: Glaucomas associated with ocular disease.
32. Kozart DM, Yanoff M. Intraocular pressure status in 100 consecutive patients with exfoliation syndrome. Ophthalmology 1982;89:214–218. [PubMed: 7088504]
33. Karger RA, Jeng SM, Johnson DH, et al. Estimated incidence of pseudoexfoliation syndrome and pseudoexfoliation glaucoma in Olmsted County, Minnesota. J Glaucoma 2003;12:193–197. [PubMed: 12782834]
34. Aasved H. The geographical distribution of fibrillopathia epitheliocapsularis, so-called senile exfoliation or pseudoexfoliation of the anterior lens capsule. Acta Ophthalmol (Copenh) 1969;47:792–810. [PubMed: 5394642]
35. Aasved H. The frequency of fibrillopathia epitheliocapsularis (so-called senile exfoliation or pseudoexfoliation) in patients with open-angle glaucoma. Acta Ophthalmol (Copenh) 1971;49:194–210. [PubMed: 5109784]
36. Blika S, Ringvold A. The occurrence of simple and capsular glaucoma in Middle-Norway. Acta Ophthalmol Suppl 1987;182:11–16. [PubMed: 2837044]
37. Colin J, Le Gall G, Le Jeune B, et al. The prevalence of exfoliation syndrome in different areas of France. Acta Ophthalmol Suppl 1988;184:86–89. [PubMed: 2853926]
38. Hansen E, Sellevold OJ. Pseudoexfoliation of the lens capsule. I. Clinical evaluation with special regard to the presence of glaucoma. Acta Ophthalmol (Copenh) 1968;46:1095–1104. [PubMed: 5756882]
39. Rouhiainen H, Terasvirta M. Presence of pseudoexfoliation on clear and opacified crystalline lenses in an aged population. Ophthalmologica 1992;204:67–70. [PubMed: 1594183]
40. Summanen P, Tonjum AM. Exfoliation syndrome among Saudis. Acta Ophthalmol Suppl 1988;184:107–111. [PubMed: 2853905]
41. Valle O. Prevalence of simple and capsular glaucoma in the Central Hospital District of Kotka. Acta Ophthalmol Suppl 1988;184:116–119. [PubMed: 2853907]
42. Jeng SM, Karger RA, Hodge DO, et al. The risk of glaucoma in pseudoexfoliation syndrome. J Glaucoma 2007;16:117–121. [PubMed: 17224761]
43. Hansen E, Sellevold OJ. Pseudoexfoliation of the lens capsule. II. Development of the exfoliation syndrome. Acta Ophthalmol (Copenh) 1969;47:161–173. [PubMed: 5819822]
44. Henry JC, Krupin T, Schmitt M, et al. Long-term follow-up of pseudoexfoliation and the development of elevated intraocular pressure. Ophthalmology 1987;94:545–552. [PubMed: 3601370]
45. Klemetti A. Intraocular pressure in exfoliation syndrome. Acta Ophthalmol Suppl 1988;184:54–58. [PubMed: 2853921]
46. Slagsvold JE. The follow-up in patients with pseudoexfoliation of the lens capsule with and without glaucoma. 2. The development of glaucoma in persons with pseudoexfoliation. Acta Ophthalmol (Copenh) 1986;64:241–245. [PubMed: 3751508]
47. Prince AM, Streeten BW, Ritch R, et al. Preclinical diagnosis of pseudoexfoliation syndrome. Arch Ophthalmol 1987;105:1076–1082. [PubMed: 3632416]
48. Speakman JS, Ghosh M. The conjunctiva in senile lens exfoliation. Arch Ophthalmol 1976;94:1757–1759. [PubMed: 973821]

49. Layden WE, Shaffer RN. Exfoliation syndrome. Am J Ophthalmol 1974;78:835–841. [PubMed: 4421811]
50. Madden JG, Crowley MJ. Factors in the exfoliation syndrome. Br J Ophthalmol 1982;66:432–437. [PubMed: 7093181]
51. Meyer E, Haim T, Zonis S, et al. Pseudoexfoliation: epidemiology, clinical and scanning electron microscopic study. Ophthalmologica 1984;188:141–147. [PubMed: 6608708]
52. Roth M, Epstein DL. Exfoliation syndrome. Am J Ophthalmol 1980;89:477–481. [PubMed: 7369310]
53. Bartholomew RS. Incidence of pseudoexfoliation in South African Negroes and Scots. Trans Ophthalmol Soc UK 1979;99:299–301. [PubMed: 298431]
54. Hietanen J, Kivela T, Vesti E, et al. Exfoliation syndrome in patients scheduled for cataract surgery. Acta Ophthalmol (Copenh) 1992;70:440–446. [PubMed: 1414287]
55. Lumme P, Laatikainen L. Exfoliation syndrome and cataract extraction. Am J Ophthalmol 1993;116:51–55. [PubMed: 8328543]
56. Moreno Montanes J, Alcolea Paredes A, Campos Garcia S. Prevalence of pseudoexfoliation syndrome in the northwest of Spain. Acta Ophthalmol (Copenh) 1989;67:383–385. [PubMed: 2801039]
57. Puska P. Lens opacity in unilateral exfoliation syndrome with or without glaucoma. Acta Ophthalmol (Copenh) 1994;72:290–296. [PubMed: 7976257]
58. Puska P, Tarkkanen A. Exfoliation syndrome as a risk factor for cataract development: five-year follow-up of lens opacities in exfoliation syndrome. J Cataract Refract Surg 2001;27:1992–1998. [PubMed: 11738916]
59. Yalaz M, Othman I, Nas K, et al. The frequency of pseudoexfoliation syndrome in the eastern Mediterranean area of Turkey. Acta Ophthalmol (Copenh) 1992;70:209–213. [PubMed: 1609569]
60. Mizuno K, Muroi S. Cycloscopy of pseudoexfoliation. Am J Ophthalmol 1979;87:513–518. [PubMed: 443315]
61. Freissler K, Kuchle M, Naumann GO. Spontaneous dislocation of the lens in pseudoexfoliation syndrome. Arch Ophthalmol 1995;113:1095–1096. [PubMed: 7661737]
62. Futa R, Furuyoshi N. Phakodonesis in capsular glaucoma: a clinical and electron microscopic study. Jpn J Ophthalmol 1989;33:311–317. [PubMed: 2796011]
63. Schlotzer-Schrehardt U, Naumann GO. A histopathologic study of zonular instability in pseudoexfoliation syndrome. Am J Ophthalmol 1994;118:730–743. [PubMed: 7977599]
64. Dvorak-Theobald G. Pseudoexfoliation of the lens capsule: relation to true exfoliation of the lens capsule as reported in the literature, and role in the production of glaucoma capsulocuticulare. Trans Am Ophthalmol Soc 1953;51:385–407. [PubMed: 13216790]
65. Gillies W. Pseudoexfoliation of the lens capsule and pigmentary glaucoma. Trans Ophthalmol Soc Austral 1962:22.
66. Horven I. Exfoliation syndrome. Incidence and prognosis of glaucoma capsulare in Massachusetts. Arch Ophthalmol 1966;76:505–511. [PubMed: 5928139]
67. Konstas AG, Dutton GN. Gonioscopic findings in Greek patients with exfoliation glaucoma. Acta Ophthalmol (Copenh) 1991;69:281–287. [PubMed: 1927308]
68. Krause U, Helve J, Forsius H. Pseudoexfoliation of the lens capsule and liberation of iris pigment. Acta Ophthalmol (Copenh) 1973;51:39–46. [PubMed: 4739675]
69. Moreno-Montanes J, Quinteiro Alonso A, Alvarez Serna A, et al. Exfoliation syndrome: clinical study of the irido-corneal angle. J Fr Ophthalmol 1990;13:183–188.
70. Raitta C, Lehto I. Laser trabeculoplasty in open angle glaucoma. Acta Ophthalmol (Copenh) 1983;61:673–677. [PubMed: 6637429]
71. Rouhiainen H, Terasvirta M. Pigmentation of the anterior chamber angle in normal and pseudoexfoliative eyes. Acta Ophthalmol (Copenh) 1990;68:700–702. [PubMed: 2080702]
72. Sampaolesi R, Amalric P, Bessou P. On early diagnosis and heredity in capsular pseudoexfoliation of the crystalline lens. Arch Oftalmol B Aires 1961;36:159–164. [PubMed: 14496647]
73. Sampaolesi R, Zarate J, Croxato O. The chamber angle in exfoliation syndrome. Clinical and pathological findings. Acta Ophthalmol Suppl 1988;184:48–53. [PubMed: 2853919]
74. Shimizu K, Kimura Y, Aoki K. Prevalence of exfoliation syndrome in the Japanese. Acta Ophthalmol Suppl 1988;184:112–115. [PubMed: 2853906]

75. Wishart PK, Spaeth GL, Poryzees EM. Anterior chamber angle in the exfoliation syndrome. Br J Ophthalmol 1985;69:103–107. [PubMed: 3966996]
76. Ye TC, Mao WS, Zhang J. Pseudoexfoliation syndrome in Chinese. Jpn J Ophthalmol 1989;33:300–310. [PubMed: 2796010]
77. Sampaolesi R. Neue untersuchungen uber das pseudokapselhautchen-glaukom (glaucoma capsulare). Ber Deutch Ophthal Ges 1959;62:177–183.
78. Puska P. The amount of lens exfoliation and chamber-angle pigmentation in exfoliation syndrome with or without glaucoma. Acta Ophthalmol Scand 1995;73:226–232. [PubMed: 7493233]
79. Shuba L, Nicolela MT, Rafuse PE. Correlation of capsular pseudoexfoliation material and iridocorneal angle pigment with the severity of pseudoexfoliation glaucoma. J Glaucoma 2007;16:94–97. [PubMed: 17224757]
80. Franks WA, Miller MH, Hitchings RA, et al. Secondary angle closure in association with pseudoexfoliation of the lens capsule. Acta Ophthalmol (Copenh) 1990;68:350–352. [PubMed: 2392917]
81. Gohdo T, Takahashi H, Iijima H, et al. Ultrasound biomicroscopy of angle closure glaucoma with pseudoexfoliation syndrome. Br J Ophthalmol 1997;81:706–707. [PubMed: 9349164]
82. Gross FJ, Tingey D, Epstein DL. Increased prevalence of occludable angles and angle-closure glaucoma in patients with pseudoexfoliation. Am J Ophthalmol 1994;117:333–336. [PubMed: 8129006]
83. Lowe RF. Primary angle-closure glaucoma with capsular exfoliation of the lens. Br J Ophthalmol 1964;48:492–494. [PubMed: 14217215]
84. Ritch R. Exfoliation syndrome and occludable angles. Trans Am Ophthalmol Soc 1994;92:845–944. [PubMed: 7886885]
85. Herbst RW. Angle closure glaucoma in a patient with pseudoexfoliation of the lens capsule. Ann Ophthalmol 1976;8:853–856. [PubMed: 962262]
86. Prince AM, Ritch R. Clinical signs of the pseudoexfoliation syndrome. Ophthalmology 1986;93:803–807. [PubMed: 3737125]
87. Aasved H. Incidence of defects in the pigmented pupillary ruff in eyes with and without fibrillopathia epitheliocapsularis (so-called senile exfoliation or pseudoexfoliation of the anterior lens capsule). Acta Ophthalmol (Copenh) 1973;51:710–715. [PubMed: 4801166]
88. Asano N, Schlotzer-Schrehardt U, Naumann GO. A histopathologic study of iris changes in pseudoexfoliation syndrome. Ophthalmology 1995;102:1279–1290. [PubMed: 9097764]
89. Brooks AM, Gillies WE. The development of microneovascular changes in the iris in pseudoexfoliation of the lens capsule. Ophthalmology 1987;94:1090–1097. [PubMed: 2446230]
90. Sakai K, Kojima K. Fluorescein angiography and electron microscopic study of the iris with pseudoexfoliation syndrome. Folia Ophthalmol Jpn 1982:33.
91. Kuchle M, Ho TS, Nguyen NX, et al. Protein quantification and electrophoresis in aqueous humor of pseudoexfoliation eyes. Invest Ophthalmol Vis Sci 1994;35:748–752. [PubMed: 8113026]
92. Kuchle M, Nguyen NX, Hannappel E, et al. The blood-aqueous barrier in eyes with pseudoexfoliation syndrome. Ophthalmic Res 1995;27(suppl 1):136–142. [PubMed: 8577452]
93. Kuchle M, Nguyen NX, Horn F, et al. Quantitative assessment of aqueous flare and aqueous ‘cells’ in pseudoexfoliation syndrome. Acta Ophthalmol (Copenh) 1992;70:201–208. [PubMed: 1609568]
94. Kuchle M, Vinores SA, Mahlow J, et al. Blood-aqueous barrier in pseudoexfoliation syndrome: evaluation by immunohistochemical staining of endogenous albumin. Graefes Arch Clin Exp Ophthalmol 1996;234:12–18. [PubMed: 8750845]
95. Knorr HL, Junemann A, Handel A, et al. Morphometric and qualitative changes in corneal endothelium in pseudoexfoliation syndrome. Fortschr Ophthalmol 1991;88:786–789. [PubMed: 1794803]
96. Miyake K, Matsuda M, Inaba M. Corneal endothelial changes in pseudoexfoliation syndrome. Am J Ophthalmol 1989;108:49–52. [PubMed: 2750833]
97. Naumann GO, Schlotzer-Schrehardt U. Keratopathy in pseudoexfoliation syndrome as a cause of corneal endothelial decompensation: a clinicopathologic study. Ophthalmology 2000;107:1111–1124. [PubMed: 10857831]

98. Schlotzer-Schrehardt UM, Dorfler S, Naumann GO. Corneal endothelial involvement in pseudoexfoliation syndrome. Arch Ophthalmol 1993;111:666–674. [PubMed: 8489451]

99. Aasved H. Intraocular pressure in eyes with and without fibrillopathia epitheliocapsularis (so-called senile exfoliation or pseudoexfoliation). Acta Ophthalmol (Copenh) 1971;49:601–610. [PubMed: 5171571]

100. Ringvold A, Blika S, Elsas T, et al. The middle-Norway eye-screening study. II. Prevalence of simple and capsular glaucoma. Acta Ophthalmol (Copenh) 1991;69:273–280. [PubMed: 1927307]

101. Stefaniotou M, Petroutsos G, Psilas K. The frequency of pseudoexfoliation in a region of Greece (Epirus). Acta Ophthalmol (Copenh) 1990;68:307–309. [PubMed: 2392907]

102. Leske MC, Heijl A, Hyman L, et al. Predictors of long-term progression in the early manifest glaucoma trial. Ophthalmology 2007;114:1965–1972. [PubMed: 17628686]

103. Pohjanpelto P. Influence of exfoliation syndrome on prognosis in ocular hypertension greater than or equal to 25 mm. A long-term follow-up. Acta Ophthalmol (Copenh) 1986;64:39–44. [PubMed: 3962617]

104. Grodum K, Heijl A, Bengtsson B. Risk of glaucoma in ocular hypertension with and without pseudoexfoliation. Ophthalmology 2005;112:386–390. [PubMed: 15745763]

105. Davanger M, Ringvold A, Blika S. Pseudo-exfoliation, IOP and glaucoma. Acta Ophthalmol (Copenh) 1991;69:569–573. [PubMed: 1776408]

106. Konstas AG, Mantziris DA, Stewart WC. Diurnal intraocular pressure in untreated exfoliation and primary open-angle glaucoma. Arch Ophthalmol 1997;115:182–185. [PubMed: 9046252]

107. Tomita G, Puska P, Raitta C. Interocular differences in optic disc configuration in the unilateral exfoliation syndrome. Acta Ophthalmol (Copenh) 1994;72:162–167. [PubMed: 8079619]

108. Konstas AG, Allan D. Pseudoexfoliation glaucoma in Greece. Eye 1989;3(Pt 6):747–753. [PubMed: 2630357]

109. Parmaksiz S, Yuksel N, Karabas VL, et al. A comparison of travoprost, latanoprost, and the fixed combination of dorzolamide and timolol in patients with pseudoexfoliation glaucoma. Eur J Ophthalmol 2006;16:73–80. [PubMed: 16496249]

110. Thomas R, Parikh R, Sood D, et al. Efficacy and safety of latanoprost for glaucoma treatment: a three-month multicentric study in India. Indian J Ophthalmol 2005;53:23–30. [PubMed: 15829743]

111. Franks WA, Renard JP, Cunliffe IA, et al. A 6-week, double-masked, parallel-group study of the efficacy and safety of travoprost 0.004% compared with latanoprost 0:005%/timolol 0.5% in patients with primary open-angle glaucoma or ocular hypertension. Clin Ther 2006;28:332–339. [PubMed: 16750448]

112. Martinez A, Sanchez M. A comparison of the safety and intraocular pressure lowering of bimatoprost/timolol fixed combination versus latanoprost/timolol fixed combination in patients with open-angle glaucoma. Curr Med Res Opin 2007;23:1025–1032. [PubMed: 17519068]

113. Petounis A, Mylopoulos N, Kandarakis A, et al. Comparison of the additive intraocular pressure-lowering effect of latanoprost and dorzolamide when added to timolol in patients with open-angle glaucoma or ocular hypertension: a randomized, open-label, multicenter study in Greece. J Glaucoma 2001;10:316–324. [PubMed: 11558817]

114. Ticho U, Nesher R. Laser trabeculoplasty in glaucoma. Ten-year evaluation. Arch Ophthalmol 1989;107:844–846. [PubMed: 2730404]

115. Damji KF, Bovell AM, Hodge WG, et al. Selective laser trabeculoplasty versus argon laser trabeculoplasty: results from a 1-year randomised clinical trial. Br J Ophthalmol 2006;90:1490–1494. [PubMed: 16899528]

116. Grinich NP, Van Buskirk EM, Samples JR. Three-year efficacy of argon laser trabeculoplasty. Ophthalmology 1987;94:858–861. [PubMed: 3658354]

117. Psilas K, Prevezas D, Petroutsos G, et al. Comparative study of argon laser trabeculoplasty in primary open-angle and pseudoexfoliation glaucoma. Ophthalmologica 1989;198:57–63. [PubMed: 2710501]

118. Robin AL, Pollack IP. Argon laser trabeculoplasty in secondary forms of open-angle glaucoma. Arch Ophthalmol 1983;101:382–384. [PubMed: 6830487]

119. Threlkeld AB, Hertzmark E, Sturm RT, et al. Comparative study of the efficacy of argon laser trabeculoplasty for exfoliation and primary open-angle glaucoma. J Glaucoma 1996;5:311–316. [PubMed: 8897230]
120. Tuulonen A, Koponen J, Alanko HI, et al. Laser trabeculoplasty versus medication treatment as primary therapy for glaucoma. Acta Ophthalmol (Copenh) 1989;67:275–280. [PubMed: 2669435]
121. Elsas T, Johnsen H. Long-term efficacy of primary laser trabeculoplasty. Br J Ophthalmol 1991;75:34–37. [PubMed: 1991084]
122. Leung KW, Gillies WE. The detection and management of the acute rise in intraocular pressure following laser trabeculoplasty. Aust NZ J Ophthalmol 1986;14:259–262.
123. Odberg T, Sandvik L. The medium and long-term efficacy of primary argon laser trabeculoplasty in avoiding topical medication in open angle glaucoma. Acta Ophthalmol Scand 1999;77:176–181. [PubMed: 10321534]
124. Svedbergh B. Argon laser trabeculoplasty in capsular glaucoma. Acta Ophthalmol Suppl 1988;184:141–147. [PubMed: 2853914]
125. Tuulonen A, Niva AK, Alanko HI. A controlled five-year follow-up study of laser trabeculoplasty as primary therapy for open-angle glaucoma. Am J Ophthalmol 1987;104:334–338. [PubMed: 3661640]
126. Budenz DL, Pyfer M, Singh K, et al. Comparison of phacotrabeculectomy with 5-fluorouracil, mitomycin-C, and without antifibrotic agents. Ophthalmic Surg Lasers 1999;30:367–374. [PubMed: 10334024]
127. Fontana H, Nouri-Mahdavi K, Caprioli J. Trabeculectomy with mitomycin C in pseudophakic patients with open-angle glaucoma: outcomes and risk factors for failure. Am J Ophthalmol 2006;141:652–659. [PubMed: 16564799]
128. Fontana H, Nouri-Mahdavi K, Lumba J, et al. Trabeculectomy with mitomycin C: outcomes and risk factors for failure in phakic open-angle glaucoma. Ophthalmology 2006;113:930–936. [PubMed: 16647135]
129. Jerndal T, Kriisa V. Results of trabeculectomy for pseudo-exfoliative glaucoma. A study of 52 cases. Br J Ophthalmol 1974;58:927–930. [PubMed: 4457105]
130. Konstas AG, Jay JL, Marshall GE, et al. Prevalence, diagnostic features, and response to trabeculectomy in exfoliation glaucoma. Ophthalmology 1993;100:619–627. [PubMed: 8493003]
131. Popovic V, Sjostrand J. Course of exfoliation and simplex glaucoma after primary trabeculectomy. Br J Ophthalmol 1999;83:305–310. [PubMed: 10365038]
132. Scott IU, Greenfield DS, Schiffman J, et al. Outcomes of primary trabeculectomy with the use of adjunctive mitomycin. Arch Ophthalmol 1998;116:286–291. [PubMed: 9514480]
133. Singh K, Mehta K, Shaikh NM, et al. Trabeculectomy with intraoperative mitomycin C versus 5-fluorouracil. Prospective randomized clinical trial. Ophthalmology 2000;107:2305–2309. [PubMed: 11097613]
134. Tornqvist G, Drolsum LK. Trabeculectomies. A long-term study. Acta Ophthalmol (Copenh) 1991;69:450–454. [PubMed: 1750313]
135. Vesti E, Raitta C. A review of the outcome of trabeculectomy in open-angle glaucoma. Ophthalmic Surg Lasers 1997;28:128–132. [PubMed: 9054484]
136. WuDunn D, Cantor LB, Palanca-Capistrano AM, et al. A prospective randomized trial comparing intraoperative 5-fluorouracil vs mitomycin C in primary trabeculectomy. Am J Ophthalmol 2002;134:521–528. [PubMed: 12383808]
137. Honjo M, Tanihara H, Inatani M, et al. Phacoemulsification, intraocular lens implantation, and trabeculotomy to treat pseudoexfoliation syndrome. J Cataract Refract Surg 1998;24:781–786. [PubMed: 9642588]
138. Landa G, Pollack A, Rachmiel R, et al. Results of combined phacoemulsification and trabeculectomy with mitomycin C in pseudoexfoliation versus non-pseudoexfoliation glaucoma. Graefes Arch Clin Exp Ophthalmol 2005;243:1236–1240. [PubMed: 16003518]
139. Gedde SJ, Herndon LW, Brandt JD, et al. Surgical complications in the Tube Versus Trabeculectomy Study during the first year of follow-up. Am J Ophthalmol 2007;143:23–31. [PubMed: 17054896]
140. Gedde SJ, Schiffman JC, Feuer WJ, et al. Treatment outcomes in the tube versus trabeculectomy study after one year of follow-up. Am J Ophthalmol 2007;143:9–22. [PubMed: 17083910]

141. Drolsum L, Haaskjold E, Sandvig K. Phacoemulsification in eyes with pseudoexfoliation. J Cataract Refract Surg 1998;24:787–792. [PubMed: 9642589]

142. Shingleton BJ, Heltzer J, O'Donoghue MW. Outcomes of phacoemulsification in patients with and without pseudoexfoliation syndrome. J Cataract Refract Surg 2003;29:1080–1086. [PubMed: 12842671]

143. Dosso AA, Bonvin ER, Leuenberger PM. Exfoliation syndrome and phacoemulsification. J Cataract Refract Surg 1997;23:122–125. [PubMed: 9100119]

144. Hyams M, Mathalone N, Herskovitz M, et al. Intraoperative complications of phacoemulsification in eyes with and without pseudoexfoliation. J Cataract Refract Surg 2005;31:1002–1005. [PubMed: 15975469]

145. Shastri L, Vasavada A. Phacoemulsification in Indian eyes with pseudoexfoliation syndrome. J Cataract Refract Surg 2001;27:1629–1637. [PubMed: 11687363]

146. Davison JA. Capsule contraction syndrome. J Cataract Refract Surg 1993;19:582–589. [PubMed: 8229711]

147. Gimbel HV, Condon GP, Kohnen T, et al. Late in-the-bag intraocular lens dislocation: incidence, prevention, and management. J Cataract Refract Surg 2005;31:2193–2204. [PubMed: 16412938]

148. Hayashi H, Hayashi K, Nakao F, et al. Anterior capsule contraction and intraocular lens dislocation in eyes with pseudoexfoliation syndrome. Br J Ophthalmol 1998;82:1429–1432. [PubMed: 9930277]

149. Cionni RJ, Osher RH. Management of profound zonular dialysis or weakness with a new endocapsular ring designed for scleral fixation. J Cataract Refract Surg 1998;24:1299–1306. [PubMed: 9795841]