PSS NEWS

A Distance Learning Format for Continuing Medical Education in Optometry

Risk Assessment and Its Role in Glaucoma

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COPE 68145-GL

2.0 Hours

Learning Objectives

1. To learn about the criteria for deciding management options for patients with glaucoma
2. To discuss risk factors for glaucoma
3. To discuss the role of risk assessment in deciding when to treat patients who are at high risk for developing glaucoma

Case Study:

D.F. is a 54-year old African-American male who initially presented for a routine eye exam. His ocular history was insignificant. His medical history was significant for adult-onset diabetes and his family history was remarkable for a mother, brother, and two sisters with open-angle glaucoma. His IOPs were 23 OD and 23 OS. Dilated fundus examination revealed a C/D ratio of .60 OD and .55 OS. Gonioscopy was Grade 4 360 degrees OU. A visual field examination was ordered and revealed no defects. GDx nerve fiber analysis was essentially normal as well - the modulation was normal and fairly symmetrical, the TSNIT was normal, and the The Number was 26 OD and 36 OS.

A S.T.A.R. calculation was done which demonstrated that this patient was at high risk of progressing to glaucoma over the next 5 years. In lieu of monitoring, the patient was started on Latanoprost (Xalatan) OU QHS and seen for a follow up at which the IOP had come down to 16 OD, 15 OS. The patient will continue medications and be followed closely.

Discussion of Case Study:

Based on the findings of the OHTS study, you must carefully weigh all risk factors when deciding on management of glaucoma patients. In some cases, this may mean starting medical therapy prophylactically. This patient is at high risk because he has many risk factors for glaucoma: age, diabetes, positive family history, elevated IOP and increased C/D ratio. Even in the absence of defects on visual field testing or nerve fiber analysis, you may choose to start treating some patients any way. The hope in these patients is to lower the IOP and prevent significant structural and functional damage before the whole

process gets going. After all, why wait until a patient actually starts to go blind from glaucoma before you decide to do something about it?

Approximately 50 million persons world wide suffer from primary open-angle glaucoma (POAG), the most common form of glaucoma. Roughly 2 million of these patients reside in the U.S. and that number is expected to swell to 3 million by the year 2020. Glaucoma is the most common form of preventable blindness that optometrists commonly see. The first part of improving our management skills for this condition involves clarifying our definition. Glaucoma is defined as "a group of ocular diseases with various causes that ultimately are associated with a progressive optic neuropathy leading to loss of vision function." This definition excludes any mention of intraocular pressure (IOP), so we must discard the notion that glaucoma is a disease of high eye pressure. We all know that it is highly possible for patients to have elevated intraocular pressure and never develop glaucoma (Ocular Hypertension) and conversely for patients to develop glaucoma without elevated intraocular pressure (Normal Tension Glaucoma).

The primary goal in glaucoma management is to slow or halt the progressive optic-nerve damage and associated visual-field loss to the point where your patient will maintain their visual function for the duration of their life. In short, you are looking to make sure that your patient does not go blind during their lifetime. Medical therapy works for roughly 80-90% of patients and is classically maximized before progressing to laser, then conventional surgical treatment. If needed, laser therapy usually consists of selective laser trabeculoplasty (SLT). The procedure is relatively safe, but has the disadvantage of uncertain effectivity and lack of longevity. Conventional surgery is usually reserved for cases where both medical and laser therapy fail.

WHO TO TREAT

1. Patients with POAG. These patients can have any number of changes to indicate they have crossed the threshold from glaucoma suspect to glaucoma. The most common of these situations is a patient with repeatable defects in visual field testing. Whether on a Humphrey, Dicon, or Octopus, these are patients who have confirmed loss of visual function in a pattern which is consistent with glaucoma. Your goal in these patients is to stop or slow the further deterioration of visual function. Another patient who falls into this category is one who demonstrates progressive cupping of the optic nerve. A patient who changes from a C/D of .20 to .40 to .50 over the course of years. Progressive deterioration of the optic nerve is highly suggestive of pathology. The importance of optic nerve assessment is highlighted by results from OHTS which told us that many patients who convert from ocular hypertension to glaucoma will only demonstrate optic nerve changes as the first sign. Lastly, many cases of glaucoma consist of patients who demonstrate progressive changes on nerve fiber analyzers such as the GDx or HRT. If you believe in the science, these are progressive structural changes which precede

changes in visual field testing by up to 5 years. Therefore any significant change from a baseline exam can be interpreted as progression of glaucoma which requires intervention. Regardless of your choice of favorite modality of choice, the decision to treat these patients is fairly clear. Many practitioners would agree that some form of interevention is required to preserve visual function.

2. Glaucoma Suspects. This is the patient with elevated IOP but no obvious optic nerve head damage or visual field change. Also included in this category are patients with increased C/D ratios but normal visual fields and normal nerve fiber layers. At what point do you treat these patients? Do you wait until these patients cross the threshold and actually develop glaucoma before you treat or do you identify high-risk patients and intervene early in the pathogenesis? In terms of patients with ocular hypertension, I think we all have had a IOP value in our mind that we would treat at even in the absence of structural or functional defect. For some practitioners this number was 30mm Hg or 32mm Hg for others it might be 28. For increased C/D, the same basic principle. You would want to be more aggressive in a patient who was a .90 ratio than somebody who is .60 or .70. The first patient has very little rim tissue to allow for error.

Pathophysiology

Although we like to think of a magical threshold a patient has to cross before a patient is diagnosed with glaucoma, the reality is that there is no such thing. Instead, the development of glaucoma is a slow and continuous process which starts long before there any detectable clinical signs. This process involves a slow but steady lifelong loss of retinal ganglion cells and their axons in all patients. This loss of retinal ganglion cells happens even in "normal" patients due to aging via the process of apoptosis, or programmed cell death. What distinguishes normal changes due to aging from the early pathological events of glaucoma is the rate of RGC loss. In glaucoma what happens is that the patient's rate of axonal loss exceeds the normal age-related rate of loss. In a sense, these patients are losing more cells at an earlier age than they are supposed to.

Even the most sophisticated diagnostic technology we currently have is incapable of detecting these early stages of glaucoma. However, just because we cannot detect the changes clinically does not mean they do not happen. Recent research has demonstrated that even during this stage, there is potential structural damage at all levels of the visual pathway. For example, there is evidence that some retinal ganglion cells are lost through apoptosis and there are some structural changes to the lamina cribrosa. Preceding these changes in early glaucomatous damage, it is believed that are some structural and functional deficits in relay neurons in the lateral geniculate nucleus.

As the glaucomatous damage continues, the patient generally remains asymptomatic while the earliest detectable changes in structure and function become manifest with appropriate testing. In the vast majority of cases of glaucoma, structural changes

precede functional deficits. Much of this discrepancy is due to redundancy in the visual system which causes overlap of some visual functions. One of the earliest identifiable structural changes to occur in patients with glaucoma is the focal loss of the RNFL. This is usually seen clinically as a nerve fiber layer bundle defect or as focal thinning or notching of the neuroretinal rim. Depending on how early these early defects are detected, they may not be associated with detectable defects on standard (white-on-white) automated perimetry. However, in some patients, the defects may become apparent when testing with more sensitive perimetric methods, such as a frequency doubling technology or short-wavelength (blue-on-yellow) automated perimetry (SWAP). However, even with these new methods, there is still considerable damage before a definitive of glaucoma is ascertained.

Left untreated, the damage caused from glaucoma progresses and the optic nerve will demonstrate the commonly seen features of glaucomatous optic neuropathy. These include enlargement of the optic cup from diffuse axonal loss (increased cup-to-disc ratio), progressive focal thinning or notching of the rim, vertical elongation of the optic cup due to the loss of the rim tissue at both the superior and inferior poles, and splinter hemorrhages around the disc margin.

Risk Assessment

Every doctor has had their own threshold at which they treated a patient with ocular hypertension even in the absence of visual field defects. The first objective study we had to help confirm our practice was OHTS whichtold us that medication was effective in delaying or preventing the onset of glaucoma in ocular hypertensive patients with moderate or high risk for developing glaucoma. 1 This does not mean that every patient with an IOP higher than normal should be treated. The reality is that 90% of patients with ocular hypertension did not develop glaucoma over the 5 year study so treating everybody in this category is excessive. Instead, it means that we must consider all factors along with IOP when making our decision to treat. In some cases, this may mean treating a patient before he or she "truly develops glaucoma" as preventative medicine. This is further supported by studies which find that the higher the IOP, the greater the percentage of patients who experience visual field loss over time.

This concept of assessing risk and intervening early in the pathogenesis of glaucoma is based on the fact that the damage which causes glaucoma is a continuum, beginning with glaucomatous damage to the first axon of the optic nerve and ending with the loss of the last axon leading to blindness. One of the key features of assessing the risk factors is to find out where a specific patient falls in the continuum and to estimate their risk of progressing to functional vision loss. One way to do this is to utilize a calculator which will analyze identifiable risk factors which are important in the conversion of ocular hypertension to glaucoma. This calculator will generate a quantitative estimate of the individual's risk of developing glaucoma. This estimate will provide additional information to doctors to help them determine who they want to treat and who they want to monitor closely.

The concept of this management protocol is based on a concept called global risk assessment. It is analogous to lowering

cholesterol for patients before they develop cardiovascular disease. Like glaucoma, cardiovascular disease is a chronic disease which occurs in a continuum that begins as undetectable disease (early atherosclerosis), progresses to detectable but asymptomatic disease, progresses to further to symptomatic end points (angina, acute myocardial infarction), and ultimately leads to permanent damage to heart muscle tissue and end stage heart disease if left untreated. One of the major risk factors for the development of these adverse cardiovascular events is increased cholesterol levels. Therefore, the way to decrease the incidence of heart disease or to delay its onset is to decrease a patient's cholesterol.

So, what are these factors which may influence your decision to treat?

Age. Both the incidence and prevalence of primary open angle glaucoma (POAG) increases with age. This trend has been consistently found in virtually every population-based study in which age was examined. Studies have found an incidence of 0.25 percent at 20 years old and 15 percent at ages 70 to 75.2 What makes age difficult to assess is that older patients are more likely to develop glaucoma, but a younger patient must be treated more aggressively because they have more potential years over which to preserve vision. Therefore, having the same risk factors except for age may make the difference between initiating treatment and monitoring. For example, you may choose not to treat an 80 year old patient because the likelihood of the patient going blind during their lifetime is less than the same patient who is 40. This second patient may have another 40, 50, or 60 years to live so your approach would change.

Race. POAG is more severe and more prevalent in African-Americans. The Baltimore Eye Survey found a three times to four times higher incidence of glaucoma in African-Americans than Caucasians. The Beaver Dam study found an overall prevalence of 2.1% in an all-Caucasian population compared to 8.8% in the St. Lucia study in which all patients were African-Caribbean. 3,4 Similar numbers have been found for the Hispanic population from the Los Angeles Latino Eye Study (LALES). These are two population groups which you must carefully examine to rule out glaucoma.

Family History. It should be no surprise to anyone that there is a genetic component to glaucoma. Exactly how much of a factor there is depends on the study. One study calculated that the lifetime risk of glaucoma was 22% higher in patients with a family history of glaucoma. 5 Others have put anywhere from 13 to 47 %. Although family history is hard to consider quantitatively, but qualitatively if you have a patient who has had a mother or other family member to go blind from this disease, they are usually much more conscientious about returning for follow up care and are much more likely to want to be treated prophylactically.

Systemic Conditions. The biggest risk factor in terms of systemic diseases is diabetes mellitus. One of the prevailing hypotheses for this mechanism involves decreased microvascular perfusion around the optic nerve head. These patients should be evaluated on an annual basis not only to evaluate the presence of

diabetic retinopathy, but also to check for signs of glaucoma. This risk is so strong for diabetes that Medicare actually instituted a special code whereby you can bring diabetic patients in for a glaucoma screening and get reimbursed for it.

Intraocular Pressure (IOP)

Although glaucoma is no longer defined as a disease of elevated intraocular pressure, IOP remains an important parameter in diagnosing and managing the progression of the disease. In fact, it is the only modifiable risk factor for the development of glaucoma. Any body with an elevated IOP must be evaluated for glaucoma. The same can be said for any patient with asymmetric IOP readings greater than 2 mm Hg. However, realizing that many patients who don't develop glaucoma don't have elevated IOP, just because your patient has a "normal" IOP reading doesn't mean that they won't develop glaucoma.

To make matters worse, IOP tends to fluctuate during the day due to diurnal or circadian rhythms and this effect is more pronounced in POAG patients. This large IOP fluctuation can lead to progressive visual field loss in a compromised nerve. This is something that should be taken into account when considering treatment schemes for patients. To get an idea of this fluctuation, you should check IOPs during different times of day. Or, you may prefer to have your patient return one day and measure IOP every hour throughout the day. In most cases, a fluctuation of 2-4 mm Hg is normal and anything larger than that should be carefully evaluated. When it comes to treating patients, remember your goal in treatment should be not only to lower IOP, but also to decrease this diurnal fluctuation (flatten the diurnal curve).

Cup-to-Disc:

Although there is considerable variation in the average cup to disc ratio, the "normal" is .30 plus or minus .10 which gives a normal range of .20 to .40. Therefore, anything over .50 must be worked up. Also, there is considerable risk if there is asymmetry between the two eyes. A difference of .10 is not a big deal, but a difference of .20 only happens in 1% of normal eyes. One aspect to consider is the measurement of the cup to disc is not a static value. A patient who has a .60 C/D which remains constant over the course of many years is much less suspicious than a patient who is .50, but was .40 2 years ago and .30 1 year prior to that. One additional aspect to consider is the health of the neural rim tissue. A .70 C/D with healthy rim tissue all around it is much less problematic than a .50 which little or no rim tissue in one quadrant. All ancillary testing aside, this is the most critical aspect of properly diagnosing glaucoma and assessing risk. The majority of patients in OHTS who converted to glaucoma demonstrated changes in the optic nerve head as the first sign.

Central Corneal Thickness

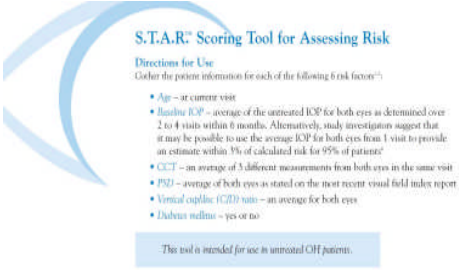
One of the major findings of OHTS was the relationship between corneal thickness and IOP. This relationship is so strong that the measurement of corneal thickness is part of the standard of care for evaluating any potential glaucoma patient. Goldmann developed tonometry based on an assumed central corneal thickness of 0.5mm. However, recent research shows us that increased corneal thickness causes high IOP readings and decreased thickness leads to low

readings. What is evolving from all of this research is the development of a correction factor for IOP considering corneal thickness. According to various reports in the literature, the amount of necessary correction ranges from 3 to 7 mm Hg for every 100 um of corneal thickness. However, most of the data are based on evaluation of normal patients, not glaucomatous eyes. One of the better correction factors I have seen is the following. For every 20 um of corneal thickness below 540 um, add 1mm Hg to the Goldmann tonometry value; conversely, subtract 1 mm Hg for every 20 um higher than 540 um. For example, a patient with an IOP of 24 mm HG and a corneal thickness of 600 um will have a corrected IOP of 21 mm Hg.

More important than the re-calibration of IOP readings is that fact that thin corneas are an independent risk factor glaucoma. Not only does the measured IOP value increase for patients with thin corneas, but these patients are more likely to develop glaucoma and thus deserve special attention.

S.T.A.R.

This program incorporates several risk factors and derives a 5-year risk of developing glaucoma. The factors it considers are age, intraocular pressure, pattern deviation on standard automated perimetry, central corneal thickness, the vertical cup to disc ratio, and if the patient has diabetes.


S.T.A.R.™ Scoring Tool for Assessing Risk

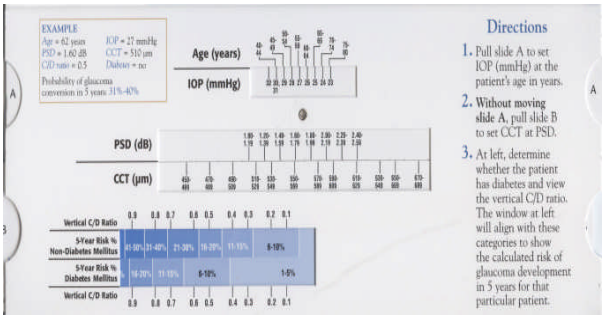
Directions for Use

Gather the patient information for each of the following 6 risk factors[1-3]:

- Age – at current visit
- Baseline IOP – average of the untreated IOP for both eyes as determined over 2 to 4 visits within 6 months. Alternatively, study investigators suggest that it may be possible to use the average IOP for both eyes from 1 visit to provide an estimate within 3% of calculated risk for 95% of patients[4]
- CCT – an average of 3 different measurements from both eyes in the same visit
- PSD – average of both eyes as stated on the most recent visual field index report
- Vertical cup/disc (C/D) ratio – an average for both eyes
- Diabetes mellitus – yes or no

This tool is intended for use in untreated OH patients.

What this program does is weigh each of the factors according to its predictive power for predicting the likelihood of ocular hypertensive patients converting to glaucoma. One should be aware, however, the global risk estimate provided by the risk calculator does not directly address whether or not to treat an individual patient; the risk calculator simples provides a number between 0 and 100 that represents the individual's risk of developing glaucoma within 5 years.



The goal in using this type of program is then to look at the risk of developing glaucoma over the next 5 years and then deciding on a course of action. The basic guidelines for this course of action is outlined below.

A patient with ocular hypertension whose risk of developing glaucoma within 5 years is less than 5% is most likely one who can be safely observed without treatment. However, these patients are still at risk for developing glaucoma so they should still undergo regular examinations of the optic nerve and nerve fiber layer. In addition, many of these patients should also have period visual field examinations and/or testing by a GDx or HRT. Practitioners should also review the risk factor status of these individuals on a regular basis, as low-risk patients can occasionally become high-

risk patients if key factors change over time. The clinician must ensure that these patients understand the importance of regular follow up to detect asymptomatic progression. Although their risk is relatively low, that risk is not zero.

Patients whose 5-year risk of progressing to glaucoma is between 5 and 15% represent a "gray" area where each practitioner may take a different course of action. These patients are at higher risk if untreated than if treated but the benefits of treatment are only moderate. The decision to treat or monitor in these patients is based on the comfort thresholds of the patient and physician after considering the risk: benefit ratio.

Patients whose individual risk of progression from ocular hypertension to glaucoma within 5 years exceeds 15% are at high risk. These patients are most likely to benefit from treatment, the risk for developing glaucoma is relatively high. Practitioners should make every effort to educate their patients about this risk and should encourage them to initiate a treatment plan. Also, these patients must understand that treatment reduces, but does not eliminate, risk and that regular follow up will still be required to continually assess the efficacy of therapy.

The glaucoma risk calculator is a useful tool for clinicians in estimating an individual patient's risk of developing glaucoma, but it is not meant to replace the clinician's own personal experience and judgment. Just like any other test, the risk calculator gives you another piece of information to help guide your decision on whether you treat or monitor. Ultimately, it still comes down to the doctor's decision on what to do.

1. Kass Ma, et al. The ocular hypertension study. Arch Ophthalmol 2002; 120: 701-713
2. Tielsch JM, Sommer A, et al. Racial variations in the prevalence of primary open angle glaucoma. JAMA. 1991;266:369-74.
3. Tielsch JM, Sommer A, et al. Racial variations in the prevalence of primary open angle glaucoma. JAMA. 1991; 266: 369-74.
4. Klein BEK, Klein R, Sponsel WE, et al. Prevalence of glaucoma. Ophthalmology. 1992; 99:1499-504.
5. Tielsch JM, Katz J, et al. Family history and risk of primary open angle glaucoma. Arch Ophthalmol. 1994;112:69-73.

CONTINUING EDUCATION QUIZ

This article is worth two (2.0) continuing education credits. This COPE-approved program is accredited by the University of Alabama at Birmingham College of Optometry.

Once you have registered for the course, you will be given an access code and go to www.flexiquiz.com where you will take the quiz. To earn credit, you must receive a grade of 70% or greater.

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MULTIPLE CHOICE QUESTIONS

1. It is estimated that roughly _____ Americans suffer from glaucoma.
    a. 20,000
    b. 200,000
    c. 2 million
    d. 20 million
2. Which one of the following is NOT included in the definition of glaucoma?
    a. A group of ocular diseases
    b. Progressive optic neuropathy
    c. Loss of visual function
    d. Elevated intraocular pressure
3. According to the author, which of the following examples constitutes confirmed cases of glauoma which should be treated?
    a. Repeatable visual field defect
    b. Progresive deterioration of the optic nerve
    c. Progressive damage seen on GDx or HRT testing
    d. All of the above
4. Which of the following pathological scenarios best describes glaucoma?
    a. The patient's rate of axonal loss exceeds the normal age-related rate of loss
    b. The patient's rate of axonal loss is less than the normal age-related rate of loss
    c. The patient's rate of axonal loss is the same as the normal age-related rate of loss
    d. There is no correlation between the patient's rate of axonal loss and the normal age-related rate of loss
5. How many people in OHTS did NOT convert to glaucoma over the 5 year span?
    a. 80%

b. 90%
c. 10%
d. 50%

6. According to the article, the concept of prophylactically treating glaucoma is based on a concept called
    a. Global risk assessment
    b. Evidence-based medicine
    c. Holistic medicine
    d. Homeopathic medicine
7. The incidence of glaucoma at age 73 estimated to be
    a. 5%
    b. 10%
    c. 15%
    d. 20%
8. According the studies in the article, what is the incidence of glaucoma for the African-American population versus the general population?
    a. 1:1
    b. 2 times greater risk for the African American population
    c. 3 times greater risk for the African-American population
    d. 4 times greater risk for the African-American population

9. Which of the following studies estimated the risk for glaucoma for the hispanic population?
    a. OHTS
    b. LALES
    c. AREDS
    d. Beaver Dam Study
10. For which systemic condition does Medicare offer a glaucoma screening"
    a. Diabetes Mellitus
    b. Thyroid disease
    c. Hypertension
    d. Multiple Sclerosis
11. Which of the following patients should be evaluated for glaucoma
    a. Someone with an IOP of 13 OU
    b. Someone with an IOP of 15 OU
    c. Someone with an IOP of 9 OU
    d. Someone with an IOP of 12 OD and 16 OS
12. In general, how much of an IOP fluctuation during the day is considered normal?
    a. There is no amount of fluctuation which is normal
    b. 2 to 4 mm Hg
    c. 6 to 10 mm Hg
    d. 12 to 16 mm Hg
13. A patient with a C/D of _____ should be evaluated for glaucoma
    a. .20
    b. .30
    c. .40

d. .50

14. In terms of corneal thickness, which patients are at increased risk for developing glaucoma?
    a. Patients with normal thickness corneas
    b. Patients with thick corneas
    c. Patients with thin corneas
    d. All patients have the same risk
15. The S.T.A.R. program calculates the risk for developing glaucoma over what time period?
    a. 1 year
    b. 3 years
    c. 5 years
    d. 7 years
16. Which one of the following factors is NOT considered by S.T.A.R
    a. intraocular pressure
    b. nerve fiber layer thickness
    c. central corneal thickness
    d. age
17. According to S.T.A.R., what is the recommendation for a patient who demonstrates a 5% risk for conversion to glaucoma?
    a. Treat aggressively with medications
    b. Treat aggressively with laser trabeculoplasty
    c. Monitor regularly
    d. Send to a glaucoma specialist for evaluation
18. According to S.T.A.R., what is the recommendation for a patient who demonstrates a 15% risk or greater for conversion to glaucoma?
    a. Treat patient and monitor continually to assess efficacy of therapy
    b. Perform the S.T.A.R. calculations again
    c. Monitor regularly with no treatment
    d. Send to a glaucoma specialist for evaluation
19. Which of the following patients would you treat most aggressively in terms of glaucoma?
    a. 40 year old patient
    b. 50 year old patient
    c. 60 year old patient
    d. 70 year old patient
20. A difference of .20 in the C/D ratio between the two eyes only happens in what percentage of normal eyes?
    a. 25%
    b. 15%
    c. 1%
    d. 10%