New Perspectives on Glaucoma Screening

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Glaucoma is defined as elevated intraocular pressure resulting in visual field defects. Elevated intraocular pressure without visual field defects is referred to as ocular hypertension. The prevalence of open-angle glaucoma in the population above the age of 40 years is less than one percent. Approximately one out of ten people with elevated ocular pressure has glaucoma. The concept of variable sensitivity explains why high ocular pressures do not always result in glaucoma. Glaucoma screening by tonometry can be justified only if used in conjunction with visual field testing.

As preventive medicine is taking on more importance, many family physicians are developing a desire to expand on the curative model of medicine and utilize methods of health maintenance and screening for early recognition of asymptomatic disease. Much of the early enthusiasm for preventive medicine was not characterized by sound scientific scrutiny of methods and results. In 1974 Frame and Carlson pioneered in the critical examination of the feasibility and justification of screening for 36 selected diseases.[1] They developed a recommended longitudinal screening program for asymptomatic adults and suggested a set of criteria deemed necessary to justify screening for any given disease. These criteria are as follows:

1. The disease must have a significant effect on quality or quantity of life.
2. Acceptable methods of treatment must be available.
3. The disease must have an asymptomatic period during which detection and treatment significantly reduce morbidity and/or mortality.
4. Treatment in the asymptomatic period must yield a therapeutic result superior to that obtained by delaying treatment until symptoms appear.
5. Tests must be available at reasonable cost to detect the condition during the asymptomatic period.
6. The incidence of the condition must be sufficient to justify the cost of screening.

On the surface glaucoma seems to be the perfect disease for health screening. It has been estimated that 13.5 percent of all blindness is due to this disease.[2] It has been assumed almost universally that by discovering glaucoma in the early stages and implementing appropriate therapy, blindness can be prevented. Various public health groups have therefore urged increased screening for glaucoma by health care providers.[3] As more knowledge about glaucoma and the course of the disease process becomes known, it becomes important to move beyond these arguments and carefully examine the data. Only in this way can a truly effective, cost-conscious, and nonharmful screening and treatment program be developed. After a brief discussion of the definition, classification, and pathophysiology of glaucoma, the epidemiological and clinical data available will be examined, and a suggested screening protocol will be offered.

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Table 1. Classification of Glaucomas

Primary Glaucoma
Open-angle
(includes "low pressure" glaucoma)
Closed-angle
Congenital
Secondary Glaucoma
Infection
Trauma
Neoplasms
Iatrogenesis

Definition and Classification

There are three criteria currently used to characterize glaucoma: (1) an increase in ocular pressure, usually defined as greater than 20 to 21 mmHg, which is two standard deviations above the mean; (2) cupping and pallor of the optic disk; and (3) typical visual field defects characteristic of glaucoma, as described by Armaly,[4] which early in the disease are asymptomatic. No longer can elevated intraocular pressure without associated visual field defects be classified as glaucoma. This entity is now referred to as ocular hypertension.

Glaucomas are classified into two main categories: primary and secondary (Table 1). Secondary glaucomas can be caused by a variety of mechanisms, including infections, trauma, neoplasms, and iatrogenesis, such as steroid induced glaucoma.

Primary glaucomas are further subdivided into three categories: open angle, closed angle, and congenital. In open-angle glaucoma the angle between the cornea and iris is normal, while in closed-angle glaucoma this angle is narrowed. Closed-angle glaucoma usually is manifested acutely as an ocular emergency but can be more insidious in onset. The most common type of glaucoma is primary open angle, followed in frequency by secondary and primary closed-angle glaucomas. Primary open-angle and the asymptomatic closed-angle and secondary glaucomas are those types for which the discussion of screening applies since they can exist in an asymptomatic state.

There is another type of glaucoma that does not neatly fit into the above classification. Low pressure glaucoma is characterized by visual field defects and cupping, yet intraocular pressure is less than 21 mmHg. Low pressure glaucoma can constitute up to 18 percent of all glaucoma cases.[5] Actually, the intraocular pressure levels of this group are higher than the mean ($\geq$17 mmHg) but lower than 21 mmHg, the commonly, though arbitrarily, set lower limit of elevated intraocular pressures.[6]

Pathophysiology

Aqueous humor is produced by the ciliary body and moves from the posterior chamber through the pupil into the anterior chamber. It then leaves the eye through the trabecular meshwork and canal of Schlemm. In glaucoma the sequence of events is believed to be as follows: the outflow of aqueous humor is decreased by some pathological process; aqueous humor continues to be produced and the intraocular pressure elevates; elevated pressure causes ocular nerve damage and cupping; and ocular nerve damage leads to visual field defects that can progress to blindness. As will be discussed later, each individual varies as to what level of pressure his or her ocular nerves can tolerate.

Epidemiological Data

The prevalence of elevated intraocular pressure (greater than 21 mmHg) varies by study between 3 percent and 12.7 percent in those over the age of 40 years.[7-10] The prevalence of elevated intraocular pressure increases with age from an average of 5 percent of the population at 40 to 44 years,

Table 2. Incidence of Glaucoma Among Patients Having Ocular Hypertension

Researcher	IOP mmHg	Causes of Glaucoma	Years
Armaly[4]	24.0-29.0	1/102 eyes (1%)	5
Norskov[19]	20.0-25.0	0/72 eyes (0%)	5
Perkins[20]	≥21.0	4/124 patients (3.2%)	5-7
Wilensky[21]	>22.0	3/50 patients (6%)	6*
Armaly[4]	>30.0	0/12 eyes (0%)	5
Graham[22]	>21.0	1/232 patients (0.5%)	3.5
Linner[23]	20.6-30.4	14/152 patients (9.2%)†	10
Kitazawa[24]	>21.0	7/75 patients (9.3%)	10
David[25]	>21.0	10/61 patients (16%) 12/117 eyes (10.2%)	3.5

IOP—Intraocular pressure
*Six-year average, five-year minimum, maximum number of years unclear
†Not clear that all 14 developed glaucoma or that all 152 were followed for ten years

10 percent at 55 to 59 years, and 15 percent at 70 to 75 years.[11]

The prevalence of chronic open-angle glaucoma in these same studies varies between 0.35 percent and 0.93 percent. The prevalence of all types of glaucoma varies from 0.84 percent to 1.30 percent. Therefore, only about 10 percent of those people with elevated intraocular pressures have some form of clinical glaucoma. Other studies have shown a higher prevalence of glaucoma, but they suffer from sampling biases and/or methodological error (some define glaucoma as elevated intraocular pressure only). As critiqued by Kahn,[12] the above mentioned data are considered more accurate. In fact, the two studies with the best design and methods show the lowest prevalence.[7-9]

The prevalence of glaucoma increases with age. In the Ferndale study there was a zero percent prevalence at age 40 to 44 years, 0.9 percent at age 55 to 59 years, and 1.3 percent at age 70 to 74 years.[11] The prevalence of glaucoma also increases with the level of intraocular pressure. Even so, at 30 mmHg only 30 percent will have visual field defects, and at 35 mmHg, 50 percent.

There are other subgroups of the population that seem to have a higher risk of glaucoma. There is an increased prevalence of diabetes among patients with open-angle glaucoma, although the reverse has not been proven.[13-16] Family history of the disease is probably an added risk factor,[17] and one study suggests an increased risk among those with thyroid disease.[18]

Table 2 summarizes the results of eight studies that have examined the incidence of glaucoma among those having ocular hypertension over a period of time. The first surprising result, consistent in all studies, is the low incidence of glaucoma in this group over a five- to ten-year period. Secondly, it can also be seen that even in the higher levels of intraocular pressure, most people having ocular hypertension do not develop visual field loss, at least within five to ten years.

Even though there is a difference in results among the studies, they all show a low incidence of glaucoma occurring among those having ocular hypertension. The studies from glaucoma referral centers show incidences of 0, 6, 9.3, and 16 percent.[19,21,24,25] The studies involving cross-sectional population surveys resulted in incidences of 0.5, 1.0, and 3.2 percent.[4,20,22] The higher incidences for

referral centers is not unexpected, but the results from cross-sectional population surveys are more likely to be applicable to populations seen by family physicians.

The ratio of glaucoma to ocular hypertension increases with age, indicating an increased susceptibility to ocular nerve damage. The increased susceptibility to glaucoma with age occurs at all pressure levels, including those normally classified as "low pressure" (17 to 21 mmHg).[10]

At first glance these combined data seem somewhat contradictory; ten percent of those with elevated intraocular pressures have glaucoma, yet a much smaller percentage of ocular hypertension patients will develop glaucoma over five to ten years. These data have been analyzed by Anderson and explained by his concept of variable sensitivity.[26] His analysis is recommended reading for all those seriously interested in the topic of glaucoma screening. To summarize briefly, it appears that each individual has his own threshold of intraocular pressure, beyond which ocular nerve damage and visual field defects are developed. For some this threshold is 21 mmHg, for others it is 18 mmHg (explaining low pressure glaucoma), and for others, 35 mmHg (explaining high intraocular pressures with no visual field loss). Approximately ten percent of the population is susceptible to ocular nerve damage at pressures above 21 mmHg. At higher pressures a greater percentage is susceptible.

If a person has elevated intraocular pressures and has no visual field defects, this means one of two things: either he has not reached his threshold and his ocular nerves can withstand this pressure without damage, or he has had this pressure for a short time and has not yet developed nerve damage. In a random screening program, most of those people with newly discovered ocular hypertension have had elevated intraocular pressure for some time and their ocular nerves have remained undamaged. If their pressures do not elevate, they are at small risk of developing visual field loss. This concept explains the low incidence of new glaucoma among those having ocular hypertension. In at least three of the prospective studies mentioned, new glaucoma cases developed among participants whose intraocular pressures increased during the study.[4,20,24] The increasing prevalence of glaucoma among older patients is mainly due to the tendency for ocular pressure to rise with age, thereby causing more individuals to cross their thresholds. However, as a person ages, an increased susceptibility to damage at constant intraocular pressures is also a factor.

Another interesting aspect of the variable sensitivity concept is that even though 30 percent of those with intraocular pressures of 30 mmHg have visual field loss, it does not mean that 30 percent of those having ocular hypertension will develop visual field loss at 30 mmHg of pressure. Those without ocular nerve damage at 30 mmHg have not crossed their thresholds and appear to be at low risk of developing glaucoma unless their pressures increase. A number of attempts have been made to find ways to predict which patients who have ocular hypertension are at increased risk of glaucoma. Various parameters studied include response to steroids, facility of outflow, cup-disk ratios, and family history of glaucoma.[21,24,27] All the attempts to find useful predictors have been unsuccessful.

Clinical Data

Considering how widely held is the belief that visual field loss can be either prevented or decreased by treating elevated intraocular pressure, the lack of supporting clinical evidence is surprising. Most authorities would agree that patients with documented visual field defects secondary to ocular pressure (those who have crossed their thresholds) should be treated. There is some evidence to support this view, although it is not so strong as one would like.[28-31]

However, there is no evidence that therapy for those having ocular hypertension with stable ocular pressures will prevent the onset of visual field defects. Two small studies have even shown no difference between treatment and control groups.[19,25] Up to this time there has not been a large controlled study to determine the advantages of preventive treatment. The number of subjects needed to achieve statistical significance can be appreciated when it is remembered that approximately 98 percent of those having ocular hypertension will not develop any visual field loss in any case. This fact probably explains why the efficacy of treatment has been unquestioned by many. If one treats all patients with ocular hypertension, not realizing that very few would develop

glaucoma without therapy, it would be easy to think therapy was preventing glaucoma in a very high percentage of cases.

Screening

For routine office screening, Schiøtz tonometry is sufficient. Spector has shown that false-positive measurements of elevated intraocular pressures can be decreased significantly if tonometry is done by someone with experience in the use of the tonometer.[32] In a clinic or office setting, therefore, tonometry should be done by one person who can develop the necessary expertise. In the same study Spector also shows the average cost and time of screening by tonometry to be $10.83 and 8.3 minutes per patient. Intraocular pressure varies with the time of day,[5] and repeat tonometry on the same individual should probably be done at approximately the same time of day, if possible.

It has been suggested that ophthalmoscopy, looking for glaucomatous cupping, can be a useful screening tool. The cup-disk ratio may be helpful in discovering active cases of glaucoma, although it is not so accurate as visual field testing; and as stated previously, it has not been useful in predicting long-term outcome of ocular hypertension.[24]

Visual field testing, which appears necessary in any serious glaucoma screening program, is not something routinely performed by family physicians. Visual field testing can be done in about five minutes per eye with 96 percent sensitivity and 88 percent specificity.[33]

Discussion

From the above data several conclusions can be drawn. (1) Screening for glaucoma with tonometry alone is unsound. If 21 mmHg is used as a cutoff, then up to one fifth of all cases of clinical glaucoma will be missed and 90 percent of those positive by tonometry will not have glaucoma. (2) Tonometry should be used as the first step in a multiple step screening protocol to determine who needs to be referred for visual field testing. (3) If a ready, low-cost, and reliable source of visual field testing cannot be found, there is little value in doing routine tonometry. (4) Treatment of everyone with stable, elevated intraocular pressures is not necessary. Treatment can wait until the onset of visual field defects. (5) Patients having ocular hypertension are at low risk of developing glaucoma unless their pressures increase.

Returning to Frame's criteria for justifying screening, if "asymptomatic period" is defined as the presence of visual field defects unnoticed by the patient, then all of the criteria can be met if tonometry and visual field testing are used together, although criteria numbers 3 and 4 have to be accepted on faith rather than on clinical evidence.

Figure 1 shows a suggested protocol for glaucoma screening. Screening should start with tonometry for those over the age of 40 years. The prevalence in the population below this age is too low to merit screening. Those with pressures of 20 mmHg or less can be rescreened every five years up to age 60 years and every two to three years thereafter. Those with pressures of 21 mmHg or greater should be referred to an ophthalmologist for two reasons: to determine if visual field defects are present, and if so, to diagnose what type of glaucoma the patient has. Appropriate therapy can be started for those with glaucoma. Follow-up should be frequent to ensure adequate control of intraocular pressures, and yearly or biyearly visual field testing is recommended to monitor the progression of the disease. Joint management of patients by the family physician and ophthalmologist would provide optimal care.

Patients having ocular hypertension (no visual field defects) should have yearly tonometry. If no change in pressure occurs, nothing else need be done. If there is an increase in pressure of greater than 2 to 3 mmHg, confirmed by repeat tonometry, then referral for visual field testing is indicated sometime within a year. Again, if visual field defects are found, treatment can be started; if no defects are found, then yearly tonometries and a repeat visual field test in one to two years is sufficient.

Treatment should be medical except in those cases in which intraocular pressures cannot be controlled with medication and there is progression of visual field loss. Surgery then can be considered.

Before instituting a screening program, it is suggested that a discussion take place with any potential referral ophthalmologist to clarify plans and expectations. It is also suggested that ar-

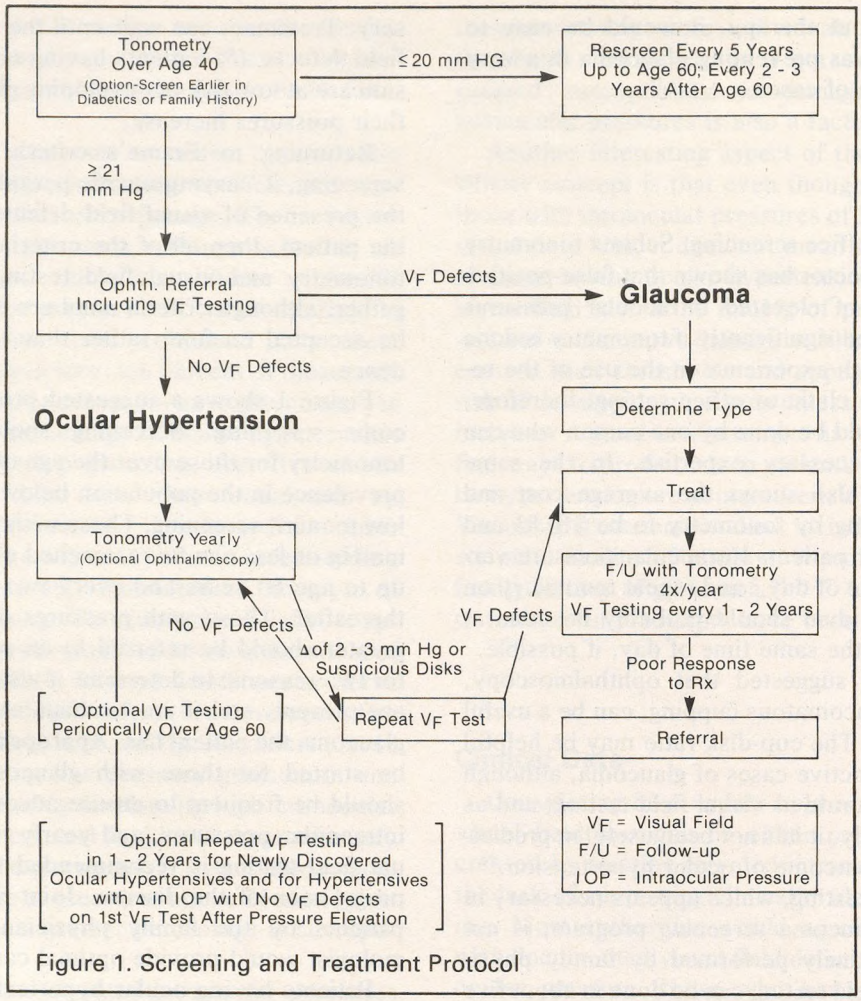

Figure 1. Screening and Treatment Protocol

rangements be made with the referral ophthalmologist for low-cost visual field testing. If the suggested protocol is followed, referrals to an ophthalmologist will be needed for the initial evaluation of those with pressures above 20 mmHg, for repeat visual field testing as needed, and for management of those with glaucoma. Follow-up tonometry, to ensure control of intraocular pressures, can be done by the ophthalmologist or family physician depending on individual preference and the geographic proximity of the referral ophthalmologist.

Variations to this basic scheme can be added. Some may feel that periodic visual field testing should be performed on all patients having ocular hypertension older than 60 years because of increasing susceptibility with age to ocular nerve damage at constant pressures. Some may feel that everyone having ocular pressures over 30 mmHg should receive treatment (although evidence for this approach is lacking). Some may want to watch diabetics and those with a family history of glaucoma more closely and start screening in these groups before they reach the age of 40 years.

Repeat visual field testing within one or two years for those with ocular hypertension could be added to eliminate the possibility of those patients with recently acquired ocular hypertension being screened before visual field defects have developed. However, this extra testing would cause a relatively large added expenditure for a small yield. Some may want to add yearly ophthalmoscopy to tonometry, to look for changes in the cup-disk ratio, although the value of this approach is unproven.

The screening approach described will detect about 80 percent of the glaucoma cases, missing only those with low pressure glaucoma. It will avoid treatment of ocular hypertension in those who have little chance of developing glaucoma. The population in the pressure range of 17 to 20 mmHg presents a special problem. It cannot be recommended that they be referred for visual field testing. Thirty percent of the population falls within the 17 to 20 mmHg pressure range.[8] While one out of ten individuals with ocular pressures $\geq$ 21 mmHg will be found to have glaucoma, roughly one out of 200 to 300 with pressures of 17 to 20 mmHg will have the disease. In this pressure range ophthalmoscopy, with referral of those with suspicious disks, might prove to be beneficial.

It is expected and hoped that this suggested screening protocol will undergo change as experience and new knowledge dictate. It is hoped that the protocol can be used as a rational starting point for those interested in doing further work in the area of glaucoma screening.

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