Risk Factors for Legal Blindness in Primary Open Angle Glaucoma

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ABSTRACT

RISK FACTORS FOR LEGAL BLINDNESS IN PRIMARY OPEN ANGLE GLAUCOMA (POAG), Karanjit S. Kooner, M.D.

Context: POAG is a leading cause of irreversible blindness worldwide. Factors associated with the damage, progression of the disease and related blindness are poorly understood.
Objective: To determine characteristics of patients with POAG that are associated with either a higher risk for blindness or preservation of visual function.
Design: Prospective observational comparative cohort study.
Participants: In all, 487 (974 eyes) consecutive incoming patients with POAG were followed for 5.5 ± 3.6 years. Exclusion criteria were 1) secondary glaucoma, 2) ocular conditions that would interfere with proper diagnosis and management, and 3) less than 3 months follow-up.
Methods: Seventy-seven pieces of information were collected on each patient and updated at every six monthly visit. Comparisons were done between 1) patients with no legal blindness (NLB) and those with legal blindness (LB); 2) stable NLB patients and those who progressed; 3) the affected eye and non-affected eye of patients with unilateral blindness; and 4) initial presenting data of new patients.
Setting: Academic (Clinic A), county hospital (Clinic B), and a Veterans Affairs hospital (Clinic C) providing primary, secondary, and tertiary care.
Main Outcome Measures: 1) Development of legal blindness in one or both eyes and 2) progression of glaucoma in one or both eyes.
Results: Compared to NLB group, LB group features were: higher mean initial intraocular pressure (IOP), ($p = 0.03$), late detection ($p = 0.006$), wide variation of IOP in the follow-up period (5.9 vs 4.1 mmHg, $p = 0.031$), poor control of IOP ($p < 0.0001$) and non-compliance ($p < 0.0003$).
Conclusions: This study suggests that some of the risk factors for legal blindness in POAG are related to the level of initial IOP, late detection of the disease, poor control of IOP and non-compliance.

Risk Factors for Legal Blindness in Primary Open Angle Glaucoma (POAG)

INTRODUCTION

The World Health Organization (WHO) estimates that nearly 71.0% of blindness in the world is from three conditions: cataract, trachoma, and glaucoma.[1] Various surveys by WHO also suggest that depending on a geographical location, glaucoma is responsible for 5.7% to 22.7% of all blindness worldwide. It may be fair to suppose that around 10% of global blindness may be from glaucoma. But there are several limitations of these statistics. First, glaucoma as a composite group includes both primary and secondary glaucomas while ways and means of clinically diagnosing these entities are not widely available in all countries. Second, the prevalence of various types of glaucomas is not uniform. For example, POAG comprises nearly 70% of all glaucomas in the West; whereas, in China it may be less than 5.0%.[2]

Definition of Legal Blindness

The definitions of **legal blindness** and visual impairment are also not standardized worldwide and therefore pose difficulties in comparing their prevalence. Legal blindness in North America is defined as best corrected visual acuity of 20/200 or less or a visual field less than 20 degrees at its widest in the better eye with the Goldmann III 4e test object or its equivalent on automated perimetry (Fig. 1).[3] Goldmann III 4e equivalent test objects are 10 mm target on the tangent screen at 1 m, size III target at threshold value of 10 dB or less on the Humphrey and size III target at 7 dB on Octopus perimeter. WHO defines blindness as visual acuity of less than 3/60 (0.05) or corresponding visual field loss in the better eye with best possible correction. Visual impairment corresponds to visual acuity of less than 6/18 (0.3) but equal to or better than 3/60 (0.05) in the better eye with best possible correction.

Definition of POAG

Based on the most current concept of POAG, this entity is still theoretically defined as a progressive optic neuropathy with characteristic optic nerve excavation, and corresponding **visual field (VF) defects.**[4] Gonioscopically, the

angles are open and the **intraocular pressure (IOP)** may be elevated in up to 60% to 70% of patients. For the study, as it was initiated in 1993, IOP levels equal to or greater than 21 mmHg were used for the definition. The disease is multifactorial, usually bilateral, though not necessarily symmetrical. All other causes of damage to the nerve fiber bundles should be excluded. In order to understand progression and blindness in POAG, it is essential to study the disease process in detail.

Etiology of POAG

The current treatments for glaucoma focus on lowering IOP. This approach may not be enough as 25% to 38% of patients may continue to lose VFs and develop blindness even when IOP has been reduced to the normal range.[5-7] The research of Hattenhauer and associates has suggested that 27% of glaucoma patients go blind in at least one eye after 20 years or more with the disease.[8] It is well known that the underlying pathology in POAG is the death of **retinal ganglion cells**. The cells preferentially damaged in glaucoma are the magnocellular retinal ganglion cells.[9-10] Both experimental animal studies of the retina and human autopsy studies of lateral geniculate nucleus in glaucoma also point to the damage of larger retinal ganglion cells that project to magnocellular layers of the lateral geniculate.[11-13]

The most prevalent theories attempting to explain glaucomatous optic neuropathy are the mechanical theory and vascular theory. In the **mechanical theory**, the emphasis is on the damage to the optic nerve neurons at the level of the lamina cribrosa by the elevated IOP.[14] Alternately, the raised IOP may attenuate the sensitive microcirculation to the optic nerve head. On the other hand, the **vascular theory** suggests that eyes with inherently poor vascular supply to the optic nerve head are more predisposed to damage by elevated or normal IOP.[15] But the cause-and-effect relationship between nerve damage and vascularity has not been established. Sponsel and co-workers[16] discovered that in patients with glaucoma or ocular hypertension, the eye with the higher velocity of retinal leukocyte flow was associated with better visual function with regard to VFs and contrast sensitivity. It is controversial whether increased blood velocity translates to enhanced perfusion pressure to a particular area. Further support

for the vascular theory came after the development of **laser Doppler flowmetry (LDF) technique** to evaluate the circulation of the optic nerve.[17] Studies have shown diminished blood flow in the optic nerves of eyes with POAG.[18,19] Similarly, optic nerve flow was decreased in patients with low systemic blood pressure and increased in patients with hypertension.[20] It is still doubtful whether LDF measures the entire blood flow to the optic nerve head, though most investigators believe LDF penetrates as far as the level of the lamina cribrosa.[21] As neither theory could explain all cases of glaucoma, the trend was to combine the two views together.

In the late 1960s and early 1970s another theory was proposed that correlated elevated IOP with blocking **axoplasmic flow** at the lamina cribrosa.[22,23] The resultant interruption of trophic factors to the ganglion cell body might cause the cells to initiate a suicidal response resulting in programmed cell death or **apoptosis**.[9]

The focus now has shifted more to understanding the response of nerve tissue to trauma and aging. Profiting from the data emerging from studies of central nervous system trauma, the new concepts of excitatory neurotoxins and apoptosis were applied to understanding the damage in glaucoma. When nervous tissue is severely injured, regardless of the cause, it follows the same common final pathway before neuronal death. The injurious events may relate to ischemia/hypoxia, trauma, hypoglycemia, stroke, and various acute or chronic degenerative and hereditary neuronal diseases.[24] The functional damage to the nervous tissue continues to progress even after the primary cause has been removed. These new concepts may help us understand why some glaucoma patients continue to exhibit progressive neuropathy even after an offending factor such as high IOP has been controlled. Moreover, there is evidence that up to 50% of retinal ganglion cell axons may be lost by the time VF loss and abnormal cupping are detected.[25,26]

The term **secondary degeneration** has been applied to progressive neuropathy that spreads to adjacent areas far beyond the initially injured neuron site. The aim of therapeutic neuroprotection is to protect these initially spared neurons from the ravages of secondary degeneration. The biochemical events

surrounding the area of nerve injury involve the release of the excitatory amino acids **glutamate** and **asparate.** These amino acids have the ability to excessively stimulate the nerve and cause neuronal fatigue, toxicity, and ultimately nerve death.[27] The cytotoxic effects of glutamate on the inner layers of the retina are well known.[28,29] Dreyer and co-workers[30] discovered significantly higher levels of glutamate in the vitreous samples of glaucoma patients compared to normal individuals. Similarly, Brooks and co-workers[31] found significantly high vitreal glutamate concentration in dogs with primary glaucoma compared to normal animals. Even relatively minor but chronic elevation of glutamate may be toxic to the retinal ganglion cells.

After the release of glutamate at the injury site, Na^+ enters the cell. There is concomitant entry of chloride ions and water, causing cellular swelling. These events constitute the acute phase of neuronal trauma. Depending on the severity of the insult, the cell may recover or proceed to further loss of function and death. In the second or delayed phase there is cellular influx of Ca^{++} and once the calcium homeostasis is altered a wide variety of abnormal biochemical reactions ensue. There is release of cytotoxic enzymes such as protease, endonuclease, and lipase that destroy cell membrane. Free radicals accumulate and further disturb the essential metabolic functions of the cells. Glutamate toxicity also releases **G protein** via its stimulation of metallotrophic receptors, which in turn activate phospholipase C. The end result is major disruption of normal cellular function.

Another important pathway for cellular death is **apoptosis.** This active process is different from necrosis and when triggered by calcium ion imbalance enables the cell to die without liberating its digestive enzymes. Apoptosis appears to be controlled by genes, which might be artificially altered in the future to prevent the initiation of the deadly program. Quigley and co-workers[9] have shown that ganglion cell death in glaucoma shares certain similarities with classic apoptosis. Retinal cells in glaucomatous optic neuropathy display chromatin condensation and involution or shrinkage. Neufeld and co-workers[32] have demonstrated increased levels of **nitric oxide synthase (NOS) isoforms 1, 2 and 3,** in the optic nerve head of patients with POAG. The presence of NOS-1 and -2 suggests that nitric oxide may reach toxic levels in the optic nerve in glaucoma.

Excitotoxicity, even when mild, can cause neuronal apoptosis.[33] Excitotoxicity of retinal ganglion cells is mediated by overstimulation of a subtype of glutamate receptor, the **N-methyl-D-asparate (NMDA)**. Dreyer and associates[34] have shown that agents that interfere with translation or transcription of these proteins are also effective in preventing NMDA-induced excitotoxicity. Overstimulation of NMDA receptors activates NOS, which mediates increased levels of nitric oxide and superoxide anion.

A new sequence of events leading to glaucomatous nerve damage has surfaced. The first stage may be triggered in susceptible patients by factors such as elevated IOP or poor blood supply to the optic nerve. In the second stage, damaged ganglion cell axons either come under the influence of neurotropin deprivation and/or the released excitatory amino acids. With the loss of neurotrophic support of the ganglion cells, slow death is inevitable. There is also the consensus among the proponents that these events are interconnected and once initiated are hard to control with present day therapy for glaucoma.

Hayreh et al[35] raised the issue of **nocturnal hypotension** in the development and progression of glaucomatous optic neuropathy. The physiologic drop in blood pressure at night, for example, may have adverse effects on a glaucoma patient with compromised optic nerve circulation. Hayreh's group[36] also prospectively investigated the effects of topical beta-blocker eyedrops on nocturnal blood pressure, heart rate, and VF function. The study showed that in patients with normal-tension glaucoma, on beta-blocker therapy, there was a significantly more marked VF progression ($p = .0003$) than in those not using topical beta-blockers. These patients also exhibited significantly greater decrease in mean diastolic blood pressure ($p = .009$) at night compared to patients with ischemic optic neuropathy.

The age-dependent reduction in the number of optic nerve fibers is also an important consideration.[37] **High-pass resolution** and histologic studies have suggested the average loss of 10,000 nerve fibers every year after the age of 40 years. As the average number of nerve fibers is approximately 1.2 million, a person in his or her mid-80s may have lost approximately 40% of neurons, due to age-related events alone.

EPIDEMIOLOGY OF POAG

Geographical distribution of POAG

There is good evidence that POAG is a worldwide disease.[38] Some estimates suggest that by the end of the 20th century, over 60 million people may be affected by glaucoma throughout the world and nearly 10% of those affected may become blind bilaterally.[39] No race, community, or continent is immune from the disease, though some races have low prevalence of POAG. A large number of glaucoma-based epidemiologic studies have been conducted in different parts of the world and have yielded useful information, though they lack uniformity of design and definition of the disease.

The **WHO Programme for the Prevention of Blindness** has tried to estimate the distribution of POAG based on the populations in nine different regions of the world as defined by the World Bank.[40] Of the total global POAG patient population, the percent distribution in the different regions is as follows: established market economies, 17.6%; former socialist economies of Europe, 7.2%; Latin America and the Caribbean, 6.7%; sub-Saharan Africa, 19.4%; Middle East/North Africa/southwest Asia, 5.2%; China, 20.1%; India, 12.9%; other Asian and Pacific countries (high income), 3.6%; and other Asian and Pacific countries (low income), 7.2%. Therefore, developing countries account for approximately 70% of the world's POAG cases.

In **Africa**, the majority of the population is black, with pockets of whites scattered throughout the continent. North Africans, for example, have Caucasian features. Due to various reasons and including socioeconomic conditions in Africa, the prevalence of blindness is the highest in the world and rates of 3.6% to 5.2% have been reported.[40] In **Ivory Coast**, Ahnoux-Zabsonre et al[41] retrospectively reviewed charts of 33,000 patients attending a private clinic. There were 24,751 black and 8,249 white subjects. They found a prevalence of 2.1% in black and 0.75% in white patients. In both groups the prevalence rate increased with age. In black patients the mean age at detection of POAG was 46.4 ±12.5 years, whereas it was 52.8 ± 12.2 years for white patients. Of the 571 patients with POAG, 38.5% had normal tension glaucoma. In an epidemiologic study in **Cameroon** looking at

causes of unilateral blindness, Moussala et al[42] found POAG responsible for 22% of cases, trailing closely those from cataract and ocular trauma. Ouertani et al[43] examined all 856 individuals over the age of 40 years for POAG in one county of **Tunisia** and detected prevalence rate of 2.68%. They also found direct correlation between the prevalence rate and increasing age. The rate was 0.54% in subjects between 40 to 50 years, 1.71% in those between 51 to 65 years and 50.63% in individuals over 65 years. Ninety-one percent of patients found to have glaucoma were unaware of the condition and 30.4% suffered from advanced disease. In the tiny nation of **Togo**, Balo and Talabe[44] noted that 66.87% of patients with POAG were under 45 years old, of which 65.23% were male and 34.86% were female. Optic nerve head cupping was significantly greater in the left eye compared to the right ($p < 0.02$). Glaucoma was responsible for 17% of blindness in 523 patients found to have visual impairment in the rural communities of Central **Ethiopia**.[45] Nwosu[46] conducted a one year study looking for new cases of blindness at a teaching hospital eye clinic in Anambra State, **Nigeria**. He found that of 257 patients with blindness, glaucoma was responsible for 22.2% of visual impairment in at least one eye. A community-based cross-sectional study in the Segou region of **Mali** examined 5,871 inhabitants of three rural districts.[47] Bilateral blindness rate was 1.7% and glaucoma accounted for 8.1% following cataract and trauma. The prevalence of POAG in central **Tanzania** during a survey of ocular diseases in adults was 3.1%.[48] The subjects were examined from six randomly selected eligible villages.

In contrast to the results of the above studies, the prevalence of POAG in South Pacific islanders is rare. During a trachoma survey in 1955, Mann and Loschdorfer[49] found only one case of POAG among 13,268 inhabitants of **Papua, New Guinea.**

Asia is populated by different races with varied facial features and skin color. **India** has a population of nearly a billion people and the WHO estimates that approximately 9 million inhabitants are blind, and that glaucoma may be responsible for 12.8% of the cases.[1] The **Vellore Eye Survey** was conducted in the city of Vellore in South India, and examined 972 individuals between the ages of 30 and 60 years.[50] The prevalence of POAG, primary angle closure glaucoma and

ocular hypertension were 4.1 (0.08 – 8.1), 43.2 (30.14 – 56.3), and 30.8 (19.8 – 41.9) per 1,000 inhabitants, respectively. The main drawbacks of the study were lack of subjects over the age of 60 years and a low response rate of only 50.3% from the eligible individuals. A similar population-based, cross-sectional study was carried out in the city of Hyderabad.[51] The investigators wanted to determine the prevalence and cause of moderate visual impairment. There were 2,522 total participants of all ages, with a high response rate of 85.4%. Primary angle closure glaucoma and POAG accounted for 0.4% and 2.0% of moderate visual impairment respectively.

China is the world's most populated nation with over a billion citizens. China contains a relatively homogeneous society and the prevalence of primary closed angle glaucoma is greater than POAG. Hu[52] conducted an epidemiologic survey in Shunyi County of Beijing and found prevalence rate of 0.41% for primary angle closure glaucoma and 0.11% for POAG. Both conditions were responsible for 9.28% of the blind and 16.67% of visually impaired patients. Compared to the glaucoma prevalence of 0.60% for the entire study population, the prevalence in subjects over 40 years was 1.40%. Another study in Tongcheng County of Anhui Province found a prevalence rate of 0.31% for primary angle-closure glaucoma and 0.07% for POAG.[53] The overall prevalence of glaucoma was 0.38%, whereas in individuals over the age of 40 years, the rate was 0.71%. Gao et al[2] examined 331 patients with glaucoma at the Third Affiliated Hospital of China Medical College and 275 patients at the eye clinic of Kyushu University in **Japan** during a two-year period. Glaucoma patients made up 1.5% of the 22,869 patients in the former institute and 1.8% of the 15,585 outpatients of the latter. At the China Medical College the distributions of the various glaucomas were primary angle closure glaucoma (76.4%), POAG (4.8%), secondary glaucoma (11.8%) and congenital glaucoma (5.7%). In comparison, the findings from Japan were primary angle closure glaucoma (34.5%), POAG (12.7%), secondary glaucoma (22.2%), exfoliation glaucoma (14.9%) and congenital glaucoma (10.9%). A well-designed nationwide glaucoma survey was carried out in Japan under the auspices of the **Japanese Glaucoma Research Club** in 1988-89.[54] Of the 5,092 subjects evaluated, 1.6% showed IOP abnormalities, whereas 5.1% had optic disc changes. On further

examination, prevalence of POAG was found to be 0.5% while 1.4% of the subjects were diagnosed with low-tension glaucoma.

The **Melbourne Visual Impairment Project** was a population-based study designed to assess the distribution and causes of eye diseases in Melbourne, Australia.[55] The investigators examined 3,271 residential subjects and 403 nursing home patients. The response rate was 83% for the former and 90.2% for the later. In the residential population the prevalence rate for POAG was 1.7% [95% confidence limits (CL) =1.21, 2.21]. Nearly half of these participants were unaware of their disease. Primary angle-closure glaucoma was detected in two persons (0.06%), whereas six (0.2%) had secondary glaucoma. Age was a significant risk factor as the prevalence rate increased from 0.1% in people between 40 to 49 years to 9.7% in those between 80 to 89 years. A person's gender played an insignificant role. The prevalence rate for glaucoma in nursing home patients was 2.36% (95% CL = 0, 4.88).

Bonomi et al[56] examined 4,297 persons (73.9% participation rate) in rural areas of northern **Italy** who were over 40 years of age. The investigators looked for ocular hypertension, POAG, primary angle-closure glaucoma, and normal-tension glaucoma, and found prevalence rates of 2.1%, 1.4%, 0.6%, and 0.6% respectively. In Western **Scotland**, Ghafour et al[57] analyzed blind registration forms of new 647 legally blind patients for the fiscal year 1980. Overall, glaucoma accounted for 14.6% of legal blindness and was the second most common cause behind senile macular degeneration (29.8%). In a geographically well-defined county in central Sweden, the investigators identified glaucoma population with the help of data from local hospitals and pharmacies.[58] The prevalence of glaucoma was 1.4% in individuals over 45 years of age.

The prevalence of glaucoma in Western developed countries was evaluated by Tuck and Crick.[59] They analyzed data from eight surveys and estimated prevalence rates for POAG in mainly white Caucasians 40 to 89 years of age to be 1.2%. This estimate ranged from 0.2% for individuals in their 40s to 4.3% for those in their 80s. The percentage of individuals with the disease and their age distributions were: 7% less than 55 years, 44% between 55 and 74 years, and 49% older. The investigators also indirectly estimated incidence from the prevalence

results (implied incidence), and calculated the rate to be 0.11% per year in persons between 55 and 74 years.

St. Lucia in the West Indies is home to a relatively homogeneous black population. The investigators used a cluster sampling method and examined 1,679 individuals older than 30 years.[60] The prevalence rate for glaucoma was high, being 8.8%.

Prevalence of POAG in the United States

In the United States, glaucoma as a composite group is the second most frequently reported principal diagnosis at office visits to ophthalmologists after cataract.[61] It makes up about 15% of all visits relating to illness or injury in ophthalmology. Among patients making return visits for the care of their previously treated eye condition, glaucoma accounted for about 20%. Among all the glaucoma-related office visits for the two year period of 1991-92, the diagnostic coding in descending order of frequency were: unspecified glaucoma (63.2%), open angle glaucoma (20.7%) and borderline glaucoma (14.0%). The open angle glaucoma category was composed of POAG (10.7%), open-angle glaucoma, unspecified (9.2%), and other open-angle glaucoma (0.8%). In individuals 65 years and older, glaucoma was the third most commonly reported principal diagnosis. Although glaucoma accounted for 3.2% of all diagnoses in persons between 65 and 74 years of age, it was higher (4.4%) in persons 75 years and over. When comparing the principal diagnosis of glaucoma with all other ophthalmic and non-ophthalmic diagnoses, it was the 13th most frequently mentioned condition. Glaucoma is also the second leading cause of legal blindness in America.[62] In African-Americans, however, it is the most common cause of blindness and visual impairment.[62] Of all adult glaucoma, POAG constitutes 60% to 70%. Approximately 80,000 Americans are blind from the disease, and 2 to 3 million have glaucoma.[63] As the majority of patients are asymptomatic during the early and intermediate stages of the disease, it is estimated that approximately half of the patients may be unaware of their disease.[64] Therefore, for physicians and government health planners alike, POAG poses a grave challenge. The population-based **Baltimore Eye Survey** examined 5,308 inhabitants of East Baltimore and

discovered 161 (3.03%) cases of POAG.[65] In 1975, the **Framingham Eye Study** had found a prevalence of 3.3% for POAG among 2,477 individual examined.[66]

Effect of time on the prevalence of POAG

There is some evidence that the prevalence (the number of established cases of a disease in a defined population at a defined point in time) or the incidence (the number of new cases of a disease during a defined period of time) of POAG has increased over the years. The sampling data collected by the **National Ambulatory Medical Care Survey (NAMCS)** of the Division of Health Care Statistics of the National Center of Health Statistics, Centers for Disease Control and Prevention, has provided useful information.[61] In patients 65 years of age and older, between 1975 and 1992, glaucoma changed from being the ninth most mentioned morbidity-related principal diagnosis to the fifth. During 1975-76 there were 2.3 million glaucoma related visits and by 1991-92 the numbers showed a 284.6% increase to 8.7 million per year. Increased visit rates were observed in all age groups over 45 years. For example, in individuals 65 years of age and older, the rate for glaucoma visits increased from 5.7 visits per 100 subjects in 1975 to 19.9 visits per 100 subjects in 1992. These increased rates were observed in both sexes. According to the **National Health Interview Survey (NHIS)** individuals reporting a glaucoma-related condition increased from 5.7 conditions per 1,000 persons in 1977 to 10.4 conditions per 1,000 persons in 1991. Between 1982 and 1991, in persons 65 years and older the reporting of a glaucomatous condition increased from 41.8 conditions per 1,000 persons to 57.8 conditions per 1,000 persons. However, more cases are also being discovered nowadays because of factors such as better detection methods, the aging population, and heightened public awareness. As glaucoma is a disease of the elderly, who are now living longer because of better health care, we can expect to encounter more cases of glaucoma in the new century.

Demographic characteristics of patients with POAG and other risk factors

There are several known risk factors for developing POAG but not every patient has all of them (Table 1). While some factors appear to complement each

other, several may very well operate independently. It is well accepted that POAG is a disease of the elderly and the risk increases with **aging**.[66-70] This high prevalence in older populations may be explained on the basis of prolonged exposure to raised IOP or deteriorating microcirculation of the optic nerve head.

Table 1. Risk factors for POAG

- Age over 40 years [37,66-70]
- Elevated IOP [64,67,69-72]
- African American ancestry [62-68,71,77-83]
- Family history of glaucoma [84-86]
- Ocular trauma [103]
- Topical, systemic or endogenous corticosteroids [100,101]
- Myopia [97,98]
- Diabetes mellitus [95]
- Hypertension [87-93]
- Dysthyroid disease [99]
- Vascular insufficiency [16-20,35,36,87,94]
- Migraine headaches [102]
- Gender [89,96]

Several studies have demonstrated that increased IOP is associated with greater prevalence of POAG [64,67,69-72] and glaucoma-related VF defects in established POAG patients.[5-7,72,73] This clinical observation is amply supported by experimental studies in primates and by experience in treating patients with acute glaucoma.[74] In practice, however, patients show great variability in response to elevated IOP. Population-based studies have shown that only one-tenth or less of individuals with raised IOP will have accompanying glaucomatous visual field loss.[64] Longitudinal studies with ocular hypertensives have revealed that barely one-tenth of such subjects develop glaucoma over a ten year period.[75] Normal IOP may be observed in almost one-sixth of well established glaucoma patients even on repeated examinations.[64] Other deficiencies pertaining to the role of IOP in glaucoma include the lack of a practical and economical means for monitoring 24-hour continuous IOP, or at least a reliable diurnal pressure. Zeimer and associates[76] reported that in some glaucoma patients, IOP may be elevated upon awakening but drop precipitously within half an hour. Thus, a physician may fail to gauge the true nature of pressure spikes.

Race is an important risk factor, and African-Americans are four to five times more likely to develop POAG than other races.[64,67,71,77-83] The disease also strikes them early and they usually present with severe damage at the first visit. Moreover, the glaucomatous process is more refractory to treatment and results in a higher rate of blindness.[67] It is estimated that one in ten elderly blacks and one

in fifty elderly whites have glaucoma. In the **Barbados Eye Study**, a population-based prevalence survey, IOP was significantly higher in the black participants compared to their white counterparts.[79,80] The mean values for the black and white individuals were 18.7 ± 5.2 mm Hg and 16.5 ± 3.0 mm Hg respectively. Similarly, IOP greater than 21 mm Hg was present in 18.4% of blacks and 4.6% of whites. The prevalence of POAG in the black population was 7% and the odds of having IOP greater than 21 mm Hg was 5 times higher in this group. Conversely, examination of 2,773 Australian aborigines revealed no case of POAG.[81] The **Health and Nutrition Examination Survey** of 1971 to 1974 also found that black Americans had slightly higher IOPs than their white counterparts.[82] Mean IOPs of all groups increased with age, and there was positive correlation with systemic blood pressure.

A **family history** of glaucoma should always raise a red flag. Such a history may be found in 13 to 25% of glaucoma patients.[84] Both autosomal recessive and dominant transmission may be involved. Miller [85] examined 75 immediate descendents of patients with POAG between the ages of 15 and 60 years and performed tonography together with careful evaluation for glaucoma. The results showed that 8% had definitive POAG, 36% had suspicious outflow value, and 56% had no evidence of glaucoma. The average ages of the three groups were 48.5, 39.6, and 32.5 years, respectively. More recently in the Baltimore Eye Survey, the investigators calculated relative risk for developing glaucoma for a person with a sibling diagnosed with POAG to be 3.7-fold.[86]

Perfusion pressure is the difference between arterial pressure and venous pressure. IOP raises venous pressure at the exit point of the eye and thus affects intraocular blood flow. Decreased intraocular blood flow lowers perfusion pressure. Even normal IOP has an impact on the perfusion pressure, because it exceeds orbital venous pressure. Similarly, IOP induced ischemia can result from impaired autoregulation in a patient because of vasospastic disease, atherosclerosis, platelet or clotting abnormalities, and systemic hypertension.[87]

There is a well-known association of both **systemic hypertension** and **hypotension** in patients with glaucoma.[87-90] Many patients with POAG and normal-tension glaucoma exhibit elevated blood pressure.[91,92] Similarly, low

systemic blood pressure is also a risk factor in glaucoma.[88,93] It is believed that chronic hypertension may cause ischemia and low systemic blood pressure may reduce local perfusion of the optic nerve head, especially when the eye has elevated IOP or poor **autoregulation.**[94] Equally important is to understand the effect of physiologic nocturnal hypotension on the progression of glaucomatous field loss. Patients who exhibit greater nocturnal hypotension tend to show progressive field loss even at well-controlled IOP.[37]

There is a close association between glaucoma and **diabetes mellitus.**[95] Clinically, diabetic patients show an almost three-fold increase in the prevalence of POAG, elevated IOP, increased IOP response to topical steroids, and large **cup-to-disc (C/D) ratios** as compared to non-diabetic individuals. The prevalence rate of diabetes in patients with glaucoma is reported to be 6% to 11%. On the other hand, glaucoma may provide a beneficial effect on the incidence of proliferative diabetic retinopathy. Patients with POAG and individuals exhibiting exaggerated IOP response to steroids both show increased prevalence of diabetes mellitus and positive glucose tolerance test. It is important to remember that both glaucoma and diabetes mellitus lead to blindness if undetected and untreated early on. Other common associated features of diabetes mellitus and POAG are hereditary components, tendency to produce eye damage over time, an asymptomatic nature, and the possibility of early detection.

Gender may be important, as some studies have found ocular hypertension more frequent in females and POAG more in males.[89,96] **Myopia** may coexist in 3% to 18% of patients with glaucoma.[97] The association between high myopia (>10 diopters [D]) and glaucoma is particularly significant ($p < 0.001$). Some of the high myopia-related factors implicated in the development of glaucoma are a structurally weak optic nerve in myopia, impaired **aqueous outflow**, choroidal vascular changes, strong familial tendency, and angle malformation. The **Blue Mountain Eye Study**, carried out in an Australian white community, found that glaucoma was associated with 4.2% of eyes with low myopia (≥ -1.0 D to <-3.0 D) and 4.4% of eyes with moderate to high myopia (≥ -3.0 D) compared to 1.5% of eyes with no myopia.[98] This two- to threefold risk of glaucoma in myopic subjects was maintained even when other risk factors and IOP were excluded.

Thyroid disorders are frequently associated with glaucoma. Cockerham and associates[99] reviewed charts of 500 patients with thyroid-associated orbitopathy and found that 125 (25%) had IOP greater than 22 mm Hg but less than 30 mm Hg. Of this group, 2% developed glaucomatous field defects over a follow-up period of 48 months. Several factors may cause raised IOP in patients with thyroid disorders, such as increased episcleral venous pressure secondary to orbital congestion, excessive mucopolysaccharide deposition in the **trabecular meshwork**, a direct thyrotoxic effect, or a genetic predisposition to glaucoma.

The **Collaborative Glaucoma Study**[69] conducted between 1960 and 1973 was a prospective study that examined 5,000 subjects in five centers for risk factors that may influence the development of POAG-like visual field defects. Such defects were seen in 1.7% of the eyes. But during a period of five years, 98.54% of eyes with initial pressure of less than 20 mm Hg showed no glaucoma-like VF defects compared to 93.34% of eyes with pressures greater than 20 mm Hg. Significant variables relating to glaucomatous VF defects were: reduced **outflow facility** (C-value 0.186 vs 0.250), age (54.56 vs 44.13 years), IOP (19.83 vs 16.74 mm Hg), C/D ratio (0.33 vs 0.24) and pressure increase after water drinking (2.72 vs 1.43 mm Hg). The authors stressed the multifactorial nature of glaucoma.

Use of **corticosteroids** may increase the risk of glaucoma by raising IOP when administered exogenously and in certain conditions of increased endogenous production, such as Cushing's syndrome.[100,101] Approximately 18% to 36% of the general population are corticosteroid responders. Patients over 40 years of age and with certain systemic diseases such as diabetes mellitus, high myopia as well as relatives of patients with POAG are more vulnerable to corticosteroid-induced glaucoma. Elevation of IOP following the use of steroids depends on the specific drug dose, frequency of administration and steroid responsiveness of the patient.

Certain vasospastic conditions such as **migraine** may be associated with POAG or normal tension glaucoma. A prospective study found that 28% of patients with normal tension glaucoma had migraine while 10% with high tension glaucoma had the condition.[102] Blunt **ocular trauma**, however trivial, may result in angle recession and ultimate elevated IOP.[103] This condition needs to be carefully excluded in unilateral glaucoma cases.

Role of immunological factors in POAG

Several immunologically based diseases such as rheumatoid arthritis, thyroid disturbances, migraine and Raynaud's phenomenon are seen in patients with POAG. Wax and co-workers[104] have found serum **antibodies to retinal proteins** and **retinal immunoglobulin** deposition in an eye with glaucoma. Similarly, an immunologic basis of glaucoma was also suggested by David and co-workers,[105] who found an association of human leukocyte antigen **HLA-DR3** allele in Caucasian patients with glaucoma. But a Spanish study found a frequency of **HLA-DQA1** alleles similar in both patients with POAG and the controls.[106] However, the study showed the association of POAG with other genetic markers such as acid phosphatase ACP*C alleles located at the chromosome 2p23. Recently Gil-Carrasco and associates[107] detected haplotype **HLA-DRB1* 0407-DQB1*0302** among Mexican Mestizo patients with POAG. They suggested that this haplotype with the disease may be the result of linkage disequilibrium or the influence of a neighboring gene.

Influence of social and/or economic factors on the development of POAG

Apart from **black** race, no socioeconomic, educational, or occupational factor appears to have any significant effect on the prevalence of POAG. Once the disease is established, all the aforementioned factors become crucial depending on the patient's ability to pay for the doctor visits and medications, access to health care, and understanding of the disease process.

Genetic considerations in POAG

There is a strong familial association in POAG.[108] The disease does not appear to follow any set familiar pattern, but a history of POAG in close relatives is much more significant than in distant relatives. Paterson[109] examined 50 siblings of patients with POAG and detected the disease in 8%. Out of 125 patients suffering from POAG, Biró [110] found that 16 (12.8%) were **hereditary** in nature.

The discovery of defective **genes** is an important milestone in the pursuit of early diagnosis and cure. It is essential to understand the genetic nomenclature of glaucoma in order to follow the recent advances and discoveries. To simplify the matter, glaucomas have been classified into POAG, primary closed-angle glaucoma, and congenital glaucoma. The corresponding prefixes for glaucoma loci are **GLC1, GLC2, and GLC3.** As new loci are discovered they are given an alphabetical letter after the GLC prefix. The first two genetic loci discovered for POAG were named **GLC1A** and **GLC1B.** Of the current eight genes or genetic regions assigned to GLC nomenclature, six relate to POAG, GLC1A-F, and two to congenital glaucoma, namely GLC3A-B. In 1993, Sheffield et al[111] mapped the GLC1A region to chromosome 1q21-q31 and the group later narrowed the region to a 3 cM region between the markers D1S3665 and D1S3664 in juvenile open-angle glaucoma patients. The mutated gene was identified as myocilin by Stone et al[112] in 1997. Escribano et al[113] had earlier isolated myocilin or **trabecular meshwork-induced glucocorticoid response protein (TIGR)** from the ocular ciliary body. The TIGR gene is made up of three exons and is capable of encoding a 501 amino acid chain protein. The third exon has been identified as the site of all glaucoma- related mutations. Yokoe and Anholt[114] found that the amino acid sequence encoded by the third exon was homologous to the frog olfactomedin gene and may form multimers. Wirtz and co-workers[115] were successful in mapping a sixth gene for POAG - GLC1F to 7q35-q36 in a family with a strong family history of glaucoma.

Community-based screening for POAG

The detection and diagnosis of POAG in population-based studies is not easy. Screening surveys that do not include **applanation tonometry**, dilated fundus evaluation, and automated visual field examination are apt to miss significant numbers of patients. The value of IOP measurement may vary according to the time of the day as both intraday and interday fluctuations are well recognized.[116] Approximately one-sixth of all POAG patients may show IOP levels below 22 mm Hg consistently during population-based studies.[64] At a single screening, almost one-third to one-half of the patients with POAG may show pressures below 22 mm

Hg.[117] On the other hand, not all patients with high pressures have glaucoma or will develop glaucomatous optic nerve damage.[64] **Optic disc** examination by direct ophthalmoscopy also has interobserver and intraobserver variations.[118] VF testing, though very useful, has its own drawbacks, such as time required for testing and short-term or long-term fluctuations. At a public glaucoma screening, Yamada et al[119] found **frequency-doubling technology perimetry** superior to Damato campimetry. The former targets larger optic nerve fibers in the magnocellular pathway, which are selectively affected in early glaucoma.[8] Glaucoma screenings in general are quite useful, but cumbersome and time consuming. It is now recommended that it would be more economical to target at-risk populations, such as subjects over 40 years of age, African-Americans and the elderly.

Prevalence of blindness in patients with POAG

In the United States there is no central agency for blindness registration. A 1970 study involving data from 16 states estimated legal blindness from glaucoma to be 16.2 cases per 100,000 population.[120] Glaucoma was the second single cause of blindness prevalence and also the second cause of blindness incidence. During 1969-1970 the annual incidence of registration for glaucoma blindness was 1.5 per 100,000 persons representing approximately 10% of all new registrations. Most experts believe that these data underestimate the real problem by 2 to 3-fold because of underreporting of blindness in the country. Glaucoma is the second most common cause of legal blindness in the United States and among African Americans it is the leading cause.[62] In 1996, approximately 80,000 Americans were legally blind from glaucoma.[39] Blindness from glaucoma is 4 to 8 times more common in African Americans than in Caucasian Americans.[67]

Knowledge about POAG in the general population

The knowledge about glaucoma is quite scanty in the general population. In Germany, Pfeiffer and Krieglstein[121] surveyed 2,600 men and women over the age of 14 years. Only 30.0% of the subjects had heard about glaucoma. The awareness was greater in individuals who wore glasses or contact lenses (44.0%).

The symptoms believed to be associated with glaucoma were blurred vision (39.0%), pain (28.0%), and difficulty in reading (22.0%). Approximately 11.0% knew that there were few subjective symptoms in glaucoma, while 29.0% thought they would be able to feel elevated IOP. Two factors responsible for poor vision were believed to be excessive reading (16.0%) and smoking (11.0%). Therapeutic measures mentioned for glaucoma included surgery (63.0%), laser treatment (26.0%), and medications (23.0%). The sources of glaucoma information were friends (44.0%), doctors (13.0%), and opticians (2.0%). There was little correlation between knowledge of glaucoma and a person's education, profession, and income.

Effect of POAG on the life expectancy of patients

Several studies have looked at the question of adverse effects of glaucoma on life expectancy of persons with glaucoma.[122,123] Hiller and associates[124] used data from the Framingham Eye Study and the **Framingham Heart Study** to see if raised IOP or a history of treatment for glaucoma is associated with decreased survival. They divided patients into 3 groups: low pressure ($\leq$ 20 mm Hg), medium pressure (20 – 24 mm Hg), and high pressure ($\geq$ 25 mm Hg). The death ratio for the group with medium IOP relative to the group with low pressure was 1.04. The group with high pressure had a corresponding death ratio of 1.56. The data suggested that high IOP or presence of glaucoma is a marker for decreased life expectancy.

Future Glaucoma Research

There is an acute need for ways to diagnose glaucoma early and to provide neuroprotection to healthy as well as injured ganglion cells. Genetic testing for defective genes opens a new avenue toward early diagnosis and possible therapy. Borrás and associates[125] have demonstrated transfer of genes to the trabecular meshwork and expression of recombinant proteins in rabbits after injection of replication-deficient adenovirus vectors into the anterior chamber. Similarly, Kaufman and co-workers[126] used a herpes viral vector (ribonucleotide reductase defective HSV-1, hrR31) to deliver the lacZ reporter gene to living cat and rat eyes.

A device that can measure IOP continuously without the patient having to visit a physician would also answer the difficult question of diurnal variation. Accordingly, medical therapy might be altered to address IOP fluctuations during the course of the day.

The field of **neuroprotection** has opened exciting possibilities. Current research is focusing on determining relevant mechanisms involved in retinal ganglion cell degeneration by studying cellular changes in the optic nerve and retina. The ultimate aim is to prevent retinal ganglion cell loss. Neufeld and associates[127] have demonstrated inducible nitric oxide synthase (NOS-2) in the optic nerve heads from human glaucomatous eyes and from rat eyes with chronic, moderately elevated pressure. They treated rats with unilateral elevated pressure with **aminoguanidine**, an inhibitor of NOS-2 for 6 months and compared that to an untreated group. At the end of the study the untreated group showed pallor and cupping; whereas, the treated group appeared normal. When they calculated retinal ganglion cell loss by labeling with Fluoro-Gold, the cell loss in the treated group was 10% compared to 36% in the other group. The investigators believe that excessive nitric oxide released by reactive astrocytes stimulates the production of peroxynitrite, which is toxic to the axons of retinal ganglion cells at the level of lamina cribrosa. This epic finding opens new doors for designing neuroprotective agents in the near future. Drugs that block excitotoxic ganglion cell loss or those that bar NOS, such as arginine analogues, may have a role in the treatment of glaucoma. **Memantine**, which blocks excessive or pathologic NMDA receptor-linked ion channel activity but relatively sparse normal or physiologic activity is being tried in clinical glaucoma trials in the United States as a potential neuroprotective agent.[128,129] It is already used for the treatment of dementia and Parkinson's disease.

Critical Analysis of studies on visual function loss in POAG

Several studies have attempted to understand risk factors for progression of glaucoma or blindness from glaucoma. The chief features and findings of the studies discussed here are presented in Table 2. As one scans through the studies, the multifactorial nature of POAG becomes very obvious. The major factors,

which have been implicated repeatedly, are: elevated IOP, large diurnal variations in IOP, poor control of IOP, non-compliance, older age, advanced VF damage at diagnosis, poor ocular perfusion pressure, black race, longer duration of the disease, and frequent disc hemorrhages. A brief critical analysis of each study follows.

Oliver JE, et al in a retrospective, community based, longitudinal study, analyzed data of 290 patients who were diagnosed with glaucoma between 1965 and 1980 in Olmsted County, Minnesota.[130] Features of patients who became legally blind in at least one eye (compared to those who did not) were: moderate to severe VF loss at the time of diagnosis, variability of IOP, and more susceptibilities to IOP.

In a multicenter, retrospective trial, Stewart et al followed 218 patients with POAG for at least five years, to look for signs of progression.[131] They found that 15.6% of patients progressed on the basis of disc cupping and VF deterioration. The mean IOP in the progressed group was 19.5 ± 3.8 mmHg, compared to 17.2 ± 3.1 mmHg in the stable group ($p = .001$). The average standard deviation of individual IOP was also greater in the progressed group: 5.1 mmHg vs 3.9 mmHg ($p = 0.012$). Levels of IOP had a significant influence on the disease progression: at levels of ≤ 12 mmHg, no patient progressed, at ≤ 17 mmHg, 6% of patients progressed, at ≥ 18 mmHg, 26% of patients progressed, while at ≥ 21 mmHg, 32% progressed. More patients who progressed required trabeculectomy (21% vs 8%) and they needed more medications, were older, had a large C/D ratio (0.9 to 1.0), and showed worse visual acuity than those in the stable group. Lower IOP was beneficial to the patient's visual status, but did not prevent progression in all patients. ALT was needed equally by both groups. The effect of race, gender, eye laterality, mean deviation and pattern standard deviation of VFs, or medical history was not significant. The IOP of the at-risk group, [larger C/D (0.9 to 1.0), older (>75 years), visual acuity worse than 20/30, or taking 2 or more glaucoma medications] did not differ significantly from the composite study population.

The **Advanced Glaucoma Intervention Study (AGIS)** investigated the association between control of IOP after surgery and VF progression.[132] They

followed 591 patients (789 eyes from 11 participating centers) over seven years. Patients on maximally tolerated medical therapy were assigned to two surgical protocols: 1) ALT–trabeculectomy–trabeculectomy or 2) trabeculectomy–ALT–trabeculectomy. The goal was to reduce IOP to <18 mmHg. The data was analyzed from two perspectives. In the **Predictive Analysis**, patients were grouped into 3 categories: a) IOP less than 14 mmHg, b) IOP between 14 and 17.5 mmHg, and c) IOP greater than 17.5 mmHg in the first 18 months of the study. The objective was to determine if early IOP levels have any effect on subsequent VF deterioration. The second analysis termed Associative Analysis grouped patients into 4 groups (A-D) in terms of percentage of times an individual patient presented with IOP less than 18 mmHg during follow- visits over 6 years: 100%, 75 to <100%, 50 to <75%, and 0 to <50%.

The Predictive Analysis study showed that patients with IOP greater than 17.5 mmHg had a higher prevalence of diabetes, higher mean IOP, a lower mean reference VF defect score, and a lower mean age than those in the other groups. Patients in the three groups maintained their distinctive ranking over the follow-up period.

By **Associative Analysis**, eyes with IOP less than 18 mmHg at each visit (100%) over six years showed no change in VF defect score, while for other groups, VF defects worsened over time. The investigators concluded that low IOP is beneficial for preserving VF over time. But a proportion of eyes still developed VF loss, stressing the interplay of factors other than pure IOP.

Quigley and Maumenee described their experience of following a select group of 16 eyes of 10 patients for a mean of 17 years (range 8 to 42 years).[133] The average IOP was kept below 20 mmHg with medical or surgical therapy. Eight (50%) eyes required cataract extraction. Thirteen (81.2%) retained their initial visual acuity of 20/40 or better. All patients were referred from other physicians, so there was no information on the initial presenting data. When first seen by the authors, even with treatment, IOPs were in the range of 26 to 52 mmHg (mean 34 ± 7 SD). They were successful in reducing IOPs by 59%, or a decrease of approximately 20 mmHg. The mean IOP during follow-up was 14 mmHg. Only 2 (12.5%) eyes experienced worsening of the VF status. All patients except one

(10%) required filtering procedures. The weakness of the study includes selection of only well-controlled patients, and lack of patient demographic information, such as race, ocular and systemic risk factors. But the authors have stressed the possible role of diurnal variations of IOP in further deterioration of visual function.

Kolker described his experience of the relative risks of medical and surgical treatments to the central vision in patients with advanced open-angle glaucoma.[134] He selected 76 patients (101 eyes) (40 male, 36 female, 58 white, 18 black, average age 60.1 years, average follow-up 7.1 years) with advanced VF loss and no prior glaucoma surgery. This VF defect was defined as loss extended within 5° of fixation. If the defect crossed the point of fixation, it was termed "split" (54 eyes); otherwise called "spared" (47 eyes). Loss of central vision, defined as visual acuity of $\leq$ 20/200, occurred in 18 (17.8%) of 101 eyes. Twelve eyes were treated medically, while six had glaucoma surgical procedures. Loss of central vision occurred in 12 (22%) eyes in the "split" group and 6 (13%) eyes of the "spared" group. A patient with **split fixation** had twice the risk of losing central vision, compared to a patient with spared fixation. All patients with spared fixation who lost central vision first developed split fixation. No patients lost central vision after surgery if the fixation was spared.

Of the 76 eyes treated medically for glaucoma, 12 (15.8%) developed loss of central vision over 4 years of follow-up. Eyes that lost central vision had higher IOP, 12.1 ± 4.1 mmHg vs 19.2 ± 2.7 mmHg in eyes that maintained central vision ($p < 0.05$). In eyes that maintained IOP of < 18 mmHg, the loss of central vision was 4%, compared to 29% in eyes with average IOP > 22 mmHg. After excluding 10 eyes because of cataract, 32 (59.3%) of the remaining medically treated eyes demonstrated progression. Nineteen patients (22 eyes) underwent various incisional glaucoma procedures for control of IOP. Three eyes (13.6%) lost central vision and two other eyes (10.5%) had further progressive VF loss.

In order to understand the causes of blindness in glaucoma patients, Spaeth did complete eye exams, including fluorescein angiography on 117 individuals (33 POAG, 23 glaucoma suspects, 26 low-tension glaucoma, 10 secondary glaucoma and 25 normals).[135] POAG patients showed prolonged arm-choroid, arm-retina

and retinal artery transit time compared to others. The dye also appeared at least two seconds earlier in the central retinal vessels than in the choroidal vessels. These features appeared to be related to raised IOP and insufficient choroidal circulation in patients with POAG. The author suggested that abnormal choroidal circulation affected the intricate blood supply of the optic nerve in the laminar and prelaminar area. He proposed that patients with POAG had compromised choroidal circulation that was made worse by elevated IOP. Ultimately, ischemia and related events damaged the tissues supplied by these compromised vessels. He also stressed sociologic factors, such as late detection of glaucoma and non-compliance. Almost 80% of patients seeking help for the first time at the Wills Eye Hospital had prior visual loss. Another 10% lost vision due to non-compliance. Ninety-three percent of glaucoma patients followed at Wills Eye Hospital could not obtain driver's licenses because of their vision being less than 20/40.

Reese and McGavic investigated the relationship of systemic blood pressure, IOP and amount of VF damage in patients with POAG.[136] They examined 132 cases with POAG and determined the percent of VF still retained. They calculated systolic coefficient by dividing mean systolic pressure by IOP and diastolic coefficient by dividing mean diastolic pressure by IOP. Eyes with 100–70% remaining field had a mean systolic coefficient of 5.65, and a mean diastolic coefficient of 3.21. Eyes with 70–35% retained field showed mean systolic coefficient of 4.61 and a mean diastolic coefficient of 2.28. Thus they were able to construct a convincing relationship, but the weaknesses of the study included possible effects of glaucoma treatment on the measurements, and lack of adjustment for wide variability of blood pressure and IOP values.

Patients with POAG who present with unilateral VF defect were the focus of interest for Harbin and co-workers.[137] They followed 21 such patients (14, male, 7 female, 11 white, 10 black, mean age 60 years), for two to seven years. Non-affected eyes of all patients showed IOP > 24 mmHg on some occasions and 17 (80.9%) had C/D ratio greater than 0.3 on initial exam. Nine (42.8%) patients had IOP > 4 mmHg in the affected eye as compared to the fellow eye. Eleven (52.4%) patients had symmetric IOP on first examination. One (4.8%) had IOP greater in

the fellow non-affected eye. Twelve (57.1%) patients had C/D ratio larger than at least 0.2 disc diameters in the damaged eye. In the rest, C/D ratio was similar. Nine (43%) patients demonstrated field loss in the non-affected eye during the follow-up period. IOP control was similar in both eyes. Other parameters such as diabetes, hypotensive episodes, race, age, length of follow-up, outflow facility, diurnal pressure range, and treatment were not significant. The presenting eyes of 16 (76.2%) patients experienced further field loss. Asymmetrical IOP control could explain this discrepancy in only 5 patients. The authors concluded that eyes with existing field loss are more prone to further damage at pressure levels that may be similar in both eyes.

In an attempt to evaluate the contribution of various factors on the progression of VF damage in normal-tension glaucoma, Araie and co-workers studied 56 patients with early stage disease.[138] They found that IOP, C/D ratio and peripapillary atrophy have positive influence on the progression of field defects in their patients.

The importance of IOP as a risk factor for optic nerve damage and visual loss was emphasized by Anderson.[138A] He also stressed equally important factors such as sensitivity of the optic nerve and rate of damage.

The rate of change of VF threshold values over time by trend analysis was studied by O'Brien and associates.[7] They followed 40 eyes of 40 patients with POAG (23 male, 17 female, 30 white, 10 black, mean IOP 16.7 ± 2.4 mmHg) for 44.9 ± 17.4 months. VF deterioration was observed in 10 (25%) while 28 (70%) remained stable and 2 (5%) showed improvement. The superonasal portion of the VF experienced the greatest loss and correlated well with standard error of the mean and the range of IOP level. The group experiencing loss had a higher mean VF threshold value and significantly less optic disc pallor and cupping at the beginning of the study than the others. The rate of loss for the whole group was -0.029 ± 0.075 dB/month while for the group showing progression was -0.116 ± 0.065 dB/month. The roles of various factors such as age, sex, race, family history of glaucoma, follow-up time, diabetes, systemic blood pressure, refractive error, initial or final visual acuity, frequency of disc hemorrhage, were not significant.

In order to understand the relationship between ocular perfusion pressure and retrobulbar blood flow in POAG patients with progressive damage, Ghergel and co-investigators used color Doppler imaging.[139] They examined 20 patients with POAG with VF deterioration in spite of IOP less than 21 mmHg. The two control groups were age-matched POAG patients with stable fields and age-matched healthy individuals. Patients with POAG had a lower mean ocular perfusion pressure ($p<0.0045$). Patients with progressive damage showed a lower mean blood pressure ($p = 0.033$) and a lower end diastolic velocity in the central retinal artery ($p = 0.0093$) compared with normals. The authors emphasized possible lack of autoregulation or vascular dysregulation in patients with progressive glaucomatous damage.

Risk factors for the development of VF defects in ocular hypertension were studied by Quigley and co-workers in 647 individuals.[75] Defects were seen in 68 (10.5%) persons. The main risk factors were moderate to severe nerve fiber layer atrophy at baseline. These factors increased the risk of development of VF loss by seven to eight times. Other significant factors were older age, large C/D ratio, smaller rim-disc area ratio, large cup asymmetry, presence of disc crescent, and higher IOP.

The importance of circulatory insufficiency and decreased blood flow in the optic nerve was stressed by Harrington.[92] He found that patients who showed the most extensive and rapid VF loss had generalized arteriosclerosis, low systemic and retinal arterial blood pressure, and increased IOP. Therefore, the delicate balance between arterial pressure in the arterioles of the optic nerve and IOP is essential for preventing ischemia and development of VF loss seen in glaucoma. Sudden reduction of systemic blood pressure resulted in rapid deterioration of VFs. The weakness of the study is that only six patients were studied.

By using discriminate analysis of various ocular, systemic and laboratory variables, Drance and associates were able to identify patients with glaucomatous VF defects.[140] The most significant variables were disc rim abnormalities, C/D ratio, family history of glaucoma, disc hemorrhage, coronary disease, and prior hemodynamic crisis.

Wilson and co-investigators studied risk factors for rate of progression of glaucomatous VF loss in 57 patients with POAG [6] and showing some degree of VF loss. Progression was defined as deterioration of VF by at least 30% from baseline. Patients with pre-existing field loss developed further loss at a faster pace. Other significant factors were family history of glaucoma, female gender, and initial IOP, but age and systemic blood pressure did not affect rate of VF loss.

A review of 750 cases of legal blindness from the Massachusetts Eye and Ear Infirmary showed that 93 (12.4%) were bilaterally blind from glaucoma, while 28 (3.7%) had blindness in one eye.[141] A third of patients who were legally blind from glaucoma presented with blindness on their initial visit to obtain help. Other investigators also had similar experiences.[142,143] There was a preponderance of black patients with a diagnosis of glaucoma and legal blindness. Black patients became blind at a younger age (67.7 years) as compared to white patients (73.7 years). The level of IOP before treatment was similar in both races. Noncompliance to treatment was noted in 39% of white patients and 46% of black patients. An analysis of glaucoma patients with and without legal blindness showed that patients who presented with cupping and field loss were more likely to develop blindness and sooner than those patients who had cupping alone. A comparison of patients with IOP > 24 mmHg, abnormal cupping but normal VF showed that patients who did not lose VF had lower tension than the group that did develop field defects. Patients who had glaucomatous VF defects whether superiorly or inferiorly continued to lose vision over 10 to 20 years, even after their tensions were reduced to mid 20s or high teens. When patients developed field defects, both above and below, they showed further loss within five years, even with controlled tensions.

In an attempt to identify basic characteristics of patients who present with late glaucoma, Fraser and co-workers reviewed the medical records of 100 patients with POAG and 100 control subjects.[144] Patients of African Caribbean origin were over four times more likely to present late than comparable white patients [R: 4.55, 95% CL (1.57, 13-18)]. Females were one-third as likely to attend late [0.34, [0.15, 0.74)], patients referred by any other source than then optometrist with the correct diagnosis were four times more likely to be late [4.32

(1.89, 9.88)], older patients were more likely to present late [1.68 (1.22, 2.20)], and patients with IOP in the 21-25 mmHg range were less likely to present early as compared to patients with IOP >31 mmHg [0.24, (0.09, 0.04)].

The influence of race in POAG was investigated by Martin and co-workers by chart review of 140 patients with POAG in Baltimore.[71] The study patients were selected from the Wilmer Clinic and the local Veterans Affairs Hospital. Twenty-five (17.6%) were white and 115 (81.6%) were black. Initial IOP in the right eyes of new black patients was 29.9 mmHg vs 25.8 mmHg in white patients ($p = 0.056$). Inter-eye IOP difference was greater in blacks (4.4 vs 3.8 mmHg; $p = 0.67$). Blacks also had a greater C/D ratio ($p = 0.002$) and more C/D ratios of >0.5 disc diameter ($p = 0.03$). Advanced VF damage was noted in 33.3% of blacks vs 18.5% of whites; $p = 0.20$. Similarly, blacks had more arcuate scotomas and nasal steps versus paracentral scotomas. POAG was diagnosed earlier in blacks 63.7 years vs 69.1 years in whites ($p = 0.006$). The investigators also found that utilization of health facilities was similar in both races and there was no age-related influence on the level of IOP at diagnosis. The weakness of the study included incomplete findings in many patients, no comparative data from private patient clinics, no other know ocular or systemic risk factors evaluated, exclusion criteria were not defined, lack of information on comparability of controls and protocol was not described. The number of patients, concurrent controls and data analysis were satisfactory.

To study the influence of IOP on visual fields, Crick and associates examined 929 patients with POAG or ocular hypertension over one to 13 years at King's College Hospital, London.[145] They found that both groups showed uniform depression of the whole field with time, and this change was pressure-related. The study failed to address exclusion criteria, measurements of other risk factors and demographic characteristics of the patients.

A prospective **discriminant analysis** of several factors was carried out by Drance and co-investigators to evaluate the predictive value for subsequent development of VF defects.[146] This was performed on 165 patients with elevated IOP and followed for five years. The second part of the study involving 146 patients was to examine discriminant function that produced the best separation

of those in whom VF defects developed from those who did not change over a period of five years. The analysis for the latter study was done with three different IOP levels: maximal IOP recorded, mean IOP and logarithm of the standard deviation of all IOP measurements on a given person. The sensitivity and specificity of the discriminant analysis in the first part of the study (165 patients) was 79% and 74% respectively. VF defects had appeared in 38 (23.0%) patients. For the second part of the study (146 patients) 34 variables were used to identify risk factors and their coefficients to separate the two samples. But only five risk factors yielded a correct separation of 79%. The sensitivity and specificity were 71% and 81%, respectively. The five determinants in order of their significance were: horizontal C/D ratio, logarithm SD of IOP, disc hemorrhage, coronary disease and family history of stroke. By including IOP, the predictive value was improved to 74% and 77% separation. In this study, the exclusion criteria and means to minimize bias were not described.

The rate of VF loss in 151 patients (112 black) was estimated from VF data obtained by Goldmann perimetry in the Baltimore Eye Survey.[147] The investigators used regression analysis to compare VF scores with age, vertical C/D ratio, treatment status, gender, race, and IOP. In black subjects, severity of VF damage was significantly associated with age ($p < 0.02$), history of glaucoma treatment ($p < 0.04$) and IOP ($p < 0.0001$). The weakness of the study was that there was a lack of white patients.

A case-finding study in central Sweden found 128 cases of POAG with VF defects.[58] Risk factors for advanced VF defects were: old age, long duration of the disease, higher mean initial IOP, and more extensive damage at the time of diagnosis. Risk of having advanced VF defect was 8-6 times greater if the initial IOP was >35 mmHg. Similarly, a patient with extensive damage at diagnosis (Bjerrum scotoma with nasal breakthrough) had 14 times greater chance of developing advanced VF defects.

A long-term (11.2 years) follow-up of 258 patients with glaucoma found 45 (17.4%) cases of blindness in Leicester, England.[148] The main risk factors were: severity of VF loss at diagnosis in the better eye ($p < 0.006$), mean IOP in the

better eye during follow-up ($p < 0.004$), extent of VF loss in the worst eye at diagnosis ($p < 0.02$), and patient's higher socio-economic class ($p < 0.03$).

In 1960, Chandler PA reviewed 20 patients with POAG retrospectively, and looked for risk factors for progression.[149] About half of the patients had surgical intervention. Major risk factors were advanced damage and cupping at presentation and wide fluctuations of IOP.

A retrospective study on 31 patients with bilateral POAG but unilateral glaucomatous VF loss was conducted by Kass et al.[150] The follow-up was from 3 years to 7 years. Twenty-nine percent of the fellow eyes developed VF changes. Initial IOP greater than 26 mmHg was associated with higher rates of development of VF loss. Similarly, on follow-up, if IOP exceeded 24 mmHg on more than 50% of the measurements, 65% of fellow eyes developed VF changes.

The role of IOP reduction after trabeculectomy was studied retrospectively in 20 patients (24 eyes) with POAG.[151] Trabeculectomy was successful in preventing progression in 14 eyes. The mean variance of all postop pressures in patients who did not progress was much better than those who progressed. However, there were no differences in the preop and postop mean IOP or the mean pressure reduction after surgery. The prevalence of progressive VF loss was significantly worse in those eyes that sometimes showed IOP greater than 21 mmHg. The weakness of the study was the small number of subjects and retrospective design.

The Collaborative Glaucoma Study prospectively followed nearly 5000 patients with POAG.[69] Significant factors associated with progression of glaucoma were age, outflow facility, IOP, C/D ratio and IOP changes after water drinking. The weakness of the study was that there was a substantial dropout rate.

Mikelberg and Drance did a retrospective study on 48 patients with POAG to evaluate the pattern of progression of VF defects.[152] Over the duration of the study (8.0 ± 3.5 years) nearly half of the patients developed new scotomas. Sixty-three percent maintained a single hemifield defect over the entire duration of the study. The scotomas became denser in 79% and 52% showed enlargement of scotomas. Longer duration of follow-up was determined to be the main risk factor for progression of VF defects.

Crichton et al retrospectively reviewed 59 patients with low tension glaucoma (LTG).[153] In eyes with unequal IOP, the VF damage was always greater on the side with higher mean IOP. But in the majority of patients, the difference was equal to or less than 1 mmHg. The authors suspected that there must be other non-IOP related factors responsible for glaucomatous damage.

The Baltimore Eye Survey evaluated the role of race in the prevalence of blindness in patients with glaucoma.[70] A detailed ophthalmic examination was performed on 5300 mixed-race neighborhood subjects in Baltimore. The prevalence of blindness in black was two-fold that of the rate in whites. Age also played a major role.

The role of IOP control in glaucomatous damage was studied by Mao et al in a retrospective manner in 55 patients with POAG.[72] These patients were followed for 4 to 11 years and had received medical therapy and laser trabeculoplasty. Those eyes with progressed uniformly had IOP greater than 21 mmHg during the follow-up period; whereas, eyes that exhibited IOP less than 17mmHg remained stable. Of those eyes that had IOP between 17 mmHg and 21 mmHg only half progressed. Another stabilizing factor was the patient's young age at diagnosis.

Factors associated with visual loss in patients with advanced glaucomatous damage were studied prospectively by Stewart et al[73] in 72 individuals. The most significant factors responsible for visual loss were higher mean and peak IOP, large standard deviation of IOP, noncompliance and history of argon laser trabeculoplasty.

A retrospective, community based study evaluated 295 patients with glaucoma, who were diagnosed between 1965 and 1980.[8] The probability of glaucoma related blindness was 27% in at least one eye after 20 years. The main weakness of the study was that all subjects were white.

A prospective study followed 113 patients with POAG for over five years.[154] Baseline VF status and peak IOP were significantly associated with progression.

A Swedish study examined 76 patients with pseudo-exfoliation glaucoma or POAG for over a two-year period.[155] Six different IOP variables were selected: IOP at start, IOP change (%), random IOP, mean IOP, peak IOP and IOP range.

The patients were treated by either ALT or pilocarpine. VF decay was more related to the range and peak of IOP and mean IOP than initial IOP or degree of IOP reduction. Elevated IOP was associated with greater VF damage with time. IOP range and mean IOP were significantly related to VF progression in capsular glaucoma but in POAG, most rapid visual decay was found in group with the lowest mean IOP. The authors emphasized that an IOP curve was preferable to single/random IOP measurements at IOP levels below 24 mmHg. If single/random IOP exceeds 24 mmHg, the value is highly correlated to mean IOP. The weaknesses of the study were 72% of patients had capsular glaucoma, a short follow-up (2 years), patients being white, and medical treatment only consisted of pilocarpine.

Hayreh et al prospectively investigated the effects of topical beta blockers on nocturnal arterial hypotension and VF deterioration in 161 patients with glaucoma and 114 patients with nonarteritic anterior ischemic optic neuropathy.[36] They concluded that topical beta blockers aggrevate nocturnal hypotension and heart rate and may stimulate VF deterioration in susceptible individuals.

A retrospective study investigated VF progression in patients with initially unilateral glaucomatous VF damage.[156] Forty-eight patients with POAG, pseudoexfoliation glaucoma or pigmentary glaucoma were included. After six years, only 6.2% of fellow eyes showed signs of progression. Twenty-one percent of the first-affected eyes progressed. The main risk factor for progression was the status of VF at initial examination.

Thirty-six patients with severe unilateral glaucomatous damage were followed for over five years by Chen and associates.[157] Significant VF deterioration was noted in 33% of the severely affected eyes and 17% of fellow eyes. The risk factors for progression in the fellow eye were larger initial C/D ratio, smaller between-eyes differences in the initial Advanced Glaucoma Interventions Study score and lower ocular perfusion pressure.

The rate of VF loss in progressive glaucoma was studied in a prospective manner in 34 patients with NTG, 68 patients with POAG, and 125 patients with OHT by Rasker et al.[158] VF progression was observed in 67% of patients with NTG, 45% of subjects with POAG and 8% of individual with OHT. The mean rate

of VF deterioration in each group respectively was 3.7%, 2.5%, and 2.3% per year. Apart from older age, neither initial VF status nor the presence of disc hemorrhage played any role in VF progression.

The Collaborative Initial Glaucoma Treatment Study (CIGITS), a randomized clinical trial, followed 607 patients with newly diagnosed POAG for over five years.[159] Nearly half were treated medically and the other half underwent trabeculectomy as an initial procedure. Both the treatment modalities resulted in similar VF outcomes. The surgery group showed greater vision loss initially, but this difference diminished after four years.

A retrospective study consisting of 40 patients with POAG was conducted by Kwan et al to evaluate long-term VF outcomes in POAG.[160] The mean follow-up was 14 years and the VF score decreased at the rate of -1.5% per year. The cumulative rate of blindness from glaucoma was 19% at 22 years. Major risk factors identified were higher IOP, greater number of antiglaucoma medications at presentation and glaucoma surgery during study period. They, however, did not exclude patients with blindness from non-glaucoma causes.

To determine the clinical factors associated with progressive optic nerve damage in glaucoma, Tezel et al retrospectively studied 93 patients with POAG and 69 subjects with normal-pressure glaucoma.[161] During the five year follow-up, 43.5% of eyes exhibited progressive optic nerve damage. Several factors at baseline were determined to be associated with progressive optic nerve damage: a smaller neural rim area - disc area ratio, larger zone β area-disc area ratio, larger parapapillary atrophy length-disc circumference ratio, and diagnosis of normal-pressure glaucoma and prior surgical treatment for glaucoma.

A long-term retrospective study examined the correlation of VF progression between eyes in 152 patients with POAG.[162] After seven years, VF progression was observed in 35.5% of the more severely affected eyes, 24.3% of the less affected eyes and 15.8% had progression in both eyes. The only significant risk factor for worse eye progression was progression in the better eye. For the better eye, a disc hemorrhage was a risk factor for progression.

In a landmark trial, the Ocular Hypertension Treatment Study (OHTS), Kass et al followed 1636 subjects with ocular hypertension prospectively for over

five years.[163] Approximately half of them were treated medically and IOP reduced by ≥ 20% from baseline. At the conclusion of the study, the cumulative probability of developing POAG was determined to be 4.4% in the treated group and 9.5% in the observation group.

Jonas et al conducted a prospective study in Germany to evaluate morphologic features of the optic disc which may predict glaucomatous damage in POAG.[164] The subjects consisted of 257 white patients (394 eyes) with POAG and were followed up for about three years. Progression on the disc was observed in 11% of patients. Small neuroretinal rim area and a large β zone of parapapillary atrophy were significantly associated with glaucomatous cupping. The main drawback of the study was in the total lack of other races.

Shin et al[165] investigated the long term results after combined cataract and glaucoma surgery (with and without mitomycin-C) in 203 patients with POAG. Fifty-nine eyes that did not receive mitomycin-C were compared with 124 eyes that did. The mitomycin-C group had better IOP control and stable VFs.

A follow-up study in St. Lucia found that nearly 50% of untreated patients with POAG or ocular hypertension had progressed in five years.[166] Old age was positively associated with progression, while gender, IOP, or baseline VF scores were not significantly associated with progression.

An Australian[167] study evaluated 438 patients with POAG and 301 subjects with ocular hypertension for risk factors responsible for progression of ocular hypertension to POAG. They concluded that older age at diagnosis, myopia, a family history of glaucoma and a high IOP were all associated with progression to POAG.

Gordon et al evaluated the results of OHTS study to understand baseline factors that may predict onset of POAG.[168] At five years of follow-up, the probability of developing POAG was 4.4% in the treated group and 9.5% in the observation group. Baseline predictive factors that were significantly associated with the development of POAG were older age, higher IOP, greater pattern standard deviation, thinner central corneal measurements and larger vertical C/D ratio. A history of diabetes was found to be significantly protective against developing POAG.

The role of IOP reduction after trabeculectomy was evaluated by Shigeeda et al in 23 patients with normal-tension glaucoma (NTG).[169] This was a retrospective, noncomparative study. Over six years of follow-up, trabeculectomy significantly slowed the progression of VF damage, but did not completely eliminate it.

The Early Manifest Glaucoma Trial (EMGT), a prospective study, randomized 255 patients with POAG to either ALT and topical betaxolol or no immediate treatment.[170] The risk for progression was halved by treatment. Each mm of Hg reduction of IOP from baseline value decreased the risk of progression by 10%. The major influencing factors were higher baseline IOP, exfoliation, bilateral disease, worse mean deviation of IOP and older age. A retrospective chart review of 186 patients diagnosed in 1975 with glaucoma was carried out between April and November, 2000.[171] Two chief causes of blindness were worse VF loss at diagnosis and non-compliance.

A prospective study by Asrani et al[172] evaluated the role of diurnal fluctuations of IOP on the progression of POAG. Sixty-four patients were taught to perform self-tonometry several times a day for a week. The diurnal IOP range and IOP range over several says were significant risk factors for progression. Patients in the upper twenty-fifth percentile IOP progressed more than those in the lower twenty-fifth percentile: 88% vs 57% over 8 years.

Objectives of the present investigation

The **primary objective** of the study was to identify significant risk factors for progression of POAG and eventual legal blindness in a cohort of patients in the Dallas metropolitan area. Progression was based on predefined criteria involving VF and optic nerve cupping (also see page 42). Progression in VF was demonstrated by reduction in the peripheral field, enlargement of scotomas or extension of the field deficit to the next level. Signs of optic nerve head progression were based on thinning of the neural rim from baseline, appearance of or deepening of notching or enlargement of C/D ratio by $\geq$0.2 disc diameters from prior exams. **Legal blindness** in North America is defined as best corrected visual acuity of 20/200 or less or a visual field less than 20 degrees at its widest in the

better eye with the Goldmann III 4e test object or its equivalent on automated perimetry (Fig. 1).[1A] Goldmann III 4e equivalent test objects are 10 mm target on the tangent screen at 1 m, size III target at threshold value of 10 dB or less on the Humphrey and size III target at 7 dB on Octopus perimeter. WHO defines blindness as visual acuity of less than 3/60 (0.05) or corresponding visual field loss in the better eye with best possible correction. Visual impairment corresponds to visual acuity of less than 6/18 (0.3) but equal to or better than 3/60 (0.05) in the better eye with best possible correction.

Various risk factors what were studied were: ocular (myopia, elevated IOP), systemic (diabetes, hypertension, vascular disease, dysthyroidism, smoking, alcohol abuse), genetic (family history of glaucoma), disease management issues (poor control, late detection, non-compliance) and socio-economic (access to healthcare, affordability of care) risk factors in POAG have a role in the progression of the disease leading to legal blindness. **Secondary aims** were to determine: (1) do socioeconomic conditions influence risk factors for POAG and (2) what are the presenting features of unilateral POAG? The role of risk factors is discussed on page 11-15.

For over a century, several convincing observations and risk factors for acquiring POAG and the damage from it have been gathered. Yet the predictive value of these factors is still unsatisfactory, suggesting yet more factors to be discovered. Only by close observation and follow-up of patients can we attempt to dismantle the multifactorial mystery of POAG. If those individuals at risk could be identified, a more aggressive therapy may prevent blindness.

PATIENTS AND METHODS

Patients with diagnosis of POAG with or without prior surgical intervention were enrolled in the study at three different institutions between January 1993 and December 1999. All the patients were seen either by me alone or by residents and fellows under my supervision. The study protocol was approved by appropriate Institutional Review Boards/Ethics Committees of the three clinics.

Clinic A is a private patient facility attached to The University of Texas Southwestern Medical Center at Dallas. It is staffed by the full-time faculty of the

Medical Center. The patients attending Clinic A have some sort of health insurance or are self-payers. They may seek health care on their own or are referred by their ophthalmologist, optometrist, or primary care physician. For the sake of this study, patients attending Clinic A were arbitrarily assumed to belong to a higher socio-economic group. As per the business office, the average annual income of Clinic A patients was $\geq$ $50,000.

The second group of patients is from **Clinic B**. This clinic is a part of Parkland Memorial Health and Hospital System, a county hospital providing health care to the inhabitants of Dallas County. It is staffed mainly by the Medical Center's ophthalmology residents under full-time supervision. The cost of health care to each patient is judged from patient's income and ability to pay. For example, individuals under the poverty line, unemployed or homeless are provided health care at no cost. Therefore, patients enrolled in Clinic B were assumed to be in a lower socio-economic group. The average income of patients in this clinic was $\leq$$12,000 per annum as per Clinic B business office.

The third facility, **Clinic C**, is the local Veterans Affairs Hospital. In the USA, the Veterans Affairs Hospitals provide free health care to the veterans of the U.S. Armed Forces. Veterans from all walks of life may be treated at these facilities provided they satisfy the prerequisites. The facility is also staffed by the Medical Center's ophthalmology residents under full-time supervision. The Veterans Affairs Hospital patients were arbitrarily considered socioeconomically to be in the middle class. The average annual income of patients at Clinic C was $\geq$$23,000 (as per Clinic C business office).

Study Design

The study was designed to be an observational prospective comparative study with no attempt to alter the current management of the patients. The various subgroups of the POAG patient population and methods of their evaluation were:

I. Patients who showed **no legal blindness (NLB)** either at the beginning of the study, nor did they develop **legal blindness (LB)** during the entire

duration of observation. NLB subgroup (control group) was compared with those patients who developed LB.

II. A subgroup of NLB patients showed progression of their disease in terms of worsening of VF or C/D ratio. They were compared with those who did not (control group). The aim was to learn about factors responsible for disease progression.

III. Patients who were legally blind in one or both eyes either before entering the study or developed the condition during the course of the study period (LB group). Of particular interest were patients who were legally blind unilaterally and presented in Dallas initially. The non-affected and affected eyes of these patients were compared. This comparison provided clues to ocular factors responsible for legal blindness as the non-affected eye acted as a control.

IV. Among the three clinics, some patients presented initially in Dallas for their care. They provided useful data in understanding the natural history of the disease in terms of initial IOP, visual acuity, status of optic nerve head and VF damage. The remainder of the patients had prior diagnosis and treatment.

V. Patients with LB in Clinic A, B, and C, were compared with each other to determine any role of socioeconomic factors.

VI. The entire population "**composite Dallas population**" was also evaluated by methods described above.

The **diagnosis of POAG** was based on: 1) signs of glaucomatous optic disc such as vertically oval cupping, disparity of cups in both eyes, neural rim thinning or notching, saucerization, nasalization of vessels or total cupping; 2) corresponding VF defects such as nasal step, paracentral or arcuate scotoma; 3) open irido-corneal angle, 4) IOP being 21 mmHg or greater. This was the acceptable definition of POAG when the study was planned.

The **exclusion criteria** were: 1) all types of secondary glaucoma, including angle recession, pigmentary glaucoma, pseudo exfoliation, or congenital glaucoma; 2) patients with less than three months of follow-up, 3) patients with eye conditions or diseases that could preclude proper ocular examination or affect

visual acuity, 4) patients with eye conditions or diseases that could produce glaucoma-like VF defects or any other type of VF changes that would impede accurate glaucoma diagnosis. Similarly, the same criterion was true if a patient developed blindness from conditions other than POAG, 5) patients with diagnosis of ocular hypertension even when they had converted to POAG as this group is being followed as part of another study; 6) patients with low-tension glaucoma; 7) patients unable to cooperate with study procedures and their inability to perform tests reliably. In 1993, low tension glaucoma was defined as an ocular condition with optic nerve and VF changes consistent with glaucoma, but IOP levels were consistently equal to or less than 21 mmHg.

Between January 1993 and December 1999, a total of 487 consecutive incoming patients were qualified: 231 in Clinic A; 98 in Clinic B; and 158 in Clinic C. The number of patients at each clinic corresponds to the amount of time spent there by me. For new patients, follow-up visits were scheduled at 1, 3, and 6 months after enrollment, and every six months thereafter. Some patients were seen more frequently, but the data was only obtained for the above-mentioned time intervals. Patients after ocular surgery were allowed to stabilize for approximately six months before resumption of their data collection. For this study, the database was closed on December 31, 1999. Those patients who were regularly followed up in the clinics before 1993 either because they were seen here initially or were referred from other sources had a retrospective review of their medical records. Any missing piece of information was noted and verified or added on their next clinic visit. Information from the medical records was transferred to patient profile forms (Fig. 2,3) and locked in a secure place.

Statistical methods

The following analyses were performed for each clinic and for all clinics combined. Primary group or subgroup comparisons were: a) legally blind versus non-legally blind, b) in unilaterally blind patients: legally blind eye versus non-legally blind eye, and c) in non-legally blind patients: group who progressed versus the group of patients who did not progress.

Categorical variables (such as gender, procedures, medications) were compared between groups with the Fisher's Exact test for 2x2 tables or assessed with Chi-square statistics for larger contingency tables. **Continuous variables** (e.g., age, C/D ratio) and some ordinal variables (vision, VFs) were compared between groups with **two-sample t-tests. Wilcoxon Rank Sum tests** were also performed if parametric assumptions were not met. For unilaterally blind patients, measurements in their legally blind eye and non-legally blind eye were compared with **paired t-tests.** First and last visits within groups were also assessed using paired t-tests. Repeated measures analysis of variance models were used to assess changes within groups and changes between groups and the interaction between group and visit. For IOP data, right and left eyes were combined in a mixed linear model with the patient as a random effect to obtain the average IOP and to adjust the standard error for correlation between eyes within a patient.[173,174] Inferences with regard to group and time and their interaction were then assessed with this model.

Data management was performed using Microsoft Access 97 & 2000 (Microsoft Corporation, Redmond, WA, USA). Statistical analysis was performed using SAS version 8.0 (SAS Institute, Cary, NC, USA). A probability value of 0.05 or less was considered statistically significant.

Glaucoma patient profile sheet with inclusive definitions (Fig 2 – 3)

This form contains 77 bits of information on each patient. The information was updated after every visit from the patient's medical chart. Shortly thereafter, data entry was completed on the computer database.

The description of the data sheet is as follows: 1) **Name of the patient** with family name or surname first; 2) **hospital number** corresponds to the number for each patient's medical record; 3) **date of birth**; 4) **gender**; 5) **Hospital** 1–3 corresponds to Clinics A–C; 6) **race** or ethnicity 1–5 correspond to white, black, Hispanic, American Indian or other races, respectively; 7) **past history of blunt ocular or facial trauma** was recorded; 8) **myopia**, any patients with refractive error of –3.00D or greater was considered a myope; 9) **diabetes**, history of diabetes mellitus was obtained; 10) **family history of glaucoma** was inquired

upon, if it was positive, 1 was designated for positive history of glaucoma in the parents, 2 for siblings, and 3 for other relatives; 11) history of **systemic hypertension** was obtained; 12) history of **systemic steroids** and 13) **topical steroids** was noted; 14) history of **dysthyroidism**; 15) history of **vascular disease** included such conditions as myocardial infarction, carotid arterial disease, myocardial ischemia, claudication, atherosclerosis, cerebrovascular disease, peripheral vascular disease, and migraine; 16) history of **alcohol abuse** (by history or on medical record); 17) history of **smoking** at least 1 pack per day (marked positive if a patient had been a smoker within the past five years); 18) history of ocular disease other than glaucoma at the initial visit was noted: 1= cataract, 2 = pseudophakia, 3 = age related macular degeneration (ARMD), 4 = others; 19) similarly, diseases developing during the follow-up period were also noted; 20) **diagnosis at the initial examination** was noted: 1 = POAG, 2 = glaucoma suspect, 3 = combined mechanism glaucoma (only POAG patients are included in this study); 21) date of diagnosis of POAG was ascertained from the patient or the medical record and duly noted; 22–24) pertain to glaucoma suspects only; 25) diagnosis in Dallas or 26) elsewhere was noted; 27) **legal blindness** in the right eye (OD) or 28) the left (OS) eye was documented. Blindness could be diagnosed at the first exam or develop during the follow-up period. 29) The definition of legal blindness (page 1) is based on visual acuity and/or VF loss. This was noted for each eye. 30) and 31) If a patient developed legal blindness from conditions other than POAG during the course of the study, this was noted, though it disqualified the patient. 32) and 33) date of diagnosis of legal blindness in OD or OS; 34-47) history of ocular surgeries was noted for each eye, e.g. cataract surgery (34,35), **argon laser trabeculoplasty (ALT)** (36,37), **laser peripheral iridotomy (LPI)** (38,39), **trabeculectomy** (40,41). Combined **cataract and trabeculectomy**. The removal of a cataractous lens was by either phacoemulsification or manual extracapsular cataract extraction (ECCE). With the former, both same-site and two-site trabeculectomy approaches were used. (42,43), other surgeries (44,45) including those pertaining to (1) setons, (2) cornea, (3) retina, (4) lids or (5) others; and cyclodestruction (46,47); 48) date first seen in Dallas, and 49) last seen in Dallas gave the duration of follow-up. 50–53) Status of **visual acuity** was noted at the first and the last visit: 1 = 20/20, 2 = 20/40, 3 =

20/60, 4 = 20/80, 5 = 20/100, 6 = 20/200, 7 = count fingers (CF), 8 = hand motion (HM), 9 = light perception (LP) and 10 = no light perception (NLP); 54–57) **vision deterioration** over the course of the study was noted. In patients who were unable to undergo VF exam or had diffusely depressed VF and total cupping, worsening visual acuity was considered a sign of progression. Causes other than POAG were designated as: 1 = cataract, 2 = age-related macular degeneration (ARMD), 3 = other. 58–61) corresponded to the **status of VF**: 1 = within normal limits (Fig. 4), 2 = relative scotoma outside 20° (Fig. 5), 3 = absolute scotoma outside 20° (Fig. 6), 4 = relative/absolute scotoma within 20° – 10° (Fig 7), 5 = relative/absolute scotoma within 10° – 5° (Fig 8), 6 = relative/absolute scotoma within 5°, 1–3 quadrants (Fig 9, Fig 9A), and 7 = relative/absolute scotoma within 5° in all quadrants (Fig 10) (automated perimetry was performed with the Humphrey Fields Analyzer (Humphrey Instruments, San Leandro, CA, USA) using program 30–2, size III white stimulus with full threshold strategy and foveal threshold test turned on. An appropriate age-related plus power lens was added to the distance refraction to obtain best corrected vision. Patients could wear their distance contact lenses. The VF examination was typically repeated yearly, but more frequently if progression or unreliability were suspected. Pupillary diameter of at least 3 mm was maintained. If a patient was unable to count fingers at 30 cm, the VF defect was recorded as 7. Criteria for **VF abnormality** were a cluster of two or more adjacent points of 5-decibels (dB) or greater loss, and by one or more points of 10 dB or greater loss from age-corrected normal reference value. 62–65) refer to the progression and worsening of VF during the study. This **progression** was demonstrated by reduction in peripheral field, enlargement of scotomas, or extension of the field defect to the next level (e.g. 2 to 3). The type of progression was reconfirmed by me and the date of occurrence was documented. Causes other than POAG were noted as 1 = cataracts, 2 = ARMD, and 3 = others. 66) **IOP** (mmHg) in each eye by Goldmann applanation tonometry at the first visit, 3 months, 6 months, and every 6 months visits thereafter were documented. The reading was rounded to the next higher integer. IOP was repeated on each patient and if there was a difference of more than 3 mmHg, a median of 2 or 3 measurements was documented. 67–72) pertain to the status of **C/D ratio** at initial and final visits and any progression during the

study. For this study, the C/D ratios were groups into 3 categories: 0.1 – 0.5; >0.5 – 0.7; and >0.7 – 1.0. Apart from an undilated optic disc examination at each visit, a dilated evaluation was done yearly by stereoscopic techniques. **Signs of progression** included thinning of the neural rim from baseline, appearance of or deepening of notching, or enlargement of C/D ratio $\geq$ 0.2 disc diameter from prior exams. The type of progression was confirmed by me and the date of occurrence was documented. 73–74) relate to **antiglaucoma medications** used by the patient: 1 = beta blockers, 2 = miotics, 3 = epinephrine class of drugs, 4 = systemic carbonic anhydrase inhibitors, 5 = topical carbonic anhydrase inhibitors, 6 = α-agonists, 7 = prostaglandin analogue, 8 = none; 75) issue of **noncompliance** is important, but there is no universal definition of noncompliance. For this study, evidence of noncompliance was obtained from various sources: patient, a close relative, documented missed appointments, refusal of treatment, or from patient's statements such as "I ran out of meds last month," "can't afford medications," "doctor did not ask me to return,"etc. Refusal for surgical intervention was also noted. 76) **poor control** related to unsatisfactory control of IOP requiring multiple medications (>2.0 meds); laser or incisional surgery, progression of C/D ratio ($\geq$ 0.2 disc diameter) or VF deterioration described above #62-65. The decision to consider usage of three or more drugs to control glaucoma as indicative of poor control is subject to criticism. The intent, however, is to warn the ophthalmologists of the danger that lies ahead for these patients. This does not mean that all patients on 3 or more drugs would progress to blindness, but a considerable number do as was noted in my pilot study. 77) **Late detection** referred to the status of vision, VF or C/D ratio at the first examination. If a patient presented with either C/D disparity of $\geq$ 0.2 or with moderate to severe VF damage in one or both eyes, this was determined to be late detection of the disease.

RESULTS

A. COMPOSITE PATIENT POPULATION IN DALLAS

Five hundred twenty-six patients qualified for the study, but 39 (7.4%) patients were dropped after enrollment because of development of conditions that interfered with proper evaluation or affected variables of interest. Out of the

remaining 487 (974 eyes) patients, 282 (57.9%) showed no legal blindness (NLB); whereas, 205 (41.1%) patients did develop or had legal blindness (LB).

I. Demographics and Characteristics of composite Dallas patient population and comparison of the three clinic patient populations (Table 3).

There were 290 (58.5%) male and 197 (40.5%) female. This gender difference is biased against the female population because Clinic C mainly consists of males; in clinic A and B, the females outnumbered males (56.7% vs 43.3% and 65.3% vs 34.7%) respectively. The racial makeup was: Caucasians 193 (39.7%), Afro-Americans 253 (51.9%), Hispanics 19 (3.9%), American Indians 1 (0.20%), and other races 21 (4.3%). In 1996, the racial composition of Texas was: Caucasians (84.7%), Afro-Americans (12.2%), Asians (2.6%), and American Indians (0.5%).[175] Persons of Hispanic origin may be of any race and that may explain their lower racial proportion of only 3.9%. In Texas, 28.8% of residents claim Hispanic roots. Dallas metropolitan area had a population of 2.9 million in 1996.[176] The racial makeup of the Dallas population was: Caucasians (73.3%), Afro-American (15.8%), American Indians (0.5%), Asians (2.5%), other races (7.9%) and Hispanics (14.0%). Based on the ethnic divisions of Texas and Dallas, Afro-Americans were disproportionately highly represented (X3-4) in the composite glaucoma population. One reason for the higher prevalence of black patients in Clinic B than the other two clinics may be economic. The U.S. national poverty rate in 1999 was 11.8%, being 9.8% for white and 23.6% for black families.[177] The racial profile of each clinic supported the study's arbitrary socio-economic divisions. The average age (years) at the diagnosis of glaucoma (mean ± SD, median, range) was 59.12 ± 12.9, 60.02, 21.1 – 90.4, while at the first visit was 63.95 ± 12.20, 65.22, 21.1 – 91.7. Similarly, the follow-up (years) was 5.5 ± 3.6, 4.5, 0.3 – 23.7. No interclinic differences were detected in terms of age at diagnosis, age at first visit, or the follow-up period.

One hundred twenty patients (24.6%) were legally blind in both eyes; whereas 85 (17.4%) were unilaterally blind.

Risk Factors

Past history of blunt ocular or facial trauma was elicited in 36 (7.4%) patients. Post-contusion glaucoma may be delayed for months or years, and is seen in approximately 2% to 10% of patients.[103] Fifty-seven (11.7%) patients had myopia and the finding correlated well with other studies.[97] Myopia was more prevalent in Clinic A patients than in Clinic B or C, $p = 0.03$. A higher level of education is strongly associated with prevalence and severity of myopia.[178] Better education, indirectly, translates into higher paying jobs and a higher socio-economic stratus. One hundred six (21.8%) patients were diabetic, with Clinic B patients showing the greatest prevalence (41.8%), $p < 0.0001$. This may be race-related, as blacks comprised the largest group in Clinic B. African-Americans have been identified with a higher prevalence of diabetes, hypertension, and cardiovascular diseases when compared with whites.[179] The diabetes prevalence rate in Dallas population was higher than the reported rate of 6% to 11% in other studies, presumably due to racial make-up, also.[95] One hundred sixty (33.2%) had a positive family history of glaucoma, the highest prevalence was 39.7% in Clinic A patients, $p = 0.005$. The prevalence rate of positive family history of glaucoma in Dallas population was also higher than the reported rate of 13% to 25%.[84] The family members affected were: parents 87 (54.4%), siblings 31 (19.4%) and other members 42 (26.2%). Two hundred forty-one (49.6%) patients had systemic hypertension, with Clinic B patients showing a prevalence rate of 59.2%, $p = 0.005$. Fifteen (3.1%) patients reported the use of systemic steroids in the past, while only 8 (1.6%) had used topical steroids. History of dysthyroidism was obtained in 27 (5.6%) patients, with Clinic A patients having a prevalence rate of 10.0%, $p < .0003$. One hundred thirty-eight (28.4%) patients gave a history of vascular disease, with Clinic C patients showing a prevalence rate of 36.3%, $p < 0.0001$. Alcohol abuse was reported by 53 (10.9%) with Clinic C patients showing a prevalence rate of 19.6%, $p < 0.0001$. One hundred twenty (24.6%) patients gave a history of smoking with Clinic C patients reporting the highest prevalence rate of 44.9%, $p < 0.0001$. US Veterans have the highest prevalence of chronic diseases among the general population.[180]

Other Ocular Diseases

Ocular diseases other than glaucoma at visit one were seen in 214 (44.0%) patients. Clinic C patients had the highest prevalence rate of 60.0%, $p < 0.0001$. These diseases were: cataract 163 (76.7%), pseudophakia 11 (4.6%), mild ARMD 2 (0.9%), and other conditions 38 (17.8%). During follow-up, another 85 (17.4%) patients showed evidence of other diseases, with Clinic C patients having the highest prevalence of 32.9%, $p < 0.0001$. These diseases were cataract in 73 (85.9%), mild ARMD in 2 (2.3%) and other diseases in 10 (11.8%), $p = 0.514$. The significance between other ocular diseases and glaucoma is not well understood, but has been previously observed.[141]

Diagnosed in Dallas

One hundred ninety-five (40.0%) patients were diagnosed initially in Dallas with Clinic B showing a larger proportion (67.3%), $p < 0.0001$. The remaining patients were diagnosed elsewhere. This large number of patients initially diagnosed in Dallas provides an excellent opportunity to study presenting features of the disease.

Ocular Surgeries

One hundred (20.5%) patients underwent cataract surgery, with 26.0% of Clinic A patients requiring this surgery, $p = 0.004$. Many patients in Clinic A are referred for a more severe form of glaucoma and accompanying diseases. These patients may also be more aggressive in demanding better vision. One hundred eighty-one (37.2%) patients needed ALT. Over 44% of Clinic C required ALT, while only 26.5% of Clinic B patients were selected for ALT. One reason for lower usage of ALT in Clinic B may be that blacks appear to exhibit higher failure rates.[181] Sixty (12.3%) patients required LPI, with 17.8% of Clinic A patients needing the surgery, p 0.001. Eighty-eight (18.1%) patients required trabeculectomy, while 57 (11.7%) needed a combined (glaucoma and cataract) procedure. Thirty (6.2%) patients also underwent other ocular procedures, such as on cornea 5 (16.7%), retina 7 (23.3%), lids 6 (20.0%) and others 12 (40.0%). Nine (1.8%) patients required cyclodestructive procedure. Overall, Clinic B patients

received fewer surgical procedures. Substantial racial disparities do exist in the use of some health services in the USA.[182] Other reasons may be physician bias and/or patient perception of the disease.

Visual Acuity

At visit 1, 345 (70.9%) patients had visual acuity between 20/20 and 20/40; whereas, 68 (14.0%) patients had visual acuity of 20/200 or less. Clinic C had the highest proportion of individuals with visual acuity equal to 20/200 or less (24.7%) compared to Clinic A (15.6%) and Clinic B (7%). At the final visit, 300 (61.6%) patients had visual acuity between 20/20 and 20/40. One hundred three (21.1%) patients had visual acuity of 20/200 or less. Over the course of the study, 35 (51.5%) more patients had their visual acuity drop to the level of legal blindness, $p = 0.004$. This trend supports the progressive nature of the disease.

Visual Acuity Deterioration

One hundred eighteen (24.2%) patients showed worsening of their visual acuity over the course of observation. Media opacities, age related changes, and disease progression were responsible.

Status of VF Defects

For description of the classification of VF defects, see Methods. Two hundred thirty-one (47.4%) patients had mild VF defects (1 and 2); whereas, 152 (31.5%) patients had severe VF defects (5 to 7) at Visit 1. At the final visit, 196 (40.3%) patients had mild VF defects (1 and 2) while 179 (36.7%) had advanced defects. VF progression was seen in 93 (19.1%) patients ($p = 0.174$). Most of the progression occurred in the moderate to severe group, as observed by other investigators.[6,137] Clinic C patients had the worst VF damage at both visits.

IOP

At visit 1, IOP mmHg (mean ± SD, range) was 23.2 ± 10.1, 2.0 – 70.0 versus 18.1 ± 3.2, 3.0 – 46.0 at final visit. IOP levels were statistically similar in all

clinics at first and last visits ($p = 0.431$), though clinically the latter pressures were lower. The wide fluctuations and rage of IOP were also impressive.

C/D Ratios

At Visit 1, 256 (52.6%) patients had C/D ratios of >0.7, while at the final visit, this group increased to 307 (63.0%). C/D ratio progression was seen in 147 (30.2%) patients, again expressing the chronic progressive nature of the disease.

Antiglaucoma Medications

The use of antiglaucoma medications was as follows: beta blockers 454 (93.2%), miotics 315 (64.7%), epinephrine 184 (37.8%); CAI systemic 128 (26.3%); CAI topical (114 (23.4%); alpha agonists 81 (16.6%) and prostaglandin analogue in 15 (3.1%). This drug usage reflects the trends and choices available during the study time. There was more use of prostaglandin analogues and alpha agonists in Clinic A patients. Formulary restrictions and cost might have been the factors in Clinics B and C.

Non-Compliance

Non-compliance with medications or recommendation for surgery was observed in 260 (53.4%) patients. The highest prevalence was in Clinic B patients (68.4%), $p = 0.002$. This coincided with the finding that fewer patients in Clinic B underwent surgical intervention, indirectly pointing to non-compliance or other socio-economic factors such as physician bias, poor patient disease perception, religious belief and/or cost involved.

Poor Control

Inadequate control of IOP, or progression of C/D ratio and VF defects were observed in 403 (82.7%) patients. No statistical differences were noted among the three clinics and reflect the progressive nature of glaucoma.

Late Detection

Late detection was noted in 443 (91.0%) patients. The highest prevalence was in Clinic B and lowest in Clinic C. Socio-economic factors may play a role in late detection. The patients in Clinic C enjoy some distinct advantages, such as free care, both acute and long term, assistance with transportation, available of physicians in all branches of medicine, and early government assistance with disability. These factors assist in early detection and prompt management of diseases.

II. Demographics and Characteristics of Composite Dallas Patient Population NLB versus LB (Table 4).

There were 282 (57.9%) NLB patients and 205 (42.1%) LB patients for a total of 487. There were fewer females than males in the LB group (32.2% vs 67.8%); the data is biased because of few female patients in Clinic C. Race played an important role, with 58.1% of black subjects in the LB group. The mean age at diagnosis was 59.3 ± 13.2, not different from NLB group, and the average follow-up was 6.1 ± 4.0 years.

Although not statistically different from the NLB group, LB patients had the following risk factors: hypertension (53.4%), family history of glaucoma (30.5%), vascular disease 30.2%), smoking (24.0%), diabetes (19.5%), alcohol abuse (13.2%), myopia (11.2%), ocular trauma (6.3%), dysthyroidism (5.4%), use of systemic steroids (4.9%) or topical steroids (2.4%).

The disease process in LB patients was difficult to manage, and they required more ALT (43.4%), trabeculectomy 29.3%), and cyclodestruction (4.4%). Their vision at visit one was also worse, with 36% recording vision $\leq$ 20/200 and only 55.4% showing vision of $\geq$ 20/40 compared to 89.4% of the NLB group. By the last visit, 40% of LB patients experienced deterioration of vision and 56% had dropped to $\leq$ 20/200.

Visual field status at visit one was as follows: mild damage (14.2%), moderate damage (23.9%) and severe damage (61.9%). At the final visit, the values were 8.3%, 20.0%, and 71.7% respectively. The progressive nature of the

disease is supported by noticing deterioration in 16.3% of NLB group and 22.9% of LB group patients.

LB patients had elevated IOP at the first visit: 24.2 ± 11.2 vs 22.1 ± 7.7 mmHg ($p = 0.03$). They showed wide fluctuation over the course of the study. The mean IOP for each patient in both groups is shown in Figure 11. Legal blindness was prevalent at all IOP levels, thus indicating patient susceptibility over a wide range of pressures. On the other hand, wide fluctuations of IOP in patients with POAG are not uncommon.[172] At pressure of 17 mmHg or less, 54 (26.3%) patients were legally blind. The average standard deviation of IOP (mmHg) over the follow-up period was different in the two groups (5.9 vs 4.0, $p = 0.031$). The relationship between IOP at visit 1 and last visit for patients in both groups is demonstrated in Figure 12. Pressure levels gradually decreased to similar values in both groups, though the standard deviation of individual IOPs was still higher in the LB group (4.8 vs 2.4 mmHg, $p = 0.02$)

Optic nerve appearance was worse in the LB group at the first visit, with 75% of patients showing C/D of ≥ 0.7. This figure approached 85.4% at the last visit. Both groups showed deterioration of C/D.

Noncompliance, poor control and late detection were worse in LB group: 63%, 95.6%, and 95.1% respectively. These factors were high in the NLB group also: 46.4%, 73.4% and 87.9% respectively. Thus noncompliance is an important overall issue in POAG.

III. Demographics and Characteristics of Composite Dallas Patient Population with NLB who did not progress versus those who did progress (Table 5)

Progression was based on VF and C/D ratio deterioration. Visual acuity deterioration was not arbitrarily considered. The main reason was the wide fluctuation in patient responses. Moreover, a patient experiencing visual acuity reduction without a corresponding glaucomatous VF change or C/D ratio progression would indicate a non-glaucoma etiology.

Of the 282 NLB patients, 148 (52.5%) did not progress, while 134 (47.5%) showed progression of the disease process. Several factors that distinguished the progressed group from the non-progressed group were: female sex (54.5% vs

45.5% males), need for more ALT (40.3% vs 25.7%), elevated IOP at first visit (23.5 ± 10.2 vs 22.1 ± 5.2 mmHg) and poor control of IOP (92.5% vs 56.1%). The mean IOP for both groups during follow-up is shown in Figure 13. Patients showed progression at all levels of IOPs, even at pressures below 17 mmHg, 32 (23.9%) patients experienced progression. This finding stresses the role of non-IOP related factors in the progression of glaucoma. There were wide pressure variations (standard deviation) in the follow-up period (6.1 vs 4.8 mmHg, p = 0.02). The relationship of IOP levels at visit 1 and the last visit is demonstrated in Figure 14. Patients in both groups achieved lower pressures with treatments. Elevated initial IOP is a significant risk factor for progression of VF.

Appearance of optic nerve head was quite varied in both groups. A majority (41.2%) of patient in the stable group had C/D ratio of >0.7 - 1.00, compared to the progressed group in which a majority (43.3%) were in the 0.1 - 0.5 C/D range. Examinations of optic nerve head features are highly subjective. There is a wide variation in the intraobserver and interobserver findings.[118] Initial C/D ratio appeared to be quite unpredictable to define the course of the disease.

IV. Demographics and Characteristics of Patients with LB Diagnosed Initially in Dallas, and comparison of patients in 3 clinics (Table 6).

Features of POAG patients who initially present at the physician's office or hospital provide a unique insight into some facets of the natural history of the disease. One may estimate how late a patient has presented for care in addition to gaining useful information about the extent of damage. Of the 205 patients with legal blindness 60 (29.3%) were initially diagnosed in Dallas: 29 (48.3%) in Clinic A, 17 (28.3%) in Clinic B, and 14 (23.4%) in Clinic C.

There were 34 (56.7%) male and 26 (43.3%) female. Blacks comprised the largest ethnic group (65.0%), with 94.1% of Clinic B patients being black. Clinic A had the highest proportion of white subjects (41.4%) The chief risk factors encountered were: hypertension (46.7%), diabetes (26.7%), vascular disease (26.7%), family history of glaucoma (21.7%), myopia (21.7%), ocular trauma (10.0%), use of systemic steroids (5.0%) or topical steroids (3.3%), and

dysthyroidism (3.3%). Clinic C patients had the highest prevalence of myopia (42.9%) and a positive family history of glaucoma (42.9%). Glaucoma related procedures were performed as follows: ALT (48.3%), trabeculectomy (20.0%), LPI (18.3%), and combined cataract/glaucoma surgery (13.3%). Clinic B patients required the most trabeculectomies (35.3%), indicating the severe nature of the disease in that clinic. Forty-two percent of Clinic C patients presented at visit 1 with visual acuity in the legal blindness range, compared to 17.6% in Clinic B, and 13.7% in Clinic A. In Clinic B, 52.9% of patients experienced deterioration of vision. Over 50% of patients had advanced VF defect at visit 1, and Clinic A patients had the worst results (58.5%). VF deterioration at the last visit was observed in 26.7% of patients, and 65% of patients had advanced loss. Clinic A had the most patients with advanced VF damage (72.3%). One reason for this may be that some patients were sent for consultation and takeover of care at the university. At visit one, IOP measured 25.6 ± 10.4 mmHg, with clinic C patients showing the highest IOP of 36.3 ± 13.2 mmHg. Sixty-five percent of patients had advanced cupping at visit one, which deteriorated to 83.3% by the last visit. Thirty-five percent of patients experienced worsening of C/D ratio. The rates of noncompliance, poor control, and late detection were 75%, 96.7% and 98.3% respectively.

V. Patients with unilateral blindness who presented initially in Dallas

Of the 85 patients with unilateral legal blindness, 26 (30.6%) presented initially in Dallas. The non-affected eye acts as a control in these patients. The measurements are given in mean ± SD, median and range in appropriate units. The first set of values corresponds to the non-affected eye. At visit 1, IOPs in mmHg: 25.0 ± 10.3, 23.5, 10.0 – 60.0 vs 29.4 ± 13.6, 25.5, 2.0 – 60.0, $p = 0.043$. The C/D ratio values at visit 1 were: 0.7 ± 0.13, 0.7, 0.5 – 0.9 vs 0.85 ± 0.09, 0.9, 0.7 – 1.0, $p < 0.0001$. Final visit C/D values were: 0.7 ± 0.14, 0.8, 0.5 – 0.9 vs 0.9 ± 0.1, 0.9, 0.7 – 1.0, $p = 0.0002$. Visual acuity and VF measurements were studied as continuous variables, respectively. For description of visual acuity measurement and VF defects, see Methods. The visual acuity values at visit 1 for the non-affected and affected eye were: 2.1 ± 0.9, 2.0, 1.0 – 4.0 vs 4.2 ± 2.9, 2.5, 1.0

– 10.0, p = 0.002. At final visit, the results were: 2.8 ± 1.9, 2.0, 1.0 – 8.0 vs 6.5 ± 2.6, 7.0, 2.0 – 10.0, p < 0.0001. VF values at visit 1 were 2.4 ± 1.1, 2.0, 1.0 – 6.0 vs 4.8 ± 2.0, 4.5, 1.0 – 7.0, p < 0.0001. At final visit, VF values were 3.0 ± 1.2, 3.0, 1.0 – 6.0 vs 5.3 ± 1.7, 6.0, 2.0 – 7.0, p <0.0001.

In summary unilaterally blind patients presented with significantly high IOP and worse visual acuity, VF defects and C/D ratio in the affected eye. Over time, they showed further worsening of all the above parameters.

B. PATIENT POPULATION AT CLINIC A

Two hundred forty-five patients qualified for the study, but 14 (5.7%) patients were dropped after enrollment because of development of conditions that interfered with proper evaluation or affected variables of interest. Out of the remaining 231 patients, 140 (60.61%) did not develop legal blindness; whereas 91 (39.39%) patients did develop legal blindness. In the latter group, 52 (57.1%) were legally blind in both eyes; whereas, 39 (42.9%) were legally blind unilaterally.

I. Demographics and characteristics of patients with NLB versus LB at Clinic A (Table 7)

There were 140 NLB and 91 LB individuals in Clinic A. The main differences between LB and NLB individuals were: higher age at diagnosis (61.60 ± 14.00 vs 58.1 ± 14.00); use of systemic steroids (8.8% vs 1.5%), more use of ALT (49.4% vs 32.1%) and trabeculectomy (30.8% vs 11.4%), worst initial and final visual acuity, worst worsening of vision (39.6% vs 15.7%), worst VF at visit one and final visit, elevated IOP at visit one (25.0 ± 11.3 vs 22.24 ± 7.3 mmHg), worst C/D ratio at visit one (68.10% vs 32.9%) and at final visit (82.4% vs 40.7%), worst non-compliance (56.0% vs 41.4%), poor control (99.00% vs 77.1%) and late detection 99.00% vs 87.1%).

II. Demographics and characteristics of NLB Clinic A patients who did not progress vs those who did (Table 8)

Of the 140 NLB subjects, 70 progressed and 70 did not progress. The distinguishing features of the group who progressed were: more use of ALT

(41.4% vs 20.0%), elevated IOP at first visit (24.9 ± 8.9 vs 21.8 ± 5.8 mmHg), non-compliance (55.7% vs 27.1%), and poor control (92.9% vs 61.4%).

III. Data Relating to Initial Presentation of Clinic A Patients in Dallas (Table 9)

Ninety-one patients presented initially at Clinic A. The average age was 60.6 ± 13.6. There were 35 (38.5%) male and 56 (61.5%) female. The racial breakdown was: Caucasian 51.6%, Afro-American 38.5%, Hispanic 5.5%, and others 4.4%. The major risk factors were: hypertension (38.5%), family history of glaucoma (32.2%), vascular disease (27.5%), history of smoking (15.4%), diabetes (14.3%), myopia (13.2%), dysthyroidism (8.8%), ocular trauma (6.6%), alcohol abuse (4.4%), and use of systemic steroids (2.2%) or topical steroids (2.2%). Twenty-three percent of patients were legally blind. The average IOP was 22.65 ± 8.6 mmHg and late detection was noted in 93.4% of patients.

C. PATIENT POPULATION AT CLINIC B

One hundred ten patients qualified for the study, but 12 (10.9%) patients were dropped after enrollment because of the development of conditions that interfered with proper evaluation or affected variables of interest. Out of the remaining 98 patients, 70 (71.4%) stayed non-legally blind, while 28 (28.6%) became legally blind.

I. Demographics and Characteristics of Patients with NLB versus LB at Clinic B (Table 10)

There were 28 LB patients in Clinic B, 12 male and 16 female. The average age was 58.4 ± 12.6. These were 26 (92.9%) Afro-American and 2 (9.1%) Hispanic. The distinguishing features from NLB patients were: need for more ALT (42.9% vs 20%) and trabeculectomy (25.0% vs 7.1%), faster deterioration of vision (42.9% vs 12.9%), and poor control (100% vs 68.6%).

II. Demographics and Characteristics of NLB Clinic B Patients who did not progress versus those who did progress (Table 11)

There were 34 patients who progressed and 36 who did not in Clinic B. In the former group, there were 7 males and 27 females. The average age was 58.8 ± 11.5. The distinguishing features from those who did not progress were: less prevalence of myopia (2.9% vs 27.8%) and smoking (20.6% vs 25.0%), required more ALT (35.3% vs 5.6%), trabeculectomy (14.7% vs 0.0%), elevated IOP at visit one (23.8 ± 9.7 vs 22.1 ± 5.0 mmHg) and poor control (94.1% vs 44.4%).

III. Data Relating to Initial Presentation of Clinic B Patients in Dallas (Table 12)

Sixty-six patients were initially seen in Clinic B. There were 23 (34.9%) male and 43 (65.1) female, 54 (81.8%) Afro-American, 5 (7.6%) Caucasian, 5 (7.6%) Hispanic and 2 (3.0%) others. The main risk factors were: hypertension (59.0%), diabetes (39.3%), family history of glaucoma (23.4%), history of smoking (15.2%), vascular disease (12.1%), myopia (16.7%), ocular trauma (9.0%), alcohol abuse (3.0%), dysthyroidism (1.5%), use of systemic steroids (1.5%), or topical steroids (1.5%). Most patients (80.3%) presented with vision $\geq$ 20/40 while 6% has visual acuity $\leq$ 20/200 at presentation. Advanced VF loss was observed in 10.6%. The average IOP was 22.85 ± 8.9 mmHg. Optic cupping $\geq$ 0.7 was seen in 43.9% of patients. Late detection was observed in 95.4% of patients.

D. PATIENT POPULATION AT CLINIC C

One hundred seventy patients qualified for the study, but 12 (7.0%) were dropped after enrollment because of the development of conditions that interfered with proper evaluation or affected variables of interest. Of the remaining 158 patients, 72 (45.6%) did not develop legal blindness, while 86 (54.4%) did become legally blind. Of the latter group, 56 (65.1%) were legally blind bilaterally, while 30 (34.9%) were blind unilaterally.

I. Demographics and Characteristics of Patients with NLB versus LB at Clinic C (Table 13)

There were 86 LB and 72 NLB patients in Clinic C. In the LB group, there were 85 (98.8%) males and 1 (1.2%) female, 58 (67.4%) Afro-American, 24 (27.9%) Caucasian, 1 (1.2%) Hispanic, 1 (1.2%) American Indian, and 2 (2.3%) others. The

average age was 57.2 ± 12.4. The main distinguishing features from NLB patients were: Afro-American race (67.4% vs 47.2%), need for more trabeculectomy (29.1% vs 11.1%), faster visual acuity deterioration (34.9% vs 1.4%), advanced VF loss at first visit (65.1% vs 6.9%) and final visit (73.2% vs 6.9%), faster rate of deterioration (22.1% vs 15.3%), elevated IOP at visit one (23.4 ± 11.8 vs 21.6 ± 7.6 mmHg), advanced C/D loss at visit one (79.0% vs 40.2%) and 84.9% vs 29.2% at the last visit, noncompliance (63.9% vs 40.3%) and poor control (90.7% vs 70.8%).

II. Demographics and Characteristics of Clinic C NLB Patient Who Did Not Progress versus Those Who Did Progress (Table 14).

Among the 72 NLB patients, 30 (41.7%) progressed and 42 (58.3%) did not in Clinic C. Of those who progressed, all were male, 17 (56%) Caucasian, 12 (40%) Afro-American and 1 (3.3%) Hispanic. The average age was 61.2 ± 11.0 years. The distinguishing features from those who did not progress were: diagnosis of hypertension (70.0% vs 38.1%), elevated IOP at visit 1, (23.9 ± 10.0 vs 21.8 ± 4.9), poor control (90% vs 57.1%) and late detection (63.3% vs 92.9%).

III. Data Relating to Initial Presentation of Clinic C Patients in Dallas (Table 15)

There were 38 patients who were initially seen in Clinic C. There were 37 97.4%) males, 1 (2.6%) female, 16 (42.1%) Caucasians, 21 (55.3%) Afro-Americans and 1 (2.6%) Hispanic. The average age was 63.9 ± 10.2. The main risk factors were hypertension (42.1%), smoking (36.8%), family history of glaucoma (35.1%), vascular disease (31.6%), diabetes (18.4%), myopia (10.5%), alcohol abuse (13.2%), ocular trauma (7.9%), dysthyroidism (5.3%), use of systemic steroids (2.6%), or topical steroids (2.6%). LB was detected in 34.2%. Over 15% had visual acuity $\leq$ 20/200, 21.1% had advanced VF loss and 50% had C/D of $\geq$ 0.7. Late detection was noticed in 92.1%.

DISCUSSION

Glaucoma is the third largest cause of blindness in the world.[1] Current estimates of the prevalence of glaucoma by meta-analysis of published data suggest that there are approximately 66.8 million people affected worldwide.[39]

Nearly 10% of them may be bilaterally blind. The public health impact is hard to assess because of the lack of a universal definition of the disease in its various forms.[40] Nearly 70% to 90% of the world's blind population lives in the developing countries.[40,183]

Approximately two-thirds of glaucoma in the Western world is POAG, while in the Asian countries it may be less than 5%.[2, 184] In the United States, the current estimates of individual with POAG is 2.47 million (1.84 million white, 619,000 black, and 11 thousand others).[185]

This study involved 487 patients in the Dallas metropolitan area, with an average follow-up of 5.5 ± 3.6 years. It is one of the larger series of glaucoma patients followed prospectively in one area. Patients were either followed by me or under my supervision. Thus, treatment style was similar and consistent in all clinics, in contrast to multicenter studies. Though arbitrary, the Clinics A-C represented: three socioeconomic groups of the society - high, low, and middle (see Patients and Methods). Therefore, the role of socioeconomic influences in POAG and resultant blindness was also studied.

A critical review of the literature on glaucoma brings out two important consistent features of the disease. First, POAG is a progressive disease in most cases, and second, it is a multifactorial complex entity. It is the second feature (whose whole gamut is far from complete) that may explain why different studies do not come up with the same results all the time.

Table 16 - Risk Factors for Blindness in Glaucoma

- IOP
  - elevated IOP [7,75,131,132,134,137-139,148,160]
  - large diurnal variations [130,132]
  - poor control of IOP [130]
  - Mean IOP in the better eye [148]
- Older age [8,75,131]
- Advanced VF damage at diagnosis [38,75,92,130, 134,141,171]
- Black race[62-64]
- Longer duration of disease [141]
- Non-compliance [135,141,171]
- Frequent disc hemorrhage[146]
- Late detection [135,141,143]
- Worse vision [141]
- Vascular insufficiency [135,136,139-141]
- Family history of glaucoma [140]
- Greater number of antiglaucoma medications [160]
- Glaucoma surgery [160]
- Higher socioeconomic class [148]
- VF loss in the worse eye [148]

Risk Factors for Blindness in POAG (Tables 3 and 4).

POAG is a progressive disease and with time, 25% to 38% of patients exhibit signs of progression and ultimate blindness in one or both eyes.[5-7] Blindness is a devastating event in the life of a patient, but the interplay of causes that lead to blindness are not completely understood (Table 2, Table 16).

Two hundred five (41.1%) patients had legal blindness by the end of the study. One hundred twenty (58.5%) were affected bilaterally and 85 (41.5%) had unilateral blindness. This study did not support the findings by Quigley et al,[147] who found that bilateral blindness was rare in patients with POAG. Clinic C patients had the highest prevalence of legal blindness (54.5%), p = 0.04. All chronic diseases are more prevalent in the Veterans Affairs population.[180] The relationship between these chronic diseases and glaucoma may be complex. One could argue that multiple chronic ailments may force noncompliance or delay in seeking medical care. The prevalence of blindness in glaucoma patients is variable (4-40%) depending on the ethnicity and inclusion criteria of the study population.[7,8,58,148]

Even though current definitions of glaucoma have downplayed the role of IOP (ostensibly to emphasize non-IOP factors) IOP with all its manifestations is still recognized as a major culprit in the progression of the disease.[64,73,130,132,148,153,155,165,169,171] But it is difficult to determine or predict the IOP level that would cease being harmful to the patient. In fact, significant numbers of patients continue to exhibit progression even with their IOP in the "normal" range; therefore, the use of terms such as "low-tension glaucoma" or "normal tension glaucoma" to describe these patients.[5,6] Strong believers in the role of IOP in POAG advocate aggressive reduction of IOP from current levels.[132,155,159] It has been suggested that each patient should be assigned a "**target pressure**," a value that in the opinion of the treating physician should prevent or slow the progression of damage.

Elevated IOP at visit one (24.2 mmHg) was very significant in LB group. These patients also had a larger variations (±11.2 mmHg) than the NLB group. This finding is consistent with several studies.[130,131,141,151] Even during the follow-up visits, LB patients showed more fluctuations in IOP (4.8 versus 2.4 mmHg, p =

0.02). When we look at patients with LB who were initially seen in Dallas, several different features come to light. The average IOP at presentation was 25.6 mmHg with SD of ±10.4 mmHg. However, Clinic C patients had the highest IOP at visit one (36.3 ± 13.2 mmHg). All the patients in Clinic C also presented late for treatment. Some of the reasons may be lack of social support, other chronic diseases requiring more attention, homelessness, etc.

The prevalence of blindness was detected at all IOP levels (Fig. 11), underlying the role of non-IOP related factors in glaucoma. At pressures of 17 mmHg or less, 54 (26.3%) patients still showed legal blindness. **Central corneal thickness** was not measured in this study. A thin cornea may lead to lower measurement of IOP by Goldmann tonometry, and thus lead to undertreatment of these individuals.[168] But the influence of elevated IOP was clearly evident; 116 (57%) patients had IOP >21mmHg. Why did so many patients have elevated mean IOP? There may be several explanations. First, these patients had poor control of IOP because of poor response to medical or surgical therapy. Second, after an eye shows a particular VF damage, e.g. split fixation, there is hesitation to intervene surgically, because of fears of "snuffing out" the remaining field. Third, when there is very advanced damage (≤HM), IOP reduction becomes less of a priority compared to keeping the patient comfortable. By this time, most patients may have accepted their fate and are quite satisfied as long as they have no pain. The AGIS investigators[132] also stressed the importance of maintaining low IOP. They found that VF progression was less if a patient maintained IOP less than 18 mmHg at each visit. But their patients had advanced glaucoma. The present study consisted of patients in different stages of the disease.

Among the patients with bilateral blindness, Clinic C had the highest prevalence (35.4%) and Clinic B the lowest (12.2%). Why did veterans show low prevalence? There may be several explanations. As discussed before, all types of chronic diseases are common in veterans.[180] They also have the encouragement and incentives to continue seeking care at their hospitals. As the follow-up period increases, there is evidence of continued glaucoma progression.[58,141,145,152] The Veterans Affairs Administration provides regular health check-ups and prompt referrals among medical specialists. They offer financial benefits associated with

visual disability. The office of blind registration assists veterans with all types of low vision aids. Therefore, veterans keep on coming back to the clinic for benefits. The lower prevalence in Clinic B may be due to the inability of a blind person to keep clinic appointments, especially when there is no social or family support, or inability to afford medications due to loss of employment.

Table 17. Univariate analysis of legal blindness in clinics

Variate	Clinic A	Clinic B	Clinic C	Total
No LB	140 (28.7%) (60.7%)	70 (14.4%) (71.4%)	72 (14.9%) (45.6%)	282 (57.9%)
Yes LB	91 (18.7%) (39.3%)	28 (5.8%) (28.6%)	86 (17.5%) (54.4%)	205 (42.1%)
Total	231 (47.4%)	98 (20.1%)	158 (32.5%)	487 (100%)
$p = 0.0001$. H_o = LB is independent of clinic; LB = legal blindness				

Older age at diagnosis may adversely affect the outcome.[8,75,131] These patients may have harbored the disease for a longer time,[58,147,156,158,166,170] which in itself is an adverse risk factor.[58,135,141,145,152] Also, the age-related loss of optic nerve fibers[37] may play a crucial role in faster deterioration of the disease. No differences in the age at diagnosis (59 ± 12.6 years) were noticed in this study.

Race was another important feature with 58% of LB patients being black, as seen in other studies.[6,7,63,70,141]

Table 18. Univariate analysis of the effect of race in all clinics.

Variable	White	Black	Hispanic	Others	Total
No LB	124 (64.3%)	134 (53%)	12 (63.2%)	12 (57.1%)	282
Yes LB	69 (35.7%)	119 (47%)	7 (26.8%)	10 (42.9%)	205
Total	193	253	19	22	487
$P = 0.120$. H_o = LB is independent of race LB = legal blindness					

Among the LB patients initially seen in Dallas, 65% of patients were black. The three clinics were surrogates for patient incomes. The average incomes were ≥$50,000, ≤$12,000, and ≥$23,000 respectively. The univariate analysis of the effects of the clinics and race are shown in Table 17 and Table 18 respectively. Legal blindness in univariate analysis is affected by clinics. The various reasons for such a disparity have been discussed above. In regard to race, univariate analysis was performed to evaluate its effect on all patients and also within each clinic. As shown in Table 18, overall effect of race on LB was not significant ($p = 0.120$). Meanwhile, only Clinic C showed that blacks tended to have more LB

than others (Table 19). Multivariate approach involved logistic regression to model the probability of blindness as a function of age, gender, race, baseline IOP, clinic and baseline VF damage. Race did not appear to play a significant role in LB, while baseline IOP, gender, and baseline VF were positively associated with LB. The gender issue may need to be ignored because of paucity of females in Clinic C. Ninety-four percent of Clinic B patients were black, reflecting socioeconomic realities of the metropolitan area. The Baltimore Eye Study[62] demonstrated that POAG accounted for 19% of all blindness among blacks. It was six times as frequent among blacks as among whites. POAG also manifested about 10 years earlier in blacks. Medicare returns were studied by Javitt et al[187] for rates of incisional and laser surgery for POAG in blacks and whites. This rate was 2.2 times higher in blacks. But compared to a six-fold high prevalence of blindness, it was realized that blacks were receiving far less care for POAG.

Table 19. Univariate analysis of the effect of race in Clinic C.

Variable	White	Black	Hispanic	Others	Total
No LB	37 (60.7%)	34 (37%)	1 (50%)	0 (0.0%)	72
Yes LB	24 (39.3%)	58 (64%)	1 (50%)	3 (100%)	86
Total	61	92	2	3	158
p = 0.02; LB = legal blindness					

Risk factors such as ocular trauma, myopia, diabetes, family history, hypertension, use of systemic steroids, and topical steroids, dysthyroidism, vascular disease, alcohol abuse, and smoking were not significant.

Table 20. Multivariate analysis of the various variables and their effects on legal blindness.

Parameter	Odds Ratio	95% confidence limit for odds ratio	P value
Age at diagnosis	1.008	0.993 – 1.024	0.281
Race	1.148	0.919 – 1.435	0.224
Baseline IOP (>22 mmHg vs < 22 mmHg	1.54	1.05 – 2.268	0.028
Clinic	1.157	0.905 – 1.478	0.244
Gender (female vs male)	0.601	0.383 – 0.943	0.0268
Baseline VF (1 scotoma or worse vs normal)	13.698	4.863 – 38.582	<0.0000 1
IOP = intraocular pressure; VF = visual field			

Poor control of IOP was seen in 196 (95.6%) of LB patients. Do LB patients have difficult and more severe glaucoma? This is also supported by the high use of ALT (43.4%), trabeculectomy (29.3%), cyclodestruction (4.4%), systemic CAIs (38.5%)

and noncompliance (63%) in that group. Trabeculectomy was used the most in Clinic B patients, indicating more difficult disease in black populations. Both the use of a greater number of antiglaucoma medications and glaucoma surgery are recognized risk factors for blindness.[160]

Thirty-six percent of composite LB patients had vision reduced to legal blindness at their first visit. Of those who were seen initially in Dallas, LB was detected at the first visit in 21.7%. Several studies have indicated that one-third of patients who were legally blind from glaucoma presented with blindness on their initial visit to obtain help.[141-143] Clinic C patients showed the most legal blindness at visit one (42.8%) and correspondingly had the highest rate of late detection (100%). This may be explained by a multitude of factors, such as blacks comprised 71.4% of the patients, myopia was present in 42.9% of the population, and there was a high prevalence of other systemic ailments: diabetes (21.4%), hypertension (42.9%), vascular disease (48.6%), and smoking (28.6%). Over 60% of patients had advanced VF damage on visit one. The highest prevalence was in Clinic A patients. One reason for this is that Clinic A is a referral center and patients with advanced damage are sent for consultation. Several investigators have pointed out the role played by advanced VF damage at diagnosis,[75,92,130,134,138,148,171] VF loss in the worst eye[148] and vascular insufficiency.[135,136,139,140]

After excluding all diseases that might interfere with the diagnosis and follow-up of glaucoma, legally blind patients had more other than glaucoma ocular diseases (53.9% vs 36.9%, $p< 0.0002$). This feature has been observed by other investigators[141] though the significance is not clear. Is this a benign finding or does it portray a broader psychosocial behavior of this group of patients? It may be that they tend to ignore medical/physical problems which are not serious enough in their minds. Later on this behavior may be translated into non-compliance.

Seventy-five percent of legally blind patients had C/D ratios greater than 0.7 at their first visit, compared to 36.2% of the non-legally blind individuals. By the end of the study, these values were 85.4% and 46.8% respectively. This

finding stresses the basic nature of POAG as a progressive optic neuropathy. Both groups of patients exhibited progression of their C/D ratios.

The wide variety of antiglaucoma medications used during the study period were similar in legally blind and not legally blind patients, except for the greater use of miotics and systemic CAIs in the former group. The systemic CAIs, though very effective, have a multitude of toxic side effect and are usually employed as a last-ditch effort to control IOP. Their use may indirectly point to the poor control of the disease in that group. Similarly, relatively inexpensive miotics may have been used for economic reasons.

Noncompliance is a poorly understood feature of glaucoma management. There is no universal definition of noncompliance, but the study definition (see page 42) revealed a noncompliance rate of 63% in legally blind patients. The significance of noncompliance has been stressed by several investigators.[135,188]

Late detection, or late presentation of the patient for medical treatment, has been a significant feature of many investigations.[135,141-143] The present study noted a high prevalence of late detection in legally blind and non-legally blind patients (95.1% vs 87.9%, $p = 0.006$). The need for early detection and early treatment cannot be stressed enough. Other factors such as age at diagnosis, history of ocular trauma, myopia, diabetes, hypertension, family history of glaucoma, vascular disease, alcohol abuse, smoking, systemic or topical steroids or dysthyroidism were not significant.

Risk Factors for POAG (Table 3)

Several risk factors were recognized in this study. The age at diagnosis (59.12 ± 12.9 years) supports the findings in other studies, that POAG is a disease of elderly.[66-68,168] Prevalence of bilateral legal blindness was 24.6% and of unilateral blindness, 17.4%. In concurrence with other studies, Afro-Americans comprised the greatest proportion of patients with POAG (51.9%),[62-68,70,71,77-80] considerably more than their representation in Dallas (15.8%). Elevated IOP (23.2 mmHg) and a large SD (±10.1) stressed the role of IOP in glaucoma.[64,67,69,71,110,168] No sexual disparities could be documented, as Clinic C patients had just two female patients. In the other two clinics, females were in

the majority (56.7% and 65%). Female propensity for POAG has been noted earlier.[95-96]

Systemic hypertension was noted in 49.6% of patients. The highest prevalence was in Clinic B (59.2%). Vascular diseases had a prevalence of 28.4% with the highest rate in Clinic C (36.6%). The prevalence of diabetes was 21.8% with the highest rate in Clinic B (41.8%), which also had disproportionately higher Afro-American population (83.7%). Systemic hypertension, vascular disease and diabetes are all well recognized risk factors.[16,19,35-37,87-90,92,94,95,132] Family history of glaucoma was positive in 33.2% of patients. Most studies have estimated that 20% to 25% of cases of POAG are hereditary.[84-86,108-110,167,189] History of ocular trauma was obtained in 7.4%. Myopia was associated with 11.7% of patients, with the highest rate in Clinic A (15.1%). A strong association of myopia to higher educational level and occupation was found in an Australian study.[190] They also noticed that the prevalence of myopia decreased from 24% in individuals 40 to 49 years old to 12% in persons 70 to 79 years. It is not known if myopia has a direct role in the prevalence of POAG or if its other features, such as increased IOP and large C/D ratios are responsible.

The role of the presence of diseases other than glaucoma is not well understood. Clinic C patients had the highest prevalence of such conditions at the first visit (60%, $p < 0.0001$) and at the last visit (32.9%, $p < 0.0001$). Compared to the other two clinics, Clinic A patients underwent more surgical procedures, such as cataract (26.0%, $p = 0.004$), ALT (36.4%, $p = 0.011$), and LPI (17.8%, $p = 0.0001$). This may have to do with access to health care and utilization of health resources because of the patients' ability to pay.[187] Afro-Americans had a substantially lower rate of eye care related outpatient visits than Caucasians (143.2 per 1000 persons per year versus 194.6 per 1000; $p < 0.01$).[191] Deterioration of visual function in the composite group was as follows: visual acuity in 118 (24.2%), VF in 93 (19.1%), and C/D ratio in 147 (30.2%) patients. This trend has been observed in other studies.[6-8,141]

Use of systemic corticosteroids was reported by 3.1% of individuals and of topical steroids by 1.6%. The role of corticosteroids to induce elevated IOP is well-documented. [100,101]

Dysthyroidism was found in 5.6% of patients, but the highest prevalence was in Clinic A (10%). Alcohol abuse also was detected in 10.9% of patients. The highest prevalence was in Clinic C. Smoking was seen in 24.6% and the highest prevalence in Clinic C.

Noncompliance was also an important issue in 260 (53.4%) patients. The highest prevalence was in Clinic B (68.4)%, and lowest in Clinic A (47.2%), p = 0.0002. In a Greek clinic based study, Konstas et al found a noncompliance rate of 44% among patients with glaucoma.[188] When compared to compliant patients, noncompliant individuals had higher IOP (22.9 vs 18.5 mmHg; p > 0.001) and worse VF defects (10.8 vs 7.0 dB; p = 0.008).

Four hundred three (82.7%) patients encountered poor control of IOP, or progression of C/D ratio and VF defects. This observation stresses the difficult task faced by ophthalmologists treating patients with glaucoma. Similarly, late detection was encountered in 443 (91.0%) patients. The combination of noncompliance, poor control and late detection epitomizes the challenge of glaucoma.

Table 21 - Risk factors for progression of POAG

- IOP
  - wide fluctuations [7,73,133,148,149,151,155,170,172]
  - elevated mean IOP [2,7,73,75,92,131-133,138,146,147,155,165,168]
  - elevated initial IOP [6,58,145,150,155,158,160]
  - range of IOP [7,74,153,155]
  - difference in IOP between eyes [181]
  - change in IOP after water drinking test [69]
- Vascular insufficiency [36,92,135,136,139,140,146,160,168]
- Large C/D ratio [6,69,75,131,138,140,141,156-158,161,164,168]
- Disc hemorrhage [140,146,162,170]
- Surgical intervention [73,131,160,161]
- Female gender [6]
- Family history of glaucoma [6,140]
- Poor outflow facility [69]
- Worse visual acuity [131]
- Older age [58,69,75,131,147,156,158,166,170]
- Fewer antiglaucoma mediations [158]
- Poor ocular perfusion [139]
- Greater number of antiglaucoma medications [131,160]
- Advanced VF loss [58,134,137,141,149,156]
- Bilateral disease[70]
- Exfoliation[170]
- History of glaucoma treatment[147]
- Progression in the better eye [162]
- Large parapapillary atrophy [161,164]
- Small neuroretinal rim area [75,161,164]
- Baseline VF [6,153]
- Noncompliance [73,141]
- Longer duration of follow-up [58,141,145,152]

Risk factors for progression of POAG (Table 5)

Several risk factors have been implicated in the progression of VF in patients with POAG (Table 21). The range of VF progression in POAG varies from 20% to 76%, depending upon duration of follow-up.[7,11,72,130,170] The major

difficulty in comparing the results of different studies of progression is that the criteria for progression vary.[83] For this study, progression was based on predefined VF and optic disc deterioration (see page 42).

There were 148 patients who remained stable and 134 patients who progressed. Their ages at diagnosis of POAG were similar 59.1 ± 12.6 vs 58.9 ± 12.6 (p = 0.90). Other studies have found older age a major risk factor for progression.[58,69,75,131,147,156,158,166,170] No racial or other known systemic risk factors were significant, in contrast to other investigators.[36,71,92,135,136,139-141,146,160] Presence of diseases other than glaucoma was also similar. IOP in the progressed group was higher than the stable group (23.5 ± 10.3 vs 22.1 ± 5.2 mmHg, p = 0.04) at their first visit. The average standard deviation of individual IOPs over the follow-up period was greater in the progressed group 6.1 vs 4.8 mmHg, p = 0.02). Both these features have been confirmed by other studies.[7,73,75,92,131-133,142,146,147,149,153,155,165,168,172] Control of IOP and disease process was worse in the progressed group, p < 0.0001 and they also required more ALT, p = 0.011. The need for greater numbers of antiglaucoma medications [131,160] and surgical interventions [21,73,161,166] for glaucoma which indirectly signify poor control of the disease are well documented.

Status of visual acuity was similar both at visit 1 (p = 0.6) and the final visit (p = 0.5). Twenty-two (16.4%) individuals from the progressed group showed visual acuity deterioration compared to 10 (6.8%) in the stable group, p = 0.014. Visual field status was similar in both groups at visit one (p = 0.37) but worsened at the final visit (p = 0.008). Compared to no patient showing VF deterioration in the stable group, 46 (34.3%) patients in the progressive group had worsening VF (p = 0.0001). As observed by other investigators,[7] the status of the optic nerve head at first visit was better in the progressed group (p = 0.004). In all, 92 (68.7%) patients in the progressed group exhibited worsening of C/D ratios (p < 0.0001).

Noncompliance and late detection were similar in both groups (p = 0.121 and P = 0.855 respectively). However, other studies have found these to be major risk factors.[73,141]

In summary, risk factors for progression were: elevated initial IOP, wide variations in IOP, and poor control of IOP. However, progression was seen at all

IOP levels (Figure 13). The progressed group and the stable group had similar visual function status at the beginning of the study. Poor control of IOP was the biggest deciding factor.

Features of patients with legal blindness diagnosed initially in Dallas (Table 6)

Sixty patients with legal blindness were initially diagnosed in Dallas. Afro-Americans comprised 65% of the group, $p = 0.034$. The average age at diagnosis of legal blindness was 61.3 ± 12.9 years. The prevalence of other risk factors were: myopia (21.7%), diabetes (26.7%), family history (21.7%), hypertension (26.7%), and vascular disease (26.7%).

Average IOP at visit one was 25.6 ± 10.4 mmHg and after treatment, it dropped to 18.1 ± 3.2 mmHg. Forty-eight percent of patients required ALT, while 20% needed trabeculectomy. Progression in visual acuity, VF, and C/D ratio was noted in 43.3%, 26.7%, and 35% respectively. There was also a high prevalence of noncompliance (75%), poor control (96.7%), and late detection (98.3%). In summary, new patients with legal blindness present with elevated IOP, advanced VF defects (28.3% had stage 6 and 16.7% had stage 7 changes), larger C/D ratio (65% had C/D ratio of >0.7 – 1.0) and exhibit noncompliance and poor control of the disease process.

Features of patients with unilateral blindness diagnosed initially in Dallas.

Patients with advanced unilateral glaucomatous damage provide unique opportunities to study the disease process in both eyes. Systemic variables being equal, it is very likely that innate properties of each eye or vascular factors are responsible for the differences. Past studies have indicated that eyes with dissimilar glaucomatous manifestations differ on the basis of large C/D ratio,[137,156,157,163] elevated IOP,[9,137,150,153,163] optic disc hemorrhage,[162] severe VF loss,[156,157] progression in the better eye,[162] and poor ocular perfusion.[157]

Twenty-six (30.6%) of the 85 patients with unilateral blindness presented initially in Dallas. The affected eye had higher IOP (29.4 ± 13.6 vs 25.0 ± 10.3, $p = 0.043$), larger C/D ratio at visit 1 (0.85 ± 0.09 vs 0.7 ± 0.13, $p < 0.0001$) and final

visit (0.9 ± 0.1 vs 0.7 ± 0.14, p = 0.0002), worse visual acuity (p = 0.002) and VF status (p < 0.0001). These parameters worsened over time.

SUMMARY AND RECOMMENDATIONS

This long-term study has emphasized the innate theme of POAG: that it is a progressive disease and has a complex array of multifactorial risk factors. Patients' lifestyle, biological makeup, psychological outlook, social interactions, monetary situations, and health status may affect the rate of progression of glaucoma.

Four hundred eighty-seven patients with POAG were followed for 5.5 ± 3.6 years in the Dallas metropolitan area. The three different clinic populations provided a good racial mixture. If we ignore Clinic C, where there were very few females, because of the male dominance among the United States war veterans, the female patients comprised 59.3% of Clinic A and B. There was a preponderance of Afro-Americans (51.9%), indicating their vulnerability to POAG. The average IOP at the first visit was 23.2 ± 10.1 mmHg, stressing the role of elevated IOP and its wide fluctuations in POAG. The current treatments were effective in reducing the pressure to 18.1 ± 3.2 mmHg at the final visit. We have still not been very successful in reducing IOP to the target pressure in every patient. Side effects and cost of glaucoma treatments, lack of awareness of the seriousness of the disease, progressive loss of vision, and many other unknown reasons may be responsible for the high prevalence of non-compliance (53.4%). Another impressive finding was that 91% of individuals presented late for treatment. Therefore, enhancing public awareness should be a high priority. The progressiveness of the disease was supported by the finding that 82.7% of patients were felt to be poorly controlled either in terms of not maintaining target pressure or worsening of C/D ratio and VF status.

All the known risk factors for glaucoma were widely prevalent; hypertension (49.6%), family history of glaucoma (33.2%), vascular disease (28.4%), smoking (24.6%), diabetes (21.8%), myopia (11.7%), alcohol abuse (10.9%), blunt ocular or facial trauma (7.4%), dysthyroidism (5.6%), and systemic steroids (3.1%). Forty-four percent of patients had non-glaucoma related ocular diseases at

the first visit. These included cataract, dry eyes, ARMD, corneal or lid conditions, but were not considered significant enough to cause interference with glaucoma management. Over the follow-up period, 24.6% more patients developed similar conditions. This suggests that a glaucoma patient has to deal with a multitude of accompanying eye problems.

Various glaucoma procedures employed to treat IOP were: ALT (37.2%), trabeculectomy (18.1%), combined surgery (11.7%), LPI (12.3%), and cyclodestruction (1.8%). Visual acuity, VF, and C/D ratio deterioration were observed in 24.2%, 17.1%, and 30.2% of patients.

Of the 205 legally blind patients, 120 (58.5%) were affected bilaterally, and 85 (41.5%) unilaterally. The average age was 59.3 ± 13.2 years, similar to the non-legally blind patients.

Fifty-eight percent of legally blind patients were Afro-Americans. Legally blind individuals had higher ocular pressures at the first visit as compared to the non-legally blind patients. Their IOP levels also showed greater variability. Though legal blindness was encountered at all IOP levels, only 26.3% were legally blind with pressures below 17 mmHg. Legally blind individuals experienced poor control of their disease process and received more glaucoma-related procedures to control IOP. Both non-compliance and late detection were very significant problems. Though not statistically different, legally blind patients had an impressive array of risk factors: family history of glaucoma (30.5%), diabetes (19.5%), hypertension (53.4%), vascular disease (30.2%), alcohol abuse (13.2%) and smoking (24.0%).

During the study, 148 (52.5%) patients of the 282 non-legally blind individuals remained stable and 134 (47.5%) progressed. Progression was noticed at all IOP levels. Nearly 24% of patients with IOP less than 17 mmHg progressed. However, central corneal thickness was not measured. Gordon et al[168] have demonstrated that thin central corneal thickness is a risk factor for progression to POAG in individuals with ocular hypertension. The group that progressed in the present study had higher initial mean IOP, wide variations in IOP in the follow-up period, worse optic nerve cupping and experienced difficulty in controlling IOP, which required more ALT.

Initial data on patients with unilateral blindness, who were first seen in Dallas, revealed that they had higher initial IOP in the affected eye, worse C/D ratio, worse visual acuity and worse VF changes. All the visual functions worsened over time. In a similar investigation, Susanna et al found the risk factors for progression in the fellow eye of patients with uniocular POAG were elevated IOP, C/D $\geq$ 0.5 or disc hemorrhage.[192]

Socioeconomic effects were also observed. There were fewer Caucasians in Clinic B (7.1%) compared to 54.1% in Clinic A and 38.6% in Clinic C. In Clinic B, 28.6% were legally blind, compared to 38.9% in Clinic A, and 54.4% in Clinic C. In the last clinic, the high prevalence is explainable by the presence of a full-time blindness coordinator and government supported benefits. In Clinic A, patients could afford to continue eye care from disability insurance, even when employment may have been affected. In Clinic B, patients either dropped out of eye care due to lack of affordability or simply ended up in government supported social services. These services may have their own eye care providers. There were fewer patients undergoing ALT, LPI and cyclodestruction in Clinic B, most probably due to affordability reasons, or non-compliance.

This study has shown that POAG is an intricately complex disease. Patients may show progression at any levels of IOP, and at any stage of the disease. Patients' susceptibility to IOP was varied. The role of non-IOP related risk factors in POAG is still poorly understood. The study suggests continuous careful monitoring of the optic nerve and visual fields. The target pressure may have to be constantly reassessed until other neuroprotective measures become available. The recent association of thin central corneal thickness[168] and susceptibilities to POAG in subjects with ocular hypertension indicates the need to measure central corneal thickness in all such patients and possibly those with POAG. The treatment for POAG should be multifaceted to counteract the multifactorial nature of the disease. Serious consideration should be given to the quality of life, cost -benefit analysis of therapy, and keeping the end point in mind, i.e., preventing progression.

STRENGTHS, WEAKNESS, AND LIMITATIONS OF THE STUDY

Strengths of the study

A large number of patients (487) were followed prospectively for 5.5 ± 3.6 years. The patients were from three different clinics within the Dallas metropolitan area. There was a good mixture of gender (120 male; 85 female) and race (193 Caucasian; 253 Afro-American; 19 Hispanic; and 22 others). Seventy-seven bits of information were collected on each patient at every visit. Presenting data on new patients has been discussed. Eligibility and exclusionary criteria were clearly defined. Controls were selected from each clinic: NLB patients (control) vs LB patients; stable patients (controls) vs those who progressed. The protocol was assiduously followed. Proper biostatistical methods were employed for analysis of data. Socioeconomic differences among the three clinics was supported by data from the business offices of each clinic.

Weaknesses and limitations of the study

There were only two female patients in Clinic C because of the make-up of the United States Armed Forces. Patients with insurance may attend Clinic B or C out of convenience. The progression of C/D ratio or VF were confirmed by the author alone; there were no other masked examiners. A standardized coding system for glaucomatous VF loss is needed. Selection bias is inevitable in studies based on a single investigator's experience. For example, changes in C/D ratio and VF could have been under- or over-estimated. Also, patients in this study may have unusually severe glaucoma, simply because they continued to be followed up at a glaucoma referral center. The apparent rates of VF loss may thus have been magnified. In addition, there may be other confounding factors that were not considered.

FUTURE STUDIES AND UNANSWERED QUESTIONS

The author wishes to continue the present study, but with the following modifications. (1) A control group of individuals without POAG will be selected at each clinic. They should provide information on the prevalence of systemic diseases at each clinic. These control persons will be age, sex, and race matched

with POAG patients. (2) As the disease process appears to be different in Afro-Americans, patients will be race matched for each category of the study. For example, Caucasians with Caucasians and Afro-Americans with Afro-Americans. (3) More detailed information will be obtained regarding systemic diseases; for example, poor control, satisfactory control or excellent control of diabetes.

The aim is to establish a large Dallas Glaucoma Patient Database and create a computer-based Glaucoma Simulation Model. This model may be used to predict effects of drugs or surgeries and their benefits to the patients.

The unanswered questions are lack of understanding of the role of non-IOP related risk factors in POAG and how to manipulate them. There is also a need to heighten awareness of glaucoma in the general public and other physicians to encourage early detection. Non-compliance should be suspected in all patients. POAG appears to be a multifactorial, multisystem disease, which calls for cooperation among different specialties.

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Table 1. Risk factors for POAG - see page 12

Table 2. Summary of Risk Factors for Progression of POAG/OHT or blindness in glaucoma

No.	Author(s) Year	Country	Study design, Total # of patients (eyes)	Gender		Race/ diagnosis	Risk factors / comments
				M	F		
1	Oliver JE, et al[130] 2002	USA	Retrospective case (56) control (234)	Case 20	36 Control 87 147	White POAG	▪ Moderate to advanced VF defects at diagnosis ▪ Variability in IOP ▪ Poor control of IOP
2	Stewart WC, et al[131] 2000	USA	Retrospective case-control - 218 case (34) control (184)	Case 12	22 Control 82 102	Case B 10 W 22 Other 2 Control B 95 W 125 Other 14 POAG	▪ Elevated IOP ▪ Large C/D ratio ▪ Greater number of medications ▪ Older age ▪ Worse VA
3	The AGIS Investigators[132] 2000	USA	Prospective Predictive analysis - 738 eyes Associative analysis - 586 eyes	Predictive analysis 318	420 Associative analysis NM NM	Predictive analysis B 420 W 306 Others 12	▪ Early average IOP > 17.5 mmHg ▪ Follow-up IOP lower than 18 mmHg, but only in fewer than 50% of visits
4	Quigley HA, et al [133] 1979	USA	Retrospective 10 (16)	6	4	Race: NM POAG	▪ Large diurnal variations of IOP ▪ Elevated IOP
5	Kolker AE [134] 1977	USA	Retrospective 76 (101)	40	36	W 58 B 18 POAG	▪ Elevated IOP ▪ Advanced VF loss

Table 2. Summary of Risk Factors for Progression of POAG/OHT or blindness in glaucoma

No.	Author(s) Year	Country	Study design, Total # of patients (eyes)	Gender		Race/ diagnosis	Risk factors / comments
				M	F		
6	Spaeth GL[135] 1971	USA	Retrospective Group A - 117 Group B - 32	NM	NM	Race = NM *Group A* Normal = 25 POAG = 33 OHT = 23 LTG = 26 Secondary glaucoma = 10 *Group B* POAG = 11 OHT = 4 LTG = 26 Secondary glaucoma = 7 Optic atrophy = 5	▪ Elevated arm - retina circulation time (abnormal blood flow) ▪ Late detection of the disease ▪ Noncompliance
7	Reese AB, et al[136] 1942	USA	Prospective 132 (132)	NM	NM	Race - NM POAG - 132	▪ Systolic coefficient lower than 5.65 (systolic coefficient = systemic pressure ÷ IOP) ▪ Diastolic coefficient lower than 3.21 (diastolic coefficient = diastolic pressure ÷ IOP)
8	Harbin TS et al[137] 1976	USA	Retrospective 21	14	7	Black = 10 White = 11 POAG	▪ VF loss ▪ Enlarged C/D ratio ▪ Elevated IOP
9	Araie M et al[138] 1993	Japan	Retrospective 56 (56)	24	32	Japanese NTG	▪ Elevated IOP ▪ Large C/D ratio ▪ Ratio of peripapillary atrophy to disc area
10	O'Brien C et al [7] 1991	USA	Retrospective 40 (40)	23	17	W = 30 B = 10 POAG = 26 Pigmentary = 10 PXG = 4	▪ Less optic nerve damage and higher initial mean threshold values in the visual fields ▪ Elevated IOP

Table 2. Summary of Risk Factors for Progression of POAG/OHT or blindness in glaucoma

No.	Author(s) Year	Country	Study design, Total # of patients (eyes)	Gender		Race/ diagnosis	Risk factors / comments
				M	F		
11	Gherghel D et al[139] 2000	Switzerland	Case-Control Case - 20 Control - 20	NM	NM	Race NM POAG	▪ Higher IOP ▪ Lower mean ocular perfusion pressure ▪ Low blood pressure ▪ Low end diastolic velocity in the central retinal artery
12	Quigley HA et al [75] 1994	USA	Prospective 647	293	354	B = 175 Others = 472 OHT	▪ Moderate or severe nerve fiber layer atrophy at baseline ▪ Older age, large cup/disc ratio, smaller rim/disc area ratio, large cup asymmetry, disc crescent ▪ High IOP
13	Harrington, DO[92] 1959	USA	Retrospective 6	4	2	NM POAG	▪ Arterial insufficiency and decreased blood flow in the anterior portions of the optic nerve
14	Drance SM et al[140] 1978	Canada	Retrospective Case = 219 Control = 100	Case NM NM Control NM NM		NM POAG = 219 Normal = 100	▪ Elevated IOP, neuroretinal rim abnormalities, large cup-to-disc ratios, family history of glaucoma, previous hemodynamic crisis, coronary heart disease and hemorrhage on the optic nerve head.
15	Wilson R et al [6] 1982	England, UK	Retrospective 57	25	32	Race = NM POAG	▪ Advanced VF defects ▪ Family history of glaucoma ▪ Initial IOP ▪ Female gender
16	Grant WM et al[141] 1982	USA	Retrospective 59	NM	NM	W = 33 B = 26 POAG = 47 Secondary glaucoma = 4 Congenital = 2 Angle closure = 6	▪ Black race ▪ Worse VF at presentation ▪ Late detection

Table 2. Summary of Risk Factors for Progression of POAG/OHT or blindness in glaucoma

No.	Author(s) Year	Country	Study design, Total # of patients (eyes)	Gender M	Gender F	Race/ diagnosis	Risk factors / comments
17	Fraser S et al[144] 1999	UK	Retrospective 200	Case 58 Control 47	42 53	*POAG* W = 45 B = 19 Other = 26 *Control* W = 77 B = 8 Others = 15	▪ Patients of African Caribbean descent presented late for treatment ▪ Females presented late ▪ Older patients ▪ Patients referred by other sources than optometrists ▪ Patients with IOP >31 mmHg
18	Martin JM et al [71] 1985	USA	Retrospective 140	NM	NM	W = 25 B = 115	▪ Black race. They had higher initial IOP, large cup-to-disc ratio, advanced VF damage and were younger than whites.
19	Crick RP et al [145] 1989	UK	Retrospective 929 (1450)	NM	NM	Race = NM POAG = 1069 OHT = 381	▪ Higher pretreatment IOP
20	Drance SM et al [146] 1981	Canada	Prospective *First part* 165 (165) *Second part* 146 (146)	*First part* 94 *Second part* NM	71 NM	NM *First part* OHT = 165 *Second part* OHT = 146	▪ Strongest predictors of development of VF defects were large cup-to-disc ratios, disc hemorrhage, family history of glaucoma, coronary disease, hemodynamic crisis, family history of diabetes, family history of stroke and euglobulin lysis time.
21	Quigley HA et al [147] 1996	USA	Prevalence survey 151	NM	NM	B = 112 W = 39	▪ In blacks, severity of VF damage was associated with age, history of glaucoma, and IOP
22	Ekström C et al [58] 1991	Sweden	Survey 128	NM	NM	White POAG = 45 Others = 83	▪ Old age, longer duration of disease, higher mean IOP, more extensive VF damage at time of diagnosis
23	King AJW et al[148] 2000	UK	Prospective 258	NM	NM	NM POAG	▪ Severity of VF loss at diagnosis in the better eye ▪ Mean IOP in the better eye during follow-up ▪ Extent of VF loss in the worst eye at diagnosis ▪ Higher socio-economic class

Table 2. Summary of Risk Factors for Progression of POAG/OHT or blindness in glaucoma

No.	Author(s) Year	Country	Study design, Total # of patients (eyes)	Gender M	Gender F	Race/ diagnosis	Risk factors / comments
24	Chandler PA[149] 1960	USA	Retrospective 20 (40)	10	10	Glaucoma	▪ Elevated IOP and advanced cupping at presentation. Wide fluctuation of IOP.
25	Kass MA et al[150] 1976	USA	Retrospective 31 Case 9 Control 22	Case 7 Control 13	24 9	Case W = 7 Others = 24 Control W = 14 Others = 8 POAG	▪ Elevated initial IOP ▪ IOP greater than 24 mmHg on more than half of follow-up visits
26	Werner EB et al[151] 1977	Canada	Retrospective 20 (24)	8	12	NM POAG	▪ Poor quality of IOP control after trabeculectomy ▪ Postop IOP ≥ 21 mmHg
27	Armaly MF et al[69] 1980	USA	Prospective 4192	1917	2275	W = 3641 Other = 551 POAG	▪ Elevated IOP ▪ Decreased outflow facility ▪ Older age ▪ Large C/D ▪ Pressure change after water drinking
28	Mikelberg FS et al[152] 1989	Canada	Retrospective 48 (48)	28	20	Race (NM) POAG	▪ longer duration of the disease
29	Crichton A et al[153] 1989	Canada	Retrospective 59	NM	NM	Race: NM LTG = 59	▪ eye with greater IOP than the fellow eye
30	Tielsch JM et al[70] 1990	USA	Prevalence survey 5300	NM	NM	B = 2390 W = 2910 POAG	▪ Blacks had two-fold excess prevalence of blindness and visual impairment than whites. ▪ Rates rose sharply with age
31	Mao LK et al[72] 1991	USA	Retrospective Case =28 Control = 27	Case 10 Control 9	18 18	Case B = 1 W = 27 Control B = 3 W = 24 POAG	▪ IOP > 21 mmHg during follow-up ▪ Older age

Table 2. Summary of Risk Factors for Progression of POAG/OHT or blindness in glaucoma

No.	Author(s) Year	Country	Study design, Total # of patients (eyes)	Gender		Race/ diagnosis	Risk factors / comments
				M	F		
32	Stewart WC et al [73] 1993	USA	Prospective 72 Case 16 Control 56	Case 6 | 10 Control 20 | 36		Case B = 14 W = 2 Control B = 46 W = 10 POAG	▪ higher mean and peak IOP ▪ high stand deviation of IOP ▪ noncompliance ▪ history of argon laser trabeculoplasty
33	Hattenhauer MG et al[8] 1998	USA	Retrospective 295	109	186	Race = W POAG = 265 Exfoliation = 25 Pigmentary = 5	▪ Longer duration of the disease ▪ Disc or VF damage at the time of diagnosis ▪ Old age
34	Martínez-Belló C et al[154] 1999	Canada	Prospective 113 (113)	55	58	POAG Race (NM)	▪ Baseline VF status ▪ Peak IOP
35	Bergea B et al[155] 1999	Sweden	Prospective 76 (76)	NM	NM	W POAG = 21 Pseudoexfoliation = 55	▪ High mean IOP and greater IOP variation (range and peak)
36	Hayreh SS et al[36] 1999	USA	Prospective 275	139	136	Race: W NTG = 131 POAG = 30 Nonarteritic optic neuropathy = 114	▪ Use of topical beta blockers, by affecting nocturnal arterial hypotension and reducing heart rate
37	Chen PP et al [156] 2000	USA	Retrospective 48	NM	NM	W = 43 B = 1 Other = 4 POAG = 31 PXG = 11 Pigmentary glaucoma = 36	▪ Level of VF loss at initial testing

Table 2. Summary of Risk Factors for Progression of POAG/OHT or blindness in glaucoma

No.	Author(s) Year	Country	Study design, Total # of patients (eyes)	Gender		Race/ diagnosis	Risk factors / comments
				M	F		
38	Chen PP et al [157] 2000	USA	Retrospective 36	21	15	WB = 30 B = 3 Others = 3 POAG = 18 Pseudoexfoliation = 14 NTG = 2 Pigmentary glaucoma = 2	▪ All had severe monocular VF defects Risk factors for progression to fellow eye if: ▪ large initial cup:disc ratio ▪ Low ocular perfusion ▪ smaller between-eyes difference in the initial Advanced Glaucoma Interventional Study Score
39	Resker MTE, et al [158] 2000	Netherlands	Prospective NTG = 34 POAG = 68 OHT = 125	NM	NM	NTG POAG OHT Race = NM	▪ Older age ▪ Rate of VF damage similar in NTG and POAG
40	Lichter PR et al [159] 2001	USA	Prospective 607 Medicine group = 307 Surgery group = 300	Medicine group 164 | 143 Surgery group 170 | 130		Medicine group White = 167 Others = 140 Surgery group W = 170 Others = 130	▪ Poor reduction in IOP from baseline
41	Kwon YH et al [160] 2001	USA	Retrospective 40 (40)	16	24	White = 40 POAG	▪ Higher IOP and smaller number of antiglaucoma medications on initial presentation ▪ Glaucoma surgery
42	Tezel G [161] 2001	USA	Retrospective POAG = 93 (186) NTG = 69 (138)	POAG 44 NTG 22	 49 47	POAG B = 9 Others = 84 NTG B = 5 Others = 64	▪ smaller neural rim area - disc area ratio at baseline ▪ larger zone β area - disc area ratio at baseline ▪ larger parapapillary atrophy length - disc circumference ratio at baseline ▪ diagnosis of NTG ▪ prior combined medical and surgical treatment

Table 2. Summary of Risk Factors for Progression of POAG/OHT or blindness in glaucoma

No.	Author(s) Year	Country	Study design, Total # of patients (eyes)	Gender		Race/ diagnosis	Risk factors / comments
				M	F		
43	Chen DP [162] 2002	USA	Retrospective 152	76	76	W = 120 B = 15 Others = 17 POAG = 90 Pseudoexfoliation = 18 Pigmentary glaucoma = 13 NTG = 31	▪ level of maximum IOP in either eye worse eye or better eye ▪ progression in the better eye ▪ large initial VF defect ▪ optic disc hemorrhage ▪ longer follow-up ▪ longer duration of disease
44	Kass MA et al [163] 2002	USA	Prospective 1636 Case (817) Control (819)	Case 359 | 458 Control 346 | 473		Case W = 577 B = 203 Other = 38 Control W = 560 B = 205 Other = 54 OHT	▪ Elevated IOP
45	Jonas JB et al [164] 2002	Germany	Prospective 257 (394) Case 39 (42) Control 218 (352)	Case 22 | 17 Control 113 | 105		White 257 POAG	▪ Small size of neuroretinal rim ▪ Large area of β zone of parapapillary atrophy
46	Shin DH et al [165] 2002	USA	Case-Control Study Case (124) Control (59)	Case 72 52 Control 23 36		POAG Case B = 71 W = 53 Control B = 23 W = 35	▪ Poor control after combined cataract and glaucoma procedures and no use of mitomycin-C
47	Wilson RM et al [166] 2002	St. Lucia, West Indies	Cohort study 155 (287)	47	108	Black POAG = 81 Suspects = 74	▪ Older age

Table 2. Summary of Risk Factors for Progression of POAG/OHT or blindness in glaucoma

No.	Author(s) Year	Country	Study design, Total # of patients (eyes)	Gender		Race/ diagnosis	Risk factors / comments
				M	F		
48	Landers J et al [167] 2002	Australia	Retrospective POAG = 438 OHT = 301	POAG 195 243 OHT 112 189		Race (NM) POAG = 438 OHT = 301	▪ Older age at diagnosis ▪ Myopia ▪ Elevated IOP ▪ Family history of glaucoma
49	Gordon MO et al [168] 2002	USA	Prospective Case = 125 Control = 1493	Case 72 53 Control 625 868		Case W = 76 B = 40 Others = 9 Control W = 1057 B = 359 Others = 78	▪ Older age, large vertical or horizontal cup:disc ratio, elevated IOP, greater pattern standard deviation, thin central corneal thickness
50	Shigeeda T et al [169] 2002	Japan	Retrospective 23	NM	NM	Japanese NTG	▪ Trabeculectomy slowed further progression of VF damage ▪ Progression did not completely stop
51	Leske MC et al [170] 2003	Sweden	Prospective Case = 129 Control = 126	NM	NM	W POAG	▪ Magnitude of initial IOP ▪ Higher baseline IOP ▪ Bilateral disease ▪ Pseudoexfoliation ▪ Worse mean deviation ▪ Older age ▪ Frequent disc hemorrhages
52	Chen PP [171] 2003	USA	Retrospective 186	95	91	W = 152 B = 14 Other = 20 POAG = 105 Pseudoexfoliation = 26 NTG = 41 Pigmentary = 14	▪ Worse VF loss at diagnosis ▪ Late detection ▪ Noncompliance
53	Asrani S [172] 2000	USA	Prospective 64 (105)	31	33	POAG W = 57 B = 5 Other = 2	▪ Large fluctuations in IOP

Table 2 Key

IOP = intraocular pressure

POAG = primary open angle glaucoma

NM = not mentioned

B = black

W = white

VA = visual acuity

C/D = cup-to-disc ratio

OHT = ocular hypertension

LTG = low tension glaucoma

NTG = normal tension glaucoma

VF = visual field

PXG = pseudoexfoliation

Table 3. Demographics and characteristics of composite Dallas patient population and comparision of the three clinic patient populations					
Characteristics	**Composite Dallas Patient Population n (%); total 487**	**Clinic A Patients n (%), total 231**	**Clinic B Patients n (%), total 98**	**Clinic C Patients n (%), total 158**	**p value**
Age at diagnosis, yr (mean ± SD, median, range)	59.12 ± 12.9, 60.02, 21.1 – 90.4	59.50 ± 14.04, 60.0, 21.1 – 90.4	59.05 ± 11.6, 60.3, 30.0 – 86.8	58.6 ± 11.8, 60.1, 24.3 – 81.40	0.460
Age at first visit, yr (mean ± SD, median, range)	63.95 ± 12.20, 65.22, 21.1 – 91.7	64.15 ± 13.62, 66.3, 21.1 – 89.9	60.3 ± 11.4, 60.9, 29.9 – 86.8	65.9 ± 9.8, 66.2, 39.6 – 91.7	0.370
Follow-up, yr	5.5 ± 3.6, 4.5, 0.3 – 23.7	5.1 ± 3.5, 4.0, 1.0 – 23.7	4.9 ± 1.8, 4.6, 0.9 – 11.3	6.4 ± 4.3, 5.4, 0.3 – 22.2	0.670
Legal blindness					
Bilateral	120 (24.6)	51 (22.0)	12 (12.2)	56 (35.4)	0.04
Unilateral	85 (17.4)	39 (16.8)	16 (16.3)	30 (19.0)	
Gender					
Male	290 (59.5)	100 (43.3)	34 (34.7)	156 (98.7)	<0.001
Female	197 (40.5)	131 (56.7)	64 (65.3)	2 (1.3)	
Race					
Caucasian	193 (39.7)	125 (54.1)	7 (7.1)	61 (38.6)	
Afro-American	253 (51.9)	79 (34.2)	82 (83.7)	92 (58.2)	
Hispanic	19 (3.9)	11 (4.8)	6 (6.1)	2 (1.3)	<0.001
American Indian	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.6)	
Other	21 (4.3)	16 (6.9)	3 (3.1)	2(1.3)	
Risk Factors					
Ocular trauma	36 (7.4)	13 (5.6)	10 (10.2)	13 (8.2)	0.310
Myopia	57 (11.7)	35 (15.1)	12 (12.2)	10 (6.3)	0.03
Diabetes	106 (21.8)	30 (13.0)	41 (41.8)	35 (22.1)	<0.0001
Family history	160 (33.2)	91 (39.7)	21 (21.9)	48 (30.6)	0.005
Hypertension	241 (49.6)	97 (42.0)	58 (59.2)	86 (54.8)	0.005

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Characteristics	**Composite Dallas Patient Population n (%); total 487**	**Clinic A Patients n (%), total 231**	**Clinic B Patients n (%), total 98**	**Clinic C Patients n (%), total 158**	**p value**
Systemic steroids	15 (3.1)	10 (4.3)	1 (1.0)	4 (2.5)	0.252
Topical steroids	8 (1.6)	4 (1.7)	1 (1.0)	3 (1.9)	0.860
Dysthyroidism	27 (5.6)	23 (10.0)	1 (1.0)	3 (1.9)	<0.0003
Vascular disease	138 (28.4)	69 (30.0)	12 (12.2)	57 (36.3)	<0.0001
Alcohol abuse	53 (10.9)	17 (7.4)	5 (5.1)	31 (19.6)	<0.0001
Smoking	120 (24.6)	32 (13.8)	17 (17.3)	71 (44.9)	<0.0001
Other Ocular Diseases					
Visit one	214 (44.0)	84 (36.4)	36 (36.7)	94 (60.0)	<0.0001
Final visit	85 (17.4)	21 (9.1)	12 (12.2)	52 (32.9)	<0.0001
Diagnosed in Dallas	195 (40.1)	91 (39.4)	66 (67.3)	38 (24.0)	<0.0001
Ocular Surgeries					
Cataract	100 (20.5)	60 (26.0)	10 (10.2)	30 (19.00)	0.004
ALT	181 (37.2)	84 (36.4)	26 (26.5)	71 (44.9)	0.011
LPI	60 (12.3)	41 (17.8)	4 (4.1)	15 (9.5)	0.001
Trabeculectomy	88 (18.1)	43 (18.6)	12 (12.2)	33 (20.9)	0.208
Combined	57 (11.7)	29 (12.5)	7 (7.1)	21 (13.3)	0.283
Other	30 (6.2)	17 (7.4)	2 (2.0)	11 (7.0)	0.163
Cyclodestruction	9 (1.8)	2 (0.9)	0 (0.0)	7 (4.4)	0.011
Visual Acuity					
Visit one					
20/20	144 (29.6)	81 (35.1)	27 (27.5)	36 (22.8)	
20/40	201 (41.3)	92 (39.8)	51 (52.0)	58 (36.7)	
20/60	47 (9.6)	20 (8.7)	10 (10.2)	17 (10.8)	
20/80	16 (3.3)	5 (2.2)	3 (3.1)	8 (5.1)	
20/100	11 (2.3)	9 (3.9)	1 (1.0)	1 (0.6)	
20/200	6 (1.2)	3 (1.3)	1 (1.0)	2 (1.3)	

Table 3. Demographics and characteristics of composite Dallas patient population and comparision of the three clinic patient populations					
Characteristics	**Composite Dallas Patient Population n (%); total 487**	**Clinic A Patients n (%), total 231**	**Clinic B Patients n (%), total 98**	**Clinic C Patients n (%), total 158**	**p value**
CF	29 (6.0)	7 (5.2)	2 (2.0)	15 (9.5)	0.002
HM	12 (2.5)	8 (1.3)	2 (2.0)	7 (4.4)	
LP	14 (2.9)	9 (2.2)	1 (1.0)	8 (5.1)	
NLP	7 (1.4)	1 (0.4)	0 (0.0)	6 (3.8)	
Final Visit					
20/20	108 (22.2)	52 (22.5)	23 (23.5)	33 (21.0)	0.004
20/40	192 (39.4)	92 (39.8)	48 (49.00)	52 (32.9)	
20/60	51 (10.5)	31 (13.4)	7 (7.1)	13 (8.2)	
20/80	20 (4.1)	12 (5.2)	4 (4.1)	4 (2.5)	
20/100	13 (2.7)	10 (4.3)	1 (1.0)	2 (1.3)	
20/200	14 (2.9)	6 (2.6)	3 (3.1)	5 (3.2)	
CF	41 (8.4)	16 (6.9)	4 (4.1)	21 (13.3)	
HM	15 (3.1)	2 (0.9)	3 (3.1)	10 (6.3)	
LP	12 (2.5)	4 (1.7)	2 (2.0)	6 (3.8)	
NLP	21 (4.3)	6 (2.6)	3 (3.1)	12 (7.6)	
Visual Acuity Deterioration	118 (24.2)	58 (25.1)	21 (21.4)	39 (24.7)	0.766
Visual Field					
Visit 1					
1	85 (17.4)	50 (21.6)	13 (13.3)	22 (13.9)	<0.0001
2	146 (30.0)	56 (24.2)	60 (61.2)	30 (19.0)	
3	52 (10.7)	21 (9.1)	8 (8.2)	23 (14.6)	
4	52 (10.7)	25 (10.8)	5 (5.1)	22 (14.0)	
5	40 (8.2)	22 (9.5)	5 (5.1)	13 (8.2)	
6	65 (13.3)	44 (19.0)	3 (3.1)	18 (11.4)	
7	47 (9.6)	13 (5.6)	4 (4.1)	30 (19.0)	
Final Visit					

Table 3. Demographics and characteristics of composite Dallas patient population and comparision of the three clinic patient populations					
Characteristics	**Composite Dallas Patient Population n (%); total 487**	**Clinic A Patients n (%), total 231**	**Clinic B Patients n (%), total 98**	**Clinic C Patients n (%), total 158**	**p value**
1	60 (12.3)	32 (13.8)	8 (8.2)	20 (12.7)	<0.0001
2	136 (27.9)	53 (22.9)	55 (56.1)	28 (17.7)	
3	58 (11.9)	27 (11.7)	12 (12.2)	19 (12.0)	
4	54 (11.1)	22 (9.5)	9 (9.2)	23 (14.6)	
5	47 (9.6)	26 (11.3)	6 (6.1)	15 (9.5)	
6	72 (14.8)	49 (21.2)	3 (3.1)	20 (12.7)	
7	60 (12.3)	22 (9.5)	5 (5.1)	33 (20.9)	
VF Progression	93 (19.1)	52 (22.5)	17 (17.3)	24 (15.2)	0.174
IOP, mmHg (mean ± SD, median, range)					
Visit 1	23.2 ± 10.1, 22,7, 2.0 – 70	23.6 ± 9.3, 22, 2 – 70	23.2 ± 8.8, 20.7, 7 – 65	22.5 ± 9.7, 20, 2 – 62	0.431
Final visit	18.1 ± 3.2, 18.1 3.0 – 46.0	18.3 ± 2.8, 18.5, 0 – 43	18.7 ± 2.2, 18.5, 11 – 29	17.7 ± 3.7, 17.6, 3 – 46	
C/D Ratios					
Visit 1					
0.1 - 0.5	110 (22.6)	57 (24.7)	22 (22.4)	31 (19.6)	0.066
>0.5 - 0.7	121 (24.8)	60 (26.0)	31 (31.6)	30 (19.0)	
> 0.7 - 1.0	256 (52.6)	114 (49.3)	45 (45.9)	97 (61.4)	
final visit					
0.1 - 0.5	61 (12.5)	36 (15.6)	13 (13.3)	12 (7.6)	0.029
>0.5 - 0.7	119 (24.4)	55 (23.8)	31 (31.6)	33 (20.9)	
> 0.7 - 1.0	307 (63.0)	140 (60.6)	54 (55.10)	113 (71.5)	
C/D Ratio Progression	147 (30.2)	79 (34.2)	28 (28.6)	40 (25.3)	0.160
Antiglaucoma Medications					

Table 3. Demographics and characteristics of composite Dallas patient population and comparision of the three clinic patient populations					
Characteristics	**Composite Dallas Patient Population n (%); total 487**	**Clinic A Patients n (%), total 231**	**Clinic B Patients n (%), total 98**	**Clinic C Patients n (%), total 158**	**p value**
Beta blockers	454 (93.2)	209 (90.5)	96 (98.0)	149 (94.3)	0.038
Miotics	315 (64.7)	128 (55.4)	65 (66.3)	122 (77.2)	<0.0001
Epinephrine	184 (37.8)	85 (36.8)	31 (3.6)	68 (43.0)	0.171
CAI systemic	128 (26.3)	52 (22.5)	29 (29.6)	47 (29.8)	0.200
CAI topical	114 (23.4)	60 (26.0)	21 (21.4)	33 (20.9)	0.444
Alpha agonists	81 (16.6)	53 (22.9)	15 (15.3)	13 (8.2)	0.0006
Prostaglandin analogue	15 (3.1)	14 (6.1)	0 (0.0)	1 (0.6)	0.001
Noncompliance	260 (53.4)	109 (47.2)	67 (68.4)	84 (53.2)	0.002
Poor Control	403 (82.7)	198 (85.7)	76 (77.5)	129 (81.6)	0.181
Late Detection	443 (91.0)	212 (91.8)	95 (96.9)	136 (86.1)	0.012

ALT = argon laser trabeculoplasty; LPI = laser peripheral iridotomy

CF = count fingers; HM = hand motions; LP = light perception; NLP = no light perception

VF - visual field; IOP = intraocular pressure; C/D = cup-to-disc; CAI = carbonic anhydrase inhibitor

Table 4. Demographics and Characteristics of Composite Patient Population: NLB versus LB			
Characteristics	**NLB n (%) total = 282**	**LB n (%) total = 205**	**p value**
Age at diagnosis, yr (mean ± SD, median, range)	59.0 ± 12.6, 59.4, 21.2 – 86.9	59.3 ± 13.2, 61.1, 28.8 – 90.4	0.52
Age at first visit, yr (mean ± SD, median, range)	62.3 ± 11.9, 62.9, 21.1 – 89.0	66.1 ± 12.3, 67.0, 26.8 – 91.7	0.431
Follow-up, yr (mean ± SD, median, range)	5.1 ± 3.1, 4.2 1.0 –18.1	6.1 ± 4.0, 5.2, 0.3 – 23.7	0.04
Gender			
Male	151 (53.5)	139 (67.8)	p<0.002
Female	131 (46.4)	66 (32.2)	
Race			
Caucasian	124 (44.0)	69 (33.7)	
Afro-American	134 (47.4)	119 (58.1)	0.120
Hispanic	12 (4.3)	7 (3.4)	
Others	12 (4.3)	10 (4.8)	
Risk Factors			
Ocular trauma	23 (8.2)	13 (6.3)	0.5
Myopia	34 (12.0)	23 (11.2)	0.90
Diabetes	66 (23.4)	40 (19.5)	0.320
Family history	98 (35.1)	62 (30.5)	0.330
Hypertension	132 (46.8)	109 (53.4)	0.20
Systemic steroids	5 (1.8)	10 (4.9)	0.1
Topical steroids	3 (1.1)	5 (2.4)	0.30
Dysthyroidism	16 (5.7)	11 (5.4)	1.000
Vascular disease	76 (27.1)	62 (30.2)	0.5
Alcohol abuse	26 (9.1)	27 (13.2)	0.2
Smoking	71 (25.2)	49 (24.0)	0.830
Other Ocular Diseases			
visit 1	104 (36.9)	110 (53.9)	<0.0002
last visit	44 (15.6)	41 (20.0)	0.230
Diagnosed in Dallas	135 (47.9)	60 (29.3)	<0.0001
Ocular Surgeries			
Cataract	52 (18.4)	48 (23.4)	0.211
ALT	92 (32.6)	89 (43.4)	0.020
LPI	29 (10.3)	31 (15.2)	0.124
Trabeculectomy	28 (9.9)	60 (29.3)	<0.0001
Combined	22 (7.8)	18 (8.8)	0.740
Cyclodestruction	0 (0.0)	9 (4.4)	<0.0004
Others	14 (5.0)	16 (7.8)	0.252
Visual Acuity - visit one			

Table 4. Demographics and Characteristics of Composite Patient Population: NLB versus LB			
Characteristics	**NLB n (%) total = 282**	**LB n (%) total = 205**	**p value**
20/20	105 (37.2)	26 (12.7)	<0.0001
20/40	156 (52.2)	67 (32.7)	<0.0001
20/60	15 (5.3)	29 (14.1)	0.001
20/80	3 (1.0)	3 (1.4)	0.70
20/100	1 (0.3)	6 (1.9)	0.20
20/200	0 (0.0)	12 (5.8)	<0.0001
CF	0 (0.0)	25 (12.2)	<0.0001
HM	0 (0.0)	18 (8.8)	<0.0001
LP	0 (0.0)	7 (2.4)	0.002
NLP	0 (0.0)	14 (6.8)	<0.0001
- last visit			
20/20	88 (31.2)	14 (6.8)	<0.0001
20/40	157 (55.7)	38 (18.5)	<0.0001
20/60	24 (8.5)	24 (11.7)	0.30
20/80	6 (2.1)	9 (4.4)	0.20
20/100	7 (2.3)	5 (2.4)	0.10
20/200	0 (0.0)	19 (9.3)	<0.0001
CF	0 (0.0)	35 (17.1)	<0.0001
HM	0 (0.0)	21 (10.2)	<0.0001
LP	0 (0.0)	17 (8.3)	0.001
NLP	0 (0.0)	23 (11.2)	<0.0001
Visual Acuity Deterioration	36 (12.7)	82 (40.0)	<0.0001
Visual Field - visit 1			
1	73 (25.9)	12 (5.8)	<0.0001
2	129 (45.8)	17 (8.3)	<0.0001
3	35 (12.4)	17 (8.3)	0.20
4	20 (7.1)	32 (15.6)	0.004
5	18 (6.4)	22 (10.7)	0.10
6	6 (2.1)	59 (28.8)	<0.0001
7	1 (0.35)	46 (22.4)	<0.0001
- final visit			
1	54 (19.1)	6 (2.9)	<0.0001
2	125 (44.3)	11 (5.4)	<0.0001
3	45 (16.0)	13 (6.3)	0.001
4	26 (9.2)	28 (13.7)	0.144
5	32 (11.4)	27 (13.2)	0.030
6	0 (0.0)	62 (30.2)	<0.0001
7	0 (0.0)	58 (28.3)	<0.0001
VF Progression	46 (16.3)	47 (22.9)	0.10
IOP mmHg (mean ± SD, median, range)			

Table 4. Demographics and Characteristics of Composite Patient Population: NLB versus LB			
Characteristics	**NLB n (%) total = 282**	**LB n (%) total = 205**	**p value**
· visit one	22.1 ± 7.7, 21.0, 2 – 70	24.2 ±11.2, 21.0, 2.0 – 70.0	0.030
· final visit	18.1 ± 2.4, 18.0, 10.0 – 26.0	17.7 ± 4.8, 18.0, 0.0 – 46.0	0.153
C/D ratios · visit one			
0.1 – 0.5	87 (30.8)	23 (11.2)	<0.0001
>0.5 – 0.7	93 (33.0)	28 (13.7)	<0.0001
>0.7 – 1.0	102 (36.2)	154 (75.0)	<0.0001
· final visit			
0.1 – 0.5	53 (18.8)	8 (3.9)	<0.0001
>0.5 – 0.7	97 (34.4)	22 (10.8)	<0.0001
> 0.7 – 1.0	132 (46.8)	175 (85.4)	<0.0001
C/D Ratio Progression	92 (32.6)	55 (26.8)	0.20
Antiglaucoma medications			
Beta blocker	262 (92.9)	192 (93.6)	0.744
Miotics	158 (56.0)	157 (76.6)	<0.0001
Epinephrine	93 (33.0)	91 (44.4)	0.10
CAI systemic	49 (17.4)	79 (38.5)	0.0001
CAI topical	59 (20.9)	55 (26.6)	0.131
Alpha agonists	43 (15.2)	38 (18.5)	0.40
Prostaglandin analogue	8 (2.8)	7 (3.4)	0.803
Non-compliance	131 (46.4)	129 (63.0)	<0.0003
Poor Control	207 (73.4)	196 (95.6)	<0.0001
Late Detection	248 (87.9)	195 (95.1)	0.006

ALT = argon laser trabeculoplasty; LPI = laser peripheral iridotomy

CF = count fingers; HM = hand motion; LP = light perception

NLP = no light perception; VF = visual field; IOP = intraocular pressure

C/D · cup-to-disc; CAI = carbonic anhydrase inhibitor

Table 5. Demographics and Characteristics of Composite Dallas Patient Population with NLB Who Did Not Progress versus those who Did Progress			
Characteristics	**Patients with no progression n (%) total = 148**	**Patients who progressed n (%) total = 134**	**p value**
Age at diagnosis, yr. (mean ± SD, median, range)	59.1 ± 12.6, 59.5, 22.1 – 86.9	58.9 ± 12.6, 59.1 21.7 – 83.3	0.90
Age at first visit, yr. (mean ± SD, median, range)	62.9 ± 11.6, 62.8, 30.6 – 88.7	61.7 ± 12.1, 63.3, 21.1 – 86.7	.403
Follow-up, yr (mean ± SD, median, range)	4.1 ± 2.5, 3.5, 1.0 – 16.4	6.2 ± 3.4, 4.9, 1.2 – 18.1	<0.0001
Gender			
Male	90 (60.8)	61 (45.5)	0.012
Female	58 (39.2)	73 (54.5)	
Race			
Caucasian	68 (45.9)	56 (41.8)	
Afro-American	68 (45.9)	66 (49.2)	0.8
Hispanic	5 (3.5)	7 (5.3)	
Others	7 (4.7)	5 (3.7)	
Risk Factors			
Ocular trauma	12 (8.1)	11 (8.2)	1.0
Myopia	22 (14.9)	12 (9.0)	0.13
Diabetes	31 (20.9)	35 (26.1)	0.305
Family history	54 (36.7)	44 (33.3)	0.552
Hypertension	64 (43.2)	68 (50.7)	0.233
Systemic steroids	5 (3.4)	0 (0.0)	0.10
Topical steroids	3 (2.0)	0 (0.0)	0.250
Dysthyroidism	9 (6.1)	7 (5.2)	0.802
Vascular disease	37 (25.2)	39 (29.3)	0.501
Alcohol abuse	17 (11.5)	9 (6.7)	0.220
Smoking	41 (22.7)	30 (22.4)	0.34
Other ocular diseases			
- visit one	52 (35.1)	52 (18.8)	0.54
- final visit	23 (15.5)	21 (15.7)	1.000
Diagnosed in Dallas	79 (53.4)	68 (50.7)	0.720
Ocular Surgeries			
Cataract	23 (15.5)	29 (21.6)	0.720
ALT	38 (25.7)	54 (40.3)	0.011
LPI	11 (7.4)	19 (14.2)	0.10
Trabeculectomy	13 (8.8)	15 (11.2)	0.553
combined	11 (7.4)	18 (13.4)	0.120
Others	6 (4.1)	8 (6.0)	0.600
Visual Acuity - visit one			
20/20	52 (35.1)	53 (39.5)	

Table 5. Demographics and Characteristics of Composite Dallas Patient Population with NLB Who Did Not Progress versus those who Did Progress			
Characteristics	**Patients with no progression n (%) total = 148**	**Patients who progressed n (%) total = 134**	**p value**
20/40	83 (56.1)	73 (54.5)	
20/60	8 (5.4)	7 (5.2)	0.6
20/80	3 (2.0)	0 (0.0)	
20/100	2 (1.3)	1 (0.7)	
- final visit			
20/20	45 (30.4)	45 (33.6)	
20/40	80 (54.0)	70 (52.2)	
20/60	15 (10.1)	12 (9.0)	
20/80	3 (2.0)	6 (4.5)	0.5
20/100	1 (0.7)	1 (0.7)	
20/200	2 (1.3)	0 (0.0)	
CF	2 (1.3)	0 (0.0)	
Visual Acuity Deterioration	10 (6.8)	22 (16.4)	0.014
VF Status - visit 1			
1	39 (26.3)	34 (25.4)	
2	68 (45.9)	61 (45.5)	
3	14 (9.5)	21 (15.7)	0.40
4	14 (9.5)	6 (4.5)	
5	13 (8.8)	12 (8.9)	
- final visit			
1	38 (25.7)	16 (11.9)	
2	69 (46.6)	56 (42.0)	
3	14 (9.5)	31 (23.1)	
4	14 (9.5)	12 (9.0)	
5	13 (8.8)	12 (9.0)	0.008
6	0 (0.0)	6 (4.5)	
7	0 (0.0)	1 (0.7)	
VF Progression	0 (0.0)	46 (34.3)	<0.0001
IOP (mean, ±SD, median, range)			
- visit one	22.1 ± 5.2, 22.0, 10.0 – 45.0	23.5 ± 10.3, 23.8, 17.0 – 60.0	0.04
- final visit	18.2 ± 3.6, 18.4, 15.0 – 35.0	18.7 ± 4.8, 18.5, 14 – 40.0	0.23
C/D ratios - visit one			
0.1 – 0.5	38 (25.7)	58 (43.3)	
>0.5 – 0.7	49 (33.1)	40 (29.8)	0.004
>0.7 – 1.0	61 (41.2)	36 (26.9)	
- final visit			
0.1 – 0.5	38 (25.7)	27 (20.1)	
>0.5 – 0.7	49 (33.1)	45 (33.6)	0.50

Table 5. Demographics and Characteristics of Composite Dallas Patient Population with NLB Who Did Not Progress versus those who Did Progress			
Characteristics	**Patients with no progression n (%) total = 148**	**Patients who progressed n (%) total = 134**	**p value**
> 0.7 – 1.0	61 (41.2)	62 (46.3)	
C/D Ratio Progression	0 (0.0)	92 (68.7)	<0.0001
Antiglaucoma medications			
Beta blocker	137 (92.6)	125 (93.3)	1.000
Miotics	66 (44.6)	92 (68.7)	<.0001
Epinephrine	34 (23.0)	59 (44.0)	<0.0002
CAI systemic	23 (15.5)	26 (19.4)	0.433
CAI topical	32 (21.6)	27 (20.1)	0.8
Alpha agonists	18 (12.2)	25 (18.7)	0.140
Prostaglandin analogue	3 (2.0)	6 (4.5)	0.123
Non-compliance	62 (41.9)	69 (51.5)	0.121
Poor Control	83 (56.1)	124 (92.5)	<0.0001
Late Detection	131 (88.5)	117 (87.3)	0.855

ALT = argon laser trabeculoplasty; LPI = laser peripheral iridotomy

VF = visual field; C/D = cup-to-disc; IOP = intraocular pressure

CAI = carbonic anhydrase inhibitor

Table 6. Demographics and Characteristics of Patients with legal blindness, diagnosed initially in Dallas, in comparison of the three Clinic Patient Populations					
Characteristics	**Composite Dallas Patient Population n (%); total 60**	**Clinic A Patients n (%), total 29**	**Clinic B Patients n (%), total 17**	**Clinic C Patients n (%), total 14**	**p value**
Age at diagnosis, yr (mean ± SD, median, range)	61.3 ± 12.9, 62.8, 29.9 – 86.7	62.7 ± 13.5, 62.9, 37.6 – 86.7	58.05 ± 13.7, 59.2, 29.9 – 82.0	62.6 ± 10.6, 65.3, 46.3 – 76.3	0.460
Follow-up, yr	6.1 ± 3.8, 5.3, 1.3 – 21.7	5.7 ± 3.2, 6.3, 1.3 – 12.2	5.9 ± 2.5, 5.6, 2.7 – 11.3	6.9 ± 5.8, 4.6, 1.3 – 21.7	0.615
Gender					
Male	34 (56.7)	12 (41.4)	9 (52.9)	13 (92.9)	0.0006
Female	26 (43.3)	17 (58.6)	8 (47.1)	1 (7.1)	
Race					
Caucasian	16 (26.7)	12 (41.4)	0 (0.0)	4 (28.6)	0.034
Afro-American	39 (65.0)	13 (44.8)	16 (94.1)	10 (71.4)	
Hispanic	4 (6.7)	3 (10.3)	1 (5.9)	0 (0.0)	
American Indian	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Other	1 (1.6)	1 (3.5)	0 (0.0)	0 (0.0)	
Risk Factors					
Ocular trauma	6 (10.0)	1 (3.4)	3 (17.6)	2 (14.3)	0.250
Myopia	13 (21.7)	6 (20.7)	1 (6.2)	6 (42.9)	0.05
Diabetes	16 (26.7)	6 (20.7)	7 (41.2)	3 (21.4)	0.30
Family history	13 (21.7)	6 (20.7)	1 (6.2)	6 (42.9)	0.05
Hypertension	28 (46.7)	13 (44.8)	9 (52.9)	6 (42.9)	0.823
Systemic steroids	3 (5.0)	2 (6.9)	0 (0.0)	1 (7.1)	0.535
Topical steroids	2 (3.3)	1 (3.4)	0 (0.0)	1 (7.1)	0.543
Dysthyroidism	2 (3.3)	1 (3.4)	0 (0.0)	1 (7.1)	0.543
Vascular disease	16 (26.7)	10 (34.5)	2 (11.8)	4 (48.6)	0.240

Table 6. Demographics and Characteristics of Patients with legal blindness, diagnosed initially in Dallas, in comparison of the three Clinic Patient Populations					
Characteristics	**Composite Dallas Patient Population n (%); total 60**	**Clinic A Patients n (%), total 29**	**Clinic B Patients n (%), total 17**	**Clinic C Patients n (%), total 14**	**p value**
Alcohol abuse	2 (3.3)	2 (6.9)	0 (0.0)	0 (0.0)	0.331
Smoking	8 (13.3)	4 (13.8)	0 (0.0)	4 (28.6)	0.10
Other Ocular Diseases					
- visit one	28 (46.7)	11 (37.9)	9 (52.9)	8 (57.1)	0.412
- final visit	8 (13.3)	3 (10.3)	1 (5.9)	4 (28.6)	0.150
Ocular Surgeries					
Cataract	10 (16.7)	7 (24.1)	2 (11.8)	1 (7.1)	0.305
ALT	29 (48.3)	14 (48.3)	8 (47.1)	7 (50.0)	1.000
LPI	11 (18.3)	7 (24.1)	2 (11.8)	2 (14.3)	0.523
Trabeculectomy	12 (20.0)	6 (20.7)	6 (35.3)	0 (0.0)	0.05
Combined	8 (13.3)	4 (13.8)	2 (11.8)	2 (14.3)	1.000
Other	6 (10.0)	4 (13.8)	1 (5.9)	1 (7.1)	0.634
Visual Acuity					
Visit one					
20/20	11 (18.3)	8 (27.6)	2 (11.8)	1 (7.1)	
20/40	27 (45.0)	12 (41.4)	12 (70.6)	3 (21.4)	
20/60	6 (10.0)	3 (10.3)	0 (0.0)	3 (21.4)	0.011
20/80	1 (1.7)	1 (3.4)	0 (0.0)	0 (0.0)	
20/100	2 (3.3)	1 (3.4)	0 (0.0)	1 (7.1)	
20/200	3 (5.0)	3 (10.3)	0 (0.0)	0 (0.0)	
CF	4 (6.7)	1 (3.4)	0 (0.0)	3 (21.4)	
HM	2 (3.3)	0 (0.0)	2 (11.8)	0 (0.0)	
LP	1 (1.7)	0 (0.0)	0 (0.0	1 (7.1)	
NLP	3 (5.0)	0 (0.0)	1 (5.9)	2 (14.3)	
Final Visit					
20/20	8 (13.3)	5 (17.2)	1 (5.9)	2 (14.3)	
20/40	15 (25.0)	9 (31.0)	2 (11.8)	4 (28.6)	

Table 6. Demographics and Characteristics of Patients with legal blindness, diagnosed initially in Dallas, in comparison of the three Clinic Patient Populations					
Characteristics	**Composite Dallas Patient Population n (%); total 60**	**Clinic A Patients n (%), total 29**	**Clinic B Patients n (%), total 17**	**Clinic C Patients n (%), total 14**	**p value**
20/60	8 (13.3)	4 (13.8)	2 (11.8)	2 (14.3)	0.50
20/80	3 (5.0)	0 (0.0)	2 (11.8)	1 (7.1)	
20/100	5 (8.3)	4 (13.8)	1 (5.9)	0 (0.0)	
20/200	3 (5.0)	1 (3.4)	2 (11.8)	0 (0.0)	
CF	4 (6.7)	3 (10.3)	1 (5.9)	0 (0.0)	
HM	3 (5.0)	0 (0.0)	2 (11.8)	1 (7.1)	
LP	3 (5.0)	1 (3.4)	1 (5.9)	1 (7.1)	
NLP	8 (6.9)	2 (6.9)	3 (17.6)	3 (21.4)	
Visual Acuity Deterioration	26 (43.3)	12 (41.4)	9 (52.9)	5 (35.7)	0.602
Visual Field					
Visit 1					
1	5 (8.3)	3 (10.3)	2 (11.8)	0 (0.0)	0.020
2	10 (16.7)	5 (17.2)	5 (29.4)	0 (0.0)	
3	4 (6.7)	1 (3.4)	2 (11.8)	1 (7.1)	
4	9 (15.0)	3 (10.3)	1 (5.9)	5 (35.7)	
5	5 (8.3)	1 (3.4)	3 (17.6)	1 (7.1)	
6	17 (28.3)	13 (44.8)	2 (11.8)	2 (14.3)	
7	10 (16.7)	3 (10.3)	1 (11.8)	5 (35.7)	
Final Visit					
1	1 (1.8)	1 (3.4)	0 (0.0)	0 (0.0)	0.121
2	7 (11.7)	3 (10.3)	4 (25.5)	0 (0.0)	
3	5 (8.3)	2 (6.9)	2 (11.8)	1 (7.1)	
4	8 (13.3)	2 (6.9)	3 (17.6)	3 (21.4)	
5	9 (15.0)	3 (10.3)	3 (17.6)	3 (21.4)	
6	16 (26.7)	13 (44.8)	2 (11.8)	1 (7.1)	
7	14 (23.3)	5 (17.2)	3 (17.6)	6 (42.9)	
VF Progression	16 (26.7)	6 (27.6)	5 (29.4)	3 (21.4)	0.90

Table 6. Demographics and Characteristics of Patients with legal blindness, diagnosed initially in Dallas, in comparison of the three Clinic Patient Populations					
Characteristics	**Composite Dallas Patient Population n (%); total 60**	**Clinic A Patients n (%), total 29**	**Clinic B Patients n (%), total 17**	**Clinic C Patients n (%), total 14**	**p value**
IOP mmHg, (mean ± SD, median, range)					
Visit 1	25.6 ± 10.4, 24.0, 10 – 60	25.6 ± 10.4, 24 10 – 60	25.2 ± 9.5, 24.3, 14 – 40	36.3 ± 13.2, 35.0, 16 – 60	0.05
Final visit	18.1 ± 3.2, 17.7, 0 – 46	18.1 ± 3.4, 18, 0 – 43	18.9 ± 2.6, 18.5, 12 – 29	17.0 ± 3.8, 17.0, 3.0 – 46.0	0.43
C/D Ratios					
Visit 1					
0.1 - 0.5	9 (15.0)	5 (17.2)	2 (11.8)	2 (14.3)	0.80
>0.5 - 0.7	12 (20.0)	6 (20.7)	2 (11.8)	4 (28.6)	
> 0.7 - 1.0	39 (65.0)	18 (62.1)	13 (76.5)	8 (57.1)	
final visit					
0.1 - 0.5	3 (5.0)	2 (6.9)	0 (0.0)	1 (7.1)	0.503
>0.5 - 0.7	7 (11.7)	3 (10.3)	1 (5.9)	3 (21.4)	
> 0.7 - 1.0	50 (83.3)	24 (82.8)	16 (94.1)	10 (71.4)	
C/D Ratio Progression	21 (35.0)	12 (43.4)	4 (23.5)	5 (35.7)	0.50
Antiglaucoma Medications					
Beta blockers	54 (90.0)	24 (82.8)	17 (100.0)	13 (92.9)	0.16
Miotics	44 (73.3)	20 (69.0)	14 (82.3)	10 (71.4)	0.602
Epinephrine	26 (43.3)	13 (44.8)	8 (47.1)	5 (35.7)	0.800
CAI systemic	22 (36.7)	9 (31.0)	6 (35.3)	7 (50.0)	0.50
CAI topical	16 (25.7)	7 (24.1)	4 (23.5)	5 (35.7)	0.70
Alpha agonists	10 (16.7)	4 (13.8)	5 (29.4)	1 (7.1)	0.215
Prostaglandin analogue	3 (5.0)	3 (10.3)	0 (0.0)	0 (0.0)	0.20
Noncompliance	45 (75.0)	20 (69.0)	15 (88.2)	10 (71.4)	0.325
Poor Control	58 (96.7)	28 (96.5)	17 (100.0)	13 (92.9)	0.544

Table 6. Demographics and Characteristics of Patients with legal blindness, diagnosed initially in Dallas, in comparison of the three Clinic Patient Populations					
Characteristics	**Composite Dallas Patient Population n (%); total 60**	**Clinic A Patients n (%), total 29**	**Clinic B Patients n (%), total 17**	**Clinic C Patients n (%), total 14**	**p value**
Late Detection	59 (98.3)	29 (100.0)	16 (94.1)	14 (100.0)	0.30

ALT = argon laser trabeculoplasty; LPI = laser peripheral iridotomy

CF = count fingers; HM = hand motions; LP = light perception; NLP = no light perception

VF = visual field; IOP = intraocular pressure; C/D = cup-to-disc; CAI = carbonic anhydrase inhibitor

Table 7. Demographics and Characteristics of Non-legally Blind (NLB) and Legally Blind (LB) Patients of Clinic A			
Characteristics	**NLB n (%) total = 140**	**LB n (%) total = 91**	**p value**
Age at diagnosis, yr (mean ± SD, median, range)	58.1 ± 14.00, 58.60, 21.2 – 86.95	61.60 ± 14.0, 61.72, 22.85 – 90.42	0.065
Age at first visit, yr (mean ± SD, median, range)	62.32 ± 13.12, 64.12, 21.14 – 88.70	66.90 ± 13.96, 69.90, 26.8 – 89.42	0.012
Follow-up, yr	4.90 ± 3.30, 3.8, 1.00 – 18.10	5.60 ± 3.73, 4.30, 1.00 – 23.70	0.116
Gender			
Male	58 (41.43)	42 (46.15)	0.500
Female	82 (58.60)	49 (53.8)	
Race			
Caucasian	80 (57.14)	45 (49.45)	
Afro-American	44 (31.43)	35 (38.46)	0.70
Hispanic	7 (5.0)	4 (4.40)	
Others	9 (6.43)	7 (7.7)	
Risk Factors			
Ocular trauma	10 (7.10)	3 (3.30)	0.300
Myopia	16 (11.40)	19 (20.9)	0.60
Diabetes	21 (15)	9 (9.90)	0.319
Family history	57 (41.0)	34 (37.80)	0.70
Hypertension	53 (37.90)	44 (48.30)	0.134
Systemic steroids	2 (1.5)	8 (8.8)	0.015
Topical steroids	1 (0.7)	3 (3.3)	0.303
Dysthyroidism	14 (10.0)	9 (10.0)	1.00
Vascular disease	37 (26.6)	32 (35.2)	0.2
Alcohol abuse	9 (6.4)	8 (8.8)	0.61
Smoking	20 (14.3)	12 (13.2)	0.85
Other ocular diseases			
- visit 1	42 (30.0)	42 (46.1)	0.02
- during follow-up	13 (9.3)	10 (11.0)	0.70
Diagnosed in Dallas	62 (44.3)	29 (31.9)	0.073
Ocular Surgeries			
Cataract	31 (22.1)	29 (31.9)	0.124
ALT	45 (32.1)	45 (49.4)	0.005
LPI	24 (17.1)	17 (18.7)	0.9
Trabeculectomy	16 (11.4)	28 (30.8)	0.002
combined	14 (10.0)	15 (16.5)	0.20
Others	8 (5.7)	9 (9.9)	0.303
cyclodestruction	0 (0.0)	2 (2.2)	0.154
Visual Acuity - visit one			

Table 7. Demographics and Characteristics of Non-legally Blind (NLB) and Legally Blind (LB) Patients of Clinic A			
Characteristics	**NLB n (%) total = 140**	**LB n (%) total = 91**	**p value**
20/20	61 (43.6)	19 (20.9)	<0.0001
20/40	68 (48.6)	31 (34.1)	
20/60	8 (5.7)	12 (13.2)	
20/80	3 (2.1)	1 (1.1)	
20/100	0 (0.0)	1 (1.1)	
20/200	0 (0.0)	11 (12.1)	
CF	0 (0.0)	5 (5.5)	
HM	0 (0.0)	7 (7.7)	
LP	0 (0.0)	0 (0.0)	
NLP	0 (0.0)	4 (4.4)	
- last visit			
20/20	46 (32.9)	10 (11.0)	< 0.0001
20/40	70 (50.0)	19 (21.0)	
20/60	17 (12.1)	12 (13.2)	
20/80	5 (3.6)	8 (8.8)	
20/100	0 (0.0)	0 (0.0)	
20/200	2 (1.4)	14 (15.4)	
CF	0 (0.0)	9 (9.9)	
HM	0 (0.0)	9 (9.9)	
LP	0 (0.0)	5 (5.5)	
NLP	0 (0.0)	5 (5.5)	
Visual Acuity Deterioration	22 (15.7)	36 (39.6)	<.0001
Visual Field - visit 1			
1	42 (30.0)	8 (8.8)	<0.0001
2	50 (35.7)	6 (6.6)	
3	18 (12.9)	3 (3.3)	
4	11 (7.9)	14 (15.4)	
5	14 (10.0)	8 (8.8)	
6	5 (3.6)	39 (42.9)	
7	0 (0.0)	13 (14.3)	
- final visit			
1	28 (20.0)	4 (4.4)	<0.0001
2	50 (35.7)	3 (3.3)	
3	24 (17.14)	3 (3.3)	
4	13 (9.3)	9 (9.9)	
5	15 (10.7)	11 (12.1)	
6	9 (6.4)	40 (44.0)	
7	1 (0.7)	21 (23.1)	
VF Progression	30 (21.4)	22 (24.2)	0.632
IOP			
- visit one	22.24 ± 7.3, 22.0, 2.0 – 70.0	25.0 ± 11.31, 22, 2 – 70	0.0001

Table 7. Demographics and Characteristics of Non-legally Blind (NLB) and Legally Blind (LB) Patients of Clinic A			
Characteristics	**NLB n (%) total = 140**	**LB n (%) total = 91**	**p value**
· final visit	18.45 ± 2.1, 19.0, 10 – 28	18.1 ± 3.5, 18, 0 – 43	0.62
C/D ratios · visit one			
0.1 – 0.5	51 (36.4)	9 (9.9)	< 0.0001
>0.5 – 0.7	43 (30.7)	20 (22.0)	
>0.7 – 1.0	46 (32.9)	62 (68.10)	
· final visit			
0.1 – 0.5	36 (25.7)	2 (2.2)	< 0.0001
>0.5 – 0.7	47 (33.6)	14 (15.4)	
> 0.7 – 1.0	57 (40.7)	75 (82.4)	
C/D Ratio Progression	50 (35.7)	29 (31.9)	0.60
Antiglaucoma medications			
Beta blocker	125 (89,3)	84 (92.3)	0.50
Miotics	68 (48.6)	60 (66.0)	0.010
Epinephrine	45 (32.1)	40 (44.0)	0.07
CAI systemic	20 (14.3)	32 (35.2)	0.0002
CAI topical	29 (20.7)	31 (34.1)	0.030
Alpha agonists	30 (21.4)	23 (25.3)	0.520
Prostaglandin analogue	8 (5.7)	6 (6.6)	0.80
Non-compliance	58 (41.4)	51 (56.0)	0.032
Poor Control	108 (77.1)	90 (99.0)	< 0.0001
Late Detection	122 (87.1)	90 (99.0)	< 0.001

ALT = argon laser trabeculoplasty; LPI = laser peripheral iridotomy

CF = count fingers; HM = hand motions, LP = light perception

NLP = no light perception; VF = visual field; IOP = intraocular pressure

C/D = cup-to-disc; CAI = carbonic anhydrase inhibitor

Table 8. Demographics and Characteristics of NLB Clinic A patients who did not progress vs those who did progress			
Characteristics	**Patients with no progression n (%) total = 70**	**Patients who progressed n (%) total = 70**	**p value**
Age at diagnosis, yr (mean ± SD, median, range)	58.3 ± 14.21, 58.71, 22.1 – 86.9	57.9 ± 13.83, 57.3 21.2 – 83.3	0.90
Age at first visit, yr (mean ± SD, median, range)	63.4 ± 12.5, 64.7, 30.6 – 88.7	61.2 ± 13.7, 64.1, 21.1 – 86.7	0.33
Follow-up, yr	3.7 ± 2.6, 3.2, 1.0 – 16.1	6.0 ± 3.4, 4.8, 1.2 – 18.1	< 0.0001
Gender			
Male	34 (48.6)	24 (34.3)	0.122
Female	36 (51.4)	46 (65.7)	
Race			
Caucasian	44 (62.9)	36 (51.4)	
Afro-American	19 (27.1)	25 (35.7)	0.400
Hispanic	2 (2.9)	5 (7.1)	
Others	5 (7.1)	4 (5.7)	
Risk Factors			
Ocular trauma	5 (7.1)	5 (7.1)	1.000
Myopia	8 (11.4)	8 (11.4)	1.000
Family history	30 (42.9)	27 (39.1)	0.731
Hypertension	23 (32.9)	30 (42.9)	0.30
Diabetes	10 (14.3)	11 (15.7)	1.000
Systemic steroids	2 (2.9)	0 (0.0)	0.50
Topical steroids	1 (1.4)	0 (0.0)	1.000
Dysthyroidism	8 (11.4)	6 (8.6)	0.80
Vascular disease	15 (21.4)	22 (31.9)	0.20
Alcohol abuse	5 (7.0)	4 (5.7)	1.000
Smoking	11 (15.7)	9 (12.9)	0.810
Other ocular diseases			
- visit one	20 (28.6)	22 (31.4)	0.854
- final visit	4 (5.7)	7 (10.0)	0.532
Diagnosed in Dallas	31 (44.3)	31 (44.3)	1.000
Ocular Surgeries			
Cataract	12 (17.1)	19 (27.1)	0.222
ALT	14 (20.0)	29 (41.4)	0.001
LPI	9 (12.9)	15 (21.4)	0.262
Trabeculectomy	7 (10.0)	8 (11.4)	1.000
combined	5 (7.1)	9 (12.9)	0.399
Others	3 (4.3)	5 (7.1)	0.718
Visual Acuity - visit one			
20/20	30 (42.9)	31 (44.3)	
20/40	32 (45.7)	36 (51.4)	

Table 8. Demographics and Characteristics of NLB Clinic A patients who did not progress vs those who did progress			
Characteristics	**Patients with no progression n (%) total = 70**	**Patients who progressed n (%) total = 70**	**p value**
20/60	5 (7.1)	3 (4.3)	0.30
20/80	3 (4.3)	0 (0.0)	
- last visit			
20/20	25 (35.7)	21 (30.0)	
20/40	35 (50.0)	35 (50.0)	
20/60	6 (8.6)	11 (15.7)	0.230
20/80	4 (5.7)	1 (1.4)	
20/200	0 (0.0)	2 (2.9)	
Visual Acuity Deterioration	6 (8.6)	17 (24.3)	0.021
Visual Field - visit 1			
1	22 (31.4)	20 (28.6)	
2	28 (40.0)	22 (31.4)	
3	5 (7.1)	13 (18.6)	0.422
4	6 (8.6)	5 (7.1)	
5	9 (12.9)	10 (14.3)	
- final visit			
1	21 (30.0)	7 (10.0)	
2	29 (41.4)	21 (30.0)	
3	5 (7.1)	19 (27.1)	
4	6 (8.6)	7 (10.0)	0.04
5	9 (12.9)	9 (12.9)	
6	0 (0.0)	6 (8.6)	
7	0 (0.0)	1 (1.4)	
VF Progression	0 (0.0)	30 (42.9)	<0.0001
IOP			
- visit one	21.8 ± 5.8, 21.0, 4.0 – 60	24.9 ± 8.9, 22, 5 – 70	0.001
- final visit	18.3 ± 2.1, 18, 2 – 45	18.7 ± 3.5, 18, 0 – 50	0.52
C/D ratios - visit one			
0.1 – 0.5	21 (30.0)	30 (42.9)	
>0.5 – 0.7	22 (31.4)	21 (30.0)	0.233
>0.7 – 1.0	27 (38.6)	19 (27.1)	
- final visit			
0.1 – 0.5	21 (30.0)	15 (21.4)	
>0.5 – 0.7	22 (31.4)	25 (35.7)	0.51
> 0.7 – 1.0	27 (38.6)	30 (42.9)	
C/D Ratio Progression	0 (0.0)	50 (71.4)	< .0001
Antiglaucoma medications			
Beta blocker	62 (88.6)	63 (90.0)	1.00

Table 8. Demographics and Characteristics of NLB Clinic A patients who did not progress vs those who did progress			
Characteristics	**Patients with no progression n (%) total = 70**	**Patients who progressed n (%) total = 70**	**p value**
Miotics	23 (32.9)	45 (64.3)	.0002
Epinephrine	16 (22.9)	29 (41.4)	0.03
CAI systemic	8 (11.4)	12 (17.4)	0.5
CAI topical	16 (22.9)	13 (18.6)	0.70
Alpha agonists	14 (20.0)	16 (22.9)	0.840
Prostaglandin analogue	2 (2.9)	6 (8.6)	0.30
Non-compliance	19 (27.1)	39 (55.7)	< .0010
Poor Control	43 (61.4)	65 (92.9)	< .0001
Late Detection	58 (82.9)	64 (91.4)	0.210

ALT = argon laser trabeculoplasty; LPI = laser peripheral iridotomy

VF = visual field; C/D = cup-to-disc

CAI = carbonic anhydrase inhibitors

Table 9 - Data Relating to Initial Presentation of Clinic A Patients in Dallas	
Characteristics	**Findings n (%)total = 91**
Age, yr (mean ±SD, median, range)	60.6 ± 13.6, 60.0, 21.1 – 86.9
Follow-up, yr (mean ± SD, median, range)	4.7 ± 3.31, 4.6, 1.0 – 18.1
Gender	
Male	35 (38.5)
Female	56 (61.5)
Race	
Caucasian	47 (51.6)
Afro-American	35 (38.5)
Hispanic	5 (5.5)
Others	4 (4.4)
Risk Factors	
Ocular trauma	6 (6.6)
Myopia	12 (13.2)
Diabetes	13 (14.3)
Family history	29 (32.2)
Hypertension	35 (38.5)
Systemic steroids	2 (2.2)
Topical steroids	2 (2.2)
Dysthyroidism	8 (8.8)
Vascular disease	24 (27.5)
Alcohol abuse	4 (4.4)
Smoking	14 (15.4)
Other ocular diseases	
Visit 1	23 (25.3)
Final visit	7 (7.7)
Legal Blindness	21 (23.1)
Visual Acuity	
20/20	40 (44.0)
20/40	40 (44.0)
20/60	4 (4.4)
20/80	2 (2.2)
20/100	1 (1.1)
20/200	3 (3.3)
CF	1 (1.1)
Status of VF Defects	
1	20 (22.0)
2	31 (34.0)
3	10 (11.0)
4	7 (7.7)
5	5 (5.5)
6	15 (16.5)

Table 9 - Data Relating to Initial Presentation of Clinic A Patients in Dallas	
Characteristics	**Findings n (%)total = 91**
7	3 (3.3)
IOP (mean ± SD, median, range)	22.65 ± 8.6, 21, 10 – 60
C/D ratios	
0.1 – 0.5	31 (34.0)
>0.5 – 0.7	28 (30.8)
>0.7 – 1.0	32 (35.2)
Late Detection	85 (93.4)

CF = count fingers; VF = visual fields

IOP = intraocular pressure (mmHg)

Table 10. Demographics and Characteristics of Patients with NLB and LB at Clinic B			
Characteristics	**NLB n (%) total = 70**	**LB n (%) total = 28**	**p value**
Age at diagnosis, yr (mean ± SD, median, range)	59.3 ± 11.30, 60.0, 35.1 – 86.8	58.4 ± 12.6, 60.6, 30.0 – 82.0	0.730
Age at first visit, yr (mean ± SD, median, range)	60.3 ± 11.2, 60.9, 35.2 – 86.8	60.5 ± 12.2, 61.3, 30.0 – 82.0	0.940
Follow-up, yr (mean ± SD, median, range)	4.5 ± 1.57, 4.4 1.0 – 8.7	5.8 ± 2.0, 5.4 2.8 – 11.3	0.003
Gender			
Male	22 (31.4)	12 (42.9)	0.349
Female	48 (69.6)	16 (57.1)	
Race			
Caucasian	7 (10.0)	0 (0.0)	
Afro-American	56 (80.0)	26 (92.9)	0.230
Hispanic	4 (5.7)	2 (9.1)	
Others	3 (4.3)	0 (0.0)	
Risk Factors			
Ocular trauma	5 (7.1)	5 (17.9)	0.143
Myopia	11 (15.7)	1 (3.6)	0.20
Diabetes	31 (44.3)	10 (35.7)	0.501
Family history	20 (28.5)	3 (10.4)	0.052
Hypertension	42 (60.0)	16 (57.1)	0.823
Systemic steroids	1 (1.4)	0 (0.0)	1.000
Topical steroids	1 (1.4)	0 (0.0)	1.000
Dysthyroidism	1 (1.4)	0 (0.0)	1.000
Vascular disease	10 (14.3)	2 (7.1)	0.500
Alcohol abuse	4 (5.7)	1 (3.6)	1.000
Smoking	16 (22.9%)	1 (3.6)	0.03
Other Ocular Diseases			
visit 1	23 (32.9)	13 (46.4)	0.250
last visit	9 (12.9)	3 (10.7)	1.000
Diagnosed in Dallas	49 (70.0)	17 (60.7)	0.50
Ocular Surgeries			
Cataract	7 (10.0)	3 (10.7)	1.000
ALT	14 (20.0)	12 (42.9)	0.041
LPI	1 (1.4)	3 (10.7)	0.10
Trabeculectomy	5 (7.1)	7 (25.0)	0.035
combined	4 (5.7)	4 (14.3)	0.220
Others	1 (1.4)	1 (3.6)	0.50
Visual Acuity			

Table 10. Demographics and Characteristics of Patients with NLB and LB at Clinic B			
Characteristics	**NLB n (%) total = 70**	**LB n (%) total = 28**	**p value**
- visit one			
20/20	26 (37.1)	3 (10.7)	0.013
20/40	42 (60.0)	16 (57.1)	0.823
20/60	2 (2.9)	1 (3.6)	1.000
CF	0 (0.0)	2 (7.1)	0.1
HM	0 (0.0)	2 (7.1)	0.1
LP	0 (0.0)	1 (3.6)	0.30
NLP	0 (0.0)	3 (10.7)	0.021
- last visit			
20/20	23 (32.9)	3 (10.7)	0.025
20/40	41 (58.6)	8 (28.6)	0.013
20/60	3 (4.3)	2 (7.1)	0.622
20/80	1 (1.4)	0 (0.0)	1.000
20/100	1 (1.4)	1 (3.6)	0.50
20/200	0 (0.0)	2 (7.1)	0.08
CF	0 (0.0)	1 (3.6)	0.30
HM	1 (1.4)	4 (14.3)	0.022
LP	0 (0.0)	2 (7.1)	0.10
NLP	0 (0.0)	5 (17.9)	0.001
Visual Acuity Deterioration	9 (12.9)	12 (42.9)	0.002
Visual Field - visit 1			
1	11 (15.7)	1 (7.1)	0.340
2	53 (75.7)	7 (25.0)	<0.0001
3	4 (5.7)	4 (14.3)	0.220
4	1 (1.4)	4 (14.3)	0.022
5	1 (1.4)	4 (14.3)	0.022
6	0 (0.0)	3 (10.7)	0.021
7	0 (0.0)	4 (14.3)	0.005
- final visit			
1	8 (11.4)	0 (0.0)	0.100
2	49 (70.0)	6 (21.4)	<0.0001
3	9 (12.9)	3 (10.7)	1.000
4	2 (2.9)	7 (25.0)	0.002
5	2 (2.9)	4 (14.3)	0.054
6	0 (0.0)	3 (10.7)	0.021
7	0 (0.0)	5 (17.9)	0.001
VF Progression	11 (15.7)	6 (21.4)	0.60
IOP			
- visit one	22.3 ± 8.45, 20, 9 – 65	24.11 ± 9.2, 21.5, 7 – 55	0.11
- final visit	18.4 ± 1.9, 18, 11 – 27	19.1 ± 2.5, 19, 13.0 – 29.0	0.53
C/D ratios			

Table 10. Demographics and Characteristics of Patients with NLB and LB at Clinic B			
Characteristics	**NLB n (%) total = 70**	**LB n (%) total = 28**	**p value**
- visit one			
0.1 – 0.5	23 (32.8)	3 (10.7)	0.025
>0.5 – 0.7	27 (38.6)	6 (21.4)	0.155
>0.7 – 1.0	20 (28.6)	19 (67.9)	<0.0003
- final visit			
0.1 – 0.5	16 (22.9)	2 (7.1)	0.10
>0.5 – 0.7	28 (40.0)	2 (7.1)	0.001
> 0.7 – 1.0	26 (37.1)	24 (85.8)	<0.0001
C/D Ratio Progression	21 (30.0)	7 (25.0)	0.805
Antiglaucoma medications			
Beta blocker	68 (97.1)	28 (100.0)	1.000
Miotics	40 (57.2)	25 (89.2)	0.002
Epinephrine	18 (25.7)	13 (46.4)	0.06
CAI systemic	14 (20.0)	15 (53.6)	0.002
CAI topical	14 (20.0)	7 (25.0)	0.6
Alpha agonists	7 (10.0)	9 (32.1)	0.001
Non-compliance	44 (62.9)	23 (82.1)	0.10
Poor Control	48 (68.6)	28 (100.0)	< 0.0001
Late Detection	68 (97.1)	27 (96.4)	1.000

ALT = argon laser trabeculoplasty; LPI = laser peripheral iridotomy

CF = count fingers; HM = hand motions; LP = light perception

NLP = no light perception; IOP = intraocular pressure

CAI = carbonic anhydrase inhibitor

Table 11. Demographics and characteristics of NLB Clinic B patients with POAG who did not progress vs those who did progress			
Characteristics	**Patients with no progression n (%) total = 36**	**Patients who progressed n (%) total = 34**	**p value**
Age at diagnosis, yr. (mean ± SD, median, range)	59.8 ± 11.26, 59.30, 35.1 – 86.8	58.8 ± 11.5, 60.8 35.2 – 80.0	0.715
Age at first visit, yr. (mean ± SD, median, range)	61.1 ± 11.18, 60.4, 38.4 – 86.8	59.4 ± 11.1, 61.2, 35.2 – 80.0	.514
Follow-up, yr (mean ± SD, median, range)	4.1 ± 1.31, 4.0, 1.0 – 7.0	4.9 ± 1.72, 4.5, 2.0 – 8.7	0.03
Gender			
Male	15 (41.7)	7 (20.6)	0.10
Female	21 (58.3)	27 (79.4)	
Race			
Caucasian	4 (11.1)	3 (8.8)	
Afro-American	27 (75.0)	29 (85.3)	0.700
Hispanic	3 (8.3)	1 (2.9)	
Others	2 (5.6)	1 (2.9)	
Risk Factors			
Ocular trauma	3 (8.3)	2 (5.9)	1.000
Myopia	10 (27.8)	1 (2.9)	0.006
Diabetes	16 (44.4)	15 (44.1)	1.000
Family history	10 (28.6)	9 (26.5)	1.000
Hypertension	25 (69.4)	17 (50.0)	0.143
Systemic steroids	1 (2.8)	0 (0.0)	1.000
Topical steroids	1 (2.8)	0 (0.0)	1.000
Dysthyroidism	0 (0.0)	1 (2.9)	0.50
Vascular disease	6 (16.7)	4 (11.8)	0.736
Alcohol abuse	2 (5.6)	2 (5.8)	1.000
Smoking	9 (25.0)	7 (20.6)	0.053
Other ocular diseases			
- visit one	13 (36.1)	10 (29.4)	0.62
- final visit	6 (16.7)	3 (8.8)	0.50
Diagnosed in Dallas	26 (72.2)	23 (67.6)	0.80
Ocular Surgeries			
Cataract	4 (11.1)	3 (8.8.)	1.000
ALT	2 (5.6)	12 (35.3)	0.002
LPI	0 (0.0)	1 (2.9)	0.50
Trabeculectomy	0 (0.0)	5 (14.7)	0.023
combined	2 (5.6)	2 (5.8)	1.000
Others	1 (2.8)	0 (0.0)	1.000
Visual Acuity - visit one			
20/20	12 (33.3)	14 (41.2)	

Table 11. Demographics and characteristics of NLB Clinic B patients with POAG who did not progress vs those who did progress			
Characteristics	**Patients with no progression n (%) total = 36**	**Patients who progressed n (%) total = 34**	**p value**
20/40	23 (63.9)	19 (55.9)	0.1
20/60	1 (2.8)	1 (2.9)	
- final visit			
20/20	11 (30.6)	12 (35.3)	0.62
20/40	22 (61.1)	19 (55.8)	
20/60	3 (8.3)	1 (2.9)	
20/80	0 (0.0)	1 (2.9)	
20/100	0 (0.0)	1 (2.9)	
Visual Acuity Deterioration	3 (8.3)	6 (17.6)	0.230
VF Status - visit 1			
1	6 (16.7)	5 (14.7)	0.73
2	27 (75.0)	26 (76.5)	
3	2 (5.6)	2 (5.9)	
4	1 (2.8)	0 (0.0)	
5	0 (0.0)	1 (2.9)	
- final visit			
1	6 (16.7)	2 (5.9)	0.12
2	27 (75.0)	22 (64.7)	
3	2 (5.6)	7 (20.6)	
4	1 (2.8)	1 (2.9)	
5	0 (0.0)	2 (5.9)	
VF Progression	0 (0.0)	11 (32.3)	<0.0001
IOP (mean ± SD, median, range)			
- visit one	22.1 ± 5.0, 21.8 5 - 40	23.8 ± 9.7, 23, 15 – 60	0.04
- final visit	18.4 ± 3.0, 17.5, 10 – 30	18.6 ± 3.5, 18, 10 – 40	0.35
C/D ratios - visit one			
0.1 – 0.5	10 (27.8)	13 (38.2)	0.55
>0.5 – 0.7	14 (38.9)	13 (38.2)	
>0.7 – 1.0	12 (33.3)	8 (23.5)	
- final visit			
0.1 – 0.5	10 (27.8)	6 (17.6)	0.60
>0.5 – 0.7	14 (38.9)	14 (41.2)	
> 0.7 – 1.0	12 (33.3)	14 (41.2)	
C/D Ratio Progression	0 (0.0)	21 (61.8)	<0.0001
Antiglaucoma medications			
Beta blocker	35 (97.2)	33 (97.0)	1.000

Table 11. Demographics and characteristics of NLB Clinic B patients with POAG who did not progress vs those who did progress			
Characteristics	**Patients with no progression n (%) total = 36**	**Patients who progressed n (%) total = 34**	**p value**
Miotics	16 (44.4)	24 (70.6)	0.032
Epinephrine	5 (13.9)	13 (38.2)	0.03
CAI systemic	7 (19.4)	7 (20.6)	1.000
CAI topical	7 (19.4)	7 (20.6)	1.000
Alpha agonists	2 (5.6)	4 (11.8)	0.422
None	1 (2.8)	0 (0.0)	1.000
Non-compliance	24 (66.7)	20 (58.8)	0.622
Poor Control	16 (44.4)	32 (94.1)	<0.0001
Late Detection	34 (94.4)	34 (100.0)	0.20

ALT = argon laser trabeculoplasty; LPI - laser peripheral iridotomy

VF = visual field; IOP = intraocular pressure; C/D = cup-to-disc

CAI = carbonic anhydrase inhibitor

Table 12 - Data Relating to Initial Presentation of Clinic B Patients in Dallas	
Characteristics	**Findings n (%)total = 66**
Age, yr (mean ±SD, median, range)	59.6 ± 11.5, 60.2, 30.0 – 86.8
Follow-up, yr (mean ± SD, median, range)	4.7 ± 1.9, 4.4, 1.0 – 11.3
Gender	
Male	23 (34.9)
Female	43 (65.1)
Race	
Caucasian	5 (7.6)
Afro-American	54 (81.8)
Hispanic	5 (7.6)
Others	2 (3.0)
Risk Factors	
Ocular trauma	6 (9.0)
Myopia	11 (16.7)
Diabetes	26 (39.3)
Family history	15 (23.4)
Hypertension	39 (59.0)
Systemic steroids	1 (1.5)
Topical steroids	1 (1.5)
Dysthyroidism	1 (1.5)
Vascular disease	8 (12.1)
Alcohol abuse	2 (3.0)
Smoking	10 (15.2)
Other ocular diseases	
Visit 1	25 (37.9)
Final visit	7 (10.6)
Legal Blindness	14 (21.2)
Visual Acuity	
20/20	18 (27.3)
20/40	35 (53.0)
20/60	5 (7.7)
20/80	3 (4.5)
20/100	1 (1.5)
20/200	1 (1.5)
CF	1 (1.5)
HM	1 (1.5)
LP	1 (1.5)
Status of VF Defects	
1	13 (19.7)
2	40 (60.0)
3	4 (6.1)
4	2 (3.0)

Table 12 - Data Relating to Initial Presentation of Clinic B Patients in Dallas	
Characteristics	**Findings n (%)total = 66**
5	3 (4.6)
6	2 (3.0)
7	2 (3.0)
IOP (mean ± SD, median, range)	22.85 ± 8.9, 21.2, 12 – 60
C/D ratios	
0.1 – 0.5	14 (21.2)
>0.5 – 0.7	23 (34.9)
>0.7 – 1.0	29 (43.9)
Late Detection	63 (95.4)

CF = count fingers; HM = hand motions; LP = light perception

IOP = intraocular pressure; C/D = cup-to-disc

Table 13. Demographics and Characteristics of non-legally Blind (NLB) patients and legally bind (LB) patients at Clinic C			
Characteristics	**NLB n (%) total = 72**	**LB n (%) total = 86**	**p value**
Age at diagnosis, yr. (mean ± SD, median, range)	60.4 ± 10.9, 60.8, 36.1 – 81.4	57.2 ± 12.4, 59.5, 24.3 – 79.5	0.10
Age at first visit, yr. (mean ± SD, median, range)	64.4 ± 9.6, 65.6, 39.6– 81.4	67.1 ± 9.9, 66.6, 42.5 – 91.7	0.10
Follow-up, yr (mean ± SD, median, range)	6.0 ± 3.8, 4.7, 1.3 – 17.6	6.7 ± 4.7, 5.5, 0.3 – 22.2	0.310
Gender			
Male	71 (98.6)	85 (98.8)	1.000
Female	1 (1.4)	1 (1.2)	
Race			
Caucasian	37 (51.4)	24 (27.9)	
Afro-American	34 (47.2)	58 (67.4)	0.03
Hispanic	1 (1.4)	1 (1.2)	
American Indian	0 (0.0)	1 (1.2)	
Others	0 (0.0)	2 (2.3)	
Risk Factors			
Ocular trauma	8 (11.1)	5 (5.8)	0.250
Myopia	7 (9.7)	3 (3.5)	0.20
Diabetes	14 (19.4)	21 (24.4)	0.60
Family history	22 (31.0)	26 (30.2)	1.000
Hypertension	37 (51.4)	49 (57.6)	0.520
Systemic steroids	2 (2.8)	2 (2.3)	1.000
Topical steroids	1 (1.4)	2 (2.3)	1.000
Dysthyroidism	1 (1.4)	2 (2.3)	1.000
Vascular disease	29 (40.8)	28 (32.6)	0.320
Alcohol abuse	13 (18.1)	18 (20.9)	0.7
Smoking	35 (48.6)	36 (41.9)	0.425
Other ocular diseases			
- visit one	40 (55.6)	56 (65.1)	0.254
- final visit	24 (33.3)	28 (32.6)	1.000
Diagnosed in Dallas	24 (33.3)	14 (16.3)	0.015
Ocular Surgeries			
Cataract	14 (19.4)	16 (18.6)	1.000
ALT	33 (45.8)	38 (44.2)	0.90
LPI	4 (5.6)	11 (12.9)	0.20
Trabeculectomy	8 (11.1)	25 (29.1)	0.05
combined	11 (15.3)	10 (11.6)	0.64
Others	5 (6.9)	6 (7.0)	1.000
Cyclodestruction	0 (0.0)	7 (8.1)	0.016

Table 13. Demographics and Characteristics of non-legally Blind (NLB) patients and legally bind (LB) patients at Clinic C			
Characteristics	**NLB n (%) total = 72**	**LB n (%) total = 86**	**p value**
Visual Acuity - visit one			
20/20	27 (37.5)	9 (10.5)	<0.0001
20/40	36 (50.0)	22 (25.6)	
20/60	6 (8.3)	11 (12.8)	
20/80	2 (2.8)	6 (7.0)	
20/100	1 (1.4)	1 (1.2)	
20/200	0 (0.0)	2 (2.3)	
CF	0 (0.0)	14 (16.3)	
HM	0 (0.0)	7 (8.1)	
LP	0 (0.0	8 (9.3)	
NLP	0 (0.0)	6 (7.0)	
- final visit			
20/20	25 (34.7)	8 (9.3)	<0.0001
20/40	39 (54.2)	13 (15.1)	
20/60	5 (6.9)	8 (9.3)	
20/80	1 (1.4)	3 (3.5)	
20/100	2 (2.8)	2 (2.3)	
20/200	0 (0.0)	4 (4.6)	
CF	0 (0.0)	20 (23.3)	
HM	0 (0.0)	10 (11.6)	
LP	0 (0.0)	6 (7.0)	
NLP	0 (0.0)	12 (13.9)	
Visual Acuity Deterioration	1 (1.4)	30 (34.9)	<0.0001
VF Status - visit 1			
1	20 (27.8)	2 (2.3)	<0.0001
2	26 (36.1)	4 (4.6)	
3	13 (18.1)	10 (11.6)	
4	8 (11.1)	14 (16.3)	
5	5 (6.9)	10 (11.6)	
6	0 (0.0)	17 (19.8)	
7	0 (0.0)	29 (33.7)	
- final visit			
1	18 (25.0)	2 (2.3)	<0.0001
2	26 (36.1)	2 (2.3)	
3	12 (16.7)	7 (8.1)	
4	11 (15.3)	12 (13.9)	
5	5 (6.9)	12 (13.9)	
6	0 (0.0)	19 (22.1)	
7	0 (0.0)	32 (37.2)	
VF Progression	11 (15.3)	19 (22.1)	0.013
IOP (mean, ±SD, median, range)			

Table 13. Demographics and Characteristics of non-legally Blind (NLB) patients and legally bind (LB) patients at Clinic C			
Characteristics	**NLB n (%) total = 72**	**LB n (%) total = 86**	**p value**
- visit one	21.6 ± 7.6, 20.0, 2.0 – 46.0	23.4 ± 11.8, 20.0, 2.0 – 62.0	0.03
- final visit	18.2 ± 2.8, 18.0, 12.0 – 26.0	17.2 ± 4.6, 17.2, 3.0 – 46.0	0.420
C/D ratios - visit one			
0.1 – 0.5	22 (30.6)	9 (10.5)	<0.0001
>0.5 – 0.7	21 (29.2)	9 (10.5)	
>0.7 – 1.0	29 (40.2)	68 (79.0)	
- final visit			
0.1 – 0.5	8 (11.1)	4 (4.6)	<0.0002
>0.5 – 0.7	24 (33.3)	9 (10.5)	
> 0.7 – 1.0	40 (55.6)	73 (84.9)	
C/D Ratio Progression	21 (29.2)	19 (22.1)	0.40
Antiglaucoma medications			
Beta blocker	69 (95.8)	80 (93.0)	0.511
Miotics	50 (69.4)	72 (83.7)	0.04
Epinephrine	30 (41.7)	38 (44.2)	0.9
CAI systemic	15 (20.8)	32 (37.2)	0.035
CAI topical	16 (22.2)	17 (19.7)	0.844
Alpha agonists	7 (9.7)	6 (7.0)	0.60
Prostaglandin analogue	0 (0.0)	1 (1.2)	1.000
Non-compliance	29 (40.3)	55 (63.9)	0.0003
Poor Control	51 (70.8)	78 (90.7)	0.0002
Late Detection	58 (80.6)	78 (90.7)	0.105

ALT = argon laser trabeculoplasty; LPI = laser peripheral iridotomy

CF = count fingers; HM = hand motions; LP = light perception

NLP = no light perception; VF = visual field; IOP = intraocular pressure

C/D = cup-to-disc; CAI = carbonic anhydrase inhibitor

Table 14: Demographics and Characteristics of Clinic C patients who did not progress vs those who did progress			
Characteristics	**Patients with no progression n (%) total = 42**	**Patients who progressed n (%) total = 30**	**p value**
Age at diagnosis, yr. (mean ± SD, median, range)	59.8 ± 10.9, 62.5, 36.1 – 76.4	61.2 ± 11.0, 59.5 36.9 – 81.4	0.60
Age at first visit, yr. (mean ± SD, median, range)	63.6 ± 10.6, 64.1, 39.6 – 81.4	65.5 ± 8.10, 67.1, 45.7 – 81.4	0.412
Follow-up, yr (mean ± SD, median, range)	4.6 ± 2.9, 4.0, 1.3 – 16.4	8.0 ± 4.0, 7.5, 2.1 – 17.6	<0.0001
Gender			
Male	41 (97.6)	30 (100.0)	1.000
Female	1 (2.4)	0 (0.0)	
Race			
Caucasian	20 (47.6)	17 (56.7)	
Afro-American	22 (52.4)	12 (40.0)	0.325
Hispanic	0 (0.0)	1 (3.3)	
Risk Factors			
Ocular trauma	4 (9.5)	4 (13.3)	0.711
Myopia	4 (9.5)	3 (10.0)	1.000
Diabetes	5 (11.9)	9 (30.0)	0.10
Family history	14 (33.3)	8 (27.6)	0.80
Hypertension	16 (38.1)	21 (70.0)	0.01
Systemic steroids	2 (4.8)	0 (0.0)	0.50
Topical steroids	1 (2.4)	0 (0.0)	1.000
Dysthyroidism	1 (2.4)	0 (0.0)	1.000
Vascular disease	16 (39.0)	13 (43.3)	0.81
Alcohol abuse	10 (23.8)	3 (10.0)	0.214
Smoking	21 (50.0)	14 (46.7)	0.815
Other ocular diseases			
- visit one	20 (47.6)	20 (66.7)	0.20
- final visit	13 (30.9)	11 (36.7)	0.623
Diagnosed in Dallas	12 (28.6)	12 (40.0)	0.325
Ocular Surgeries			
Cataract	7 (16.7)	7 (23.3)	0.522
ALT	16 (38.1)	17 (56.7)	0.152
LPI	3 (7.1)	3 (10.0)	0.70
Trabeculectomy	4 (9.5)	5 (16.7)	0.50
combined	5 (11.9)	6 (20.0)	0.510
Others	2 (4.8)	3 (10.0)	0.643
Visual Acuity - visit one			
20/20	10 (23.8)	8 (26.7)	
20/40	28 (66.7)	18 (60.0)	

Table 14: Demographics and Characteristics of Clinic C patients who did not progress vs those who did progress			
Characteristics	**Patients with no progression n (%) total = 42**	**Patients who progressed n (%) total = 30**	**p value**
20/60	2 (4.8)	3 (10.0)	0.60
20/80	2 (4.8)	0 (0.0)	
20/100	0 (0.0)	1 (3.3)	
- final visit			
20/20	14 (33.3)	11 (36.7)	
20/40	23 (54.7)	16 (53.3)	0.72
20/60	3 (7.1)	2 (6.7)	
20/80	5 (11.9)	1 (3.3)	
Visual Acuity Deterioration	0 (0.0)	1 (3.3)	0.417
VF Status - visit 1			
1	9 (21.4)	7 (23.3)	
2	13 (30.9)	6 (20.0)	
3	14 (33.3)	12 (40.0)	0.73
4	6 (14.4)	5 (16.7)	
- final visit			
1	11 (26.2)	6 (20.0)	
2	11 (26.2)	6 (20.0)	
3	14 (33.3)	7 (23.3)	0.20
4	5 (11.9)	9 (30.0)	
5	1 (2.4)	2 (6.7)	
VF Progression	0 (0.0)	11 (36.7)	<0.0001
IOP (mean ± SD, median, range)			
- visit one	21.8 ± 4.9, 21.0, 10 – 50	23.9 ± 10.0, 23, 10 – 60	0.03
- final visit	18.7 ± 3.1, 18, 10 – 35	18.3 ± 3.7, 18, 10 – 30	0.430
C/D ratios - visit one			
0.1 – 0.5	7 (16.7)	15 (50.0)	
>0.5 – 0.7	13 (30.9)	6 (20.0)	0.01
>0.7 – 1.0	22 (52.4)	9 (30.0)	
- final visit			
0.1 – 0.5	7 (16.7)	6 (20.0)	
>0.5 – 0.7	13 (30.9)	6 (20.0)	0.6
> 0.7 – 1.0	22 (52.4)	18 (60.0)	
C/D Ratio Progression	0 (0.0)	23 (76.7)	<0.0001
Antiglaucoma medications			
Beta blocker	40 (95.2)	29 (96.7)	1.000
Miotics	27 (64.3)	23 (76.7)	0.30

Table 14: Demographics and Characteristics of Clinic C patients who did not progress vs those who did progress			
Characteristics	**Patients with no progression n (%) total = 42**	**Patients who progressed n (%) total = 30**	**p value**
Epinephrine	13 (30.9)	17 (56.7)	0.05
CAI systemic	8 (19.0)	7 (23.3)	0.800
CAI topical	9 (21.4)	7 (23.3)	1.000
Alpha agonists	2 (4.8)	5 (16.7)	0.120
Non-compliance	19 (45.2)	10 (33.3)	0.340
Poor Control	24 (57.1)	27 (90.0)	0.002
Late Detection	39 (92.9)	19 (63.3)	0.002

ALT = argon laser trabeculoplasty; LPI = laser peripheral iridotomy

VF = visual field; IOP = intraocular pressure; C/D = cup-to-disc

CAI = carbonic anhydrase inhibitor

Table 15. Data Relating to Initial Presentation of Clinic C Patients in Dallas	
Characteristics	**Findings n (%)total = 38**
Age, yr (mean ±SD, median, range)	63.9 ± 10.2, 65.3, 39.6 – 81.4
Follow-up, yr (mean ± SD, median, range)	6.5 ± 4.4, 5.5, 1.3 – 21.7
Gender	
Male	37 (97.4)
Female	1 (2.6)
Race	
Caucasian	16 (42.1)
Afro-American	21 (55.3)
Hispanic	1 (2.6)
Risk Factors	
Ocular trauma	3 (7.9)
Myopia	4 (10.5)
Diabetes	7 (18.4)
Family history	13 (35.1)
Hypertension	16 (42.1)
Systemic steroids	1 (2.6)
Topical steroids	1 (2.6)
Dysthyroidism	2 (5.3)
Vascular disease	12 (31.6)
Alcohol abuse	5 (13.2)
Smoking	14 (36.8)
Other ocular diseases	
Visit 1	17 (44.7)
Final visit	15 (39.5)
Legal Blindness	13 (34.2)
Visual Acuity	
20/20	6 (15.8)
20/40	21 (55.3)
20/60	4 (10.5)
20/80	0 (0.0)
20/100	1 (2.6)
20/200	0 (0.0)
CF	3 (7.9)
HM	0 (0.0)
LP	1 (2.6)
NLP	2 (5.3)
Status of VF Defects	
1	7 (18.4)
2	11 (28.9)
3	5 (13.2)

Table 15. Data Relating to Initial Presentation of Clinic C Patients in Dallas	
Characteristics	**Findings n (%)total = 38**
4	7 (18.4)
5	1 (2.6)
6	2 (5.3)
7	5 (13.2)
IOP (mean ± SD, median, range)	30.7 ± 11.6, 29.5, 15.0 – 60.0
C/D ratios	
0.1 – 0.5	12 (31.6)
>0.5 – 0.7	7 (18.4)
>0.7 – 1.0	19 (50.0)
Late Detection	35 (92.1)

CF = count fingers; HM = hand motions; LP = light perception

NLP = no light perception; IOP = intraocular pressure

C/D = cup-to-disc

Table 16 - Risk Factors for Blindness in Glaucoma – See page 57.

Table 17 – Univariate analysis of legal blindness in clinics – See page 60.

Table 18 – Univariate analysis of the effect of race in all clinics – See page 60.

Table 19 – Univariate analysis of the effect of race in Clinic C – See page 61.

Table 20 – Multivariate analysis of the various variables and their effects on legal blindness – See page 61.

Table 21 - Risk factors for progression of POAG - See page 65.

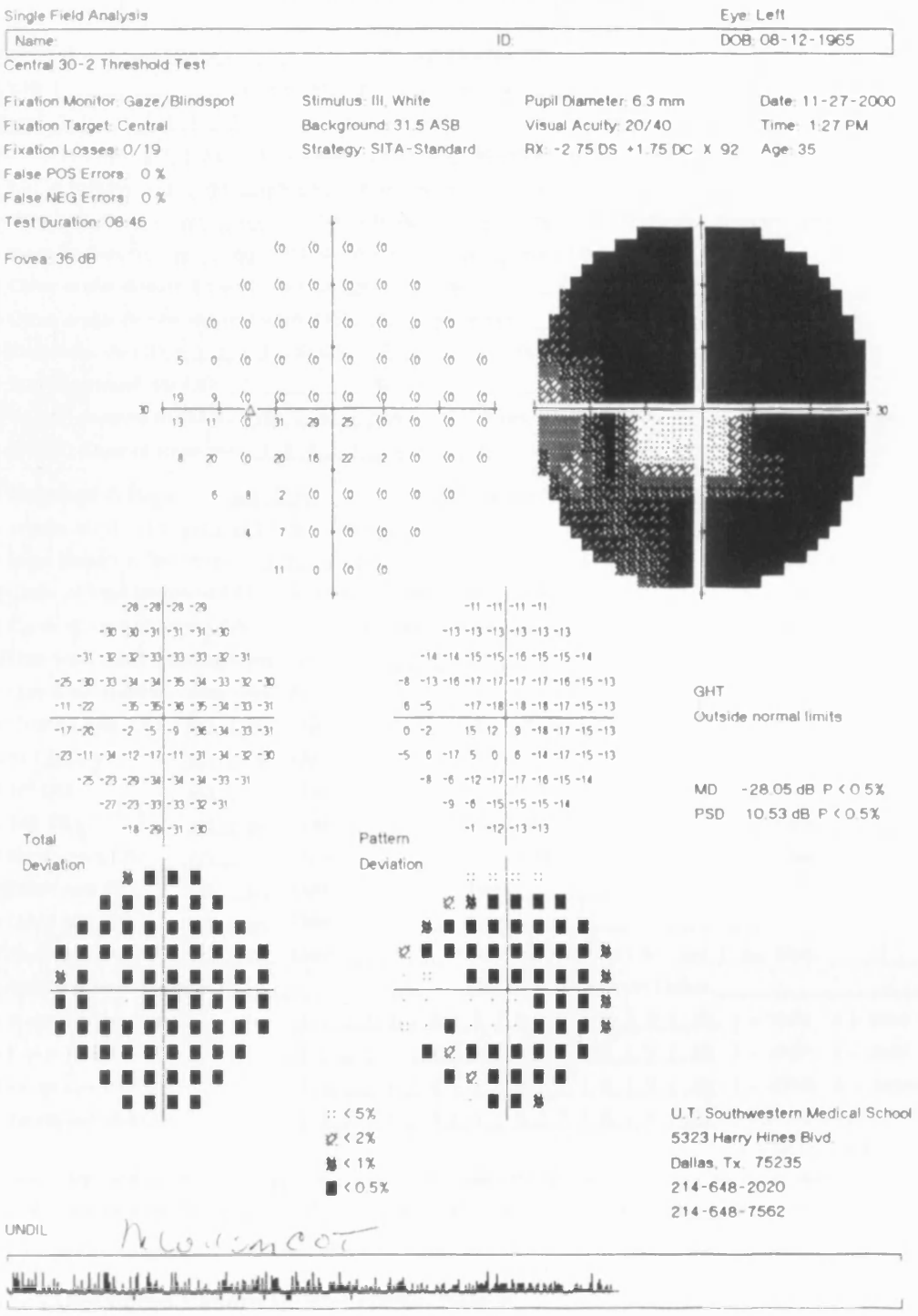

Fig. 1 - An example of a remaining VF less than 10 degrees in width

GLAUCOMA PATIENT PROFILE SHEET

Kooner

(1) Name: _____ (2) Hospital No.: _____

(3) DOB: _____ (4) Sex: M | F (5) Hospital: 1 | 2 | 3 1 = Aston, 2 = PMH, 3 = VA

(6) Race: 1 | 2 | 3 | 4 | 5 1 = White, 2 = Black, 3 = Hispanic, 4 = American Indian, 5 = Other

(7) Ocular trauma: yes | no (8) Myopia: yes | no (9) Diabetes: yes | no

(10) Family history: yes | no | unknown If yes, who? _ (11) Hypertension: yes | no

(12) Steroids systemic: yes | no (13) Steroids topical: yes | no (14) Dysthyroid disease: yes | no

(15) Vascular disease: yes | no (16) Alcohol abuse: yes | no (17) Smoking: yes | no

(18) Other ocular disease 1st visit: (A) OD yes | no If yes, ____ (B) OS yes | no If yes, _____

(19) Other ocular disease during f-u: (A) OD yes | no If yes, __ (B) OS yes | no If yes, _____

(20) Diagnosis: (A) OD 1 | 2 | 3 (B) OS 1 | 2 | 3 1 = POAG, 2 = OHT, 3 = CMG

(21) Date diagnosed: (A) OD _____; (B) OS _____

(22) If OHT, progress to POAG yes | no | N/A (23) If yes, when? 1 = date _____ 2 = N/A

(24) If OHT, cause of suspicion: 1 | 2 | 3 | 4 | 5 | 6 1 = ↑ IOP, 2 = ↑ C/D, 3 = disparity C/D, 4 = VF changes, 5 = FH, 6 = N/A

(25) Diagnosed in Dallas: yes | no (26) Diagnosed elsewhere: yes | no

(27) Legally blind: OD: yes | no | N/A (28) OS: yes | no | N/A

(29) Legal blindness definition: 1 | 2 | 3 | 4 | 5 1 = VAOD, 2 = VAOS, 3 = VFOD, 4 = VFOS, 5 = N/A

(30) Cause of legal blindness OD: 1 = POAG, 2 = other. If other, cause _____ 3 = N/A

(31) Cause of legal blindness OS: 1 = POAG, 2 = other. If other, cause _____ 3 = N/A

(32) Date legal blindness diagnosed OD: 1: _____ 2: N/A

(33) Date legal blindness diagnosed OS: 1: _____ 2: N/A

(34) Cataract surg. OD: yes | no Date: _____ (35) Cataract surg. OS: yes | no Date: _____

(36) ALT OD: yes | no Date: _____ (37) ALT OS: yes | no Date: _____

(38) LPI OD: yes | no Date: _____ (39) LPI OS: yes | no Date: _____

(40) TAE OD: yes | no Date: _____ (41) TAE OS: yes | no Date: _____

(42) Comb. surg OD: yes | no Date: _____ (43) Comb. surg OS: yes | no Date: _____

(44) Other surg OD: yes | no Date: _____ Type: _____

(45) Other surg OS: yes | no Date: _____ Type: _____

(46) Cyclodestruct OD: yes | no Date: _____ (47) Cyclodestruct OS: yes | no Date: _____

(48) Date first seen in Dallas: _____ (49) Date last seen in Dallas: _____

(50) Vision first visit OD: 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 1 = 20/20 2 = 20/40

(51) Vision first visit OS: 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 3 = 20/60 4 = 20/80

(52) Vision last visit OD: 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 5 = 20/100 6 = 20/200

(53) Vision last visit OS: 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 7 = CF 8 = HM 9 = LP 10 = NLP

(54) Vision deterioration OD: yes | no (55) If yes, cause: glaucoma yes | no, other yes | no, if yes, diag _____

(56) Vision deterioration OS: yes | no (57) If yes, cause: glaucoma yes | no, other yes | no, if yes, diag _____

Fig. 2 - Glaucoma Patient Profile Form: Side A

(58) VF first visit OD: 1 | 2 | 3 | 4 | 5 | 6 | 7 1 = WNL; 2 = Rel scotoma outside 20°;

(59) VF first visit OS: 1 | 2 | 3 | 4 | 5 | 6 | 7 3 = Abs scotoma outside 20°; 4 = Rel/abs scotoma

(60) VF last visit OD: 1 | 2 | 3 | 4 | 5 | 6 | 7 within 20°-10°; 5 = Rel/abs scotoma within 10°-5°;

(61) VF last visit OS: 1 | 2 | 3 | 4 | 5 | 6 | 7 6 = Rel/abs scotoma within 5° in 1-3 quadrants;

7 = Rel/abs scotoma within 5° in all quadrants

(62) Progression VF OD: yes | no (63) If yes, cause glaucoma: yes | no, Other yes | no, diag _____

(64) Progression VF OS: yes | no (65) If yes, cause glaucoma: yes | no, Other yes | no, diag _____

(66)

Time	IOP OD	IOP OS	Time	IOP OD	IOP OS	Time	IOP OD	IOP OS
1st			10 yr			21 yr		
1M			10.5 yr			21.5 yr		
3M			11 yr			22 yr		
6M			11.5 yr			22.5 yr		
1 yr			12 yr			23 yr		
1.5 yr			12.5 yr			23.5 yr		
2 yr			13 yr			24 yr		
2.5 yr			13.5 yr			24.5 yr		
3 yr			14 yr			25 yr		
3.5 yr			14.5 yr			25.5 yr		
4 yr			15 yr			26 yr		
4.5 yr			15.5 yr			26.5 yr		
5 yr			16 yr			27 yr		
5.5 yr			16.5 yr			27.5 yr		
6 yr			17 yr			28 yr		
6.5 yr			17.5 yr			28.5 yr		
7 yr			18 yr			29 yr		
7.5 yr			18.5 yr			29.5 yr		
8 yr			19 yr			30 yr		
8.5 yr			19.5 yr			30.5 yr		
9 yr			20 yr			31 yr		
9.5 yr			20.5 yr			31.5 yr		

(67) C/D Ratio Initial OD: _____ (68) C/D Ratio Initial OS: _____ (69) C/D Ratio Final OD: _____

(70) C/D Ratio Final OS: _____ (71) Progression OD: yes | no (72) Progression OS: yes | no

(73) Meds OD: 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 1 = ß blockers, 2 = miotics, 3 = epi, 4 = CAI sys

(74) Meds OS: 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 5 = CAI top, 6 = α agonist, 7 = prostaglandins, 8 = none

(75) Noncompliance: yes | no (76) Poor control: yes | no (77) Late detection: yes | no

Fig. 3 - Glaucoma Patient Profile Form: Side B

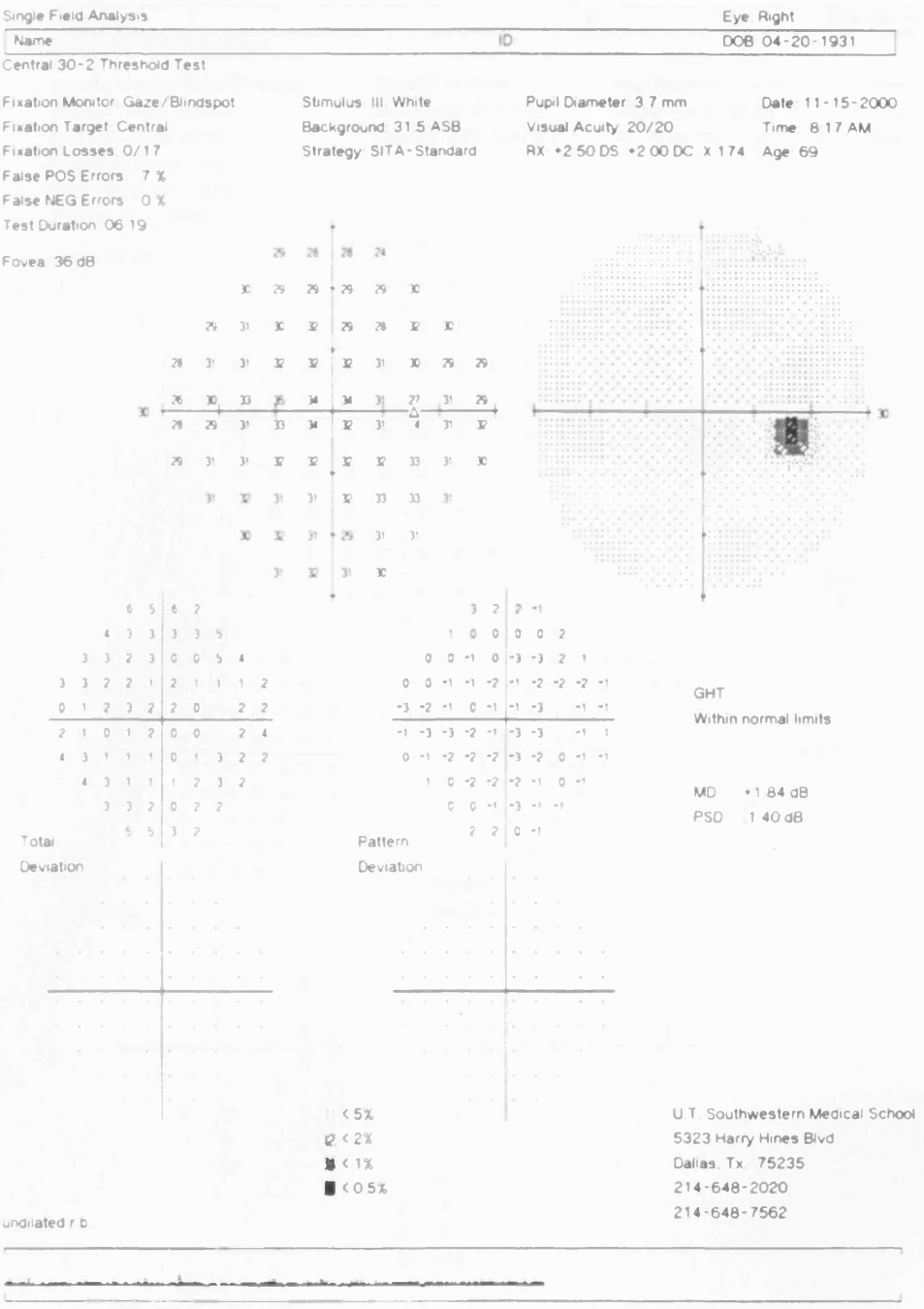

Fig. 4 - An example of a normal VF

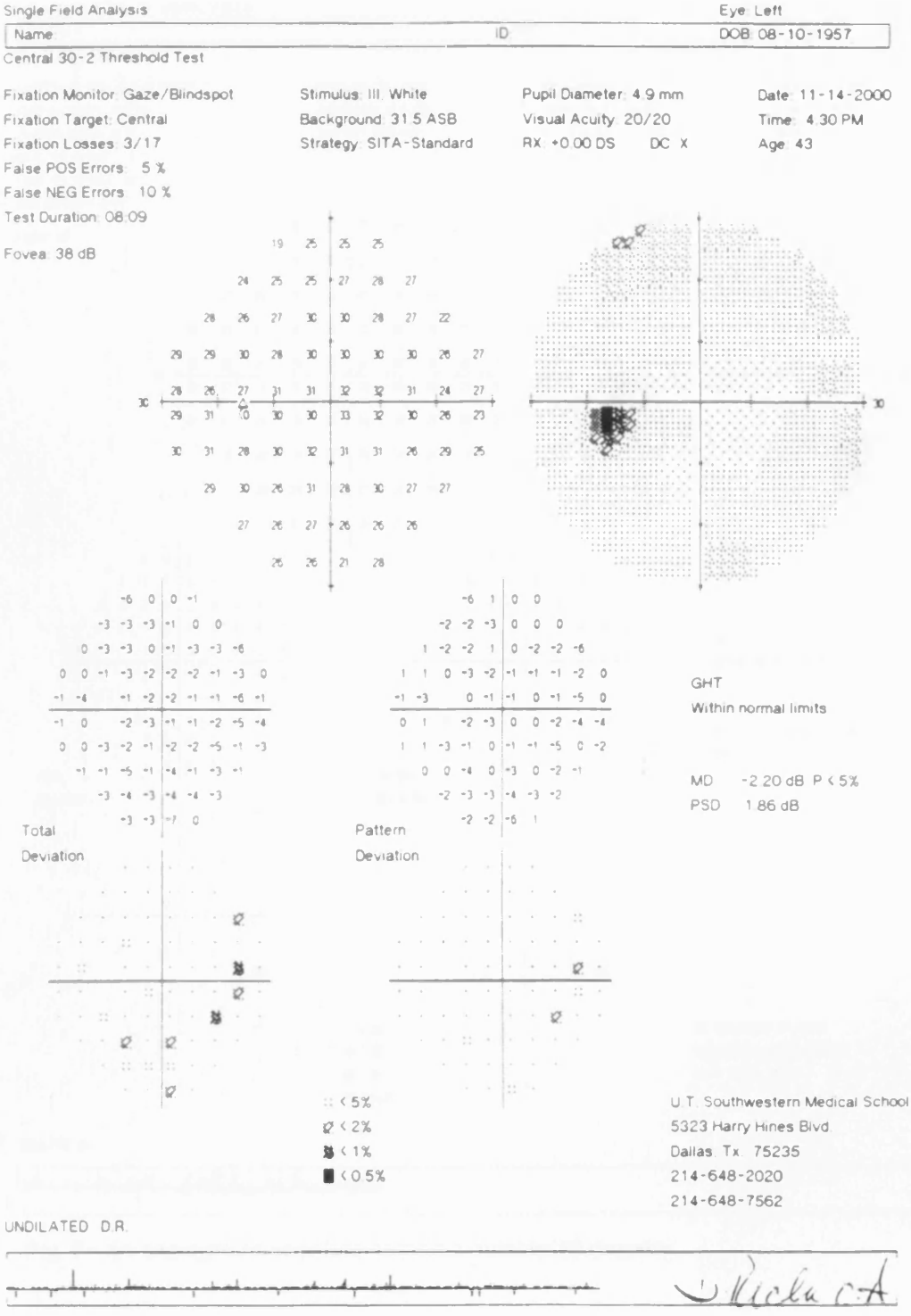

Fig. 5 - An example of relative scotoma outside 20 degrees

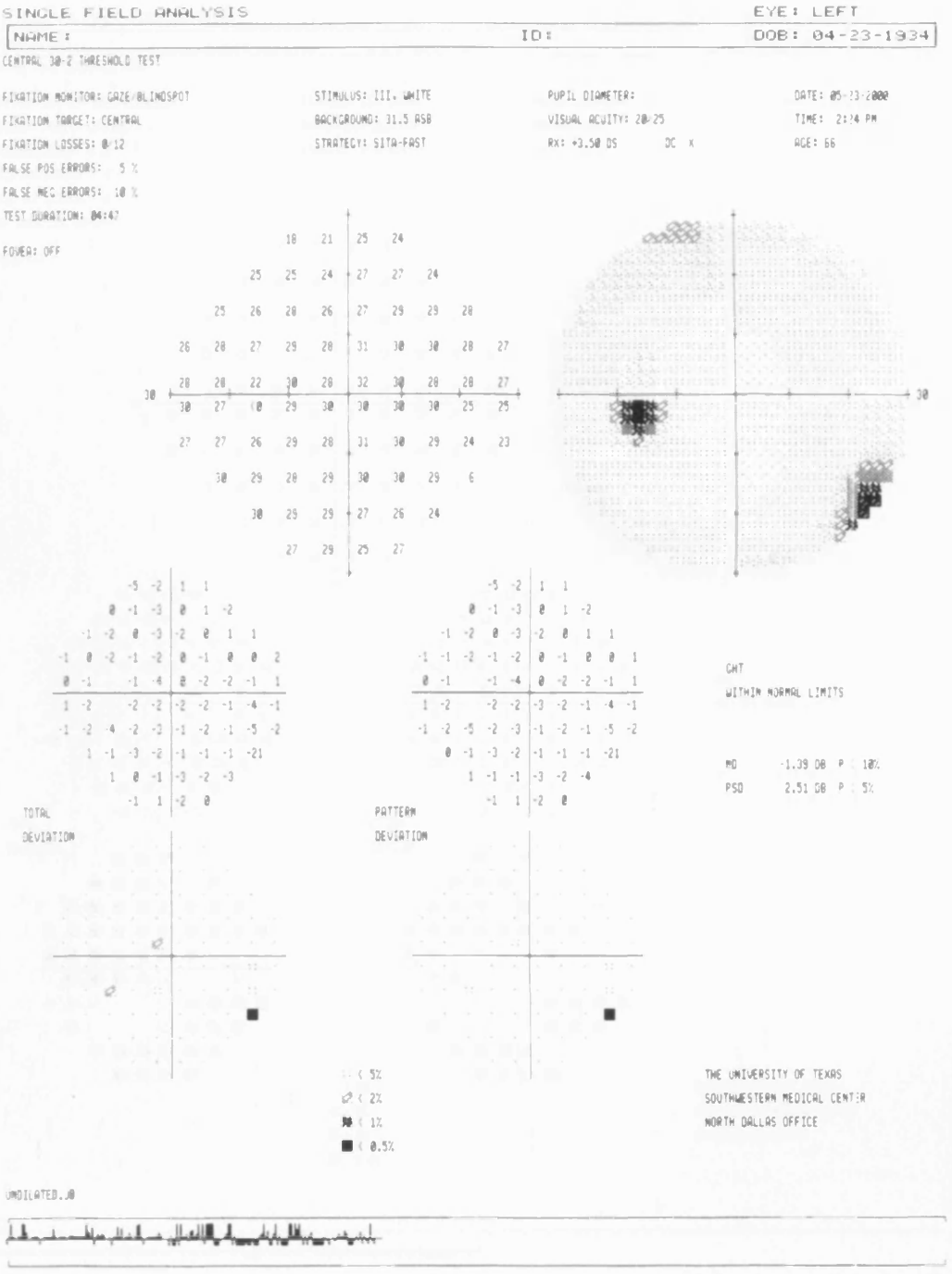

Fig. 6 - An example of absolute scotoma outside 20 degrees

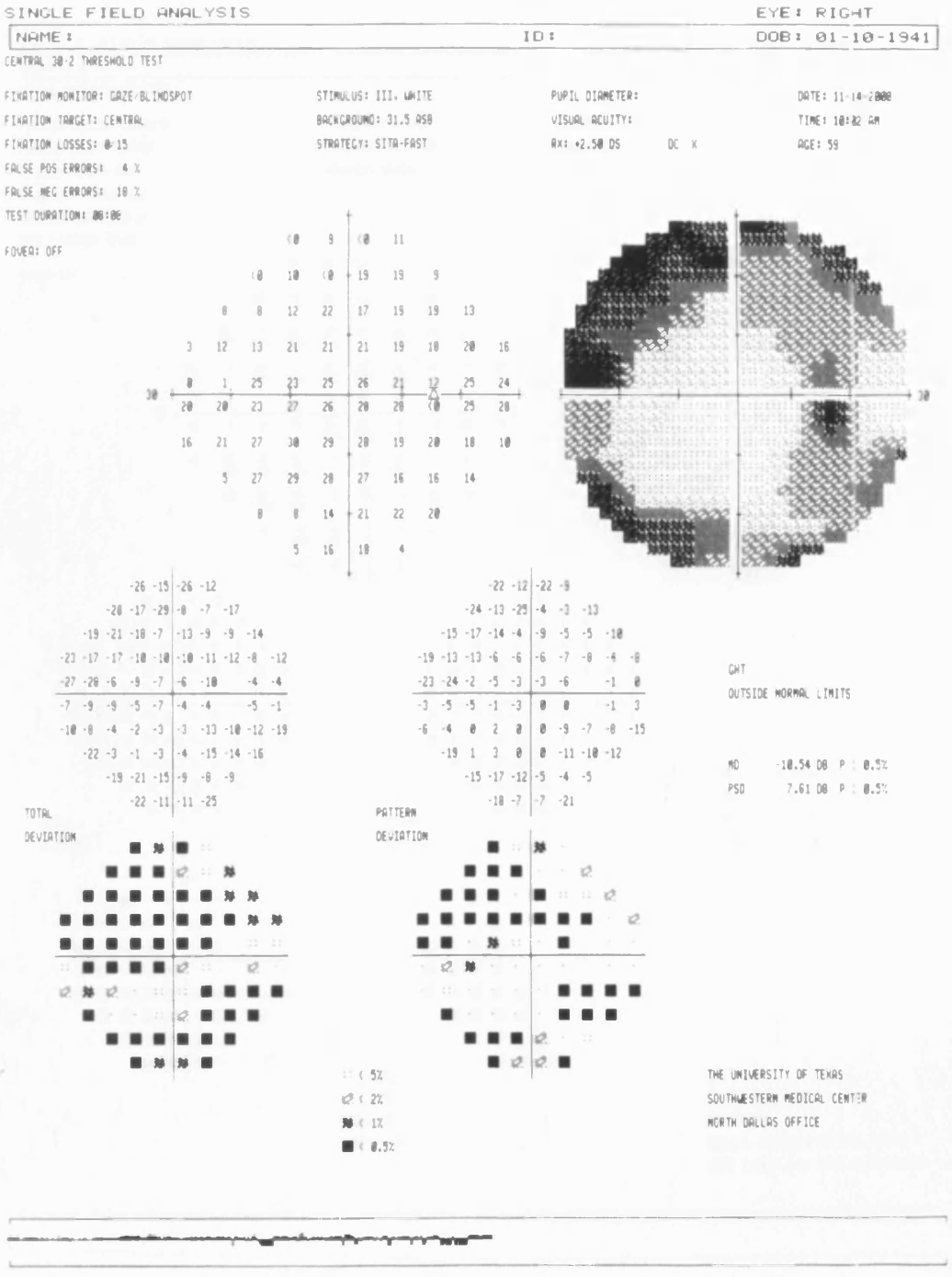

Fig. 7 - An example of relative/absolute scotoma within 20-10 degrees

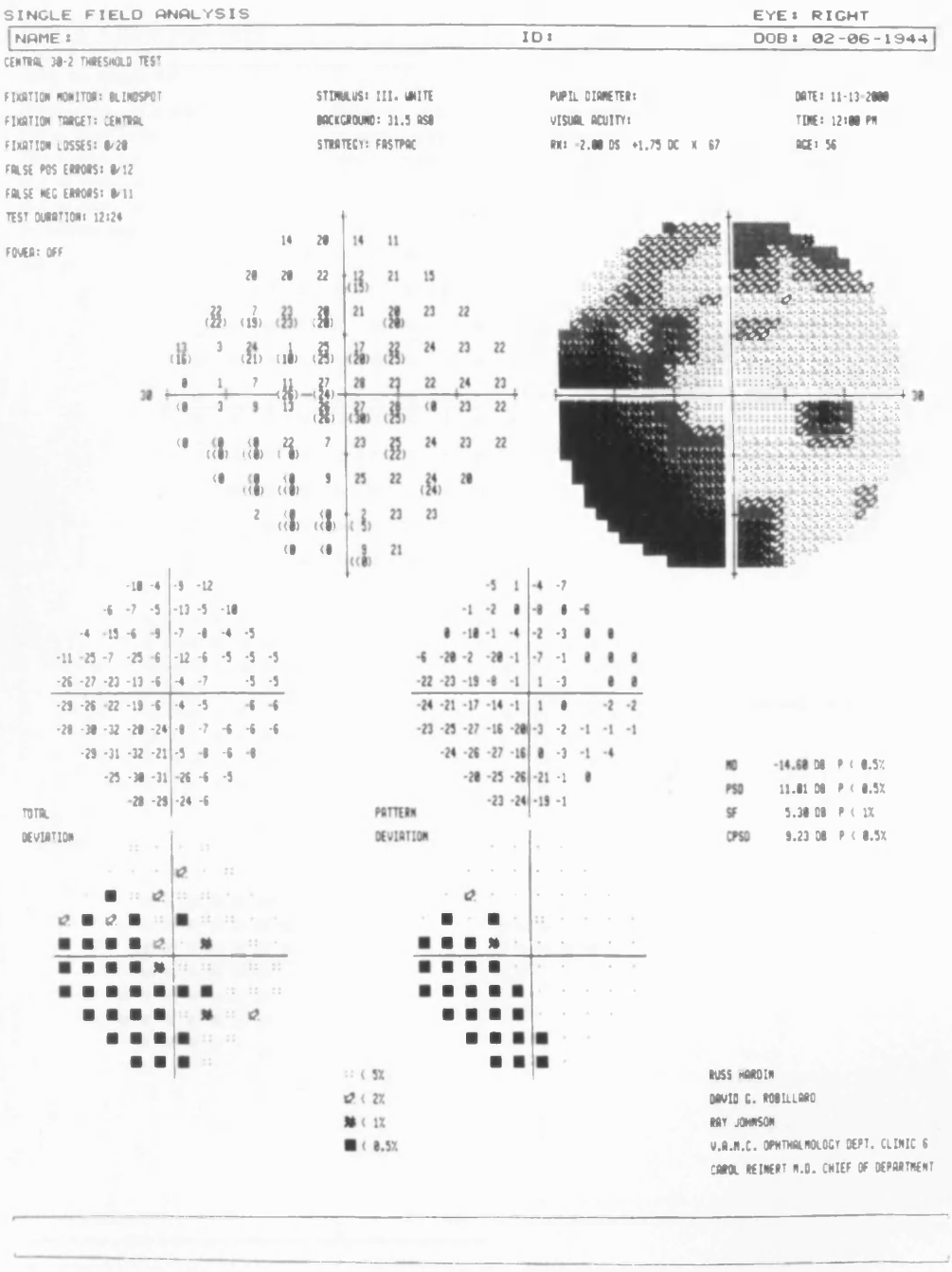

Fig. 8 - An example of relative/absolute scotoma within 10-5 degrees

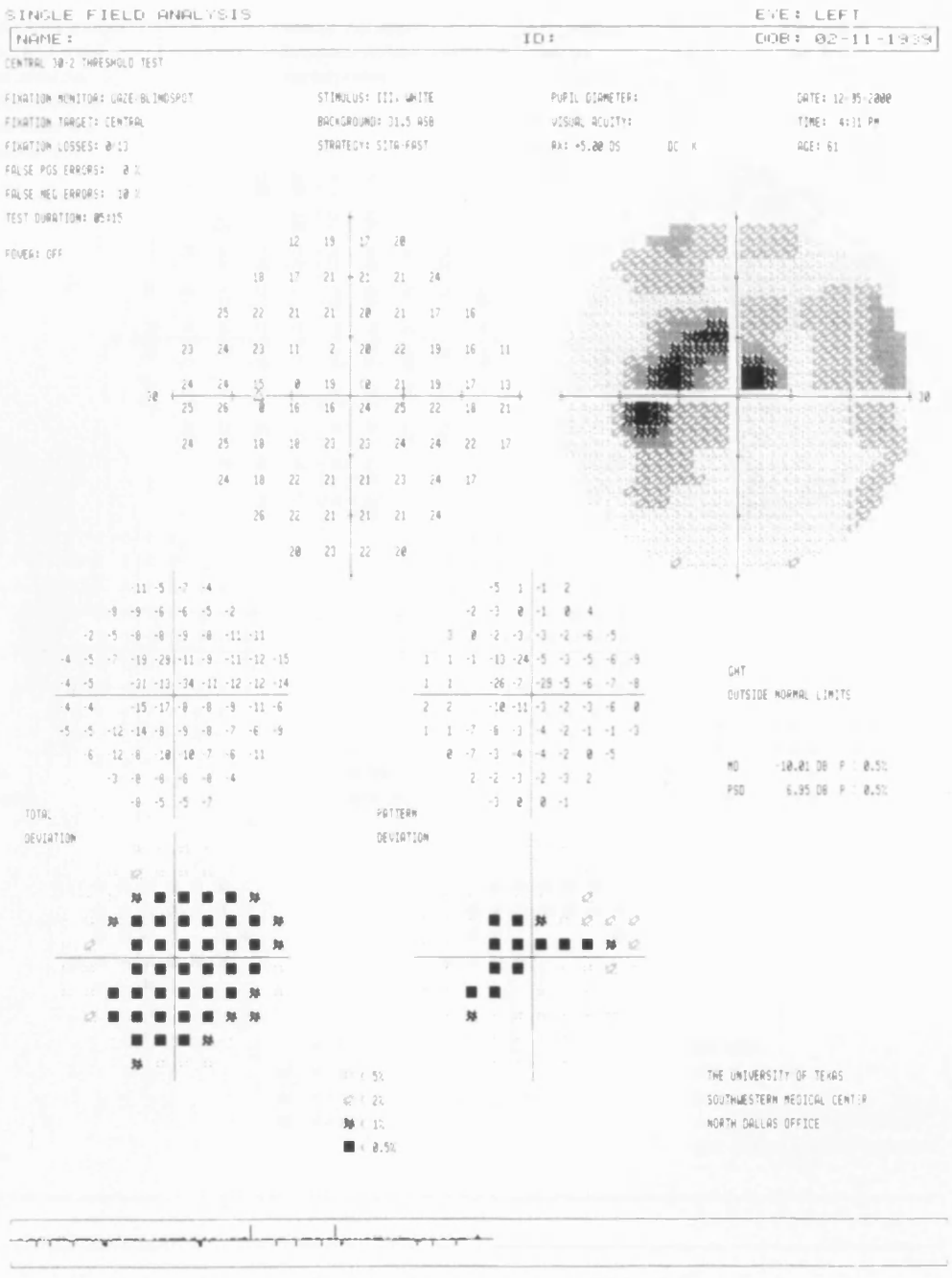

Fig. 9 - An example of relative/absolute scotoma within 5 degrees in 1-3 quadrants

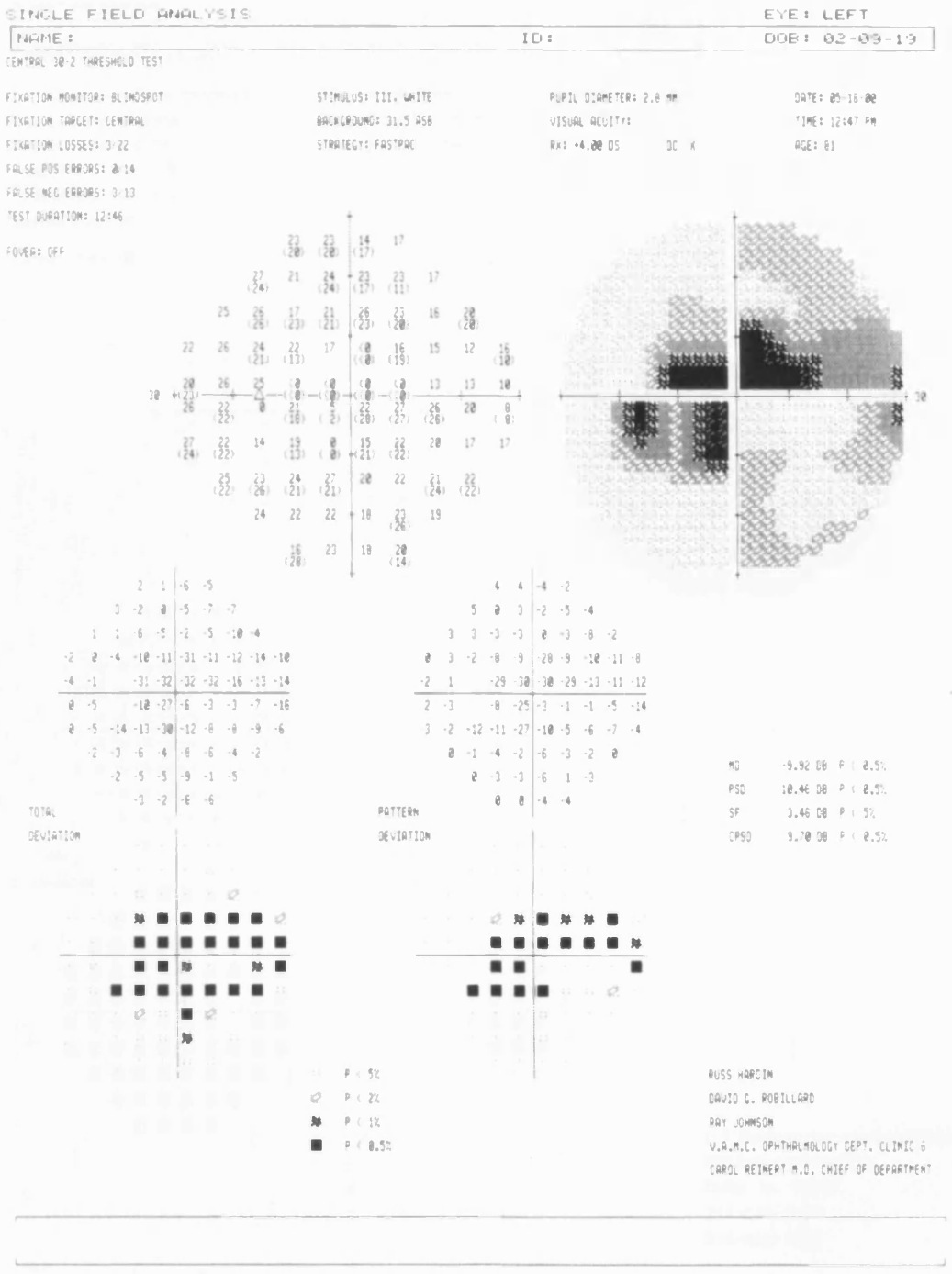

Fig. 9a - An example of relative/absolute scotoma within 5 degrees in 1-3 quadrants

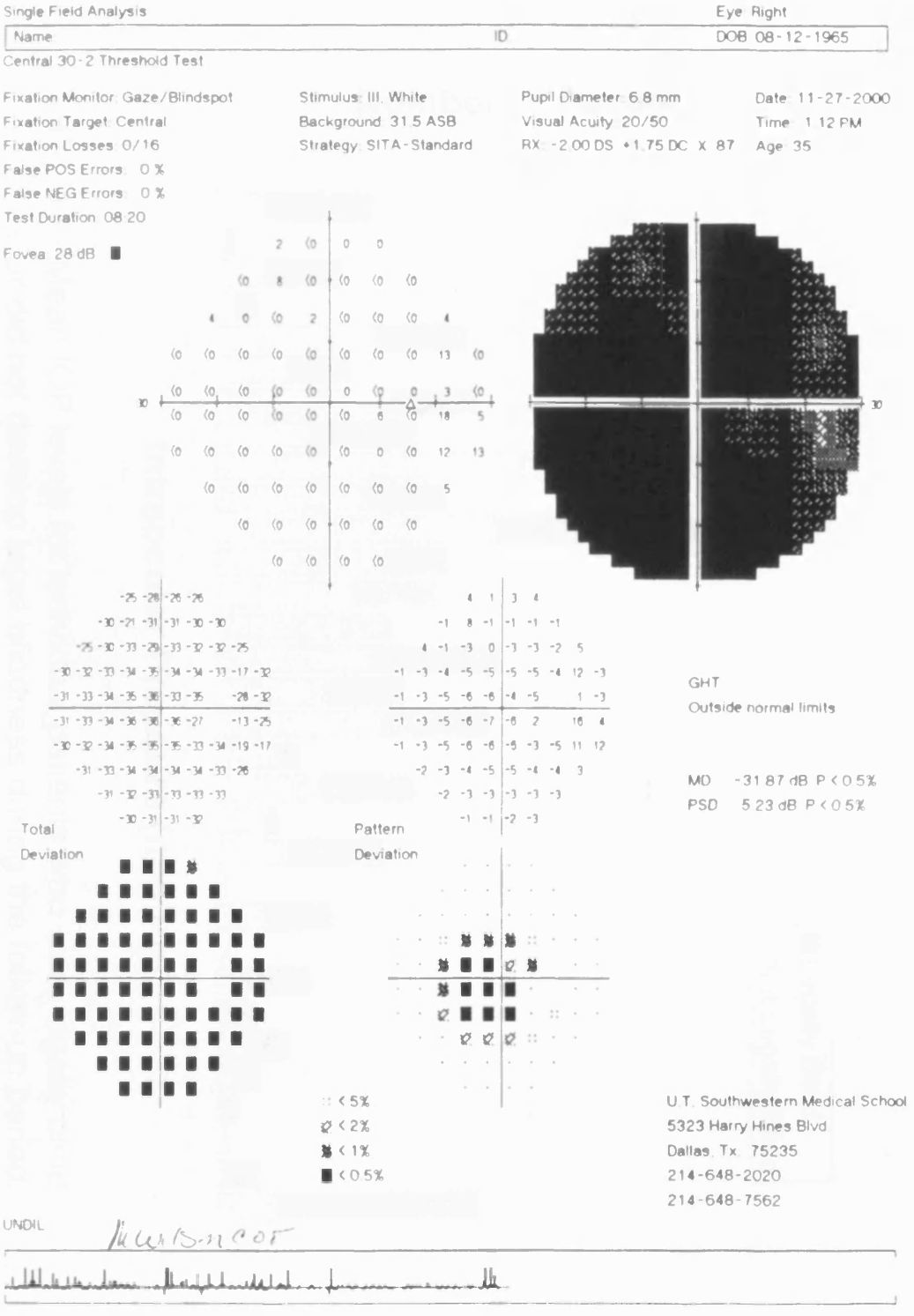

Fig. 10 - An example of relative/absolute scotoma within 5 degrees in all segments

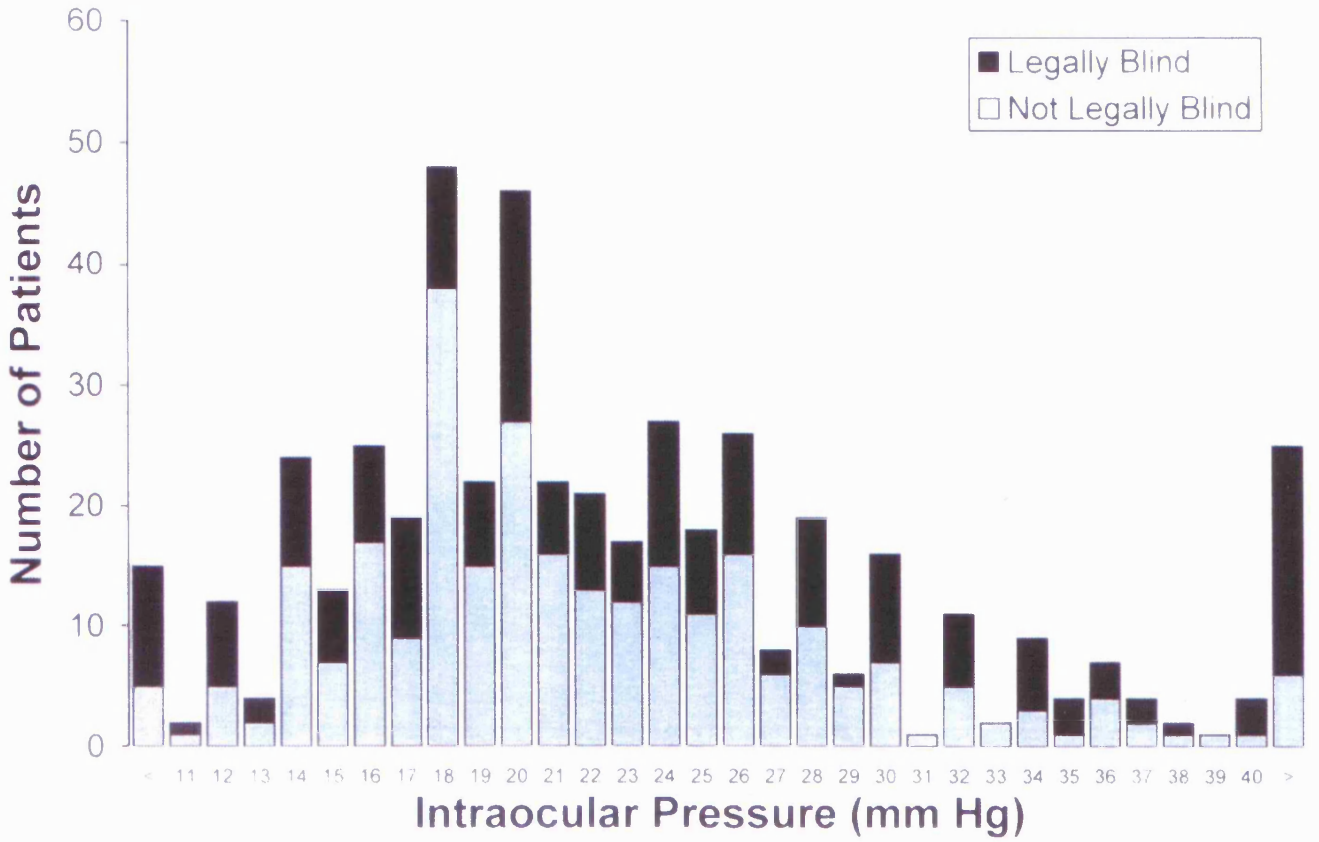

Fig. 11 - Mean IOP levels for individual patients who were legally blind or did not develop legal blindness during the follow-up period.

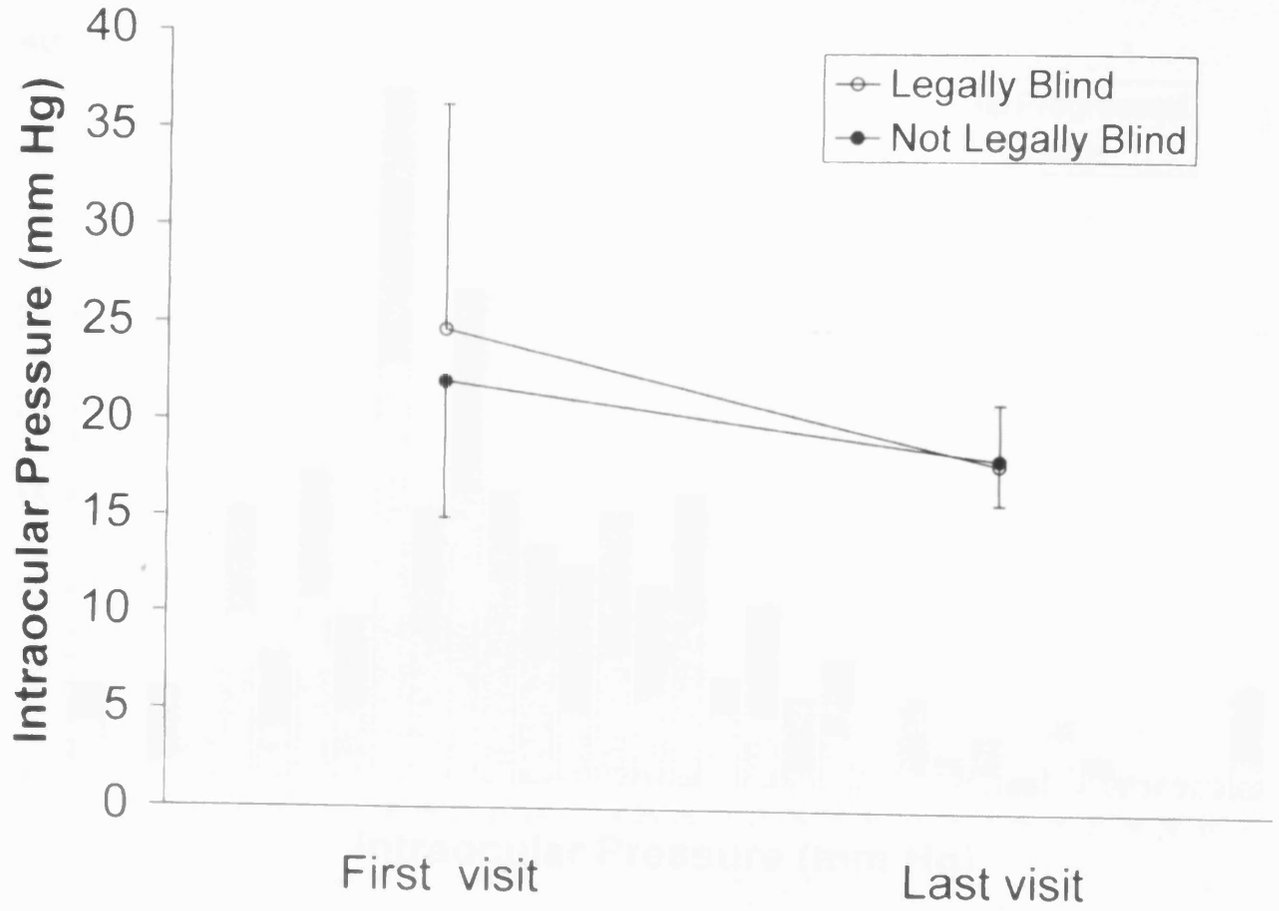

Fig. 12 - Mean IOP levels at first and last visits for individual patients who were legally blind or did not develop legal blindness during the follow-up period.

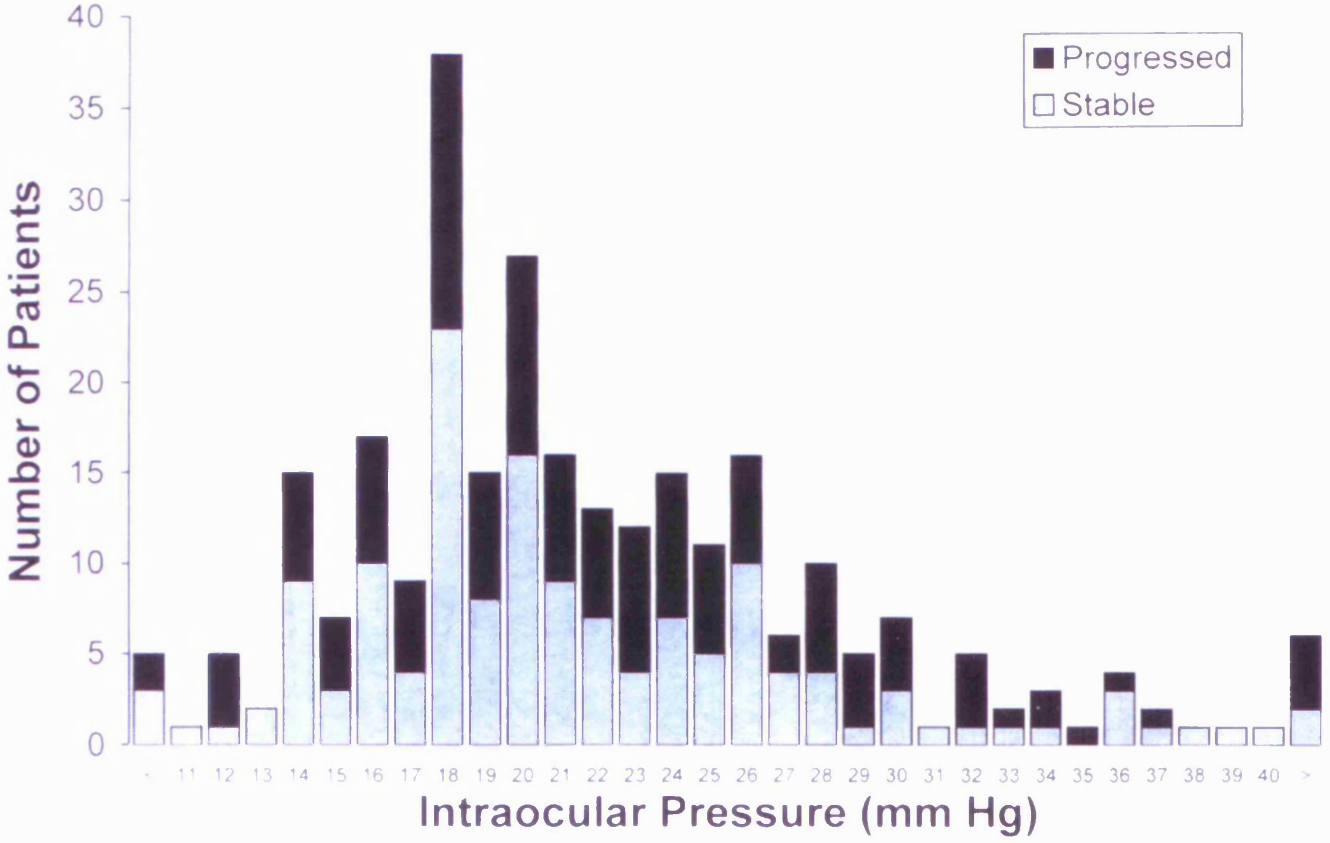

Fig. 13 - Mean IOP levels for individual patients who progressed or stayed stable during the follow-up period.

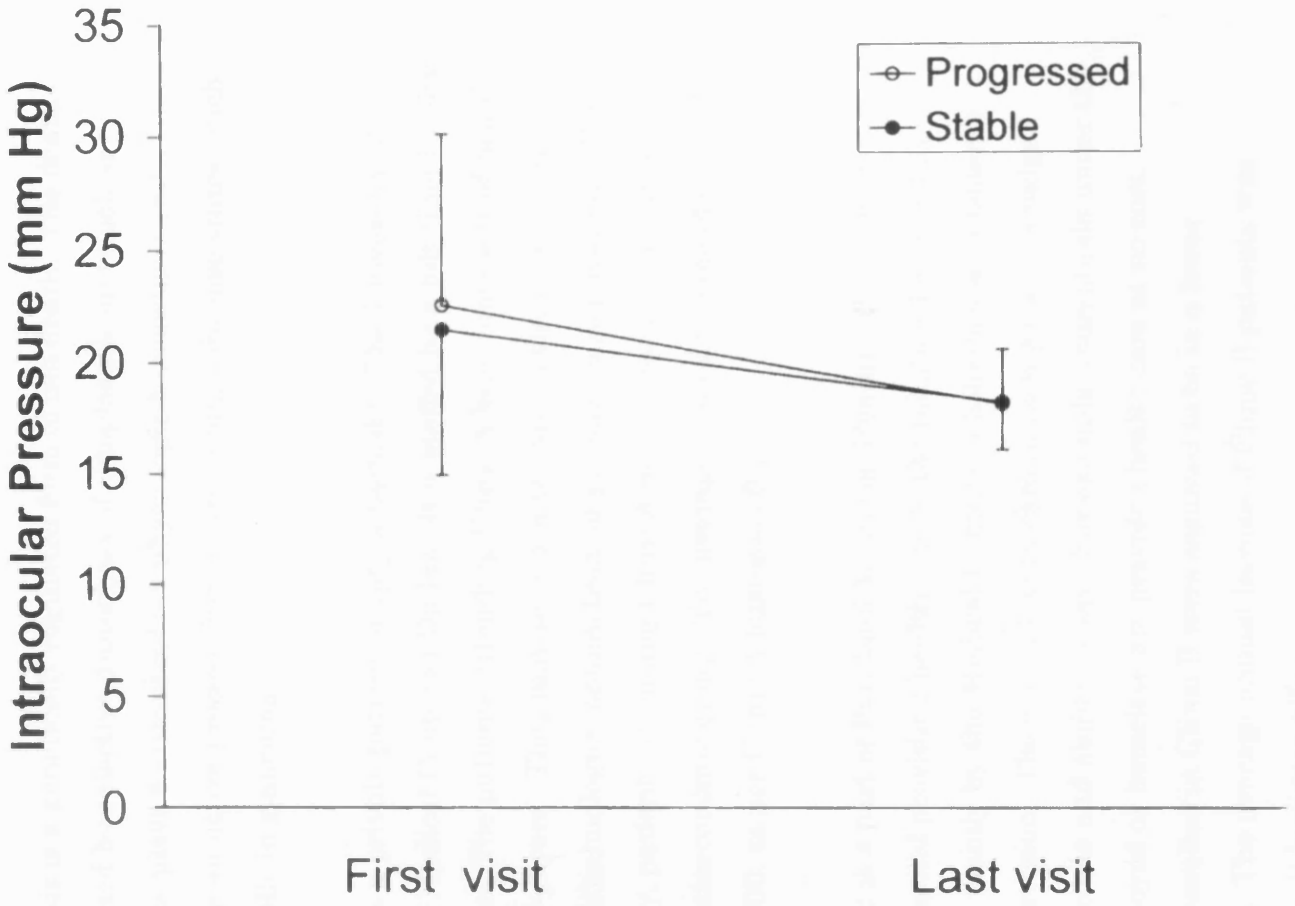

Fig. 14 - Mean IOP levels at first and last visits for individual patients who progressed or remained stable during the follow-up period.

GLOSSARY OF TERMS

Apoptosis: Apoptosis is a genetically regulated form of cell death. The death process is characterized by selective proteolysis of cytoplasmic and nuclear substrates. Apoptosis plays a crucial role in physiologic homeostasis and embryogenesis and is an active process that occurs in many disease states, such as loss of ganglion cells in glaucoma.

Clinic A: Clinic A is a private patient facility attached to The University of Texas Southwestern Medical Center at Dallas. It is staffed by a full-time faculty of the Medical Center. The patients attending Clinic A have some sort of health insurance or are self-payers. They may seek health care on their own or are referred by their ophthalmologist, optometrist, or primary care physician. For the sake of this study, patients attending Clinic A were arbitrarily assumed to belong to a higher socioeconomic group. The average annual income of Clinic A patients was $\geq$ $50,000, as per Clinic A business office.

Clinic B: This clinic is a part of Parkland Memorial Health and Hospital System, a county hospital providing health care to the inhabitants of Dallas County. It is staffed mainly by the Medical Center's ophthalmology residents under full-time supervision. The cost of health care to each patient is judged from the patient's income and ability to pay. For example, individuals under the poverty line, unemployed or homeless are provided health care at no cost. Therefore, patients enrolled in Clinic B were assumed to be in a lower socioeconomic group. The average annual income of Clinic B patients was $12,000, as per Clinic B business office.

Clinic C: Clinic C is the local Veterans Affairs Hospital. In the USA, the Veterans Affairs Hospitals provide free health care to the veterans of the U.S. Armed Forces. Veterans from all walks of life may be treated at these facilities provided they satisfy the prerequisites. The facility is also staffed by the Medical Center's ophthalmology residents under full-time supervision. The Veterans

Affairs patients are arbitrarily considered socioeconomically to be in the middle class. The average annual income of Clinic C patients was $23,000 as per Clinic C business office.

Late detection of glaucoma: Late detection referred to the status of visual field or C/D ratio at the first examination. If a patient presented with either C/D disparity of ≥ 0.2 or with moderate to severe VF damage in one or both eyes, this was determined to be late detection of the disease.

Legal blindness: The definitions of legal blindness and visual impairment are not standardized worldwide, and therefore pose difficulties in comparing their prevalence. Legal blindness in North America is defined as best corrected visual acuity of 20/200 or less or a visual field less than 20 degrees at its widest in the better eye with the Goldmann III 4c test object or its equivalent on automated perimetry (Fig 1).[1A] Goldmann III 4e equivalent test objects are 10 mm targets on the tangent screen at 1 m, size III target at threshold values 10 dB or less on the Humphrey and sizes III target at 7 dB on the Octopus perimeter. WHO defines blindness as visual acuity of less that 3/60 (0.05) or corresponding visual field loss in the better eye with best possible correction. Visual impairment corresponds to visual acuity of less than 6/18 (0.3) but equal to or better than 3/60 (0.05) in the better eye with best possible correction.

Mechanical theory of glaucoma: Proposed by Mueller in 1858, this theory emphasizes the core role played by elevated intraocular pressure in damaging the optic nerve fibers at the level of the lamina cribrosa.

Noncompliance: The concept of noncompliance or nonadherence to therapy is important in glaucoma. There is no universal definition of noncompliance. For this study, evidence of noncompliance was obtained from various sources: patient, a close relative, documented missed appointments, refusal of treatment or from patient's statements such as, "I ran out of meds last month," "can't afford medications," "doctor did not ask me to return," etc.

Objectives of the present investigation

The **primary objective** of the study was to identify significant risk factors for progression of POAG and eventual legal blindness in a cohort of patients in the Dallas metropolitan area. Progression was based on predefined criteria involving VF and optic nerve cupping (also see page 42). Progression in VF was demonstrated by reduction in the peripheral field, enlargement of scotomas or extension of the field deficit to the next level. Signs of optic nerve head progression were based on thinning of the neural rim from baseline, appearance of or deepening of notching or enlargement of C/D ratio by $\geq$0.2 disc diameters from prior exams.

Various risk factors what were studied were: ocular (myopia, elevated IOP), systemic (diabetes, hypertension, vascular disease, dysthyroidism, smoking, alcohol abuse), genetic (family history of glaucoma), disease management issues (poor control, late detection, non-compliance) and socio-economic (access to healthcare, affordability of care) risk factors in POAG have a role in the progression of the disease leading to legal blindness. **Secondary aims** were to determine: (1) do socioeconomic conditions influence risk factors for POAG and (2) what are the presenting features of unilateral POAG? The role of risk factors is discussed on page 11-15.

Optic nerve description: The status of the cup-to-disc ratios at initial and final visits were grouped into 3 categories: 0.1 - 0.5; >0.5 - 0.7; and >0.7 - 1.0.

Optic nerve progression: Signs of progression included thinning of the neural rim or enlargement of cup-to-disc ratio $\geq$ 0.2 disc diameter from prior exams.

Poor control of glaucoma: Poor control related to unsatisfactory control of IOP requiring multiple medications (>2.0 meds); laser or incisional surgery, progression of C/D ratio ($\geq$ 0.2 disc diameter) or VF deterioration. The decision to consider usage of three or more drugs to control glaucoma as indicative of poor control is subject to criticism. The intent, however, is to warn the

ophthalmologists of the danger that lies ahead for these patients. This does not mean that all patients on 3 or more drugs would progress to blindness, but a considerable number do as was noted in my pilot study.

Primary open angle glaucoma (POAG): POAG is defined as a progressive optic neuropathy with characteristic optic nerve excavation, and corresponding visual field (VF) defects.[3] Gonioscopically, the angles are open and the intraocular pressure (IOP) may be elevated in up to 60% to 70% of patients. For the study, as it was initiated in 1993, IOP levels equal to or greater than 21 mmHg were used for the definition. The disease is multifactorial, usually bilateral, though not necessarily symmetrical.

Study exclusion criteria: The exclusion criteria were: 1) all types of secondary glaucoma, including angle recession, pigmentary glaucoma, pseudo exfoliation, or congenital glaucoma; 2) patients with less than three months of follow-up, 3) patients with eye conditions or diseases that could preclude proper ocular examination or affect visual acuity, 4) patients with eye conditions or diseases that could produce glaucoma-like VF defects or any other type of VF changes that would impede accurate glaucoma diagnosis. Similarly, the same criterion was true if a patient developed blindness from conditions other than POAG, 5) patients with diagnosis of ocular hypertension even when they had converted to POAG as this group is being followed as part of another study; 6) patients with low-tension glaucoma; 7) patients unable to cooperate with study procedures and their inability to perform tests reliably. In 1993, low tension glaucoma was defined as an ocular condition with optic nerve and VF changes consistent with glaucoma, but with IOP levels consistently equal to or less than 21 mmHg.

Study inclusion criteria: The diagnosis of POAG was based on: 1) signs of glaucomatous optic disc, such as vertically oval cupping, disparity of cups in both eyes, neural rim thinning or notching, saucerization, nasalization of vessels or total cupping; 2) corresponding VF defects such as nasal step, paracentral or

arcuate scotoma; 3) open irido-corneal angle; 4) IOP being 21 mmHg or greater. This was the acceptable definition of POAG when the study was planned.

Vascular theory of glaucoma: Suggested by von Jaeger in 1858, the vascular theory underlines the role of inherently poor vascular supply to the optic nerve interlinked with normal or elevated intraocular pressure.

Visual acuity: Status of visual acuity was noted at the first and the last visit: 1 = 20/20, 2 = 20/40, 3 = 20/60, 4 = 20/80, 5 = 20/100, 6 = 20/200, 7 = count fingers (CF), 8 = hand motion (HM), 9 = light perception (LP) and 10 = no light perception (NLP); 54–57) vision deterioration over the course of the study was noted. In patients who were unable to undergo VF exam or had diffusely depressed VF and total cupping, worsening visual acuity was considered a sign of progression. Causes other than POAG were designated as: 1 = cataract, 2 = age-related macular degeneration (ARMD), 3 = other.

Visual field description: VF changes were divided into seven subgroups as follows: 1 = within normal limits (Fig. 4), 2 = relative scotoma outside 20° (Fig. 5), 3 = absolute scotoma outside 20° (Fig. 6), 4 = relative/absolute scotoma within 20° – 10° (Fig 7), 5 = relative/absolute scotoma within 10° – 5° (Fig 8), 6 = relative/absolute scotoma within 5°, 1–3 quadrants (Fig 9, Fig 9A), and 7 = relative/absolute scotoma within 5° in all quadrants (Fig 10) (automated perimetry was performed with the Humphrey Fields Analyzer (Humphrey Instruments, San Leandro, CA, USA) using program 30–2, size III white stimulus with full threshold strategy and foveal threshold test turned on. An appropriate age-related plus power lens was added to the distance refraction to obtain best corrected vision. Patients could wear their distance contact lenses. The VF examination was typically repeated yearly, but more frequently if progression or unreliability were suspected. Pupillary diameter of at least 3 mm was maintained. If a patient was unable to count fingers at 30 cm, the VF defect was recorded as 7.

Visual field abnormality: For this study, VF was considered to be abnormal if a cluster of two or more adjacent points of 5-decibels (dB) or greater loss, and by one or more points of 10 dB or greater loss from age-corrected normal reference value was detected in two consecutive automated perimetry tests.

Visual field progression: Progression was based on reduction in peripheral field, enlargement of scotomas, or extension of the field defect to the next level (e.g. 2 to 3). The type of progression was reconfirmed by me and the date of occurrence was documented. Causes other than POAG were noted as 1 = cataracts, 2 = age-related macular degeneration, and 3 = others.

Optic disc progression: Signs of progression based on optic disc included thinning of the neural rim, appearance or deepening of disc notching, or enlargement of C/D ratio to $\geq$ 0.2 disc diameter from prior exams.

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