

# Clinical Challenges and Priorities in Managing Glaucoma Patients

Fotis Topouzis · Pelagia Kalouda · Christina Keskini

Laboratory of Research and Clinical Applications in Ophthalmology, A' Department of Ophthalmology, Aristotle University of Thessaloniki, AHEPA Hospital, Thessaloniki, Greece

## Abstract

There are challenges in managing glaucoma patients and priorities need to be determined. Early in the course of the disease, managing subjects with ocular hypertension (OHT) is a challenge. The risk calculator is a useful guide to decide on early preventive treatment in those with OHT and to recommend treatment in patients at high risk for progression to glaucoma. Moreover, although well-accepted clinical criteria defining glaucomatous optic disk damage contribute to diagnostic accuracy, clinical diagnosis remains subjective relying on qualitative assessment of the optic disk. As a result, even among glaucoma experts, agreement in optic disk assessment is not excellent. In addition, visual field (VF) damage due to glaucoma has recently been associated with quality of life (QoL) measures, although a specific threshold of VF damage beyond which QoL is affected has not been determined yet. On the other hand, risk factors for glaucoma have been identified in major clinical trials, as well as the potential role of setting an individual target in lowering intraocular pressure (IOP). Despite this knowledge, we are not able to predict the rate of VF progression of the individual patient at baseline. In addition, glaucoma progresses at widely different rates among individual patients even within the same glaucoma type. Therefore,

monitoring of VF changes is important to be able to detect progression and measure the rate of progression. This would allow the clinician to verify if the target IOP has been chosen correctly and to adjust/reset the target if needed.

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## Goal of Treatment/Who Should Be Treated

Glaucoma is one of the leading causes of blindness worldwide and presents with significant prevalence in the population. It is therefore essential to accurately define and detect the population that should be treated for glaucoma and to precisely define the goal of our intervention.

It is a fact that the question of whether subjects with ocular hypertension (OHT) have to be treated is a matter of substantial controversy. OHT is defined as an elevated intraocular pressure (IOP; >21 mm Hg) in the absence of glaucoma damage [absence of damage to the optic disk or retinal nerve fiber layer (RNFL) and absence of visual field (VF) defect]. According to large epidemiological studies, the prevalence rates of OHT vary

**Table 1.** Reported prevalence rates of OHT from large epidemiological studies

Study	Age, years	Race/origin	Prevalence of OHT, %
Beaver Dam Eye Study [1]	≥43	White	4.5
Los Angeles Latino Eye Study [2]	≥40	Hispanic	3.56
Barbados Eye Study [3, 4]	≥40	White	4.6
		Black	18.4
Andhra Pradesh Eye Disease Study [5]	All ages	Indian	0.42
Thessaloniki Eye Study [6]	≥60	White	2.9
Blue Mountains Eye Study [7]	≥50	White	3.7

considerably (table 1), while some of these studies have also reported an age-related increase in OHT prevalence [1–4]. Overall, the prevalence of OHT in the population is significant, and the management of OHT patients poses important challenges to everyday clinical practice.

Elevated IOP is the leading risk factor for the development of glaucoma and the only modifiable risk factor at present [8]. However, the treatment of all OHT individuals is neither medically indicated nor economically justified because of the high prevalence of the condition, the low conversion rate to glaucoma, and the cost, inconvenience, and possible adverse effects of treatment [8]. A useful approach to further understanding the impact of treating all individuals with OHT is the ‘number needed to treat’ (NNT). NNT indicates how many individuals need to be treated before 1 patient will experience a benefit [9]. According to the Ocular Hypertension Treatment Study (OHTS), the NNT is 19.6, suggesting that IOP-lowering therapy would need to be prescribed to 20 patients with demographics similar to those in the study to prevent progression to glaucoma in 1 patient in the next 5 years [9]. Moreover, for OHT patients, the NNT to prevent 1 patient from progressing to unilateral blindness over a 15-year period is estimated at 83 according to both OHTS and St Lucia Study data [10].

In 2007, a quantitative risk model for the development of primary open-angle glaucoma

(POAG) in OHT patients based on data from the OHTS and Early Glaucoma Prevention Study (EGPS) was published. This model can be helpful in deciding on who is at increased risk to develop glaucoma and, therefore, in whom preventive treatment might be justified. Although the aforementioned risk calculator might provide significant help, it is important that clinicians take other factors into consideration beyond the ones included in the risk calculator. A positive family history of glaucoma, pseudoexfoliation syndrome, and cardiovascular disease appeared to be risk factors for developing glaucoma in many studies [11–16]. Furthermore, patient’s health, life expectancy, and preferences should always be taken into account in any clinical decision [8].

Besides knowing which subjects are more likely to develop glaucoma and, consequently, may benefit from treatment, it is necessary to determine if there is a ‘price to pay’ when delaying treatment for OHT. The phase II OHTS aimed to give an answer to this fundamental question. In this study, medication was offered to all participants in the observation group of phase I OHTS while participants in the medication group continued treatment. It was, therefore, possible to compare the cumulative incidence of POAG in subjects of the first group, who were only offered medication during phase II OHTS (median, 7.5 years of observation, then 5.5 years on treatment) with those in the second group, who were treated

for the entire duration of OHTS (median, 13.0 years) [17].

The results of the study suggest that delaying treatment had only an impact in the high-risk group (40% conversion rate in those with delayed treatment versus only 28% in those with treatment starting at baseline). The high-risk group was defined based on baseline characteristics and according to the risk calculator. This confirms the appropriateness of using the risk calculator as a guide to decide on early preventive treatment in those with OHT and to recommend treatment only in patients presenting with a high risk for conversion to glaucoma. The necessity of treating high-risk OHT patients was confirmed by the RAND study group [18]. In this study, 1,800 scenarios of glaucoma suspects were created based on a systematic review of the literature regarding potentially important factors to consider when deciding to initiate treatment, including age, life expectancy, IOP, central corneal thickness, cup/disk ratio (CDR), disk size, and family history. An 11-member panel composed of recognized international leaders in the field of glaucoma rated the appropriateness of initiating treatment for glaucoma suspects through a two-round modified Delphi method. The panel rated 587 (33%) scenarios as appropriate, 585 (33%) as uncertain, and 628 (35%) as inappropriate for treatment initiation. The results indicated that values associated with a higher predicted risk of glaucoma [greater IOP, greater CDR, and thinner central corneal thickness (CCT)] are associated with higher mean appropriateness scores, with IOP having greater impact than any other variable on panel decisions. According to the experts' decisions, simple criteria for appropriateness of treatment included IOP >26 mm Hg and a 5-year risk of mortality <90%. Finally, a point system was created for predicting panel ratings of appropriateness for a glaucoma suspect that showed a sensitivity and specificity of 96 and 93%, respectively.

## Guidelines

There are many country- or region-specific guidelines for the management of glaucoma. All agree that visual function should be preserved or maintained. The 2014 Guidelines of the European Glaucoma Society (EGS) state: 'The goal of glaucoma treatment is to maintain the patient's visual function and related quality of life, at a sustainable cost. The cost of treatment in terms of inconvenience and side effects as well as financial implications for the individual and society requires careful evaluation. Quality of life is closely linked with visual function and, overall, patients with early to moderate glaucoma damage have good visual function and modest reduction in quality of life, while quality of life is considerably reduced if both eyes have advanced visual function loss' [19]. As such, the aim of glaucoma treatment should be to prevent or to delay progression to the stage of disease which is going to affect the patient's quality of life (QoL). According to the EGS Guidelines, patients who should be treated are those with diagnosed or suspected glaucoma who are:

- Patients at risk of developing functional impairment that will lead to a deterioration in visual function related QoL
- Patients with definitive glaucomatous VF, particularly in patients with progressive disease
- Patients with significant changes in the optic nerve head (ONH) and RNFL characteristic of glaucoma

## Definitions of Normal and Glaucoma Subjects

Adopting clear definitions and classifying patients is crucial for management decisions. In the following, clinical profiles of patients with diagnosed and suspected glaucoma, and normal subjects with and without risk factors are outlined comprehensively.